平成 29 年度厚生労働科学研究費補助金（厚生労働科学特別研究事業）
臨床試験の結果の公開における電子的様式の構築のための研究

米国・EU の試験結果の公開に関する研究

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研究要旨

目的：本研究では、新しい臨床試験登録のあり方を模索するため、すでに独自形式で結果を公開している米国と EU の公開項目の動向を調査することを目的とする。

方法：本研究の調査対象機関を、ICTRP と米国の ClinicalTrials.gov と EU の EU- CTR を調査の対象機関とし、ClinicalTrials.gov と EU- CTR が設定している臨床試験結果の登録項目につい内容を調査する。調査方法は、web 上で公開されている項目を調査する。調査項目は、登録項目、形式（項目の詳細）、報告画面のインターフェースの 3 つとした。

結果：本研究から得られた結果から、米国の ClinicalTrials.gov と EU の EU- CTR の臨床試験に関する結果登録の項目は、参加フローやベースラインデータ、結果のアウトカム、有害事象の報告などが共通しており、項目に大きな違いはないと考えられた。しかしながら、項目やその定義にも差が認められ、統一性は希薄だと考えられた。

結論：臨床試験の結果登録の項目について、参加フローやベースラインデータ、結果のアウトカム、有害事象の報告などの項目を必要と考えられる。報告項目の内容や定義には慎重な検討が求められる。

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A.研究目的

WHO 臨床試験登録データセットの version 1.3 が ICTRP によって 2017 年 11 月 9 日に公表された。今回の改訂で 4 つの登録項目が追加され、従来の 20 項目から 24 項目となった。この改訂により、各国のプライマリ・レジストリはシステムの変更対応を進めており、本邦でも臨床試験の結果の登録システムの変更が必要となっている。

本研究では、新しい臨床試験登録のあり方を模索するため、すでに独自形式で結果を公開している米国と EU の公開項目の動向を調査することを目的とする。

B.研究方法

本研究の調査対象機関を、ICTRP と米国の ClinicalTrials.gov、EU の EU- CTR を調査の対象機関とする。

ClinicalTrials.gov と EU- CTR が設定している臨床試験結果の登録項目につい内容を調査する。調査方法は、web 上で公開されている項目を調査する。調査項目は、登録項目、形式（項目の詳細）、報告画面のインターフェースの 3 つとした。

(倫理面への配慮)本研究は個人のデータを扱っていないことから倫理面への配慮は必要ない。

C.研究結果

1. ClinicalTrials.gov で規定されている結果項目

ClinicalTrials.gov では、結果データの登録が求められている。また各項目には詳細な定義づけがなされていた。

（ https://prsinfo.clinicaltrials.gov/results_definitions.html ）

1）登録項目

記載されている内容は以下の 8 項目であった。

1. Participant flow
2. Baseline characteristics
3. Outcome measures (and Statistical Analysis)
4. Adverse event information
5. Limitations and caveats

6. Certain agreements
7. Results point of contact
8. Delayed results

2）記載されている項目について、大項目は、参加者フロー、ベースライン特性、結果の措置、有害事象、限界と警告、特定の契約、結果の連絡先（問い合わせ先）、遅延（オプション）の 8 項目であった。小項目は、合計 117 項目が設定されており、各大項目に対する内訳としては、参加者フローが 17 項目、ベースライン特性は 21 項目、結果の措置は 43 項目、有害事象は 23 項目、リミテーションと警告は 1 項目、特定の契約は 3 項目、結果の問い合わせ先は 4 項目、遅延（オプション）は 5 項目であった。試験結果の項目の詳細は付表 1 と 2 のとおりであった。

3）インターフェース

試験結果の報告画面のインターフェース例は付表 3 のとおりであった。

2. EU-CTR で規定されている結果項目

EU 臨床試験登録簿は、2011 年 9 月以降、世界保健機関（WHO）レジストリ・ネットワークの主要登録簿となっている。

（http://www.who.int/ictrp/trial_reg/en/index1.html）

試験結果の登録についてはスポンサー自身がデータベースに入力し、スポンサーがデータを検証した後にこの登録簿に掲載されるようになっている。

1）登録項目

Trial Results に記載されている内容は以下の項目であった。

Summary
EudraCT number
Trial protocol
Global completion date

Results information
Results version number
This version publication date
First version publication date
Other versions
Summary report(s)

Paediatric regulatory details として、次の項目が設定されていた。

Paediatric regulatory details
Is the trial part of an agreed EMA paediatric investigation plan?
Is the trial in scope of article 45 of Regulation (EC) No 1901/2006?
Is the trial in scope of article 46 of Regulation (EC) No 1901/2006?

Summary report(s)には、さらに次のセクションが含まれていた。

- ✓ trial information
- ✓ subject disposition
- ✓ baseline characteristics
- ✓ endpoints
- ✓ adverse events
- ✓ additional information
- ✓ summary attachment(s)

2）形式

項目の詳細は付表 4 の通りであった。

3）インターフェース

項目の詳細は付表 5 の通りであった。

Summary report(s)に、レポートの PDF を貼付している形式と、web 上へ直接入力している形式の二つの報告型が存在していた。

D.考察

本研究では、米国の ClinicalTrials.gov と EU の EU- CTR について、臨床試験結果の登録項目につい内容を調査した。調査項目は、登録項目、形式（項目の詳細）、報告画面のインターフェースとした。

海外の臨床研究登録機関で最も参考となったのは米国の Clinicaltrials.gov である。米国の Clinicaltrials.gov は、臨床試験情報の登録において世界で最も構造化が進んでおり、特に結果の公開に関しては WHO 以上に詳細な項目を設定していた。これはメタ・アナリシスなど試験結果を用いた 2 次的な分析に有益な形式だと考えられる。他の臨床試験登録機関と異なり、データフォーマ

ットを明確に、かつ詳細に定めていることも特筆すべきと思われる。

EU-CTR (EU Clinical Trials Register)では、世界のどのレジストリと比較しても詳細かつ高度に構造化されたデータ形式を採用している。ただ、5 階層以上に階層化された複雑極まりない構造化データは、入力する研究者に多大な負担を強いるものとなっている。筆者の研究によると EU 各国の臨床試験登録は米国に登録されることが最も多く、次いで自国の臨床試験登録機関に登録されることが多い（自国で登録機関を持っている国の場合)。新薬の販売市場として米国は最大であり、その米国での新薬承認には Clinicaltrials.gov への試験登録が求められることが影響していると考えられる。ただ、法的に EU-CTR での登録が求められる試験でない場合は、より簡便な自国のレジストリへの登録が多くなっていることからも、煩雑すぎる形式が敬遠されていることが推測される。

本研究から得られた結果から、米国の ClinicalTrials.gov と EU の EU- CTR の臨床試験に関する結果登録の項目は、参加フローやベースラインデータ、結果のアウトカム、有害事象の報告などが共通しており、項目に大きな違いはないと考えられた。しかしながら、項目やその定義にも差が認められ、統一性は希薄だと考えられた。

また、報告形式については、ClinicalTrials.gov では web 上への入力を基本としているが、EU- CTR では、PDF ファイルの貼付による方法と web 上への入力の双方の形式が見受けられたことから、報告形式については検討が必要であると考えられた。

E.結論

臨床試験の結果登録の項目について、参加フローやベースラインデータ、結果のアウトカム、有害事象の報告などの項目を必要と考えられる。報告項目の内容や定義には慎重な検討が求められる。

F．健康危険情報

特になし

G．研究発表

1. 論文発表

特になし

2. 学会発表

特になし

H．知的財産権の出願・登録状況

特になし

付表 1. ClinicalTrials.gov で規定されている試験結果の登録項目の詳細

各項目の詳細については以下の通りである。

#	大項目	小項目	データ定義（日本語）	データ定義（英語）	データ形式
1	参加者フロー	リクルート詳細	試験情報を提供するために、募集期間の日付や場所のタイプ(例えば、診療所)など、全体的な調査の募集プロセスに関連する重要な情報。 制限：350 文字。	Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and types of location (For example, medical clinic), to provide context. Limit: 350 characters.	日付、場所、期間など
2		事前割り当ての詳細	参加者の登録後に、参加者がアームやグループに割り当てられている場合は、その前に発生する重要なイベント(例えば、ウォッシュアウト、導入期間）の説明。 例えば、登録された参加者が、アームやグループに割り当てられる前に、研究から除外された理由の説明。 制限：350 文字。	Description of significant events in the study (for example, wash out, run-in) that occur after participant enrollment, but prior to assignment of participants to an arm or group, if any. Limit: 350 characters.	イベントの説明、記述
3		アームグループ情報	臨床研究を通じて参加者の流れを記述するアームまたはグループ。 一般に、各アームには割り当てられた参加者を含む必要があります。	Arms or groups for describing the flow of participants through the clinical study. In general, it must include each arm to which participants were assigned.	記述
4		アームグループタイトル	各アームまたは群を識別するために使用される説明的なラベル。 制限：> = 4 および<= 62 文字。	Descriptive label used to identify each arm or group. Limit: >=4 and <= 62 characters	記述
5		アームグループ説明	各アームまたはグループの簡単な説明。 一般に、参加者が割り当てられた各アームと、各アームに使用される介入内容を理解できるよう十分な詳細を含める必要があります。 制限：999 文字。	Brief description of each arm or group. In general, it must include sufficient details to understand each arm to which participants were assigned and the intervention strategy used in each arm. Limit: 999 characters.	記述

6		割り当てられるユニットのタイプ	参加者が参加者以外のユニットに基づいている場合は、割り当て単位(目、病変、インプラントなど)の説明。 制限：40 文字。	If assignment is based on a unit other than participants, a description of the unit of assignment (for example, eyes, lesions, implants). Limit: 40 characters.	記述
7		期間	特定の重要な事象または時点における参加者の数が報告される臨床研究の個々のステージ。	Discrete stages of a clinical study during which numbers of participants at specific significant events or points of time are reported.	期間、時間、数
8		期間タイトル	研究の段階を記述するタイトル。 期間が 1 つだけ定義されている場合、デフォルトのタイトルは Overall Study です。 研究に 1 つ以上の期間がある場合、期間タイトルのどれも全般的な研究ではありません。 制限：40 文字。	Title describing a stage of the study. If only one period is defined, the default title is Overall Study. When a study has more than one period, none of the Period Titles should be Overall Study. Limit: 40 characters.	記述
9		開始	当該期間を開始する参加者の数。 最初の期間では、それは各アームまたはグループに割り当てられた参加者の数です。 割り当てが参加者以外の単位に基づいている場合は、期間の初めに単位数も含めます。	Number of participants initiating the period. In the first period, it is the number of participants assigned to each arm or group. If assignment is based on a unit other than participants, also include the number of units at the beginning of the period.	開始参加者の数
10		完了	期間終了時の参加者の数。 割り当てが参加者以外の単位に基づいている場合は、期間の最後に単位数も含めます。	If assignment is based on a unit other than participants, also include the number of units at the end of the period.	終了参加者の数
11		完了していない（自動計算）	研究または期間を完了しなかった参加者の数(および該当する場合は、単位）。 これは、開始から完了を引いて自動的に計算されます。	Number of participants (and units, if applicable) that did not complete the study or period. This is calculated automatically by subtracting Completed from Started.	期間中に終了しなかった参加者の数

12		追加マイルストーン	参加者の数(および該当する場合は、単位) が報告されたときの研究における特定の事象または時点。1 つの期間に使用できるマイルストーンの数に制限はありませんが、各期間内に 2 つのマイルストン、開始と完了が必要です。	While there is no limit to the number of milestones that may be used in a single period, data are required for two milestones, Started and Completed, within each period.	期間内の開始と完了
13		マイルストーンタイトル	マイルストーンを記述するラベル 制限：40 文字。	Label describing the milestone Limit: 40 characters.	記述
14		マイルストーンデータ	マイルストーンに到達する参加者の数、各アーム/グループ。 割り当てが参加者以外の単位に基づいている場合は、マイルストーンに到達する単位数も含めます。	Number of participants to reach the milestone, in each arm/group. If assignment is based on a unit other than participants, also include the number of units to reach the milestone.	マイルストーンに到達する参加者の数
15		完了しなかった理由	研究または期間を完了しなかった参加者に関する追加情報。 理由が得られている場合は、未完了として記載されている全ての参加者が、いずれかの未完了の理由によって説明されなければなりません。	Additional information about participants who did not complete the study or period. If reasons are provided, the total number of participants listed as Not Completed must be accounted for by all reasons for non-completion.	記述記述
16		その他の理由	その他の理由が完了していない理由 」が選択されている場合、未完了の理由の簡単な説明。 制限：40 文字。	A brief description of the reason for non-completion, if "Other" Reason Not Completed Type is selected. Limit: 40 characters.	記述
17		完了していない理由のデータ	完了していない各理由について、 研究または期間を完了しなかった各アームまたはグループの参加者の数。	Number of participants in each arm or group that did not complete the study or period, for each Reason Not Completed.	期間を完了しなかった各アームまたはグループの参加者の数。
18	ベースライン特性	アームグループ情報	事前指定されたプロトコルおよび/または統計分析計画で指定されたベースラインで評価されたすべての参加者を含む、研究のアームまたは比較グループ。	Arms or comparison groups in the study, including all participants assessed at baseline as specified in the pre-specified protocol and/or statistical analysis plan.	アーム、比較グループのデータ
19		アームグループタイトル	各アームまたは比較群を識別するために使用される説明的なラベル。	Descriptive label used to identify each arm or comparison group.	記述

			制限：> = 4 および<= 62 文字	Limit: >= 4 and <= 62 characters.	
20		アームグループ説明	各アームまたは比較グループの簡単な説明。 一般に、参加者が参加者フロー（異なる場合）に割り当てられたアームや各アーム/グループの介入戦略からアームや比較グループがどのように導出されたかを理解するのに十分な詳細を含める必要があります。 制限：999 文字。	Brief description of each arm or comparison group. In general, it must include sufficient detail to understand how the arm(s) or comparison groups were derived from the arm(s) to which participants were assigned in Participant Flow (if different) and the intervention strategy in each arm/group. Limit: 999 characters.	記述
21		参加者総数	ベースライン特性が測定された参加者の総数。各アーム/グループおよび全体として。	Total number of participants for whom baseline characteristics were measured, in each arm/group and overall.	参加者数
22		分析対象ユニット数	分析が参加者以外のユニットに基づいている場合、ベースライン測定値が測定され、分析されたユニットの数（各アーム/グループおよび全体）。	If the analysis is based on a unit other than participants, the number of units for which baseline measures were measured and analyzed, in each arm/group and overall.	各アームのユニット数
23		分析対象ユニット種類	分析が参加者以外のユニットに基づいている場合、分析単位の説明（目、病変、インプラントなど）。 制限：40 文字。	If the analysis is based on a unit other than participants, a description of the unit of analysis (for example, eyes, lesions, implants). Limit: 40 characters.	各アームのユニットの種類
24		ベースライン分析集団の説明	ベースライン参加者（またはユニット）の総数が、アームまたは比較グループに割り当てられた参加者（またはユニット）の数と全体的に異なる場合、分析対象集団の決定方法についての簡単な説明。 制限：350 文字。	If the Overall Number of Baseline Participants (or units) differs from the number of participants (or units) assigned to the arm or comparison group and overall, a brief description of the reason(s) for the difference such as how the analysis population was determined. Limit: 350 characters.	記述

25		ベースライン測定情報	臨床研究で測定された各ベースラインまたは人口統計的特徴の記述。必要なベースライン指標には、年齢、性別、人種、民族性(プロトコルの下で収集された場合)、およびベースライン時に評価され、主要アウトカム指標の分析に使用されるその他の尺度が含まれる。	A description of each baseline or demographic characteristic measured in the clinical study. Required baseline measures include Age, Sex/Gender, Race, Ethnicity (if collected under the protocol), and any other measure(s) that were assessed at baseline and used in the analysis of the primary outcome measure(s).	各ベースラインまたは人口統計的特徴の記述
26		ベースライン指標タイトル	臨床試験で測定されたベースラインまたは人口統計的特徴の名前。 必要な数だけ選択する。	The name of the baseline or demographic characteristic measured in the clinical study. Select as many as needed.	人口統計的特徴の名前
27		研究に特有のベースライン指標	「Study-Specific Measure」が選択されている場合は、測定項目を入力します。 制限：100 文字。	If "Study-Specific Measure" is chosen, provide the name of the measure. Limit: 100 characters.	記述
28		ベースラインの指標説明	特定のベースライン指標を特徴づけるために使用される指標の説明など、ベースライン指標に関する追加の説明的情報。 制限：600 文字。	Additional descriptive information about the baseline measure, such as a description of the metric used to characterize the specific baseline measure. Limit: 600 characters.	記述
29		メジャータイプ＊１つ選択	ベースライン指標のデータタイプ。 一つ選択してください。	The type of data for the baseline measure. Select one.	選択式
30		分散尺度＊１つ選択	一つ選択してください。	Select one.	選択式
31		ベースライン参加者数	ベースライン指標を分析した参加者の数(ベースライン参加者の総数と、各アーム/グループおよび全体で異なる場合）。	The number of participants analyzed for the baseline measure, if different from the Overall Number of Baseline Participants, in each arm/group and overall.	基本尺度について分析された参加者の数
32		分析対象ユニット数	分析されたユニットの総数と、各アーム/グループおよび全体としてのベースライン尺度について分析されたユニットの数。	The number of units analyzed for the baseline measure, if different from the Overall Number of Units Analyzed, in each arm/group and overall.	ユニットの総数、ユニットの数

33		分析集団タイプ	ベースライン測定分析が参加者または参加者以外のユニットに基づいているかどうかを示す。“Type of Units Analyzed”が指定されている場合にのみ適用されます。 参加者/その他のユニットを選択します。	Indicate whether the baseline measure analysis is based on participants or units other than participants. Only applies if Type of Units Analyzed is specified. Select Participants/Other Units.	選択式
34		測定分析集団の説明	Participants [または Units] Analyzed の総数と異なる場合、分析のための参加者(またはユニット)数の決定方法の説明。 制限：350 文字。	Explanation of how the number of participants (or units) for analysis was determined, if different from the Overall Number of Participants [or Units] Analyzed. Limit: 350 characters.	記述
35		カテゴリまたはタイトル	ベースライン指標の異なるカテゴリまたは行の名前（存在する場合）。 カテゴリタイトルは、「参加者数」または「ユニット数」の、測定に基づく型を使用してデータ要約する際に、除外したものと全体のカテゴリを表す為に用いる。行タイトルは、あらゆる種類のデータに用いる。 制限：50 文字。	Name of distinct category or row for a baseline measure, if any. Category Titles are only for mutually exclusive and exhaustive categories summarizing data using the Measure Type of a "Count of Participants" or "Count of Units." Row Titles are for any type of data. Limit: 50 characters.	記述
36		ベースライン測定データ	各尺度（各アーム/群および全体）の値。	The value(s) for each baseline measure, for each arm/group and overall.	各尺度の値
37		NA 説明	ベースライン測定データに対して「NA」が報告された場合、ベースライン測定データが利用できない理由を説明します。 制限：250 文字。	Explain why baseline measure data are not available, if "NA" is reported for Baseline Measure Data. Limit: 250 characters.	記述
38		測定単位	各ベースライン指標について、データ（例：参加者、mmHg）によって定量化されたものの説明。 制限：40 文字。	An explanation of what is quantified by the data (for example, participants, mm Hg), for each baseline measure. Limit: 40 characters.	記述
39	結果の措置	結果測定情報	各アウトカム測定の説明。	A description of each outcome measure.	記述

40		結果測定タイプ＊1つ選択	結果の尺度のタイプ。 一つ選択してください。	The type of outcome measure. Select one.	選択式
41		結果測定タイトル	特定のアウトカム指標の名前。 制限：255 文字。	Name of the specific outcome measure. Limit: 255 characters.	記述
42		結果測定の説明	アウトカム測定に関する追加情報。アウトカム測定のタイトルに含めていない場合、特定のアウトカム測定に用いられるメトリックの説明を含めるようにする。 制限：999 文字	Additional information about the outcome measure, including a description of the metric used to characterize the specific outcome measure, if not included in the Outcome Measure Title. Limit: 999 characters.	記述
43		結果測定時間枠	使用された特定のメトリックについて測定が評価された時点。評価の時点の記述は、結果測定に特定のものでなければならず、一般に各研究参加者が評価測定される特定の期間になる（研究の全期間ではありません）。 制限：255 文字	Time point(s) at which the measurement was assessed for the specific metric used. The description of the time point(s) of assessment must be specific to the outcome measure and is generally the specific duration of time over which each participant is assessed (not the overall duration of the study). Limit: 255 characters.	記述
44		予想報告日	アウトカム測定データがアウトカム測定に含まれていない場合、それらが測定されるはずだった予定の月と年を指定します。	If Outcome Measure Data are not included for an outcome measure, provide the expected month and year they will be submitted.	予定の年と月
45		アームグループ情報	予め指定されたプロトコールおよび/または統計分析計画に基づく全ての群または比較群を含む、研究におけるアームまたは比較群。	Arms or comparison groups in the study, including all arms or comparison groups based on the pre-specified protocol and/or statistical analysis plan.	記述
46		アームグループタイトル	各アームまたは比較群を識別するために使用される説明的なラベル。 制限：> = 4 および<= 62 文字。	Descriptive label used to identify each arm or comparison group. Limit: >= 4 and <= 62 characters.	記述

47		アームグループ説明	各アームまたは比較グループの簡単な説明。 一般に、参加者フローにおいて､参加者が割り当てられたアームおよび各アーム/グループの介入戦略から、アームまたは比較グループがどのように割付られ（異なる場合）、各アーム/グループにおいてどののような介入を受けたかを理解できるよう十分詳細に記載する必要があります。 制限：999 文字。	Brief description of each arm or comparison group. In general, it must include sufficient detail to understand how the arm(s) or comparison groups were derived from the arm(s) to which participants were assigned in Participant Flow (if different) and the intervention strategy in each arm/group. Limit: 999 characters.	記述
48		分析対象の総数	アウトカム指標が測定され、分析された参加者の数。各アウトカム指標および各群/グループ。	Number of participants for whom an outcome measure was measured and analyzed, for each outcome measure and each arm/group.	アウトカム指標が測定され、分析された参加者の数
49		分析対象ユニット種類	分析が参加者以外のユニットに基づいている場合、分析単位の説明(目、病変、インプラントなど）。 制限：40 文字。	If the analysis is based on a unit other than participants, a description of the unit of analysis (for example, eyes, lesions, implants). Limit: 40 characters.	記述
50		分析対象ユニット数	分析が参加者以外のユニットに基づいている場合、各結果測定値および各群/群について、結果が測定および分析された単位の数。	If the analysis is based on a unit other than participants, the number of units for which an outcome was measured and analyzed, for each outcome measure and each arm/group.	対象ユニット数
51		分析集団の説明	分析された参加者数または分析されたユニット数が、アームまたは比較グループに割り当てられた参加者またはユニットの数と異なる場合、その差の理由の簡単な説明(分析集団の決定方法など）。 制限：350 文字。	If the Number of Participants Analyzed or Number of Units Analyzed differs from the number of participants or units assigned to the arm or comparison group, a brief description of the reason for the difference (such as how the analysis population was determined). Limit: 350 characters.	記述
52		メジャータイプ＊１つ選択	アウトカム測定のデータ型。 一つ選択してください。	The type of data for the outcome measure. Select one.	選択式
53		分散精度の尺度＊１つ	一つ選択してください。	Select one.	選択式

		選択			
54		その他信頼区間レベル	その他の信頼区間レベル」が選択されている場合、信頼区間レベルの数値。結果測定の説明でこのレベルを選択するための論理的根拠を提供してください。	The numerical value for the confidence interval level, if "Other Confidence Interval Level" is selected. Provide a rationale for choosing this level in the Outcome Measure Description.	信頼区間レベルの数値
55		カテゴリまたはタイトル	ベースライン指標の異なるカテゴリまたは行の名前（存在する場合）。 カテゴリタイトルは、「参加者数」または「ユニット数」を使用してデータ要約する際に、除外したものと全体のカテゴリを表す為に用いる。行タイトルは、あらゆる種類のデータに用いる。 制限：50 文字。	Name of distinct category or row for an outcome measure, if any. Category Titles are only for mutually exclusive and exhaustive categories summarizing data using the Measure Type of a "Count of Participants" or "Count of Units". Row Titles are for any type of data. Limit: 50 characters.	記述
56		分析対象者数	分析された参加者の総数と異なる場合、行の結果尺度および各アーム/グループについて分析された参加者の数。 制限：50 文字。	The number of participants analyzed for the outcome measure in the row and for each arm/group, if different from the overall Number of Participants Analyzed. Limit: 50 characters.	記述
57		分析対象ユニット数	分析されたユニットの総数と異なる場合、行および各アーム/グループの結果尺度について分析されたユニット数。	The number of units analyzed for the outcome measure in the row and for each arm/group, if different from the overall Number of Units Analyzed.	ユニット数
58		結果データ	各カテゴリ/行および各アーム/グループを含む、各アウトカム測定の測定結果。	The measurement value(s) for each outcome measure, including each category/row and each arm/group.	成果の測定値
59		NA 説明	結果データに「NA」が報告された場合、結果測定データが利用できない理由を説明します。 制限：250 文字。	Explain why outcome measure data are not available, if "NA" is reported for Outcome Data. Limit: 250 characters.	記述
60		測定単位	各成果尺度のデータ（例：参加者、mmHg）によって定量化されたものの説明。 制限：40 文字	An explanation of what is quantified by the data (for example, participants, mm Hg), for each outcome measure. Limit: 40 characters.	記述

61		統計分析	主要評価項目および副次評価項目の統計的有意性に関する科学的に適切なテスト結果（該当する場合)。そのような分析には以下のようなケースが考えられる:プロトコルおよび/または統計解析計画書に予め指定されたもの、スポンサーまたは責任者によって公に作成された、FDA の要請により主要評価項目の解析。 統計分析が報告された場合、「比較グループ選択」と「統計テストのタイプ」の報告が必要になる。さらに、関連情報とともに、「P 値」、「推定パラメータ」または「その他の統計分析」という次のデータ要素の 1 つを報告しなければならない。	Result(s) of scientifically appropriate tests of statistical significance of the primary and secondary outcome measures, if any. Such analyses include: pre-specified in the protocol and/or statistical analysis plan; made public by the sponsor or responsible party; conducted on a primary outcome measure in response to a request made by FDA. If a statistical analysis is reported "Comparison Group Selection" and "Type of Statistical Test" are required. In addition, one of the following data elements are required with the associated information: "P-Value," "Estimation Parameter," or "Other Statistical Analysis."	記述
62		統計分析の概要	実行された分析の概要説明	Summary description of the analysis performed.	記述
63		比較グループ選択	統計分析に含まれるアームまたは比較グループ(すべてをチェックして「オムニバス」分析を示す）。	The arms or comparison groups involved in the statistical analysis (check all to indicate an "omnibus" analysis).	記述
64		統計テストの種類＊1つ選択	分析のタイプを識別します。 一つ選択してください。	Identifies the type of analysis. Select one.	選択式
65		仮説の統計的検定	結果データおよび計算された p 値の統計分析に使用される手順。	Procedure used for statistical analysis of outcome data and the calculated p-value.	統計分析の手順
66		P 値	帰無仮説を仮定して計算された p 値	Calculated p-value given the null-hypothesis	P 値
67		メソッド＊1つ選択	P値が報告された場合にp値を計算するために使用される統計検定。一つ選択してください	The statistical test used to calculate the p-value, if a P-Value is reported. Select one.	選択式
68		その他のメソッド名	"その他"を選択した場合は、統計テストの名前を入力します。 制限：40 文字。	If "Other" is selected, provide name of statistical test. Limit: 40 characters.	記述

69		推定方法	介入の効果を推定するために使用される手順。	Procedure used to estimate effect of intervention.	手順
70		測定パラメーター	一つ選択してください。	Select one.	選択式
71		その他のパラメーター	"Other" Estimation Parameter が選択されている場合、推定パラメータの名前。 制限：40 文字。	The name of the estimation parameter, if “Other” Estimation Parameter is selected. Limit: 40 characters.	記述
72		見積もり値	推定パラメータの計算値	The calculated value for the estimation parameter.	推定パラメータの計算値
73		レベル	パーセンテージで表示。	Expressed as a percentage.	パーセンテージで表されます。
74		辺の数	片側または両側を選択します。	Select 1-sided or 2-sided.	片方 or 両方
75		下限	信頼区間が「両側」である場合、または信頼区間が「片側」であり、上限が入力されていない場合は必須です。	Required if confidence interval is "2-sided" or if confidence interval is "1-sided" and no Upper Limit is entered.	信頼区間
76		上限	信頼区間が「両側」である場合、または信頼区間が「片側」で下限が入力されていない場合は必須です。	Required if confidence interval is "2-sided" or if confidence interval is "1-sided" and no Lower Limit is entered.	信頼区間
77		NA 説明	"NA"が報告されて"両側"信頼区間の上限が得られない場合、上限のデータが利用できない理由を説明する。 制限：250 文字。	Explain why the upper limit data are not available, if "NA" is reported as upper-limit of "2-sided" confidence interval. Limit: 250 characters.	記述
78		パラメーター分散タイプ＊１つ選択	一つ選択してください。	Select one.	選択式
79		分散値	推定されたパラメータの分散の計算値。	The calculated value for the dispersion of the estimated parameter.	推定されたパラメータの分散の計算値

80		見積もりコメント	比較の方向を含む、他の関連する推定情報（例えば、相対リスクの分子および分母を表すアームまたは比較グループを記述する）。 制限：250 文字。	Any other relevant estimation information, including the direction of the comparison (for example, describe which arm or comparison group represents the numerator and denominator for relative risk). Limit: 250 characters.	記述
81		その他の統計分析	統計学的仮説検定または推定のオプションを使用した統計解析が報告できない場合は、統計学的有意に関する科学的に適切なテストの説明と結果を提供する。	If the statistical analysis cannot be submitted using the Statistical Test of Hypothesis or Method of Estimation options, provide a description and the results of any other scientifically appropriate tests of statistical significance.	記述
82	有害事象	時間枠	有害事象データが収集された特定の期間。 制限：500 文字。	The specific period of time over which adverse event data were collected. Limit: 500 characters.	記述
83		有害事象報告の説明	臨床試験で収集された有害事象情報が、以下の有害事象の定義とは異なる有害事象および/または重大な有害事象の異なる定義に基づいて収集される場合、その定義がどのように異なるかについて簡単に説明する。また、有害事象収集に関する追加の関連情報を提供するために使用することができます(例えば、毎日のアンケートなど)、分析集団がどのように決定されたかに関する情報(リスクのある参加者の数がアームまたは比較群に割り当てられた参加者の数）。 制限：500 文字。	If the adverse event information collected in the clinical study is collected based on a different definition of adverse event and/or serious adverse event than the Adverse Events definition below, a brief description of how the definitions differ. May also be used to provide any additional relevant information about adverse event collection, including details about the method of systematic assessment (for example, daily questionnaire) or information about how the analysis population was determined (if the Number of Participants at Risk differs from the number of participants assigned to the arm or comparison group). Limit: 500 characters.	記述

84		テーブルデフォルトのソースボキャブラリ名	標準用語、統制語彙、または有害事象用語がある場合はその分類およびバージョン（例えば、SNOMED CT、MedDRA 10.0）「重大な有害事象」および「（重大な有害事象を含まない)その他の有害事象」表に入力された､全ての有害事象に適用される元の報告された名称に対するデフォルトの値。必要に応じて、報告された名称を特定の有害事象用語を指定することもできます。 制限：20 文字。	Standard terminology, controlled vocabulary, or classification and version from which adverse event terms are drawn, if any (for example, SNOMED CT, MedDRA 10.0). Default value for Source Vocabulary Name to be applied to all adverse event terms entered in the "Serious Adverse Event" and "Other (Not Including Serious) Adverse Event" tables. If necessary, Source Vocabulary Name may also be specified for specific Adverse Event Terms. Limit: 20 characters.	記述
85		テープルデフォルト＊ １つ選択	有害事象情報を収集するためにとられるアプローチのタイプ。 「重大な有害事象」または「重大な有害事象を含まないその他の有害事象」表に入力されたすべての有害事象条件に適用される有害事象情報を収集するために取られるアプローチのタイプのデフォルト値(システマティックまたは非システマティック・アセスメント）。 必要に応じて、特定の有害事象条件についても回収方法を指定することができる。一つ選択してください。	The type of approach taken to collect adverse event information. Default value for the type of approach taken to collect adverse event information (Systematic or Non-Systematic Assessment) to be applied to all adverse event terms entered in the "Serious Adverse Event" or "Other (Not Including Serious) Adverse Event" tables. If necessary, Collection Approach may also be specified for specific Adverse Event Terms. Select one.	記述
86		アームグループ情報	予め指定されたプロトコールおよび/または統計分析計画に基づく全ての群または比較群を含む、研究におけるアームまたは比較群。	Arms or comparison groups in the study, including all arms or comparison groups based on the pre-specified protocol and/or statistical analysis plan.	記述
87		アームグループタイトル	各アームまたは比較群を識別するために使用されるラベル。 制限：> = 4 および<= 62 文字。	Label used to identify each arm or comparison group. Limit: >=4 and <= 62 characters.	記述

88		アームグループ説明	各アームまたは比較グループの簡単な説明。 一般に、参加者フローで参加者が割り当てられたアームおよび各アーム/グループの介入戦略からアームまたは比較グループがどのように導出されたかを理解するのに十分な詳細情報を含める必要があります。 制限：999 文字。	Brief description of each arm or comparison group. In general, it must include sufficient detail to understand how the arm(s) or comparison groups were derived from the arm(s) to which participants were assigned in Participant Flow and the intervention strategy in each arm/group. Limit: 999 characters.	記述
89		有害事象	研究に参加した人に一時的に関連する異常な兆候（例：異常な身体検査や検査所の所見）、症状、または疾患、参加者の研究参加との一時的な関連、研究参加の関連の検討を含む。。	Any untoward or unfavorable medical occurrence in a participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participant's participation in the research, whether or not considered related to the participant's participation in the research.	症状など
90		全死亡率の影響を受ける総数	何らかの原因で死亡した各アーム/群の全体的な参加者数。	Overall number of participants, in each arm/group, who died due to any cause.	死亡者数
91		全死亡率のリスク総数	すべての原因による死亡の評価(すなわち、全原因死亡率の頻度を計算するための分母)に含まれる、各群/群の全参加者数。	Overall number of participants, in each arm/group, included in the assessment of deaths due to any cause (that is, the denominator for calculating frequency of all-cause mortality).	死亡率
92		重大な有害事象の影響を受けた総数	1 つまたは複数の重篤有害事象の影響を受けた参加者の総数。	Overall number of participants affected by one or more Serious Adverse Events, for each arm/group.	有害事象数
93		重大な有害事象	重篤な有害事象の評価に含まれる参加者の総数(すなわち、重篤な有害事象の頻度を計算するための分母）、各群/群。	Overall number of participants included in the assessment of serious adverse events (that is, the denominator for calculating frequency of serious adverse events), for each arm/group.	有害事象数

94		他の有害事象の報告頻度閾値	他の有害事象(重篤なものを除く)が、他の有害事象（重篤なものを除く)の表で報告されるべきアームまたは比較群内での事象の発生頻度を指定する。発生頻度の閾値は、許容最大値（5%）以下でなければなりません。データフィールドに記号（例：>または%)を含めないでください。パーセント記号で表示される。	Specify the frequency of occurrence that an Other (Not Including Serious) Adverse Event must exceed, within any arm or comparison group, to be reported in the Other (Not Including Serious) Adverse Event table. The number for the frequency threshold must be less than or equal to the allowed maximum (5%). Do not include symbols (for example, > or %) in the data field, it will be expressed as a percentage.	有害事象の%
95		頻度閾値以上の他の有害事象の影響を受けた総数	各群/群の、少なくとも 1 件の他の有害事象(重篤なものを除く)が報告された参加者の総数。この表に報告された有害事象は、少なくとも 1 つのアームまたは比較群において、指定された頻度閾値(例えば、5%）を超える頻度で発生した有害事象である。	Overall number of participants affected, for each arm/group, by at least one Other (Not Including Serious) Adverse Event(s) reported in the table. Adverse events reported in the table are those that occurred at a frequency exceeding the specified Frequency Threshold (for example, 5%) within at least one arm or comparison group.	有害事象数
96		重大な有害事象を含まない有害事象	研究期間中にその他の有害事象（重篤なものを除く)の評価に含まれる各群/群の全参加者数。（その他の有害事象(重篤なものを除く)の発生頻度の報告に必要な分母となる）	Overall number of participants, for each arm/group, included in the assessment of Other (Not Including Serious) Adverse Events during the study (that is, the denominator for calculating frequency of Other (Not Including Serious) Adverse Events).	有害事象数
97		有害事象期間	有害事象の記述語句。 制限：100 文字。	Descriptive word or phrase for the adverse event. Limit: 100 characters.	期間の記述
98		オルガンシステム	身体または臓器システムによって有害事象の用語をグループ化するために使用される上位レベルのカテゴリ。 一つ選択してください。	High-level categories used to group adverse event terms by body or organ system. Select one. (Adverse events that affect multiple systems should be classified as "General disorders.")	選択式

99		有害事象用語追加の説明	有害事象に関する追加の関連情報。 制限：250 文字。	Additional relevant information about the adverse event. Limit: 250 characters.	記述
100		ソースボキャブラリー名	標準用語、統制語彙、または有害事象用語がある場合はその分類およびバージョン（例えば、SNOMED CT、MedDRA 10.0）。空白にすると、報告された用語が使用されます。 制限：20 文字。	Standard terminology, controlled vocabulary, or classification and version from which adverse event terms are drawn, if any (for example, SNOMED CT, MedDRA 10.0). Leave blank to indicate that the value specified as the Source Vocabulary for Table Default should be used. Limit: 20 characters.	記述
101		コレクションアプローチ＊1 つ選択 or 空白	有害事象情報を収集するためにとられるアプローチのタイプ。1 つを選択するか空白のままにします。空白にすると評価収集方法として特定された値が使用されます。	The type of approach taken to collect adverse event information. Select one or leave blank to indicate that the value specified as the Assessment Type for Table Default should be used.	選択式
102		影響を受ける参加者の数	少なくとも 1 つのイベントが報告されている、各アーム/グループ内の参加者の数。	Number of participants, in each arm/group, experiencing at least one event being reported.	イベント数
103		リスクのある参加者の数	各群/群において有害事象が評価された参加者の数（有害事象の頻度を計算するための分母）。 空白の場合、表のアーム/グループにおけるリスクのある集団の値が使用されます。	Number of participants assessed, in each arm/group, for adverse events (that is, the denominator for calculating frequency of adverse events). Leave blank to indicate that the value specified as the total at risk in the arm/group for the table should be used.	参加者数
104		イベント数	報告されている有害事象の各群/群における発生数。	Number of occurrences, in each arm/group, of the adverse event being reported.	イベント数
105	限界と警告	全体的な制限と警告	研究の重大な limitation を記述する。 このような limitation の中には、検出力や統計的に信頼できる結果、信頼性の低い、または理解が難しいデータが得られた場合の技術的な問題が含まれる。 制限：250 文字。	Describe significant limitations of the study. Such limitations may include not reaching the target number of participants needed to achieve target power and statistically reliable results or technical problems with measurements leading to unreliable or uninterpretable data. Limit: 250 characters.	記述

106	特定の契約	すべてのPIのスポンサーは従業員か	研究責任者がスポンサーの従業員であるかどうかを示します。 一つ選択してください。	Indicate whether the principal investigator is an employee of the sponsor. Select one.	選択肢
107		PI開示制限	スポンサーまたはその代理人と研究責任者（PI）との間で、第 1 次完了日後に、PI が学会やフォーラム、学術ジャーナルでの臨床試験の結果を公表することの合意(臨床研究に参加する参加者のプライバシーを保護する法律を遵守することのみを目的とした取り決めを除く)が存在するか。 はい/いいえを選択します。	Indicate whether there exists any agreement (other than an agreement solely to comply with applicable provisions of law protecting the privacy of participants participating in the clinical study) between the sponsor or its agent and the principal investigator (PI) that restricts in any manner the ability of the PI to discuss the results of the clinical study at a scientific meeting or any other public or private forum or to publish in a scientific or academic journal the results of the clinical study, after the Primary Completion Date. Select Yes/No.	はい、いいえを選択
108		PI開示制限タイプ	結果開示制限に関する追加情報。様々な契約がある場合は、最も制限の厳しい契約(例えば、厳しい貿易禁止期間に関する契約)を表す以下の種類を選択します。一つ選択してください。	Additional information about the results disclosure restriction. If there are varying agreements, choose the type below that represents the most restrictive of the agreements (for example, the agreement with the greatest embargo time period). Select one.	選択式
109	結果の連絡先（問い合わせ先）	名前または公式のタイトル	窓口として指定された人。これは、特定の人物の名前（例えば、ジェーン・スミス博士)や役職名（例えば､臨床試験の責任者）でもよいです。	The person who is designated the point of contact. This may be a specific person's name (for example, Dr. Jane Smith) or a position title (for example, Director of Clinical Trials).	連絡先の人物の名前
110		組織名	指定された個人の所属組織の名称。	Full name of the designated individual's organizational affiliation.	組織名
111		電話番号	指定された個々のオフィスの電話番号。米国およびカナダ内のフォーマット123-456-7890を使用してください。米国およびカナダ以外の場合は、国コードを含む電話番号を提供します。	Office phone number of the designated individual. Use the format 123-456-7890 within the United States and Canada. If outside the United States and Canada, provide the full phone number, including the country code.	電話番号

112		メール	指定された個々の電子メールアドレス。	Electronic mail address of the designated individual.	メールアドレス
113	遅延（オプション）	遅延タイプ ＊1つ選択	いずれかを選択	Select one	選択式
114		介入の名前	証明書が発行される 1 種類以上の薬物、生物学的製剤または機器の名前を入力します。薬の場合は、一般名を入力します。それ以外の場合、簡潔に名称を入力します。名称は、プロトコル記載欄に設けられた介入名と一致しなければいけない。	Provide the name of one or more drugs, biological products or devices to which the certification applies. For drugs use generic name; for other types of interventions provide a brief descriptive name. The name(s) entered should match Intervention Name(s) provided in the protocol section.	薬物名
115		FDA 申請番号	結果の遅延が「初回承認の認定」または「新規使用の認定」であって、可能な場合は、少なくとも 1 つの FDA 申請番号（例えば、NDA 、 BLA 、 または PMA 番号）を指定します。	Provide at least one FDA application number (for example, NDA, BLA, or PMA number), if available, when Delay Results Type is "Certify Initial Approval" or "Certify New Use."	FDA 申請番号
116		要求された提出日	結果の遅延が"延長"の場合、臨床試験の結果情報の提出予定日。	Estimate of the date on which the clinical study results information will be submitted, if the Delay Results Type is "Extension".	提出日
117		説明	臨床研究の結果情報が締切までに入力できない理由。理由は延長を正当化するのに十分な理由と延長依頼を評価ができるように詳細を入力する。 特定されていない原因による「出版保留」とデータ分析の遅延は、延長の正当な理由とはならないことに注意してください。 制限：999 文字。	Description of the reason(s) why clinical study results information cannot be provided according to the deadline, with sufficient detail to justify good cause for the extension and to allow for the evaluation of the request. Note that "pending publication" and delays in data analysis for unspecified causes are not considered good cause for an extension. Limit: 999 characters.	記述

付表 2. ClinicalTrials.gov で規定されている試験結果の登録項目の説明画面

ClinicalTrials.gov Results Data Element Definitions for Interventional and Observational Studies

June 29, 2017

This document describes the definitions for results data elements submitted to ClinicalTrials.gov for interventional studies (clinical trials) and observational studies. These definitions are mostly adapted from 42 CFR Part 11.

Data element entries are annotated with symbols to indicate generally what information is required to be submitted and under which circumstances. The responsible party must ensure that the information provided complies with any applicable laws, regulations, or policies. For more information about various requirements and definitions of regulatory terms under 42 CFR Part 11, see Support Materials.

Note: The term "clinical study" is used to refer to both interventional and observational studies. The term "participant" is used to refer to a human subject.

* Required

*§ Required if Primary Completion Date is on or after January 18, 2017

[*] Conditionally required

1. Participant Flow

Information to document the progress of research participants through each stage of a study in a tabular format, including the number of participants who started and completed the clinical study. (Identical in purpose to a CONSORT flow diagram, but represented as tables).

The tabular presentation may be separated into "periods," each of which comprises an interval of study activity. Each period consists of "milestones" for reporting numbers of participants at particular points in time within that period.

Recruitment Details
Definition: Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and types of location (For example, medical clinic), to provide context.
Limit: 350 characters.

Pre-assignment Details [*]
Definition: Description of significant events in the study (for example, wash out, run-in) that occur after participant enrollment, but prior to assignment of participants to an arm or group, if any. For example, an explanation of why enrolled participants were excluded from the study before assignment to arms or groups.
Limit: 350 characters.

Arm/Group Information *
Definition: Arms or groups for describing the flow of participants through the clinical study. In general, it must include each arm to which participants were assigned.

Arm/Group Title *
Definition: Descriptive label used to identify each arm or group.
Limit: >=4 and <= 62 characters.

Arm/Group Description *§
Definition: Brief description of each arm or group. In general, it must include sufficient details to understand each arm to which participants were assigned and the intervention strategy used in each arm.
Limit: 999 characters.

Type of Units Assigned [*]
Definition: If assignment is based on a unit other than participants, a description of the unit of assignment (for example, eyes, lesions, implants).
Limit: 40 characters.

Period(s) *
Definition: Discrete stages of a clinical study during which numbers of participants at specific significant events or points of time are reported.

There is no limit to the number of periods that may be used to describe a single study. Each subsequent period represents a study stage following the previous period. That is, participants "flow" from earlier to later periods.

Period Title *
Definition: Title describing a stage of the study. If only one period is defined, the default title is Overall Study. When a study has more than one period, none of the Period Titles should be Overall Study.
Limit: 40 characters.

Started *
Definition: Number of participants initiating the period. In the first period, it is the number of participants assigned to each arm or group. If assignment is based on a unit other than participants, also include the number of units at the beginning of the period.

Comments
Definition: Additional information about the Started milestone or Milestone Data.
Limit: 100 characters.

Completed *
Definition: Number of participants at the end of the period. If assignment is based on a unit other than participants, also include the number of units at the end of the period.

Comments
Definition: Additional information about the Completed milestone or Milestone Data.
Limit: 100 characters.

Not Completed *(calculated automatically)*
Definition: Number of participants (and units, if applicable) that did not complete the study or period. This is calculated automatically by subtracting Completed from Started.

Additional Milestone(s)
Definition: Any specific events or time points in the study when the numbers of participants (and units, if applicable) are reported. While there is no limit to the number of milestones that may be used in a single period, data are required for two milestones, Started and Completed, within each period.

Milestone Title [*]
Definition: : Label describing the milestone
Limit: 40 characters.

Milestone Data [*]
Definition: Number of participants to reach the milestone, in each arm/group. If assignment is based on a unit other than participants, also include the number of units to reach the milestone.

Comments
Definition: Additional information about the milestone or data.
Limit: 100 characters.

Reason Not Completed
Definition: Additional information about participants who did not complete the study or period. If reasons are provided, the total number of participants listed as Not Completed must be accounted for by all reasons for non-completion.

Reason Not Completed Type [*]
Definition: Reason why participants did not complete the study or period. Select one.

- Adverse Event
- Death
- Lack of Efficacy
- Lost to Follow-Up
- Physician Decision
- Pregnancy
- Protocol Violation
- Withdrawal by Subject
- Other

Other Reason [*]
Definition: A brief description of the reason for non-completion, if "Other" Reason Not Completed Type is selected.
Limit: 40 characters.

Reason Not Completed Data [*]
Definition: Number of participants in each arm or group that did not complete the study or period, for each Reason Not Completed.

▼ 2. Baseline Characteristics

A table of demographic and baseline measures and data collected by arm or comparison group and for the entire population of participants in the clinical study.

Arm/Group Information *
Definition: Arms or comparison groups in the study, including all participants assessed at baseline as specified in the pre-specified protocol and/or statistical analysis plan.

Arm/Group Title *
Definition: Descriptive label used to identify each arm or comparison group.
Limit: >= 4 and <= 62 characters.

Arm/Group Description *§
Definition: Brief description of each arm or comparison group. In general, it must include sufficient detail to understand how the arm(s) or comparison groups were derived from the arm(s) to which participants were assigned in Participant Flow (if different) and the intervention strategy in each arm/group.
Limit: 999 characters.

Baseline Analysis Population Information

Overall Number of Baseline Participants *

Definition: Total number of participants for whom baseline characteristics were measured, in each arm/group and overall.

Overall Number of Units Analyzed [*]

Definition: If the analysis is based on a unit other than participants, the number of units for which baseline measures were measured and analyzed, in each arm/group and overall.

Type of Units Analyzed [*]

Definition: If the analysis is based on a unit other than participants, a description of the unit of analysis (for example, eyes, lesions, implants).
Limit: 40 characters.

Baseline Analysis Population Description [*]

Definition: If the Overall Number of Baseline Participants (or units) differs from the number of participants (or units) assigned to the arm or comparison group and overall, a brief description of the reason(s) for the difference such as how the analysis population was determined.
Limit: 350 characters.

Baseline Measure Information *

Definition: A description of each baseline or demographic characteristic measured in the clinical study. Required baseline measures include Age, Sex/Gender, Race, Ethnicity (if collected under the protocol), and any other measure(s) that were assessed at baseline and used in the analysis of the primary outcome measure(s).

Baseline Measure Title *

Definition: The name of the baseline or demographic characteristic measured in the clinical study. Select as many as needed.

- Study-Specific Measure *§ *(Select as many as needed)*
- Age * *(Select at least one of the following):*
  - Age, Continuous: For example - mean or median age
  - Age, Categorical:
    - <=18 years
    - >18 and <65 years
    - >=65 years
  - Age, Customized: Customizable age categories
- Sex/Gender * *(Select at least one of the following):*
  - Sex: Female, Male
  - Sex/Gender, Customized
- Race and Ethnicity *§
  - Race (NIH/OMB): U.S. National Institutes of Health and U.S. Office of Management and Budget Classification Categories
  - Ethnicity (NIH/OMB): U.S. National Institutes of Health and U.S. Office of Management and Budget Classification Categories
  - Race/Ethnicity, Customized
  - Race and Ethnicity Not Collected
- Region of Enrollment

Study-Specific Baseline Measure Title(s) [*]
Definition: If "Study-Specific Measure" is chosen, provide the name of the measure.
Limit: 100 characters.

Baseline Measure Description
Definition: Additional descriptive information about the baseline measure, such as a description of the metric used to characterize the specific baseline measure.
Limit: 600 characters.

Measure Type *
Definition: The type of data for the baseline measure. Select one.

- Count of Participants
- Mean
- Median
- Least Squares Mean
- Geometric Mean
- Geometric Least Squares Mean
- Number
- Count of Units

Measure of Dispersion *
Select one.

- Not Applicable (only if Measure Type is "Number", "Count of Participants", or "Count of Units")
- Standard Deviation
- Inter-Quartile Range
- Full Range

Number of Baseline Participants [*]
Definition: The number of participants analyzed for the baseline measure, if different from the Overall Number of Baseline Participants, in each arm/group and overall.

Number of Units Analyzed [*]
Definition: The number of units analyzed for the baseline measure, if different from the Overall Number of Units Analyzed, in each arm/group and overall.

Analysis Population Type [*]
Definition: Indicate whether the baseline measure analysis is based on participants or units other than participants. Only applies if Type of Units Analyzed is specified. Select Participants/Other Units.

Measure Analysis Population Description [*]
Definition: Explanation of how the number of participants (or units) for analysis was determined, if different from the Overall Number of Participants [or Units] Analyzed.
Limit: 350 characters.

Category or Row Title [*]
Definition: Name of distinct category or row for a baseline measure, if any. Category Titles are only for mutually exclusive and exhaustive categories summarizing data using the Measure Type of a "Count of Participants" or "Count of Units." Row Titles are for any type of data.
Limit: 50 characters.

Baseline Measure Data *

Definition: The value(s) for each baseline measure, for each arm/group and overall.

NA (Not Available) Explanation [*]

Definition: Explain why baseline measure data are not available, if "NA" is reported for Baseline Measure Data.
Limit: 250 characters.

Unit of Measure *

Definition: An explanation of what is quantified by the data (for example, participants, mm Hg), for each baseline measure.
Limit: 40 characters.

▼ 3. Outcome Measures

A table of data for each primary and secondary outcome measure by arm (that is, initial assignment of participants to arms or groups) or comparison group (that is, analysis groups), including the result(s) of scientifically appropriate statistical analyses that were performed on the outcome measure data, if any.

Note: Outcome measure information from the Protocol Section of the record will be copied into the Results Section the first time results are created.

Outcome Measure Information *

Definition: A description of each outcome measure.

Note: "Outcome measure" means a pre-specified measurement that is used to determine the effect of an experimental variable on participants in the study. Post-hoc (that is, not pre-specified) outcome measures may also be reported.

Outcome Measure Type *

Definition: The type of outcome measure. Select one.

- Primary
- Secondary
- Other Pre-specified
- Post-Hoc

Outcome Measure Title *

Definition: Name of the specific outcome measure.
Limit: 255 characters.

Outcome Measure Description [*]

Definition: Additional information about the outcome measure, including a description of the metric used to characterize the specific outcome measure, if not included in the Outcome Measure Title.
Limit: 999 characters.

Outcome Measure Time Frame *

Definition: Time point(s) at which the measurement was assessed for the specific metric used. The description of the time point(s) of assessment must be specific to the outcome measure and is generally the specific duration of time over which each participant is assessed (not the overall duration of the study).
Limit: 255 characters.

Anticipated Reporting Date

Definition: If Outcome Measure Data are not included for an outcome measure, provide the expected month and year they will be submitted.

Arm/Group Information *

Definition: Arms or comparison groups in the study, including all arms or comparison groups based on the pre-specified protocol and/or statistical analysis plan.

Arm/Group Title *

Definition: Descriptive label used to identify each arm or comparison group.
Limit: >= 4 and <= 62 characters.

Arm/Group Description *§

Definition: Brief description of each arm or comparison group. In general, it must include sufficient detail to understand how the arm(s) or comparison groups were derived from the arm(s) to which participants were assigned in Participant Flow (if different) and the intervention strategy in each arm/group.
Limit: 999 characters.

Analysis Population Information

Overall Number of Participants Analyzed *

Definition: Number of participants for whom an outcome measure was measured and analyzed, for each outcome measure and each arm/group.

Type of Units Analyzed [*]

Definition: If the analysis is based on a unit other than participants, a description of the unit of analysis (for example, eyes, lesions, implants).
Limit: 40 characters.

Overall Number of Units Analyzed [*]

Definition: If the analysis is based on a unit other than participants, the number of units for which an outcome was measured and analyzed, for each outcome measure and each arm/group.

Analysis Population Description [*]

Definition: If the Number of Participants Analyzed or Number of Units Analyzed differs from the number of participants or units assigned to the arm or comparison group, a brief description of the reason for the difference (such as how the analysis population was determined).
Limit: 350 characters.

Outcome Measure Data Table

Measure Type *

Definition: The type of data for the outcome measure. Select one.

- Count of Participants
- Mean
- Median
- Least Squares Mean
- Geometric Mean
- Geometric Least Squares Mean
- Number
- Count of Units

Measure of Dispersion/Precision *

Select one.

- Not Applicable (only if Measure Type is "Number," "Count of Participants," or "Count of Units")
- Standard Deviation
- Standard Error
- Inter-Quartile Range
- Full Range
- 80% Confidence Interval
- 90% Confidence Interval
- 95% Confidence Interval
- 97.5% Confidence Interval
- 99% Confidence Interval
- Other Confidence Interval Level
- Geometric Coefficient of Variation (only when Measure Type is "Geometric Mean")

Other Confidence Interval Level [*]

Definition: The numerical value for the confidence interval level, if "Other Confidence Interval Level" is selected. Provide a rationale for choosing this level in the Outcome Measure Description.

Category or Row Title [*]

Definition: Name of distinct category or row for an outcome measure, if any. Category Titles are only for mutually exclusive and exhaustive categories summarizing data using the Measure Type of a "Count of Participants" or "Count of Units". Row Titles are for any type of data.
Limit: 50 characters.

Number of Participants Analyzed [*]

Definition: The number of participants analyzed for the outcome measure in the row and for each arm/group, if different from the overall Number of Participants Analyzed.
Limit: 50 characters.

Number of Units Analyzed [*]

Definition: The number of units analyzed for the outcome measure in the row and for each arm/group, if different from the overall Number of Units Analyzed.

Outcome Data *

Definition: The measurement value(s) for each outcome measure, including each category/row and each arm/group.

NA (Not Available) Explanation [*]

Definition: Explain why outcome measure data are not available, if "NA" is reported for Outcome Data.
Limit: 250 characters.

Unit of Measure *

Definition: An explanation of what is quantified by the data (for example, participants, mm Hg), for each outcome measure.
Limit: 40 characters.

Statistical Analyses [*]
Definition: Result(s) of scientifically appropriate tests of statistical significance of the primary and secondary outcome measures, if any. Such analyses include: pre-specified in the protocol and/or statistical analysis plan; made public by the sponsor or responsible party; conducted on a primary outcome measure in response to a request made by FDA.

If a statistical analysis is reported "Comparison Group Selection" and "Type of Statistical Test" are required. In addition, one of the following data elements are required with the associated information: "P-Value," "Estimation Parameter," or "Other Statistical Analysis."

Statistical Analysis Overview
Definition: Summary description of the analysis performed.

Comparison Group Selection [*]
Definition: The arms or comparison groups involved in the statistical analysis (check all to indicate an "omnibus" analysis).

Comments
Definition: Additional details about the statistical analysis, such as null hypothesis and description of power calculation.
Limit: 500 characters.

Type of Statistical Test [*]
Definition: Identifies the type of analysis. Select one.

- Superiority
- Non-inferiority
- Equivalence
- Other (for example, single group or other descriptive analysis)
- Non-Inferiority or Equivalence (*legacy selection*)
- Superiority or Other (*legacy selection*)

Comments [*]
Definition: If, "Non-inferiority" or "Equivalence," provide additional details, including details of the power calculation (if not previously provided), definition of non-inferiority or equivalence margin, and other key parameters.
Limit: 500 characters.

Statistical Test of Hypothesis (*or Method of Estimation or Other Statistical Analysis required*)
Definition: Procedure used for statistical analysis of outcome data and the calculated p-value.

P-Value [*]
Definition: Calculated p-value given the null-hypothesis

Comments
Definition: Additional information, such as whether the p-value is adjusted for multiple comparisons and the *a priori* threshold for statistical significance
Limit: 250 characters.

Method [*]
Definition: The statistical test used to calculate the p-value, if a P-Value is reported. Select one.

- ANCOVA
- ANOVA
- Chi-Squared
- Chi-Squared, Corrected
- Cochran-Mantel-Haenszel
- Fisher Exact
- Kruskal-Wallis
- Log Rank
- Mantel Haenszel
- McNemar
- Mixed Models Analysis
- Regression, Cox
- Regression, Linear
- Regression, Logistic
- Sign Test
- t-Test, 1-Sided
- t-Test, 2-Sided
- Wilcoxon (Mann-Whitney)
- Other

Other Method Name [*]
Definition: If "Other" is selected, provide name of statistical test.
Limit: 40 characters.

Comments
Definition: Any other relevant information about the statistical test, such as adjustments or degrees of freedom.
Limit: 150 characters.

Method of Estimation (*or Statistical Test of Hypothesis or Other Statistical Analysis required*)
Definition: Procedure used to estimate effect of intervention.

Estimation Parameter [*]
Select one.

- Cox Proportional Hazard
- Hazard Ratio (HR)
- Hazard Ratio, Log
- Mean Difference (Final Values)
- Mean Difference (Net)
- Median Difference (Final Values)
- Median Difference (Net)
- Odds Ratio (OR)
- Odds Ratio, Log
- Risk Difference (RD)
- Risk Ratio (RR)
- Risk Ratio, Log
- Slope
- Other

Other Parameter Name [*]
Definition: The name of the estimation parameter, if “Other” Estimation Parameter is selected.
Limit: 40 characters.

Estimated Value [*]
Definition: The calculated value for the estimation parameter.

Confidence Interval (*If applicable*)

Level [*]
Expressed as a percentage.

Number of Sides [*]
Select 1-sided or 2-sided.

Lower Limit [*]
Definition: Required if confidence interval is "2-sided" or if confidence interval is "1-sided" and no Upper Limit is entered.

Upper Limit [*]
Definition: Required if confidence interval is "2-sided" or if confidence interval is "1-sided" and no Lower Limit is entered.

NA (Not Available) Explanation [*]
Definition: Explain why the upper limit data are not available, if "NA" is reported as upper-limit of "2-sided" confidence interval.
Limit: 250 characters.

Parameter Dispersion Type
Select one.

- Standard Deviation
- Standard Error of the Mean

Dispersion Value
Definition: The calculated value for the dispersion of the estimated parameter.

Estimation Comments
Definition: Any other relevant estimation information, including the direction of the comparison (for example, describe which arm or comparison group represents the numerator and denominator for relative risk).
Limit: 250 characters.

Other Statistical Analysis
Definition: If the statistical analysis cannot be submitted using the Statistical Test of Hypothesis or Method of Estimation options, provide a description and the results of any other scientifically appropriate tests of statistical significance.

▼ 4. Adverse Event Information

Information for completing three tables summarizing adverse events.

1. All-Cause Mortality: *§ A table of *all* anticipated and unanticipated deaths due to any cause, with number and frequency of such events in each arm/group of the clinical study.

2. Serious Adverse Events: * A table of *all* anticipated and unanticipated serious adverse events, grouped by organ system, with number and frequency of such events in each arm/group of the clinical study. (*See Adverse Events definition below*).

3. Other (Not Including Serious) Adverse Events: * A table of anticipated and unanticipated events (not included in the serious adverse event table) that exceed a frequency threshold (for example, 5 %) within any arm of the clinical study, grouped by organ system, with number and frequency of such events in each arm/group of the clinical study.

Time Frame *§
Definition: The specific period of time over which adverse event data were collected.
Limit: 500 characters.

Adverse Event Reporting Description [*]
Definition: If the adverse event information collected in the clinical study is collected based on a different definition of adverse event and/or serious adverse event than the Adverse Events definition below, a brief description of how the definitions differ. May also be used to provide any additional relevant information about adverse event collection, including details about the method of systematic assessment (for example, daily questionnaire) or information about how the analysis population was determined (if the Number of Participants at Risk differs from the number of participants assigned to the arm or comparison group).
Limit: 500 characters.

Source Vocabulary Name for Table Default
Definition: Standard terminology, controlled vocabulary, or classification and version from which adverse event terms are drawn, if any (for example, SNOMED CT, MedDRA 10.0). Default value for Source Vocabulary Name to be applied to all adverse event terms entered in the "Serious Adverse Event" and "Other (Not Including Serious) Adverse Event" tables. If necessary, Source Vocabulary Name may also be specified for specific Adverse Event Terms.
Limit: 20 characters.

Collection Approach for Table Default *§ (*or Collection Approach for each Adverse Event Term required*)
Definition: The type of approach taken to collect adverse event information. Default value for the type of approach taken to collect adverse event information (Systematic or Non-Systematic Assessment) to be applied to all adverse event terms entered in the "Serious Adverse Event" or "Other (Not Including Serious) Adverse Event" tables. If necessary, Collection Approach may also be specified for specific Adverse Event Terms. Select one.

- Systematic Assessment: Any method of routinely determining whether or not certain adverse events have occurred, for example through a standard questionnaire, regular investigator assessment, regular laboratory testing, or other method
- Non-Systematic Assessment: Any non-systematic method for determining whether or not adverse events have occurred, such as self-reporting by participants or occasional assessment/testing

Arm/Group Information *

Definition: Arms or comparison groups in the study, including all arms or comparison groups based on the pre-specified protocol and/or statistical analysis plan.

Arm/Group Title *

Definition: Label used to identify each arm or comparison group.
Limit: >=4 and <= 62 characters.

Arm/Group Description *§

Definition: Brief description of each arm or comparison group. In general, it must include sufficient detail to understand how the arm(s) or comparison groups were derived from the arm(s) to which participants were assigned in Participant Flow and the intervention strategy in each arm/group.
Limit: 999 characters.

Adverse Events

Definition: Any untoward or unfavorable medical occurrence in a participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participant's participation in the research, whether or not considered related to the participant's participation in the research.

Three types of adverse event data are to be reported: "All-Cause Mortality," "Serious," and "Other (Not Including Serious)" Adverse Events.

1. All-Cause Mortality: The occurrence of death due to any cause.
2. Serious Adverse Events: Include adverse events that result in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
3. Other (Not Including Serious) Adverse Events: Adverse events that are not Serious Adverse Events.

Total Number Affected by All-Cause Mortality *§

Definition: Overall number of participants, in each arm/group, who died due to any cause.

Total Number at Risk for All-Cause Mortality *§

Definition: Overall number of participants, in each arm/group, included in the assessment of deaths due to any cause (that is, the denominator for calculating frequency of all-cause mortality).

Total Number Affected by Any Serious Adverse Event *

Definition: Overall number of participants affected by one or more Serious Adverse Events, for each arm/group.

Total Number at Risk for Serious Adverse Events * (*or Number at Risk for each Serious Adverse Event Term required*)

Definition: Overall number of participants included in the assessment of serious adverse events (that is, the denominator for calculating frequency of serious adverse events), for each arm/group.

Frequency Threshold for Reporting Other (Not Including Serious) Adverse Events *

Definition: Specify the frequency of occurrence that an Other (Not Including Serious) Adverse Event must exceed, within any arm or comparison group, to be reported in the Other (Not Including Serious) Adverse Event table. The number for the frequency threshold must be less than or equal to the allowed maximum (5%). Do not include symbols (for example, > or %) in the data field, it will be expressed as a percentage.

For example, a threshold of 5 percent indicates that all Other (Not Including Serious) Adverse Events with a frequency greater than 5 percent within at least one arm or comparison group are reported.

Total Number Affected by Any Other (Not Including Serious) Adverse Event Above the Frequency Threshold *

Definition: Overall number of participants affected, for each arm/group, by at least one Other (Not Including Serious) Adverse Event(s) reported in the table. Adverse events reported in the table are those that occurred at a frequency exceeding the specified Frequency Threshold (for example, 5%) within at least one arm or comparison group.

Total Number at Risk for Other (Not Including Serious) Adverse Events * (*or Number at Risk for each Other, [Not Including Serious], Adverse Event Term required*)

Definition: Overall number of participants, for each arm/group, included in the assessment of Other (Not Including Serious) Adverse Events during the study (that is, the denominator for calculating frequency of Other (Not Including Serious) Adverse Events).

Adverse Event Term *

Definition: Descriptive word or phrase for the adverse event.
Limit: 100 characters.

Organ System *

Definition: High-level categories used to group adverse event terms by body or organ system. Select one. (Adverse events that affect multiple systems should be classified as "General disorders.")

- Blood and Lymphatic System Disorders
- Cardiac Disorders
- Congenital, Familial and Genetic Disorders
- Ear and Labyrinth Disorders
- Endocrine Disorders
- Eye Disorders
- Gastrointestinal Disorders
- General Disorders
- Hepatobiliary Disorders
- Immune System Disorders
- Infections and Infestations
- Injury, Poisoning and Procedural Complications
- Investigations
- Metabolism and Nutrition Disorders
- Musculoskeletal and Connective Tissue Disorders
- Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps)
- Nervous System Disorders
- Pregnancy, Puerperium and Perinatal Conditions
- Product Issues
- Psychiatric Disorders
- Renal and Urinary Disorders
- Reproductive System and Breast Disorders
- Respiratory, Thoracic and Mediastinal Disorders
- Skin and Subcutaneous Tissue Disorders
- Social Circumstances
- Surgical and Medical Procedures
- Vascular Disorders

Adverse Event Term Additional Description
Definition: Additional relevant information about the adverse event.
Limit: 250 characters.

Source Vocabulary Name
Definition: Standard terminology, controlled vocabulary, or classification and version from which adverse event terms are drawn, if any (for example, SNOMED CT, MedDRA 10.0). Leave blank to indicate that the value specified as the Source Vocabulary for Table Default should be used.
Limit: 20 characters.

Collection Approach *§ (*or Collection Approach for Table Default required*)
Definition: The type of approach taken to collect adverse event information. Select one or leave blank to indicate that the value specified as the Assessment Type for Table Default should be used.

- Systematic Assessment: Any method of routinely determining whether or not certain adverse events have occurred, for example through a standard questionnaire, regular investigator assessment, regular laboratory testing, or other method
- Non-Systematic Assessment: Any non-systematic method for determining whether or not adverse events have occurred, such as self-reporting by participants or occasional assessment/testing

Adverse Event Data

Number of Participants Affected *
Definition: Number of participants, in each arm/group, experiencing at least one event being reported.

Number of Participants at Risk *
Definition: Number of participants assessed, in each arm/group, for adverse events (that is, the denominator for calculating frequency of adverse events). Leave blank to indicate that the value specified as the total at risk in the arm/group for the table should be used.

Number of Events
Definition: Number of occurrences, in each arm/group, of the adverse event being reported.

▼ 5. Limitations and Caveats

Overall Limitations and Caveats
Definition: Describe significant limitations of the study. Such limitations may include not reaching the target number of participants needed to achieve target power and statistically reliable results or technical problems with measurements leading to unreliable or uninterpretable data.
Limit: 250 characters.

▼ 6. Certain Agreements

Information indicating whether there exists an agreement between the sponsor or its agent and the principal investigators (unless the sponsor is an employer of the principal investigators) that restricts in any manner the ability of the principal investigators (PIs), after the completion of the study, to discuss the results of the study at a scientific meeting or any other public or private forum, or to publish in a scientific or academic journal information concerning the results of the study. This does not include an agreement solely to comply with applicable provisions of law protecting the privacy of participants.

Are all PIs Employees of Sponsor? *

Definition: Indicate whether the principal investigator is an employee of the sponsor. Select one.

- Yes: The principal investigator is an employee of the sponsor
- No: The principal investigator is not an employee of the sponsor

If "No" the following information is required:

Results Disclosure Restriction on PI(s)? [*]

Definition: Indicate whether there exists any agreement (other than an agreement solely to comply with applicable provisions of law protecting the privacy of participants participating in the clinical study) between the sponsor or its agent and the principal investigator (PI) that restricts in any manner the ability of the PI to discuss the results of the clinical study at a scientific meeting or any other public or private forum or to publish in a scientific or academic journal the results of the clinical study, after the Primary Completion Date. Select Yes/No.

If there are agreements with multiple PIs who are not employees of the sponsor and there is a disclosure restriction on at least one PI, select "Yes."

PI Disclosure Restriction Type

Definition: Additional information about the results disclosure restriction. If there are varying agreements, choose the type below that represents the most restrictive of the agreements (for example, the agreement with the greatest embargo time period). Select one.

- The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding study results for a period that is ***less than or equal to 60 days*** from the date that the communication is submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot unilaterally extend the embargo.
- The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding study results for a period that is ***more than 60 days but less than or equal to 180 days*** from the date that the communication is submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot unilaterally extend the embargo.
- Other disclosure agreement that restricts the right of the PI to disclose, discuss, or publish study results after the study is completed

  Other Disclosure Restriction Description

  Definition: If "Other disclosure agreement..." is selected, describe the type of agreement including any provisions allowing the sponsor to require changes, ban the communication, or extend an embargo.
  Limit: 500 characters.

▼ 7. Results Point of Contact

Point of contact for scientific information about the clinical study results information.

Name or Official Title *

Definition: The person who is designated the point of contact. This may be a specific person's name (for example, Dr. Jane Smith) or a position title (for example, Director of Clinical Trials).

Organization Name *

Definition: Full name of the designated individual's organizational affiliation.

Phone: *§ Office phone number of the designated individual. Use the format 123-456-7890 within the United States and Canada. If outside the United States and Canada, provide the full phone number, including the country code.

Extension (Ext.): Phone extension, if needed

Email: *§ Electronic mail address of the designated individual.

▼ **8. Delayed Results** (*Optional*)

A responsible party may delay the deadline for submitting results information if one of the two certification conditions below applies to the clinical study. Alternatively, the responsible party may request an extension of the results submission deadline for good cause. The extension must be granted by the NIH Director.

Delay Results Type [*] : Select one

- Certify Initial Approval: Trial studies an FDA-regulated drug product (including a biological product) or device product that was not approved, licensed or cleared by FDA for any use before the Primary Completion Date of the trial, and the sponsor intends to continue with product development and is either seeking, or may at a future date seek, FDA approval, licensure, or clearance of the drug product (including a biological product) or device product under study.
- Certify New Use: Trial studies an FDA-regulated drug product (including a biological product) or device product that previously has been approved, licensed, or cleared, for which the manufacturer is the sponsor of the trial and for which an application or premarket notification seeking approval, licensure, or clearance of the use being studied (which is not included in the labeling of the approved, licensed, or cleared drug, product (including a biologic product) or device product) has been filed or will be filed within one year with FDA.
- Extension: Request, for good cause, an extension of the deadline for submitting results information

Note: If a responsible party who is both the manufacturer of the drug product (including a biological product) or device product studied in an applicable clinical trial and the sponsor of the applicable clinical trial submits a certification under "Certify New Use," that responsible party must submit such a certification for each applicable clinical trial that meets the following criteria: (1) the applicable clinical trial is required to be submitted in an application or premarket notification seeking approval, licensure, or clearance of a new use; (2) the applicable clinical trial studies the same drug product (including a biological product) or device product for the same use as studied in the applicable clinical trial for which the initial certification was submitted. [42 U.S.C. 282 (j)(3)(E)(v)(II) and 42 CFR 11.44(b)(3)]

Intervention Name(s)
Definition: Provide the name of one or more drugs, biological products or devices to which the certification applies. For drugs use generic name; for other types of interventions provide a brief descriptive name. The name(s) entered should match Intervention Name(s) provided in the protocol section.

FDA Application Number(s)
Definition: Provide at least one FDA application number (for example, NDA, BLA, or PMA number), if available, when Delay Results Type is "Certify Initial Approval" or "Certify New Use."

Requested Submission Date [*] (*Required when Delay Results Type is "Extension."*)
Definition: Estimate of the date on which the clinical study results information will be submitted, if the Delay Results Type is "Extension".

Explanation [*] (*Required when Delay Results Type is "Extension."*)
Definition: Description of the reason(s) why clinical study results information cannot be provided according to the deadline, with sufficient detail to justify good cause for the extension and to allow for the evaluation of the request. Note that "pending publication" and delays in data analysis for unspecified causes are not considered good cause for an extension.
Limit: 999 characters.

▼ A.1 Document Upload Information *§

The full study protocol and statistical analysis plan must be uploaded as part of results information submission, for studies with a Primary Completion Date on or after January 18, 2017. The protocol and statistical analysis plan may be optionally uploaded before results information submission and updated with new versions, as needed. Informed consent forms may optionally be uploaded at any time.

Documents must be uploaded in Portable Document Format Archival (PDF/A) format. It is strongly encouraged that the PDF/A file also be consistent with the PDF Universal Accessibility (PDF/UA) format, to optimize accessibility.

For each uploaded document, provide the following information.

Document Type *
Definition: Type of uploaded study document. Select one.

- Study Protocol: The written description of the clinical study, including objective(s), design, and methods. It may also include relevant scientific background and statistical considerations (if the protocol document includes the statistical analysis plan, use "Study Protocol with SAP and/or ICF" option). Note: All amendments approved by a human subjects protection review board (if applicable), before the time of submission and that apply to all clinical trial Facility Locations must be included.

- Statistical Analysis Plan (SAP): The written description of the statistical considerations for analyzing the data collected in the study. Includes how data are analyzed, what specific statistical methods are used for each analysis, and how adjustments are made for testing multiple variables. If some analysis methods require critical assumptions, the written description should allow data users to understand how those assumptions were verified.

- Informed Consent Form (ICF): The final version of the legal document approved by a human subjects protection review board. It is written in lay language and describes, among other things, the study's purpose, procedures, risks and potential benefits.

- Study Protocol with SAP and/or ICF: The study protocol that also includes a statistical analysis plan (SAP) and/or an informed consent form (ICF). Select one or both.
  - Statistical Analysis Plan (SAP)
  - Informed Consent Form (ICF)

Document Date *
Definition: The date on which the uploaded document was most recently updated and, if needed, approved by a human subjects protection review board.

Subtitle [*]

Definition: If there is more than one document for a study of the same Document Type, provide additional descriptive information to differentiate between documents. For example, there may be more than one document of the same Document Types if there are two populations studied in the same study (such as, infants and mothers). Do NOT use Subtitles for uploading a new version of the same document.

Document *

Definition: The study protocol, statistical analysis plan, and/or informed consent form document(s) uploaded in Portable Document Format Archival (PDF/A) format. It is strongly encouraged that the PDF/A file also be consistent with the PDF Universal Accessibility (PDF/UA) format, to optimize accessibility. Each document must include a cover page with the Official Title of the study, NCT number (if available), and date of the document.

Note: The study document may include redaction of names, addresses, and other personally identifiable information, as well as any trade secret and/or confidential commercial information (as those terms are defined in the Freedom of Information Act (5 U.S.C. 552) and the Trade Secrets Act (18 U.S.C. 1905)) contained in the protocol or statistical analysis plan. Information that is otherwise required to be submitted as part of clinical trial registration or results information may not be redacted.

▼ **History of Changes**

January 18, 2017: Document updated with data element changes per the FDAAA 801 final rule (42 CFR Part 11).

April 18, 2017: Modified Outcome Measure Description definition to describe when the Description is required.

June 29, 2017: Added Document Upload Information data elements as Appendix 1 (A.1.).

付表 3. ClinicalTrials.gov における試験結果の報告例

Show definition National Library of Medicine

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site

Home > Search Results > Study Record Detail

Save this study

Trial record **24 of 836** for: Completed, Terminated Studies | Studies With Results | breast cancer

◂ Previous Study | Return to List | Next Study ▸

Abraxane, Avastin, and Gemcitabine as First-Line Therapy for Patients With Metastatic Breast Cancer

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT00503906

Recruitment Status: Completed
First Posted: July 19, 2007
Results First Posted: April 2, 2013
Last Update Posted: May 12, 2017

Sponsor:
University of Miami

Information provided by (Responsible Party):
University of Miami

Study Details | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Study Type:	Interventional
Study Design:	Intervention Model: Single Group Assignment; Masking: None (Open Label); Primary Purpose: Treatment
Condition:	**Breast Cancer**
Interventions:	Drug: Avastin Drug: Gemcitabine Drug: Abraxane

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Participant Flow: Overall Study

	Abraxane, Avastin and Gemcitabine
STARTED	30
COMPLETED	29
NOT COMPLETED	1
Withdrawal by Subject	1

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Baseline Measures

	Abraxane, Avastin and Gemcitabine
Overall Participants Analyzed [Units: Participants]	**30**
Age [Units: Participants] Count of Participants	
<=18 years	**0** 0.0%
Between 18 and 65 years	**27** 90.0%
>=65 years	**3** 10.0%
Age [Units: Years] Mean (Standard Deviation)	**52.3 (9.2)**
Age [Units: Years] Median (Full Range)	**53.8** **(34 to 69)**
Sex: Female, Male [Units: Participants] Count of Participants	
Female	**29** 96.7%
Male	**1** 3.3%
Race (NIH/OMB) [Units: Participants] Count of Participants	
American Indian or Alaska Native	**0** 0.0%
Asian	**1** 3.3%
Native Hawaiian or Other Pacific Islander	**0** 0.0%
Black or African American	**8** 26.7%
White	**20** 66.7%
More than one race	**0** 0.0%
Unknown or Not Reported	**1** 3.3%
Region of Enrollment [Units: Participants]	
United States	**30**

Outcome Measures

Hide All Outcome Measures

1. **Primary: Median Progression-Free Survival [Time Frame: Up to 24 months]**

Measure Type	Primary
Measure Title	Median Progression-Free Survival
Measure Description	Progression-free survival will be measured from the first dose date to the earliest date of documented evidence of progressive disease or the date of death due to any causes, whichever occurs first.
Time Frame	Up to 24 months

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Measured Values

	Abraxane, Avastin and Gemcitabine
Participants Analyzed [Units: Participants]	**29**
Median Progression-Free Survival [Units: Months] Median (95% Confidence Interval)	**10.4** **(5.6 to 15.2)**

No statistical analysis provided for Median Progression-Free Survival

2. **Secondary: Rates of Partial Response (PR), Complete Response (CR) and Overall Response (ORR) in Study Participants [Time Frame: After two cycles, about 60 days]**

Measure Type	Secondary
Measure Title	Rates of Partial Response (PR), Complete Response (CR) and Overall Response (ORR) in Study Participants
Measure Description	Rates of partial response (PR), complete response (CR) and overall response (PR+CR = ORR) in study participants according to Response Evaluation Criteria In Solid Tumors (RECIST) version 1.0.
Time Frame	After two cycles, about 60 days

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Evaluable patients are study-eligible patients who receive an initial infusion of combination chemotherapy consisting of Gemcitabine, NAB paclitaxel and Bevacizumab and have had at least one CT scan for evaluation of disease status.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Measured Values

	Abraxane, Avastin and Gemcitabine
Participants Analyzed [Units: Participants]	**29**
Rates of Partial Response (PR), Complete Response (CR) and Overall Response (ORR) in Study Participants [Units: Percentage of participants]	
Overall Response Rate (ORR)	**75.6**
Complete Response (CR)	**27.6**
Partial Response (PR)	**48.3**

No statistical analysis provided for Rates of Partial Response (PR), Complete Response (CR) and Overall Response (ORR) in Study Participants

3. **Secondary: Rate of Toxicity in Study Participants [Time Frame: Over the course of study treatment.]**

Measure Type	Secondary
Measure Title	Rate of Toxicity in Study Participants
Measure Description	Determination of safety and side effect profile of the protocol therapy including the rate of toxicity in study participants. The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 will be utilized for adverse event reporting.
Time Frame	Over the course of study treatment.

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Measured Values

	Abraxane, Avastin and Gemcitabine
Participants Analyzed [Units: Participants]	**29**
Rate of Toxicity in Study Participants [Units: Percentage of participants]	
Alopecia, Grade 1/2	**65.5**
Fatigue, Grade 1/2	**37.9**
Bone Pain, Grade 1/2	**31**
Nausea, Grade 1/2	**31**
Skin rash/lesions, Grade 1/2	**27.6**
Neutropenia, Grade 1/2	**10.3**
Grade 3/4 Toxicities	**27.6**

No statistical analysis provided for Rate of Toxicity in Study Participants

4. **Secondary: Relationship Between Circulating Tumor Cells (CTC) and Disease Progression as Measured by Presence of CTC at Baseline and Over the Course of Study Treatment [Time Frame: Baseline, over the course of Treatment, about 1 year]**

Measure Type	Secondary
Measure Title	Relationship Between Circulating Tumor Cells (CTC) and Disease Progression as Measured by Presence of CTC at Baseline and Over the Course of Study Treatment
Measure Description	Exploration of the relationship between circulating tumor cells (CTC) and disease progression, by measuring CTC at baseline and over the course of treatment.
Time Frame	Baseline, over the course of Treatment, about 1 year

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Data were not collected for this outcome measure.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Measured Values

	Abraxane, Avastin and Gemcitabine
Participants Analyzed [Units: Participants]	**0**
Relationship Between Circulating Tumor Cells (CTC) and Disease Progression as Measured by Presence of CTC at Baseline and Over the Course of Study Treatment	

No statistical analysis provided for Relationship Between Circulating Tumor Cells (CTC) and Disease Progression as Measured by Presence of CTC at Baseline and Over the Course of Study Treatment

5. **Secondary: Relationship Between SPARC Expression and Response to Protocol Therapy. [Time Frame: Baseline, over the course of treatment, about 1 year]**

Measure Type	Secondary
Measure Title	Relationship Between SPARC Expression and Response to Protocol Therapy.
Measure Description	Relationship between SPARC expression and response to this chemotherapy combination and relation to progression free survival.
Time Frame	Baseline, over the course of treatment, about 1 year

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Data were not collected for this outcome measure.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle. Avastin Gemcitabine Abraxane

Measured Values

	Abraxane, Avastin and Gemcitabine
Participants Analyzed [Units: Participants]	**0**
Relationship Between SPARC Expression and Response to Protocol Therapy.	

No statistical analysis provided for Relationship Between SPARC Expression and Response to Protocol Therapy.

6. **Post-Hoc: Rate of Overall Survival in Study Participants [Time Frame: 18 months]**

Measure Type	Post-Hoc
Measure Title	Rate of Overall Survival in Study Participants
Measure Description	Rate of overall survival in study participants. Overall survival will be measured from the date of enrollment to the date of death from any cause, or the date of last contact (censored observations.)
Time Frame	18 months

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Measured Values

	Abraxane, Avastin and Gemcitabine
Participants Analyzed [Units: Participants]	**29**
Rate of Overall Survival in Study Participants [Units: Percentage of participants] Median (95% Confidence Interval)	**77.2** **(51.1 to 90.5)**

No statistical analysis provided for Rate of Overall Survival in Study Participants

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Serious Adverse Events

	Abraxane, Avastin and Gemcitabine
Total, Serious Adverse Events	
# participants affected / at risk	8/29 (27.59%)
Blood and lymphatic system disorders	
Leukopenia † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Thrombocytopenia † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Infections and infestations	
Abscess † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Breast Abscess † 1	
# participants affected / at risk	1/29 (3.45%)
Fever/Sepsis † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Neutropenic Fever † 1 [4]	
# participants affected / at risk	1/29 (3.45%)
Nervous system disorders	
Peripheral Neuropathy † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Seizure/Syncope † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Renal and urinary disorders	
Hematuria † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
UTI † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Respiratory, thoracic and mediastinal disorders	
Shortness of breath † 1 [3]	
# participants affected / at risk	1/29 (3.45%)
Skin and subcutaneous tissue disorders	
PortAcath infection † 1 [3]	
# participants affected / at risk	2/29 (6.90%)
Surgical and medical procedures	
Tamponade † 1	
# participants affected / at risk	1/29 (3.45%)

† Events were collected by systematic assessment
1 Term from vocabulary, CTCAE (3.0)
[3] Grade 3
[4] Grade 4

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	3%

Reporting Groups

	Description
Abraxane, Avastin and Gemcitabine	Each treatment cycle is 28 days. Participants will be treated until disease progression: • Gemcitabine: 1500 mg/m2 body surface area (BSA) intravenously (IV) over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Abraxane: 150 mg/m2 IV over 30 minutes (+/- 5 minutes) on days 1 and 15 of each cycle, followed by; • Avastin: 10 mg/kg IV on days 1 and 15 of each cycle.

Other Adverse Events

	Abraxane, Avastin and Gemcitabine
Total, Other (not including serious) Adverse Events	
# participants affected / at risk	29/29 (100.00%)
Blood and lymphatic system disorders	
Neutropenia † 1	
# participants affected / at risk	3/29 (10.34%)
Leukopenia † 1	
# participants affected / at risk	1/29 (3.45%)
Thrombocytopenia † 1	
# participants affected / at risk	1/29 (3.45%)
Anemia † 1	
# participants affected / at risk	1/29 (3.45%)
Lymphedema † 1	
# participants affected / at risk	2/29 (6.90%)
Cardiac disorders	
Chest Pain † 1	
# participants affected / at risk	1/29 (3.45%)
Pericardial effusion † 1	
# participants affected / at risk	1/29 (3.45%)
Tachycardia † 1	
# participants affected / at risk	1/29 (3.45%)
Tricuspid Regurg † 1	
# participants affected / at risk	1/29 (3.45%)
Endocrine disorders	
Heat intolerance † 1	
# participants affected / at risk	1/29 (3.45%)
Hot flashes † 1	
# participants affected / at risk	1/29 (3.45%)
Eye disorders	
Blurred Vision † 1	
# participants affected / at risk	2/29 (6.90%)
Conjunctivitis † 1	
# participants affected / at risk	1/29 (3.45%)
Scotoma † 1	
# participants affected / at risk	1/29 (3.45%)
Gastrointestinal disorders	
Nausea † 1	
# participants affected / at risk	8/29 (27.59%)
Diarrhea † 1	
# participants affected / at risk	4/29 (13.79%)
Constipation † 1	
# participants affected / at risk	1/29 (3.45%)
Heartburn † 1	
# participants affected / at risk	1/29 (3.45%)
Reflux † 1	
# participants affected / at risk	1/29 (3.45%)
Regurgitation (valve) † 1	
# participants affected / at risk	1/29 (3.45%)
Vomiting † 1	
# participants affected / at risk	1/29 (3.45%)

General disorders	
Fatigue [†] [1]	
# participants affected / at risk	11/29 (37.93%)
Headache [†] [1]	
# participants affected / at risk	7/29 (24.14%)
Insomnia [†] [1]	
# participants affected / at risk	4/29 (13.79%)
Cough [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Weight Loss [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Pelvic pain [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Hepatobiliary disorders	
Jaundice [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Infections and infestations	
Abscess [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Flu-like symptoms [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Oral infection [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Rhinorrhea [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Mucositis [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Painful edema [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Pedal edema [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Metabolism and nutrition disorders	
Dysgeusia [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Loss of appetite [†] [1]	
# participants affected / at risk	2/29 (6.90%)

Musculoskeletal and connective tissue disorders	
Bone Pain [†] [1]	
# participants affected / at risk	9/29 (31.03%)
Hand/Foot syndrome [†] [1]	
# participants affected / at risk	7/29 (24.14%)
Nervous system disorders	
Peripheral Neuropathy [†] [1]	
# participants affected / at risk	5/29 (17.24%)
Psychiatric disorders	
Anxiety [†] [1]	
# participants affected / at risk	3/29 (10.34%)
Depression [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Renal and urinary disorders	
Acute renal insufficiency [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Reproductive system and breast disorders	
Amenorrhea [†] [1]	
# participants affected / at risk	2/29 (6.90%)
Respiratory, thoracic and mediastinal disorders	
Shortness of breath [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Pharyngitis [†] [1]	
# participants affected / at risk	1/29 (3.45%)
Upper respiratory infection [†] [1]	
# participants affected / at risk	1/29 (3.45%)

Skin and subcutaneous tissue disorders	
Alopecia † 1	
# participants affected / at risk	19/29 (65.52%)
Skin rash/lesion † 1	
# participants affected / at risk	8/29 (27.59%)
PortAcath Disorder † 1	
# participants affected / at risk	1/29 (3.45%)
Skin discoloration † 1	
# participants affected / at risk	2/29 (6.90%)
Vascular disorders	
Epistaxis † 1	
# participants affected / at risk	6/29 (20.69%)
Hypertension † 1	
# participants affected / at risk	3/29 (10.34%)
Thrombus † 1	
# participants affected / at risk	1/29 (3.45%)

† Events were collected by systematic assessment
1 Term from vocabulary, CTCAE (3.0)

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

All Principal Investigators **ARE** employed by the organization sponsoring the study.

Results Point of Contact:

Name/Title: Stefan Gluck MD
Organization: UM/Sylvester Comprehensive Cancer CEnter
phone: 305-243-4909
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Publications of Results:

Lobo C, Lopes G, Baez O, Castrellon A, Ferrell A, Higgins C, Hurley E, Hurley J, Reis I, Richman S, Seo P, Silva O, Slingerland J, Tukia K, Welsh C, Glück S. Final results of a phase II study of nab-paclitaxel, bevacizumab, and gemcitabine as first-line therapy for patients with HER2-negative metastatic breast cancer. Breast Cancer Res Treat. 2010 Sep;123(2):427-35. doi: 10.1007/s10549-010-1002-0. Epub 2010 Jun 29.

Responsible Party: University of Miami
ClinicalTrials.gov Identifier: NCT00503906 History of Changes
Other Study ID Numbers: 20060913
SCCC-2006081 (Other Identifier: University of Miami Sylvester Comprehensive Cancer Center)
First Submitted: July 17, 2007
First Posted: July 19, 2007
Results First Submitted: January 22, 2013
Results First Posted: April 2, 2013
Last Update Posted: May 12, 2017

付票 4. EU- CTR で規定されている項目

Trial Information

Section	**EudraCT UI (user interface) field name**	**EudraCT Data type/description** characters (length), numeric, list of terms (single or multiple selection), Y/N selection	**Comments**	**Mandatory fields** M=mandatory R= conditionally required O=optional	**EudraCT UI Text (Tooltip)**
Trial identification				R	No tool tip
	Full title of trial	2000 characters	This field is prepopulated from field A.3 of the CTA and can be amended by the user	M	Update the full title of the trial, if necessary. The title of the trial should be the same as the one specified in the trial protocol and /or the clinical study report.
	EudraCT number	YYYY-XXXXXX-XX	This field is prepopulated from section A.2 of the CTA and it is read-only	R	no tool tips
	Sponsor protocol code	35 characters	This field is prepopulated from field A.4.1 of the CTA and can be amended by the user	M	Update the sponsor protocol code, if necessary. The sponsor protocol code should be the same as the one specified in the trial protocol and /or the clinical study report.
Additional study identifiers				O	
	ISRCTN number	The value entered should have the format: ISRCTNxxxxxxxx where x is a digit	This field is prepopulated from the A.5 subsection of the CTA and can be amended/added by the user	O	If the trial is registered on the Current Controlled Trials website, enter the International Standard Randomised Controlled Trial Number (ISRCTN) using the following format: ISRCTNxxxxxxxx where 'x' is a number (0-9 inclusive). Otherwise, leave this blank.
	ClinicalTrials.gov identifier (NCT number)	The value entered should have the format: NCTxxxxxxxx where x is a digit	This field is prepopulated from the A.5 subsection of the CTA and can be amended/added by the user	O	Provide the US National Clinical Trial (NCT) unique identifier in the format of "NCT" followed by an 8-digit number, e.g.: NCT00000419, if available. Otherwise, leave this blank.
	WHO universal trial number (UTN)	The value entered should have the format: Uxxxx-xxxx-xxxx where x is a digit	This field is prepopulated from the A.5 subsection of the CTA and can be amended/added by the user	O	Enter the WHO Universal Trial Reference number if the trial is registered on the WHO Clincal Trials portal. Otherwise, leave this blank. For more information visit the WHO ICTRP website.
Other trial identifiers				O	
	Other identifier name	50 characters	This field is prepopulated from the A.5.4 of the CTA and can be amended [Comment GUE: UC 29 reads: Read-write: Y]	O	If other identifiers for this trial are available, click in the left-hand field and enter the name of the identifier, then enter the identification code in the right-hand field. Otherwise, leave this blank. To add addional fields, click the + button.

					To delete any fields added in error click the X button.
	Other identifier code	50 characters	This field is prepopulated from the A.5.4 of the CTA and can be amended [Comment [GUE: UC 29 reads: Read-write: Y]	O	If other identifiers for this trial are available, click in the left-hand field and enter the name of the identifier, then enter the identification code in the right-hand field. Otherwise, leave this blank. To add addional fields, click the + button. To delete any fields added in error click the X button.
Sponsor details			All the fields for the Sponsor details are prepopulated from section B.5	M	
	N/A	N/A	this field is prepopulated from B.5.1 and can be amended	M	
	Name of organisation	160 characters		M	
	Street address	100 characters	this field is prepopulated from B.5.3.1 and can be amended	M	
	Town/city	100 characters	this field is prepopulated from B.5.3.2 and can be amended	M	
	Postcode	20 characters	this field is prepopulated from B.5.3.3 and can be amended	O	
	Country	picklist (prepopulated)	this field is prepopulated from B.5.3.4 and can be amended	M	
	Another Sponsor	a new display of the same information			
Scientific contact point				M	
	Name of organisation	100 characters	This field is prepopulated from field B.5.2 of the CTA and can be amended	M	Enter the name of the organisation responsible for addressing scientific and/or technical questions.
	Functional contact point name	100 characters	This field is prepopulated from field B.5.1 of the CTA and can be amended	M	Enter the name of the functional contact point for scientific and/or technical questions (e.g. clinical trial disclosure desk).
	Telephone number/country code	8 characters (country code) & 8 characters Telephone number	This field is prepopulated from field B.5. of the CTA and can be amended	O	no tool tip
	Email address	100 characters	This field is prepopulated from field B.5.6 of the CTA and can be amended	O	no tool tip
	Another Sponsor	a new display of the same information		O	
Public contact point				M	
	Name of organisation	100 characters		M	Enter the name of the organisation responsible for addressing general questions from members of the public.

	functional contact point name	100 characters		M	Enter the name of the functional contact point for general questions from members of the public (e.g. clinical trial disclosure desk).
	telephone number country code	8 characters (country code) & 8 characters Telephone number	This field is prepopulated from field B.5.4 of the CTA and can be amended	O	No tool tip
	email address	100 characters	This field is prepopulated from field B.5.6 of the CTA and can be amended	O	No tool tip
	Another Sponsor	a new display of the same information			
Paediatric regulatory details				M	No tool tip
	Is trial part of an agreed paediatric investigation plan (PIP)? (Y/N)	radio button Y/N	This field is prepopulated from field A.7 of the CTA and can be amendedby the user	M	Select 'Yes' for a trial which is part of an agreed paediatric investigation plan (PIP), otherwise select 'No'. An agreed paediatric investigation plan is a development plan agreed with the European Medicines Agency (EMA), aimed at ensuring the necessary data is obtained to evaluate a medicine for use in children. For more information, visit the EMA's paediatric medicine webpages.
	EMA paediatric investigation plan(s)	the actual PIP number character is EMEA-nnnnnn-PIPnn-yy where nnnnnn is an integer between 1 and 999999, leading zeros allowed; nn is exactly tow numerals each between 0 and 9; yy is exactly two numerals each between 0 and 10		R	Enter the EMA paediatric investigation plan number(s) (PIP) using the following format: EMEA-xxxxxx-PIPxx-xx, where x is a number (0-9 inclusive).
	Does Article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	radio button Y/N	this field is defaulted to NO	M	Select 'Yes' for a trial which is in the scope of Article 45 of said Regulation, otherwise select 'No'. Article 45 of Regulation (EC) 1901/2006 (Paediatric Regulation) applies to paediatric studies in respect of products authorised in the European Union, which were completed by 26 January 2007.
	Does Article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	radio button Y/N	this field is defaulted to NO	M	Select 'Yes' for a trial which is in scope of Article 46 of said Regulation, otherwise select 'No'. Article 46 of Regulation (EC) 1901/2006 (Paediatric Regulation) applies to marketing authorisation holder sponsored paediatric studies in respect of products authorised in the European Union, which were

					completed after 26 January 2007.
Results analysis stage			this section has been incorporated into the General information about trial (simple form)	M	No tool tip
	Analysis stage	radio button Y/N	Validation rule (see last column right)	M	If you are reporting on an interim analysis, select 'interim'. An interim analysis is an analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to the formal completion of a trial . Otherwise select 'final'.
	Date of interim/final analysis	drop-down calendar		M	Select the date for the cut-off data point for the reported analysis.
	Is this the analysis of the primary completion data?	radio button Y/N		M	Select 'Yes' if you are reporting data collected up to the primary completion date, otherwise select 'No'. The primary completion date is the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary end point.
	Primary completion date	drop-down calendar		R	Enter the final date on which data was collected.
	Global end of trial date reached?	radio button Y/N		M	The global end of trial date is when the last subject in the trial was examined, or received an intervention globally. Select 'Yes' if the global end of the trial has been reached, otherwise select 'No'.
	Global end of trial date	drop-down calendar	Validation rule (see last column right)	R	No tool tip
	Was the trial ended prematurely?	N/A		O	
General Information about trial				M	
	Main objective of the trial	1000 characters	This field is prepopulated from field E.2.1 of the CTA and can be amended	M	Enter a description for the main objective(s) of the trial
	Actual start date of recruitment	Format dd-mmm-yyyy, date field	For EEA CTA this field is prepopulated from E.8.10.1 OR E.10.2; for 3rd countries file this field is prepopulated from E.8.10.2	M	Select the date when the recruitment of subjects began. The recruitment date is to be defined by the sponsor and can correspond to the date the subjects were consented, enrolled or screened in the trial.
	Long term follow up planned?	radio button Y/N	the process of long-term monitoring the progress of a patient after a period of active treatment. This field is defaulted to NO	M	Select 'Yes' if long-term monitoring of patients is planned, otherwise select 'No'.
	long term follow up rationale	pick-list: Safety	If answer is YES one or several items from	O	Select the main reason(s) for long-term follow up.

		Efficacy Ethical reason Regulatory reason Scientific research	the rationale drop-down list should be selected (safety/efficacy/ethical reason/regulatory reason/scientific research)		
	long term follow up duration	select from a list of integers only. Range 1-100 and indicate the duration months or years		O	
	Independent data monitoring committee (IDMC) involvement?	radio button Y/N	Y/N	M	
	Protection of trial subjects	Free text (2000 characters)		M	
	Background therapy	Free text (2000 characters)		O	
	Evidence for comparator(s)	Free text (2000 characters)		O	
Population of trial subjects	**Subject number per country**			M	
	country	pick list (as per EU-TCT list)	The system will pull in countries from the CTAs and 3rd Country files related to the trial and show the planned number of subjects as it appears in the CTA and which are derived from fields F.4.1, F4.2.1 and F4.2.2	R	Provide the actual number of subjects enrolled in each country. Enter "0" if no subjects were enrolled.
	actual number of subjects enrolled	integer and >=0		M	The table of countries has been pre-populated according to the protocol data for this trial in EudraCT. If a country is missing from the table, select it from the list and add it to the table.
	Total: EEA ONLY	derived value		M	no tool tip
	Total: whole clinical trial	derived value	This field is prepopulated from field F.4.2.2 of the CTA	R/O	No tool tip
Age group breakdown for trial	**Age range**		The system pulls the planned number of subjects per age categories as it appears in the CTA and which are derived from fields F.1.1.1.1 up to field F.1.3.1 respectively.	M	Provide the actual number of subjects enrolled in each age group. Enter "0" if no subjects were enrolled.
	in utero	integer and >=0		M	No tooltip.
	preterm newborn - gestational age <37 wk	integer and >=0		M	No tooltip.
	newborns (0-27 days)	integer and >=0		M	No tooltip.
	infants and toddlers (28 days - 23 months)	integer and >=0		M	No tooltip.
	children (2-11 years)	integer and >=0		M	No tooltip.
	Adolescents	integer and >=0		M	No tooltip.

	(12-17 years)				
	Adults (between 18 and 64 years)	integer and >=0		M	No tooltip.
	From 65 years	this field is a title, no entry available		M	No tooltip.
	from 65 to 84 years	integer and >=0	NEW CATEGORY not present in the CTA	M	No tooltip.
	85 years and over	integer and >=0	NEW CATEGORY not present in the CTA	M	No tooltip.

Subject Disposition

Section	EudraCT UI (user interface) field name	EudraCT Data type/description characters (length), numeric, list of terms (single or multiple selection), Y/N selection	Comments	Mandatory fields M=mandatory R=conditionally required O=optional	EudraCT UI Text (Help tip)
Recruitment		**Title**	Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and types of location to provide context	O	
	Recruitment details	350 Characters	screening details are required if the results will not contain a pre-assignment period.	O	Enter key information relevant to the recruitment process for the trial (e.g. dates of recruitment period and territories).
Pre-assignment					
	Screening details	350 Characters		O	Enter relevant information related to screening (e.g. screening criteria, significant events and approaches (e.g. wash-out, run-in)). It may also be relevant to provide the number of subjects screened for inclusion and a breakdown of the reasons for excluding subjects during screening by completing the pre-assignment period fields. This could help clarify the appropriate patient population for eventual drug use.
Pre-assignment period				O	
	Number of subjects at each milestone				
	Started (number of subjects)	integer and >=0		M	Enter the number of subjects enrolled at the beginning of the pre-assignment period.
	Intermediate milestone title	40 characters		O	Enter a title for any specific event or time point that defines an intermediate milestone within the pre-assignment period for which the numbers of subjects will be reported.
	Number of subjects	integer and >=0		O	Enter the number of subjects that reached the specific event, or time point.
	Completed (number of subjects)	integer and >=0		M	Enter the number of subjects at the end of the pre-assignment period.
	Subject non-completion reasons		derived data (started-completed)	R	
	Reason for non-completion	picklist: Adverse event, not fatal Adverse event, serious fatal Consent withdrawal by subject Physician decision Pregnancy Protocol deviation Other (please specify)		O	Select one or more reasons for non-completion.
	Number of subjects	integer and >=0		O	No tooltip.
Periods				M	
	Period details			R	
	Period title	40 characters		M	Enter a title describing the stage of the trial. If only one period is defined, the default title should be "overall trial".
	Is this the baseline	tick box		R	Check this box if this is the

	period				baseline period (i.e. the period for which you wish to report baseline characteristics). Otherwise, leave it un-checked. One period must be defined as the baseline period. It is expected that the baseline period is the first period after assignment. Select the most appropriate period as a baseline period, from the ones created in subject disposition.
	Allocation method	picklist: randomised-controlled Non-randomised controlled Not applicable		M	Select the method of assigning subjects to treatment group in this period.
	Blinding used	picklist: double-blind single-blind not-blinded		M	Select the blinding method used in this period.
	Roles blinded	picklist: subject, investigator, monitor, data analyst, carer, assessor		O	Select the role(s) that were blinded in this period.
	Blinding implementation details	500 characters		O	If relevant, provide details about the specific procedures used to carry out blinding (e.g. double dummy techniques, measures to prevent unblinding by laboratory measurements)
Milestones				R	
	Milestone title			N/A	
	Started	this field is a title, no entry available		M	No tooltip.
	Enter intermediate milestone title	40 characters		O	Enter a title for any specific event or time point that defines an intermediate milestone for which the numbers of subjects will be reported.
	Completed	this field is a title, no entry available		M	No tooltip.
Arms				M	
	Arm information			M	
this is displayed when more than one arm is present	Are the arms mutually exclusive? (Y/N)	radio button Y/N	this field is defaulted to NO	R	Only answer "No" if the subjects are present in more than one arm in a period. If the arms are not mutually exclusive, the total number of subjects in the period will not automatically be calculated.
	Arm title	62 characters		M	Enter a title to identify the arm.
	Arm description	999 characters		O	Enter a brief description of the arm to distinguish it from other arms in the trial.
	Arm type	picklist: Experimental active comparator placebo no intervention other		M	No tooltip.
	if 'other' specify	50 characters		R	No tooltip.
Products				M	
	IMP name	160 characters		M	Enter the name of an investigational medicinal product (IMP) administered in this arm.
	IMP code	50 characters		O	Enter the code for the investgational medicinal product (IMP).
	Other names	160 characters		O	No tooltip.
	Route of Administration	picklist: as per EU-TCT list		M	No tooltip.
	Pharmaceutical forms	picklist: as per EU-TCT list		M	No tooltip.
	Dosage and administration details	1000 characters		M	Enter details of the dosage and administration (e.g. frequency of dosing, formulation details).
Milestones				R	

	Number of subjects at each milestone			M	
	Started	Started		M	Enter the number of subjects enrolled in the arm.
	Intermediate milestone(s)	40 characters		R	Enter the number of subjects that reached the specific event or time point.
	Completed	Completed		M	Enter the number of subjects who have completed the arm.
	Subject non-completion reasons			R	
	Subject non-completion reason	picklist: Adverse event, not fatal Adverse event, serious fatal Consent withdrawal by subject lack of efficacy Lost to follow up Physician decision Pregnancy Protocol deviation Transferred to another arm/group Other (please specify)		O	Select one or more reasons for non-completion.
	Number of subjects	integer and >=0		O	No tooltip.
	Subject joining reasons			O	
	Subject joining reason	picklist: late recruitment transferred in from another group/arm other (please specify)		O	Complete these fields only to report a number of subjects who have joined the arm although they were not counted in the started milestone (e.g. transferred from another group because of incorrect treatment allocation).
	Number of subjects	integer and >=0		O	No tooltip.

Baseline characteristics

Section	EudraCT UI (user interface) field name	EudraCT Data type/description characters (length), numeric, list of terms (single or multiple selection), Y/N selection	Comments	Mandatory fields M=mandatory R=conditionally required O=optional	EudraCT UI Text (Help tip)
Baseline characteristics - settings				M	
	Select baseline period			R	
Change baseline period settings	Select baseline period	Select the period	derived from subject disposition but the baseline period can be amended	O	Select change baseline period to select a different period as baseline.
Change baseline characteristics settings	How are baseline characteristics being reported?	radio button: Per Arm in the baseline period OR For the overall baseline period		O	You can report per arm in the baseline period or for the overall baseline period.
Reporting groups				M	
	Reporting group title	Reporting group title		M	No tooltip
	Number of subjects at the baseline	derived from subject disposition		M	No tooltip
	Reporting group description	derived from subject disposition or to be completed in the text field provided 999 characters		O	No tooltip
Subject analysis sets				O	
	Add subject analysis set			O	Add a subject analysis set if you wish to additionally report on groups different from the reporting groups defined above.
	Subject analysis set title	62 characters	The subject analysis sets are used in both the end points and baseline characteristics sections. Is it required to mention it in both places.	M	Enter a title for a subject analysis set.
	Subject analysis set type	picklist: intent to treat per protocol full analysis safety analysis sub-group analysis modified intention-to-treat		M	Select the subject analysis set type.
	Subject analysis set description	999 characters		M	No tooltip
	Number of subjects in subject analysis set	positive integer		M	No tooltip
Age characteristics			Complete either the age categorical, age continuous or complete both these characteristics in order to collect values for the reporting groups and optionally the subject analysis sets.	M	
	Age categorical characteristic			R	
	Characteristic title	prepopulated	this field is a title, no entry available	M	No tooltip
	Units	prepopulated	this field contains the units, no entry available	M	No tooltip
	Description	600 characters		O	Enter additional details about the collection method, or subject population.
	Age category title	50 characters	can add as many age categories as d	R	Enter a title for a distinct category if you want to report on a category other than the default ones.

	Age categories In Utero Preterm newborn-gestational age < 37 wk Newborns (0-27days) Infants and toddlers (28days – 23months) Children (2-11 years) Adolescents (12-17 year) From 18 - 64 years From 65 – 84 years Over 85 years	Age categories In Utero Preterm newborn-gestational age < 37 wk Newborns (0-27days) Infants and toddlers (28days – 23months) Children (2-11 years) Adolescents (12-17 year) From 18 - 64 years From 65 – 84 years Over 85 years	Age categories In Utero Preterm newborn-gestational age < 37 wk Newborns (0-27days) Infants and toddlers (28days – 23months) Children (2-11 years) Adolescents (12-17 year) From 18 - 64 years From 65 – 84 years Over 85 years	O	No tooltip
	Value	integer (>= 0)		R	No tooltip
	Age continuous characteristic			R	
	Characteristic title	prepopulated	these categories can be replaced and are not mandatory	M	
	Description	600 characters	[description not required]	O	Enter additional details about the collection method, or subject population.
	Units	picklist: years/months/weeks/days/hours/minutes	[description not required]	M	No tooltip
	Central tendency type	Picklist: arithmetic mean, median, least squares mean, geometric mean, log mean	Central tendency type	M	No tooltip
	Central tendency type value	Decimal	Central tendency type value	R	No tooltip
	Dispersion type	picklist: standard deviation, inter-quartile range (Q1-Q3), full range (min-max)	Dispersion type	M	No tooltip
	Dispersion type value	decimal (>= 0)	Dispersion type value	R	No tooltip
	Gender characteristic			M	
	Characteristic title	Gender categorical	this field is a title, no entry available	M	No tooltip
	Units	Subjects	this field contains the units, no entry available	M	No tooltip
	Description	600 characters	[description not required]	O	Enter additional details about the collection method, or subject population.
	Gender category title	50 characters	[description not required]	M	Enter a title for a distinct category if you want to report on a category other than the default ones.
	Gender categories	Customised picklist: male/female	the list can be amended and customised as required	M	No tooltip
	Value	integer and >=0	[description not required]	M	No tooltip
Study specific characteristics				O	
	Study specific categorical characteristic			O	
	Characteristic title	100 characters		M	Enter a title to describe a characteristic measured at the start of the trial (e.g. ethnic group).
	Units	prepopulated with the word 'Subjects'	this field contains the units, no entry available	M	No tooltip
	Description	600 characters	[description not required]	O	Enter additional details about the collection method, or subject population.
	Category title	50 characters	Category title	R	Enter a title for a distinct category.
	Value	integer and >=0	[description not required]	R	No tooltip
Study specific continuous characteristic				O	
	Characteristic title	100 characters		M	Enter a title to describe a

					characteristic measured at the start of the trial.
	Description	600 characters	[description not required]	O	Enter additional details about the collection method, or subject population.
	Units	40 characters	[description not required]	M	
	Central tendency type	picklist: arithmetic mean geometric mean least squares mean log mean median	[description not required]	M	No tooltip
	Central tendency value	decimal	[description not required]	R	No tooltip
	Dispersion type	picklist: standard deviation, inter-quartile range (Q1-Q4), full range (min-max)	Dispersion type	M	No tooltip
	Dispersion type value	decimal (>= 0)	Dispersion type value	R	No tooltip

Endpoints

Section	EudraCT UI (user interface) field name	EudraCT Data type/description characters (length), numeric, list of terms (single or multiple selection), Y/N selection	Comments	Mandatory fields M=mandatory R=conditionally required O=optional	EudraCT UI Text (Tooltip)
Reporting groups	**Periods/Arms**	derived from subject disposition		O	
	Subject analysis sets			O	
	Add subject analysis set				Add a subject analysis set if you wish to report on groups different from the reporting groups defined above.
	Subject analysis set title	62 characters		M	Enter a title for a subject analysis set.
	Subject analysis set type	picklist: intent to treat per protocol full analysis safety analysis sub-group analysis set modified intention-to-treat		M	Select the subject analysis set type.
	Subject analysis set description	999 characters		M	Enter a clear description which defines this set of subjects.
	Number of subjects in subject analysis set	integer (> 0)		M	No tooltip
End point definition				M	
	Add end point			M	No tooltip
	End point title	255 characters		M	Enter an end point title. An end point is used to assess the effect of experimental variables in a trial. For example 'change in measure A between time point X and time point Y', 'proportion of patients with outcome B at time point X', 'disease-free survival at time point X', 'pharmacokinetic parameter C'.
	countable or measurable?	radio button		M	The selection of either countable or measurable determines the type of input for the end point data. Select countable when the end point represents data that that contains distinct values. In this case the end point accepts positive integers (i.e. whole numbers greater than zero) usually for the different categories representing the distinct values. Select measurable when the end point represents data that can assume any value within a range. In this case the end point can report decimal numbers for a measure of central tendency together with a dispersion or precision value. Note that the system does not support the input of countable data expressed as a percentage. Instead select countable and enter the totals for each of the discrete categories of the data recorded for this end point.
	Countable units	40 characters	Unit of measure	M	Select measurable when the end point represents data that can assume any value within a range. In this case the end point can report decimal numbers for a measure of central tendency together with a dispersion or precision value.
	Measurable units	40 characters	Unit of measure	M	Note that the system does not support the input of countable data expressed as

					a percentage. Instead select countable and enter the totals for each of the discrete categories of the data recorded for this end point.
	Measure type	picklist: arithmetic mean geometric mean least squares mean Log mean Median Number		M	Select the measure of central tendency type.
	Precision/Dispersion type	For measurable variable only: when the meaure type is a number, the picklit includes not applicable, confidence interval ; otherwise the picklist includes standard deviation, inter-quartile range (Q1-Q3), full range (min-max), standrad error, confidence interval (This applies only when the user choose 'measurable' type = number)	The precision type of confidence interval requires a percentage level, which is a value between 0 and 100. Dispersion type = full range or interquartile range	M	Select the precision/dispersion type. The precision/ dispersion indicates how stretched, or squeezed a distribution is.
	End point type	picklist: primary secondary post-hoc other pre-specified		M	Select the end point type. The primary end point should be the end point providing evidence directly related to the primary objective of the trial. In general, there should be one primary end point per trial.
	Timeframe	255 characters		M	Enter the time point(s) or periods of assessment for the end point. This information is to supplement the end point title.
	Description	999 characters		O	Enter details for the end point if required.
	Category title	50 characters - Option to add more than one category in the Categories box		O	Enter as many distinct category titles as required. Categories could be for example 'size reduction of lesion by > 5%', 'size reduction of lesion by 2.5 to 5%', 'size reduction of lesion by < 2.5%.
	Reporting groups	Specify the groups of subjects applicable to this end point		M	No tooltip
End point values				M	
	Number of subjects analysed	integer and >=0		M	No tooltip
	Measure type value	Number (integer if countable otherwise decimal depending on kind of measure type used)		M	No tooltip
	Precision/disperion type value	Decimal		M	No tooltip
	Confidence interval min. value	Decimal		M	No tooltip
	Confidence interval max. value	Decimal		M	No tooltip
Statistical analyses				O	
	Statistical analysis details			M	
	Statistical analysis title	50 characters		M	Enter a statistical analysis title.
	Analysis description	500 characters		O	Enter a description for the analysis. If necessary provide additional details on the analysis to include information on the null hypothesis, power calculation, adjustments for covariates, handling of missing data or adjustments for multiple comparisons. If the number of subjects in this analysis differs from the number of subjects in the selected comparison groups

					enter a reason.
	Comparison groups	Specify the groups of subjects applicable to this analysis		M	Select the arms or subject analysis sets involved in the analysis. If you are reporting a single arm study and there is no comparison, select the one arm.
	Analysis specification	radio buttons: pre-specified post-hoc		M	No tooltip
	Analysis type	picklist: equivalence non-inferiority superiority other		M	No tooltip
	Analysis type comment	500 characters		O	Enter additional details about the analysis, including definition of non-inferiority margin (if applicable), and other key parameters.
Statistical hypothesis test				O	
	P-value	picklist: = > < ≤ ≥		O	The p-value is the probability of obtaining a test statistic at least as extreme as the one actually observed, assuming that the null hypothesis of the study is true. Enter the p-value that corresponds to the primary comparison of the analysis. If you want to report other p-values (e.g. for multiple comparisons or multiple time points) then enter the additional p-values in the 'p-value comment' field.
	P-value comment	250 characters		O	Enter additional p-values (e.g. for multiple comparisons or multiple time points) in the 'p-value comment' field.
	Method	picklist: ANCOVA ANOVA Chi-squared Chi-squared corrected Cochran-Mantel-Haenszel Fisher exact Kruskal-wallis Logrank Mantel-Haenszel Mcnemar Mixed models analysis Regresssion, cox Regression, Linear Regression, Logistic Sign test t-test, 1-sided t-test, 2 sided Wilcoxon (Mann-Whitney) Other (specify)		O	Select or specify the procedure/test used for statistical analysis of end point data.
	Other method	40 characters		O	No tooltip
	N/A	N/A			
Parameter estimate				O	
	Parameter type	picklist: Cox proportional hazard Hazard ratio (HR) Log hazard ratio Mean difference (final values) Mean difference (net) Median difference (final values) Median difference (net) Odds ratio (OR) Log odds ratio Risk difference (RD) Risk ratio (RR) Log risk ratio Slope Other (please specify)		O	Select the type of parameter estimate provided by the statistical analysis. Parameter Hazard ratio log, Odds ratio log and Risk ration log has been changed to Log hazard ratio, Log odds ratio and Log risk ratio in order to clarify potential misinterpretation of the values to be provided in this specific part of the system.
	Other parameter type	40 characters		O	No tooltip
	Point estimate	Decimal		O	Enter the parameter point estimate.

	Confidence interval:sides	radio buttons: 1-sided 2-sided		O	No tooltip
	Confidence interval:level	Decimal		O	No tooltip
	lower limit	Decimal		O	For 1-sided enter either the lower or the upper limit, for 2-sided enter both limits.
	Upper limit	Decimal		O	For 1-sided enter either the lower or the upper limit, for 2-sided enter both limits.
	Variability estimate	radio buttons: Standard deviation Standard error of the mean		O	No tooltip
	Dispersion value	Decimal		O	No tooltip
	N/A	N/A			
Charts				O	
	Add attachments	50 MB	PDF, DOC, DOCX, RTF, TXT, PPT, PPTX, XLS, XLSX, TIFF, TIF, PNG, GIF, JPEG, JPG, BMP	O	

Adverse Events

Section	EudraCT UI (user interface) field name	EudraCT Data type/description characters (length), numeric, list of terms (single or multiple selection), Y/N selection	Comments	Mandatory fields M=mandatory R=conditionally required O=optional	EudraCT Text (Tooltip)
Adverse events information				O	
	Timeframe for adverse event reporting	255 characters	Timeframe for adverse event reporting	M	Enter the time point(s) or time period for adverse events assessment.
	Adverse events reporting additional description	350 characters	Adverse events reporting additional description	O	Enter information about the adverse event collection and provide details about the method of assessment and monitoring (e.g. daily questionnaire).
	Assessment type	picklist: Systematic Non-systematic	Method	M	Select the default adverse events assessment type to apply to adverse event terms entered in the serious and non-serious adverse event tables, unless otherwise specified. Systematic Assessment: Any method to routinely determine if certain adverse events have happened, for example through a standard questionnaire, regular investigator assessment, regular laboratory testing, or other method. Non-systematic Assessment: Any non-systematic method to determine if adverse events have happened, such as self-reporting by participants or occasional assessment/testing.
	Frequency threshold for reporting non-serious adverse event	Decimal (no more than 5%)	Frequency threshold for reporting non-serious adverse event	M	Enter the frequency of non-serious adverse events that, when exceeded within any arm or reporting group, are reported in the results database for all arms or reporting groups. The number must be less than or equal to the allowed maximum (5%), and must not include any symbols (e.g., >= , %).
	Dictionary name	picklist: snomed, MedDRA, other		M	Select or specify the name of the default dictionary name (e.g., SNOMED CT, MedDRA 10.0) to apply to adverse event terms entered in the serious and non-serious adverse event tables, unless otherwise specified. If Other is selected, the Other dictionary field must be completed.
	Dictionary name - if other	20 characters		R	No tooltip.
	Dictionary version	10 characters		M	No tooltip.
Adverse events reporting groups				R	
	Reporting group title	62 characters		M	Enter a title for the reporting group.
	Reporting group description	999 characters		O	Enter a description to define this group of subjects.
	Subjects exposed	integer and >=0		M	Enter the number of subjects in this reporting group exposed to the treatment. It is assumed that all subjects who received at least one dose of the treatment are included in the reporting group.
	subjects affected by serious adverse events	integer and >=0		M	Enter the number of subjects in this reporting group for whom at least one serious adverse event was reported.
	subjects affected by non-serious	integer and >=0		M	Enter the number of subjects in this reporting group for

	adverse events				whom at least one non-serious adverse event was reported.
	Total number of deaths (all causes)	integer and >=0		M	Enter the number of deaths in this reporting group. This includes deaths not related to the trial.
	Total number of deaths resulting from adverse events	integer and >=0		O	Enter the number of deaths from adverse events in this reporting group regardless of causality.
Serious adverse events				O	
	Serious adverse event details			R	
	System organ class	Picklist: MedDRA high-level categories		M	Select a system organ class (SOC). Adverse events that affect multiple systems should be classified as 'general disorders'. SOCs are high-level categories (derived from the Medical Dictionary for Regulatory Activities (MedDRA)) used to group adverse event terms by body or organ system.
	Event term	100 characters		M	Enter an event term, (e.g. headache, diarrhoea). This field is predictively populated based on the letters entered. Select the correct option from the drop-down list, if possible. Duplicate serious adverse event terms are accepted only if they belong to a different system organ class.
	Additional description	350 characters		O	
	Assessment type	picklist - Systemic/Non systemic		O	This field is populated based on your selection for the default assessment type in the adverse events information section. Change the assessment type for this adverse event if required.
	Dictionary name	default dictionary (already specified in the main page of the Adverse Events)		R	Select or specify the name of the dictionary name (e.g., SNOMED CT, MedDRA 10.0) to apply to this adverse event. If Other is selected, the Other dictionary field must be completed.
	Other dictionary if required	20 characters		R	No tooltip.
	Version	10 characters		R	No tooltip.
Values for Serious adverse event per reporting group				R	
	Arm/Group title	62 characters		R	
	subjects affected, number	integer and >=0		M	Enter the number of subjects in this reporting group affected by any occurrence of this adverse event.
	subjects exposed, number	prepopulated/option to edit		M	In most cases the number of subjects exposed is the same as the number of subjects in this reporting group. However, the number of subjects can be amended if a justification is provided.
	occurences - all, number	integer and >=0		M	Enter the number of occurences of this adverse event in this reporting group.
	occurences causally related to treatment, number	integer and >=0		M	Enter the number of occurrences of this adverse event in this reporting group thought to be causally related to the treatment.
	fatalities, number	integer and >=0		M	Enter the number of fatalities (deaths) related to this adverse event recorded during the assessment period for this reporting group.
	fatalities causally related to treatment,	integer and >=0		M	**Enter the number of fatalities (deaths) related to the serious adverse**

	number				**event thought to be causally related to the treatment.** *Under the table 'Values for serious adverse event per reporting group' the number of 'Fatalities causally related to treatment number' should not be higher than the number in the 'Fatalities number' field.*
Non-serious adverse events				O	
	Non-serious adverse event details			R	
	System organ class	picklist: MedDRA high level categories		M	Select a system organ class (SOC). Adverse events that affect multiple systems should be classified as 'general disorders'. SOCs are high-level categories (derived from the Medical Dictionary for Regulatory Activities (MedDRA)) used to group adverse event terms by body or organ system.
	Event term	100 characters		M	Enter an event term, (e.g. headache, diarrhoea). This field is predictively populated based on the letters entered. Select the correct option from the drop-down list, if possible. Duplicate serious adverse event terms are accepted only if they belong to a different system organ class.
	Additional description	350 characters		O	No tooltip.
	Assessment type	picklist: systematic, non-systematic		O	This field is populated based on your selection for the default assessment type in the adverse events information section. Change the assessment type for this adverse event if required.
	Dictionary name	picklist MedDRA SNOMED CT Other (specify)		R	Select or specify the name of the dictionary name (e.g., SNOMED CT, MedDRA 10.0) to apply to this adverse event. If Other is selected, the Other dictionary field must be completed.
	Other dictionary	20 characters		R	No tooltip.
	Version	10 characters		R	No tooltip.
Values for non-serious adverse event per reporting group	Arm/Group title	prepopulated		R	
	Arm/Group title	prepopulated	number of subjects affected by non- Serious adverse events	R	Enter the number of subjects in this reporting group affected by any occurrence of this adverse event.
	Arm/Group description	999 characters	number of subjects exposed	M	In most cases the number of subjects exposed is the same as the number of subjects in this reporting group. However, the number of subjects can be amended if a justification is provided.
	subjects affected, number	integer and >=0	occurrences - all	M	Enter the number of occurences of this adverse event in this reporting group.
	subjects exposed, number	prepopulated/option to edit	N/A	M	
	occurences - all, number	integer and >=0	N/A	M	

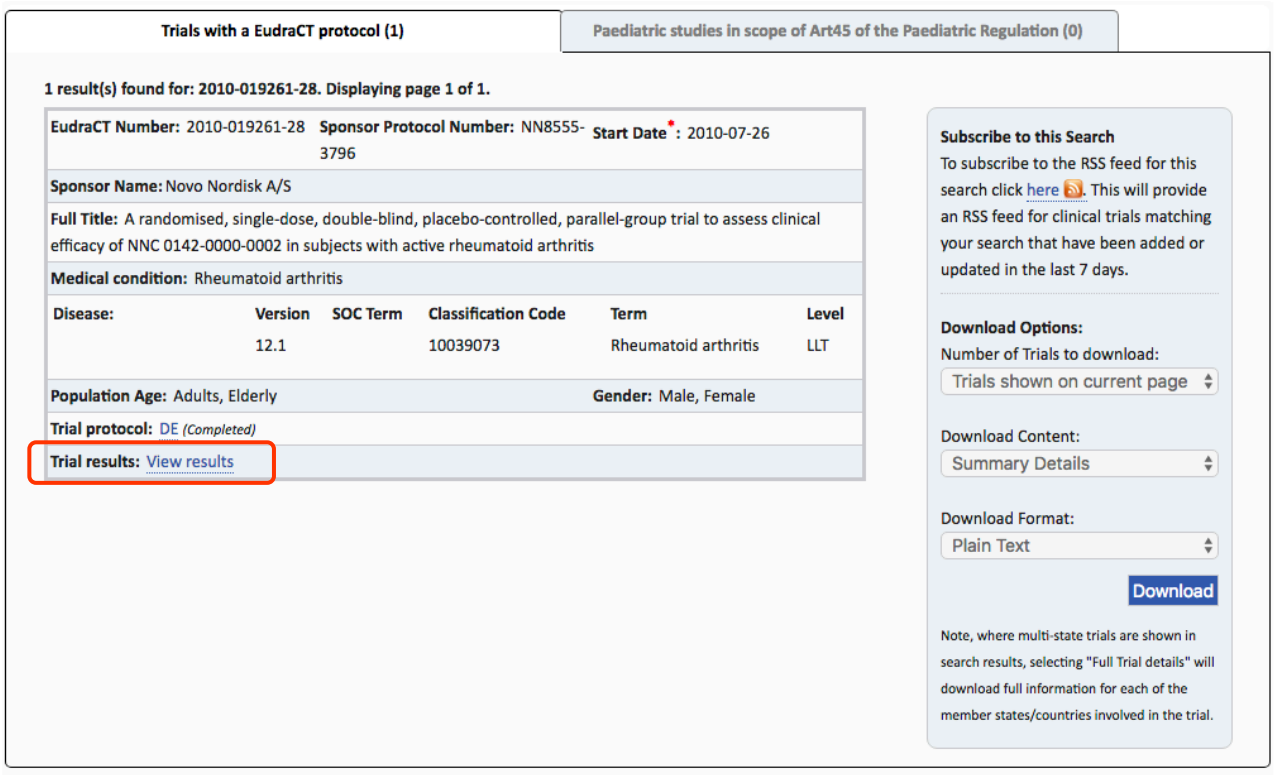
More Information

Section	EudraCT UI (user interface) field name	EudraCT Data type/description characters (length), numeric, list of terms (single or multiple selection), Y/N selection	Comments	Mandatory fields M=mandatory R=conditionally required O=optional	EudraCT Text (Tooltip)
Substantial protocol amendments (globally)				M	
	Were there any global substantial amendments to the protocol?	radio button (Y/N)		M	Amendments are considered substantial when they are likely to have an impact on the safety of the trial subjects, or to change the interpretation of the scientific documents in support of the conduct of the trial. Select 'Yes' if any substantial amendments to the protocol globally affected the trial, otherwise select 'No'.
	Add global substantial protocol amendment	add button		M	No tooltip.
	Amendment date	<dd-mmm-yyyy> (10/11 characters)		M	Select the date when the substantial amendment was first approved by a regulatory authority.
	Amendment description	200 characters, if longer truncated description		M	Enter a description and a reason for the main changes to the protocol.
Interruptions (globally)				M	
	Were there any global interruptions to the trial?	radio button (Y/N)		M	Select 'Yes' if there were any interruptions that globally affected the trial, otherwise select 'No'.
	Add global interruption	add button		M	No tooltip.
	Interruption date	<dd-mmm-yyyy> (10/11 characters)		M	Select the date when the interruption took effect.
	Interruption description	200 characters, if longer truncated description		M	Enter a description and reason for the interruption.
	Restart date	<dd-mmm-yyyy> (10 characters)		R	Select the restart date if the trial was restarted after an interruption.
Limitations and caveats				O	
	Limitations and caveats applicable to this summary of the results	250 characters		O	Describe any significant limitations of the trial (e.g. early termination leading to a small number of subjects analysed; technical problems with measurement leading to unreliable, or uninterpretable data).
Online references				O	
	PubMed identifier (PMID)	8 numerical characters		O	Enter the unique number (PubMed identifier) of a PubMed record related to this trial and click on add this link.
	N/A	N/A			

付表 5. EU- CTR の結果登録画面のインターフェース

Summary report(s)に、レポートの PDF を貼付している形式と、web 上へ直接入力している形式の二つの報告型が存在していた。

(1) レポートの PDF を貼付している形式



Clinical Trial Results:
A randomised, single-dose, double-blind, placebo-controlled, parallel-group trial to assess clinical efficacy of NNC 0142-0000-0002 in subjects with active rheumatoid arthritis

Summary	
EudraCT number	2010-019261-28
Trial protocol	DE
Global completion date	17 Apr 2012
Paediatric regulatory details	
Is the trial part of an agreed EMA paediatric investigation plan?	No
Is the trial in scope of article 45 of Regulation (EC) No 1901/2006?	No
Is the trial in scope of article 46 of Regulation (EC) No 1901/2006?	No
Results information	
Results version number	v1(current)
This version publication date	29 Jan 2016
First version publication date	29 Jan 2016
Other versions	
Summary report(s)	Synopsis

Note: The legislation allows summary attachments to be posted instead of the full dataset for this trial. Refer to Commission Guideline 2012/C 302/03 for further information.

Synopsis をクリックすると、次のような PDF ファイルがダウンロードされた。
ClinicalTrials.gov の結果画面の PDF がダウンロードしている試験も見受けられた。

Clinical trial report synopsis

Trial registration ID-number NCT01181050	**UTN**: U1111-1114-9194 **EudraCT number**: 2010-019261-28

TITLE OF TRIAL
A randomised, single-dose, double-blind, placebo-controlled, parallel-group trial to assess clinical efficacy of NNC 0142-0000-0002[a] in subjects with active rheumatoid arthritis
[a]*will hereinafter be referred to as: NNC0142-0002*

INVESTIGATOR
Signatory/principal investigator: Prof Dr [redacted]

TRIAL SITES
The trial was conducted at 8 trial sites in 3 different countries (Germany, the Russian Federation and Ukraine) as follows: Germany: 1 site, the Russian Federation: 6 sites, and Ukraine: 1 site. All sites enrolled, randomised and dosed at least 1 subject.

PUBLICATIONS
None

TRIAL PERIOD	**DEVELOPMENT PHASE**
Initiation date: 16 August 2010 Completion date: 17 April 2012	Phase 2a

OBJECTIVES
Primary objective
- To evaluate the change in disease activity following a single s.c. dose of NNC0142-0002 compared to placebo in subjects with active RA on background MTX therapy, measured 12 weeks after administration

Secondary objectives
- To assess the following in subjects with active RA on background MTX treatment, up to 24 weeks after administration of a single s.c. dose of NNC0142-0002 compared to placebo:
  - Signs of clinical efficacy, as measured by change in disease activity over time, and clinical responses determined at various time points up to Week 24
  - Signs of effects as assessed by imaging and various PD biomarkers
  - Safety and tolerability, including immunogenicity of NNC0142-0002
  - Quality of life
  - PK of NNC0142-0002 and occupancy of the NKG2D receptor by NNC0142-0002

METHODOLOGY
This was a randomised, single-dose, double-blind, placebo-controlled, parallel-group trial to assess the clinical efficacy of NNC0142-0002 in subjects with active RA concomitantly treated with methotrexate (MTX). The trial included two parallel treatment arms, and subjects were randomised in a 2:1 ratio with 41 subjects allocated to treatment with NNC142-0002 and 22 subjects to placebo treatment. Subjects received a single dose of 4 mg/kg NNC0142-0002 or placebo via subcutaneous injection into the abdominal wall. All subjects were closely monitored for 24 hours after dosing for clinical and laboratory safety assessments, pharmacokinetics and receptor occupancy. Local tolerability was assessed before the subject left the clinic. The dosing visit was followed by regular out-patient visits for 20 weeks (at Weeks 1, 2, 4, 6, 8, 12, 16 and 20), and a final visit at 24 weeks after dosing. An internal safety committee performed ongoing safety surveillance, and all safety laboratory data were reviewed at least every 3 months. The primary endpoint, change in DAS28 (based on C-reactive protein; CRP) from baseline to Week 12, was evaluated in an interim analysis conducted after Week 12-assessments had been performed for the last dosed subject.

NUMBER OF SUBJECTS PLANNED AND ANALYSED
The trial was planned for a total of 160 screened, 63 randomised and exposed, and 51 completing subjects. A total of 86 subjects were screened for the trial and 63 subjects were randomised and exposed (41 subjects to NNC0142-002 and 22 subjects to placebo). All 63 subjects completed the trial and were included in the full analysis set and the safety analysis set.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION

Men and women (not pregnant and not nursing) between ≥18 and ≤75 years of age, with active RA meeting the ACR1987 diagnosis criteria and characterised by a DAS28-CRP ≥4.5 and at least five tender/swollen joints, including one swollen wrist or at least two swollen ipsilateral metacarpophalangeal joints (second to fifth). Subjects should receive treatment with MTX (7.5–25 mg/week) for at least 12 weeks during the trial, and should have been treated with a stable MTX dose for at least 4 weeks prior to receiving trial product. They should not have failed any biologic therapy for RA and no more than two non-biologic DMARDs (primary or secondary failure to therapy). Further, they should not have any other chronic inflammatory autoimmune disease than RA (except secondary Sjögren's syndrome or stable and appropriately treated hypothyroidism).

Withdrawal criteria

The subject could withdraw at will at any time. The subject could be withdrawn from the trial at the discretion of the investigator or the sponsor due to a safety concern or if judged non-compliant with trial procedures. A subject had to be withdrawn if the following applied: i) Non-compliance with protocol procedures, which in the clinical judgement of the investigator and/or after discussion with the sponsor may invalidate the trial; ii) Sponsor closure of the trial; iii) Withdrawal of informed consent; iv) Pregnancy or intention of becoming pregnant.

INVESTIGATIONAL MEDICINAL PRODUCT, DOSE AND MODE OF ADMINISTRATION, BATCH NUMBER

All doses of NNC0142-0002 were administered s.c. in the abdominal wall, at 4 mg/kg. NNC0142-0002 was provided as freeze-dried powder in 12 mL vials, which was reconstituted with sterile water to a final concentration of 100 mg/mL per vial. Batches of NNC0142-0002 used in the trial were VLDP031 and YLDP017.

DURATION OF TREATMENT

Subjects received a single dose of trial product.

REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, BATCH NUMBER

All doses of placebo were administered s.c. in the abdominal wall. Placebo was provided as a liquid formulation in 12 mL vials. The batch of placebo used in the trial was VLDP033.

CRITERIA FOR EVALUATION – EFFICACY

Primary efficacy assessments

- tender joint count (28 joints assessed) (TJC28)
- swollen joint count (28 joints assessed) (SJC28)
- C-reactive protein (CRP) level
- subject's global assessment of disease activity (VAS) (PtGA)

Secondary efficacy assessments

- swollen joint count (SJC66)
- tender joint count (TJC68)
- subject's assessment of pain (VAS)
- subject's global assessment of disease activity (VAS) (PtGA)
- physician's global assessment of disease activity (VAS) (PhGA)
- subject's self-assessed disability using a health-assessment questionnaire-disability index (HAQ-DI) questionnaire
- CRP level
- patient-reported outcomes: HAQ-DI, short form 36 (SF-36) health survey, RA quality of life (RAQoL), multidimensional assessment of fatigue (MAF)
- MRI assessment of synovitis, oedema and erosion
- ultrasonography

Secondary pharmacodynamic assessments

- NKG2D receptor occupancy by NNC0142-0002
- CRP level
- Cell markers
- Cytokines, chemokines and other proteins, including anti-cyclic citrullinated peptide (a-CCP), rheumatoid factor (RF), soluble MICA (sMICA) and Granzyme B
- Genomic biomarkers: mRNA expression levels

Secondary pharmacokinetic assessments

- Serum concentrations of NNC0142-0002

CRITERIA FOR EVALUATION – SAFETY

- Adverse events (AEs) including local tolerability
- Physical examination including vital signs
- Clinical laboratory safety (haematology, biochemistry, urinalysis, coagulation, lipids and viral screening)
- Electrocardiogram (ECG)
- Antibodies against NNC0142-0002

STATISTICAL METHODS

The sample size calculation was based on the primary endpoint. Under the assumption of a standard deviation of 1.3 and based on a two-sided t-test, a significance level of 5%, a difference in DAS28 score of 1.2 and a 2:1 randomisation ratio, completion of a total of 51 subjects with a DAS28 ≥4.5 in the trial was expected to ensure 85% power to detect a difference between treatment with NNC0142-0002 and placebo at Week 12. Accounting for drop outs, 63 subjects were to be enrolled in the trial. The following analysis sets were defined:

- The safety analysis set: All randomised patients exposed to at least one dose of the trial product
- The full analysis set (FAS): All randomised subjects exposed to at least one dose of trial product and with at least one post-treatment measurement

All tests were two-sided and a significance level of 5% was used. No adjustment for multiplicity was made, as all secondary endpoints were regarded as supportive. The treatment effect was quantified in terms of the estimated difference (NNC0142-0002 – placebo) or, if the endpoint was log transformed, the ratio (NNC0142-0002 / placebo), together with the 95% confidence interval and p-value.

Primary endpoint – change in DAS28-CRP from baseline to Week 12

The primary model was a mixed-effect model repeated measures (MMRM). The effect at Week 12 (active – placebo) was estimated from this model and presented together with the 95% confidence interval and the p-value for testing no treatment effect.

Supportive efficacy endpoints

- Change in DAS28-CRP from baseline to Weeks 6 and 24
- ACR20 response at Weeks 6, 12 and 24
- ACR50 and ACR70 responses at Week 12
- EULAR responses at Weeks 6, 12 and 24
- Change in patient-reported outcome from baseline to Week 12, using Health Assessment Questionnaire – Disability Index (HAQ-DI), Short Form 36 (SF-36), Rheumatoid Arthritis Quality of Life (RAQoL) questionnaire and Multidimensional assessment of fatigue (MAF) scale

The analyses of change in DAS28 from baseline to Weeks 6 and 24 was based on the MMRM model used for the primary analysis of the primary endpoint, and the ANOVA model using LOCF imputation.

ACR20/50/70 responders at Week 12 were compared between the two treatment groups using the Fisher's exact test. The odds ratios for achieving ACR20/50/70 for active versus placebo (active/placebo) were estimated by fitting a logistic regression model. The same analysis was also implemented to ACR20 at Week 6 and Week 24, respectively.

The EULAR response at each timepoint (Weeks 6, 12 and 24) was compared between the two groups by fitting a proportional odds model. A supplementary analysis not specified in the trial protocol was implemented for comparing the two treatment arms using a Cochran-Mantel-Haenszel test. The change from baseline to Week 12 in patient-reported outcome using HAQ-DI and SF-36 questionnaires was each compared by fitting an ANOVA. The same analysis was conducted for the RAQoL questionnaire and MAF scale (not specified in the protocol).

Supportive efficacy endpoints not specified in the protocol

- Remission scores according to various criteria: DAS28-CRP ≤2.6 and ≤2.0, SDAI ≤3.3, CDAI ≤2.8 and $DA_{All\ comp\ \leq 1}$ (the latter being a Boolean-based definition stating that at any time point, a subject had to satisfy all of the following criteria to be in remission: TJC28 ≤1, SJC28 ≤1, CRP ≤1 [mg/dL] and PtGA ≤1[cm])

The number and percentage of subjects reaching remission scores were summarised by treatment groups.

Supportive efficacy endpoints associated with imaging

- Change in the synovitis RAMRIS from baseline to Week 12
- Change in the oedema RAMRIS from baseline to Week 12 (endpoint not specified in the trial protocol)

- Change in the erosion RAMRIS from baseline to Week 12 (endpoint not specified in the trial protocol)
- Change in ultrasound assessment of joint inflammation from baseline to Week 12

Change in the RAMRIS score from baseline to Week 12 was analysed using an ANOVA model. No statistical analysis was performed for the ultrasound assessment, as this was done only for subjects at the trial site in Germany.

PD endpoints

- Level of NNC0142-0002 occupancy of NKG2D receptor on circulating leukocyte subsets, up to Week 24
- Biomarkers: CRP; ESR; cell markers; cytokines and chemokines; genomic biomarkers (polymorphic DNA sequences [optional] and gene expression); and levels of anti-CCP, RF, sMICA and MMP-3.

PD effect was evaluated by fitting an ANOVA to the maximum concentration (E_{max}), and the minimum concentration (E_{min}) of the respective parameter.

Changes in NKG2D receptor occupancy, CRP, ESR, cell markers, cytokines, anti-CCP, RF, sMICA and MMP-3 after 12 weeks were each analysed using an ANOVA, where serum concentrations of CRP, anti-CCP, RF, sMICA and MMP-3 were logarithmic-transformed before analysis (analysis not specified in the trial protocol).

Safety endpoints

- AEs including local tolerability
- Physical examination, incl. vital signs; ECG
- Clinical laboratory safety (haematology, biochemistry, urinalysis, lipids and viral screening)
- Antibodies against NNC0142-0002

All safety endpoints were summarised descriptively based on all collected data. The PD effect based on the safety parameters was investigated using the same statistical methods as described for the PD effect based on the efficacy parameters (analysis not specified in the trial protocol).

PK endpoints

- AUC, C_{max}, t_{max} and $t_{½}$
- $AUC/AUC_{(0-W12)}$ (endpoint not specified in the trial protocol)

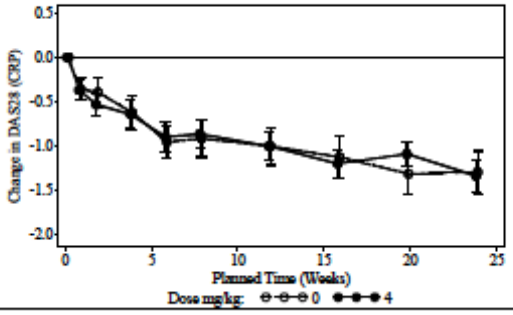
All PK endpoints were summarised descriptively.

DEMOGRAPHY OF TRIAL POPULATION

All subjects were White with a mean age of 52 years and a mean BMI of 27.5 kg/m^2. The majority of subjects (63.5%) were enrolled from the Russian Federation, followed by Ukraine (19.0%) and Germany (17.5%). More females than males (90% versus 10%) were included. Subjects had been diagnosed with RA for a mean of 7.1 years, had a mean DAS28 of 5.4, and approximately 80% of the subjects were seropositive (positive for RF or antibodies against CCP). Subjects had been treated with stable doses of MTX for a mean of 3.3 years (range: 0.3 to 13.4 years), and the time from RA diagnosis to initiation of MTX therapy was 3.8 years (range: 0 to 24 years). The two dose groups were comparable with respect to demography, disease profile and MTX treatment.

EFFICACY RESULTS

- A single subcutaneous administration of 4 mg/kg NNC0142-0002 did not result in a statistically significant reduction in disease activity in terms of DAS28-CRP at 12 weeks after treatment, when compared to placebo. Neither was any reduction observed at 6 or 24 weeks after treatment.



- No statistically significant difference in ACR20/50/70 or EULAR responses was observed during the trial, when compared to placebo.
- No statistically significant difference in change in patient-reported outcomes (HAQ-DI, SF-36 and MAF) was observed during the trial when compared to placebo, with the exception of significant improvements in the RA quality of life (RAQoL) for the placebo group at 12 and 20 weeks after treatment.
- Numbers of subjects achieving remission according to the different remission criteria were comparable between the two treatment groups. 3 (7%) actively treated subjects and 1 (5%) placebo-treated subject achieved remission according to the DAS28 $\leq$ 2.6 remission criterion. Single or no subjects achieved remission according to the other remission criteria applied (DAS28 $\leq$2.0, SDAI $\leq$3.3, CDAI $\leq$2.8 and $DA_{(All\ comp \leq 1)}$). The single remissions occurred in the group with actively treated subjects.
- No statistically significant difference in change in MRI (RAMRIS) scores on synovitis, oedema or erosion were observed during the trial, when compared to placebo.
- Full (i.e., above 95%) mean NKG2D receptor occupancy by NNC0142-0002 was observed at Week 1 and maintained throughout the 12 weeks after dosing. A mean NKG2D receptor occupancy of above 90% was maintained in blood for 13.2 weeks (SD: 3.3 weeks). For 85% of the subjects, the occupancy had declined below 20% by Week 24. For 15% of the subjects, occupancies were $\geq$20% at Week 24.
- No statistically significant difference in changes in biomarker parameters (anti-CCP, sMICA, MMP-3, CRP or ESR) was observed at Week 12 or in the follow-up period when compared to placebo, with the exception of a reduction in RF at Week 12 (ratio: 1.2; 95% CI: 1.02, 1.42; p=0.032) in placebo-treated subjects.
- Statistically significant reductions in the mean E_{min} of NKG2D receptor-expressing fraction (%) of $CD8^+$ T cells and NK cells, respectively, were observed when compared to placebo (overall cell numbers remained within normal range). In addition, a statistically significant reduction in the E_{min} of the absolute (MEF) mean NKG2D receptor expression was evident for the pooled $CD8^+$ T cell and NK cell fraction when compared to placebo. At Week 24, the proportion of NKG2D receptor-expressing NK cells approached normalisation.
- No statistically significant reduction of the mean fraction (%) $NKG2D^+CD28^-$ T cells of $CD4^+$ T cells was observed when compared to placebo. However, $NKG2D^+CD28^-CD4^+$ T cells levels were relatively low throughout the trial.
- No statistically significant differences in surface expression of CD69, CCR3/CCR5, CD45RA/CCR7 or VLA-4 at E_{min} or E_{max} were observed when compared to placebo. However, most cell markers were measured only in subjects enrolled at the German trial site because of lacking cell-marker stability during shipment.
- No effect of treatment with NNC0142-0002 on peripheral blood gene-expression profiles was observed. No genotyping was performed.
- The mean observed maximum serum concentration (C_{max}) was 27.8 µg/mL (95% CI: 25.0, 30.9), and the median time to maximum observed serum concentration (t_{max}) was approximately 7 days (95% CI: 6.9, 7.0). An average of 94% of NNC0142-0002 was eliminated at 12 weeks after treatment.

SAFETY RESULTS

- A single subcutaneous administration of NNC0142-0002 at 4 mg/kg was well tolerated in subjects with active RA concomitantly treated with MTX.
- A total of 53 AEs were reported for 33 (52%) subjects during the trial. Comparable proportions of subjects with AEs were observed for the two treatment groups, with 31 AEs reported for 22 (54%) actively treated subjects, and 22 AEs reported for 11 (50%) placebo-treated subjects. The mean time of trial participation was comparable between actively treated subjects (24.1 weeks; range: 23.1 to 25.3 weeks) and placebo-treated subjects (24.1 weeks; range: 23.3 to 24.3 weeks).
- Comparable proportions of subjects experiencing possibly/probably related AEs were observed for the two treatment groups, with 3 AEs reported for 3 (7%) actively treated subjects (single events of moderate rheumatoid arthritis, moderate stomatitis and moderate headache), and 2 AEs reported for 2 (9%) placebo-treated subjects (single events of moderate herpes zoster and mild viral respiratory tract infection). None of these possibly/probably AEs were evaluated as severe; 1 (rheumatoid arthritis) was classified as serious.
- AEs were mainly mild (49% of events) or moderate (42% of events) in severity. A total of 5 (9% of events) events were evaluated as severe: single events of musculoskeletal [shoulder] pain and [aggravated] RA in 2 (5%) actively treated subjects, and single events of [aggravated] rheumatoid arthritis, portal hypertension and hepatic fibrosis in 2 (9%) placebo-treated subjects. All severe AEs were resolved at end of trial, with the exception of the portal hypertension and hepatic fibrosis ([redacted]). None of the severe events were

evaluated as possibly or probably related to trial product; 2 severe events (portal hypertension and musculoskeletal pain) were classified as SAEs.

- A total of 5 SAEs were reported for 4 (6%) subjects: single events of moderate erosive gastritis, moderate chronic pancreatitis, severe musculoskeletal pain and moderate rheumatoid arthritis, in a total of 3 (7%) actively treated subjects; and severe portal hypertension in 1 (5%) placebo-treated subject. All SAEs were evaluated as unlikely related to the trial product, with the exception of the rheumatoid arthritis event, which was evaluated possibly related to the trial product.
- There were no deaths, AEs leading to withdrawal of a subject or medical events of special interest (such as medication errors or suspected transmission of an infectious agent via a trial product) reported during the trial.
- A total of 2 injection-site reactions were reported for 2 (3%) subjects, both administered placebo: 1 event of redness and 1 event of haematoma.
- Statistically significant decreases in mean E_{min} of B cells and sodium were observed in actively treated subjects when compared to placebo, but were not considered clinically relevant. Infrequent and transient levels outside the normal range were observed for various cell subtypes, but there were no consistent trends indicative of relationship to treatment with NNC0142-0002.
- Urinalysis parameters, viral screen, physical exam and ECG results were without remarks throughout the trial. No statistically significant difference in coagulation, lipid or cytokines, body weight, body temperature, pulse, diastolic or systolic blood pressure was observed for the actively treated group when compared to placebo.
- Treatment-induced anti-drug antibodies of low titre (titre: 1) were observed in samples collected from 3 (7%) of the subjects: at Week 12 for 1 subject, Week 16 for 1 subject and Weeks 20 and 24 for 1 subject. The anti-drug antibodies were not neutralising; i.e. did not interfere with NNC0142-0002 binding to the NKG2D receptor *in vitro*.

CONCLUSIONS

- A single subcutaneous administration of 4 mg/kg NNC0142-0002 did not result in a statistically significant reduction in disease activity in terms of DAS28-CRP at 12 weeks after treatment, when compared to placebo. Neither was any reduction observed at 6 or 24 weeks after treatment. No statistically significant difference in ACR20/50/70 or EULAR responses was observed for subjects treated with NNC0142-0002 when compared to placebo.
- Elimination of NNC0142-0002 in serum was almost complete after 12 weeks. Full (i.e., above 95%) mean NKG2D receptor occupancy by NNC0142-0002 was maintained throughout the 12 weeks after dosing.
- Treatment with NNC0142-0002 reduced the NKG2D receptor-expressing fraction of $CD8^+$ T cells and NK cells, respectively. There were no significant differences in changes of the biomarkers investigated, and no effect of treatment with NNC0142-0002 on peripheral blood gene-expression profiles or MRI scores on synovitis, oedema or erosion.
- No statistically significant improvement in patient-reported outcomes for actively treated subjects was observed for subjects treated with NNC0142-0002 when compared to placebo.
- No safety concerns were raised during the trial, and NNC0142-0002 was well tolerated within the context of the trial. Treatment-induced, non-neutralising anti-drug antibodies of low titres were observed in 3 (7%) subjects.

The trial was conducted in accordance with the Declaration of Helsinki (2008) and ICH Good Clinical Practice (1996). The results presented reflect the data available in the clinical database as of 12-June-2012.

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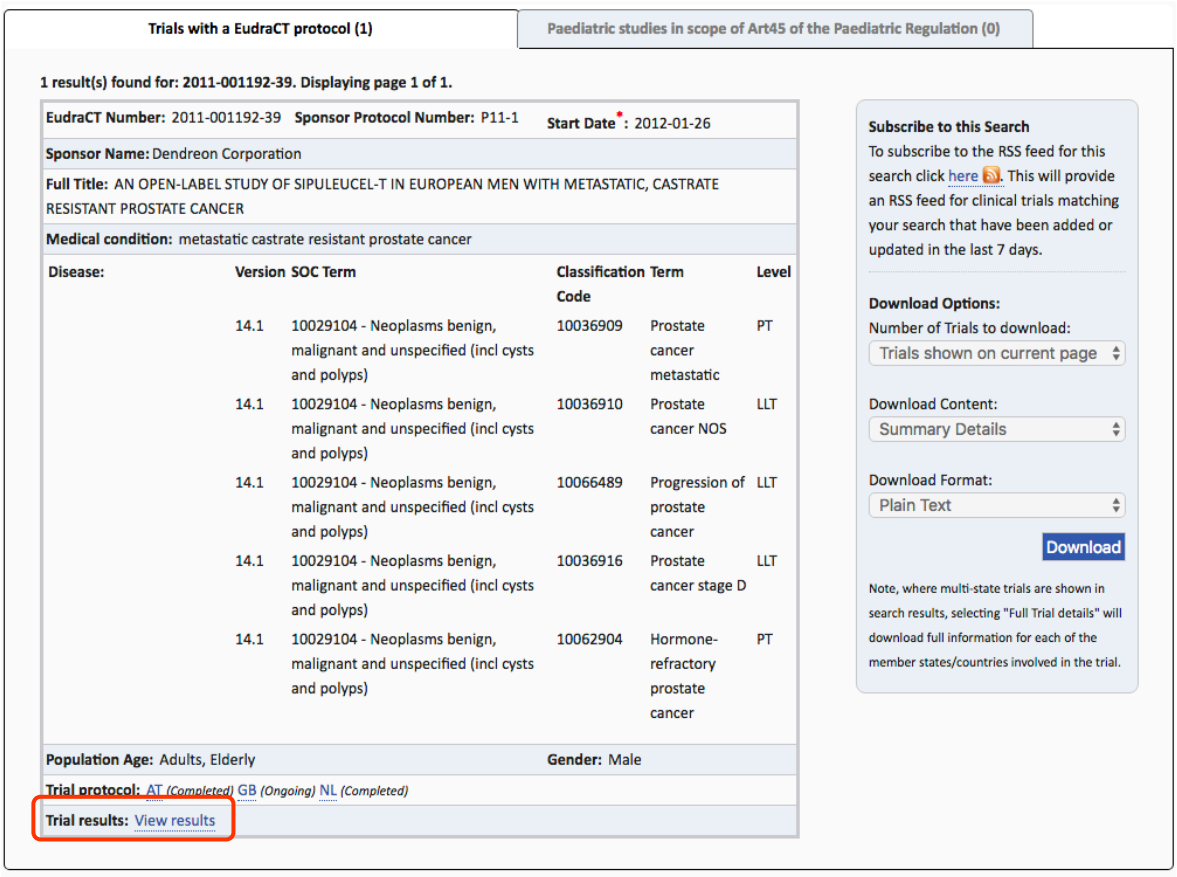

Trials with a EudraCT protocol (1) | Paediatric studies in scope of Art45 of the Paediatric Regulation (0)

1 result(s) found for: 2011-001192-39. Displaying page 1 of 1.

EudraCT Number: 2011-001192-39 **Sponsor Protocol Number:** P11-1 **Start Date*:** 2012-01-26

Sponsor Name: Dendreon Corporation

Full Title: AN OPEN-LABEL STUDY OF SIPULEUCEL-T IN EUROPEAN MEN WITH METASTATIC, CASTRATE RESISTANT PROSTATE CANCER

Medical condition: metastatic castrate resistant prostate cancer

Disease:	Version	SOC Term	Classification Code	Term	Level
	14.1	10029104 - Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10036909	Prostate cancer metastatic	PT
	14.1	10029104 - Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10036910	Prostate cancer NOS	LLT
	14.1	10029104 - Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10066489	Progression of prostate cancer	LLT
	14.1	10029104 - Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10036916	Prostate cancer stage D	LLT
	14.1	10029104 - Neoplasms benign, malignant and unspecified (incl cysts and polyps)	10062904	Hormone-refractory prostate cancer	PT

Population Age: Adults, Elderly **Gender:** Male

Trial protocol: AT *(Completed)* GB *(Ongoing)* NL *(Completed)*

Trial results: View results

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Clinical Trial Results:
AN OPEN-LABEL STUDY OF SIPULEUCEL-T IN EUROPEAN MEN WITH METASTATIC, CASTRATE RESISTANT PROSTATE CANCER

Summary	
EudraCT number	2011-001192-39
Trial protocol	AT GB NL
Global end of trial date	10 Jun 2014
Results information	
Results version number	v1(current)
This version publication date	14 Dec 2016
First version publication date	27 Jun 2015
Other versions	

Trial Information
Subject Disposition
Baseline Characteristics
End Points
Adverse Events
More Information

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Trial information

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Trial identification	
Sponsor protocol code	P11-1
Additional study identifiers	
ISRCTN number	-
US NCT number	-
WHO universal trial number (UTN)	-
Sponsors	
Sponsor organisation name	Dendreon Pharmaceuticals, Inc
Sponsor organisation address	1301 2nd Avenue, Seattle, United States,
Public contact	Jennifer Lill, Dendreon Pharmaceuticals, Inc, +1 206-455-2174, jlill@dendreon.com
Scientific contact	Jennifer Lill, Dendreon Pharmaceuticals, Inc, +1 206-455-2174, jlill@dendreon.com
Paediatric regulatory details	
Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Results analysis stage	
Analysis stage	Final
Date of interim/final analysis	10 Jun 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 Jun 2014
Global end of trial reached?	Yes
Global end of trial date	10 Jun 2014
Was the trial ended prematurely?	No
General information about the trial	
Main objective of the trial	To demonstrate that sipuleucel-T can be successfully manufactured for subjects with mCRPC at a European manufacturing facility.
Protection of trial subjects	Utilization of an Independent Data Monitoring Committee that met at 3 month intervals and established procedures regarding chain of identity to ensure autologous product is delivered correctly.
Background therapy	-
Evidence for comparator	-
Actual start date of recruitment	13 Jun 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes
Population of trial subjects	
Number of subjects enrolled per country	
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	France: 8
Worldwide total number of subjects	47
EEA total number of subjects	47
Number of subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	34
85 years and over	1

Subject disposition

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Recruitment	
Recruitment details	-
Pre-assignment	
Screening details	Administration of informed consent, evaluation of inclusion criteria, clinical evaluations and assorted laboratory tests.
Period 1	
Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Arm title	sipuleucel-T
Arm description	Each dose of sipuleucel-T contains a minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF. The recommended course of therapy for sipuleucel-T is 3 complete doses, given at approximately 2-week intervals. sipuleucel-T: Each dose of sipuleucel-T contains a minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF. The recommended course of therapy for sipuleucel-T is 3 complete doses, given at approximately 2-week intervals.
Arm type	Experimental
Investigational medicinal product name	Sipuleucel-T
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Dispersion for infusion
Routes of administration	Intravenous use
Dosage and administration details	3 250 mL doses infused approximately 2 weeks apart.

Number of subjects in period 1	sipuleucel-T
Started	47
Completed	43
Not completed	4
Started a medication restricted per the protocol	4

Baseline characteristics

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Baseline characteristics reporting groups		
Reporting group title	Overall Trial	
Reporting group description	-	
Reporting group values	Overall Trial	Total
Number of subjects	47	47
Age categorical		
Units: Subjects		
In utero	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0
Newborns (0-27 days)	0	0
Infants and toddlers (28 days-23 months)	0	0
Children (2-11 years)	0	0
Adolescents (12-17 years)	0	0
Adults (18-64 years)	12	12
From 65-84 years	34	34
85 years and over	1	1
Age continuous		
Units: years		
arithmetic mean (standard deviation)	67.2 ± 7.8	-
Gender categorical		
Units: Subjects		
Female	0	0
Male	47	47

Subject analysis sets	
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description	All subjects registered were included in the analysis.
Subject analysis sets values	Full analysis
Number of subjects	47
Age categorical	
Units: Subjects	
In utero	0
Preterm newborn infants (gestational age < 37 wks)	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65-84 years	34
85 years and over	1
Age continuous	
Units: years	
arithmetic mean (standard deviation)	67.2 ± 7.8
Gender categorical	
Units: Subjects	
Female	0
Male	47

End points

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End points reporting groups	
Reporting group title	sipuleucel-T
Reporting group description	Each dose of sipuleucel-T contains a minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF. The recommended course of therapy for sipuleucel-T is 3 complete doses, given at approximately 2-week intervals. sipuleucel-T: Each dose of sipuleucel-T contains a minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF. The recommended course of therapy for sipuleucel-T is 3 complete doses, given at approximately 2-week intervals.
Subject analysis set title	Full analysis
Subject analysis set type	Full analysis
Subject analysis set description	All subjects registered were included in the analysis.

Primary: Cumulative CD54 Upregulation

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End point title	Cumulative CD54 Upregulation [1]
End point description	
End point type	Primary
End point timeframe	Over 3 infusions of Sipuleucel-T

Notes
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Cumulative CD54 Upregulation parameters will be summarized descriptively (mean, median, standard deviation, minimum, and maximum) by infusion (1, 2, and 3) and cumulative (summed across infusions). Descriptive statistics are sufficient for this single-arm study.

End point values	Full analysis
Number of subjects analysed	47
Units: Ratio	
arithmetic mean (standard error)	34.1 ± 1.24

No statistical analyses for this end point

Primary: CD54+ cell count

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End point title	CD54+ cell count [2]
End point description	
End point type	Primary
End point timeframe	Cumulative through infusion 3

Notes
[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: CD54+ cell count parameters will be summarized descriptively (mean, median, standard deviation, minimum, and maximum) by infusion (1, 2, and 3) and cumulative (summed across infusions) Descriptive statistics are sufficient for this single-arm study.

End point values	Full analysis
Number of subjects analysed	
Units: 10^9	
arithmetic mean (standard error)	1.58 ± 0.1

No statistical analyses for this end point

Primary: Total nucleated cell count	Top of page
End point title	Total nucleated cell count [3]
End point description	
End point type	Primary
End point timeframe	Cumulative through infusion 3
Notes [3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Total nucleated cell count parameters will be summarized descriptively (mean, median, standard deviation, minimum, and maximum) by infusion (1, 2, and 3) and cumulative (summed across infusions) Descriptive statistics are sufficient for this single-arm study.	
End point values	Full analysis
Number of subjects analysed	
Units: 10^9	
arithmetic mean (standard error)	12.54 ± 0.74

No statistical analyses for this end point

Primary: Product viability (percentage)	Top of page
End point title	Product viability (percentage) [4]
End point description	
End point type	Primary
End point timeframe	Infusion 3
Notes [4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Product viability (percentage) parameters will be summarized descriptively (mean, median, standard deviation, minimum, and maximum) by infusion (1, 2, and 3). Descriptive statistics are sufficient for this single-arm study.	
End point values	Full analysis
Number of subjects analysed	
Units: percentage	
arithmetic mean (full range (min-max))	96.75 (90.4 to 99.53)

No statistical analyses for this end point

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Adverse events

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Adverse events information	
Timeframe for reporting adverse events	From informed consent to last visit
Assessment type	Systematic
Dictionary used for adverse event reporting	
Dictionary name	MedDRA
Dictionary version	14.1
Reporting groups	
Reporting group title	All subjects
Reporting group description	-

Serious adverse events	All subjects
Total subjects affected by serious adverse events	
subjects affected / exposed	3 / 47 (6.38%)
number of deaths (all causes)	0
number of deaths resulting from adverse events	
Injury, poisoning and procedural complications	
Gastroenteritis radiation	
subjects affected / exposed	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1
deaths causally related to treatment / all	0 / 0
General disorders and administration site conditions	
Fatigue	
subjects affected / exposed	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1
deaths causally related to treatment / all	0 / 0
Gastrointestinal disorders	
Pain	
subjects affected / exposed	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1
deaths causally related to treatment / all	0 / 0
Renal and urinary disorders	
Calculus urinary	
subjects affected / exposed	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1
deaths causally related to treatment / all	0 / 0
Urinary Tract Obstruction	
subjects affected / exposed	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1
deaths causally related to treatment / all	0 / 0

Frequency threshold for reporting non-serious adverse events: 5%	
Non-serious adverse events	All subjects
Total subjects affected by non serious adverse events	
subjects affected / exposed	40 / 47 (85.11%)
Vascular disorders	
Hypertension	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Injury, poisoning and procedural complications	
Citrate Toxicity	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Blood and lymphatic system disorders	
Anaemia	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Nervous system disorders	
Dizziness	
subjects affected / exposed	5 / 47 (10.64%)
occurrences all number	5
General disorders and administration site conditions	
Fatigue	
subjects affected / exposed	14 / 47 (29.79%)
occurrences all number	14
Chills	
subjects affected / exposed	10 / 47 (21.28%)
occurrences all number	10
Influenza like illness	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Pain	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Gastrointestinal disorders	
Nausea	
subjects affected / exposed	5 / 47 (10.64%)
occurrences all number	5
Constipation	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Musculoskeletal and connective tissue disorders	
Back pain	
subjects affected / exposed	11 / 47 (23.40%)
occurrences all number	11
Myalgia	
subjects affected / exposed	4 / 47 (8.51%)
occurrences all number	4
Arthralgia	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3

Bone pain	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Pain in extremity	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3
Infections and infestations	
Nasopharyngitis	
subjects affected / exposed	3 / 47 (6.38%)
occurrences all number	3

More information

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Substantial protocol amendments (globally)	
Were there any global substantial amendments to the protocol? Yes	
Date	**Amendment**
01 Jun 2012	Quality of Life questionnaire assessments added. Clarification of sample size from 10 up to 45 subjects in the statistical analysis (justification for 45 subjects). Statistical clarification for the decision to stop enrollment.
09 Jul 2013	Added thromboembolic and CVE reporting criteria of all countries to align with IB, edition 18.
02 Dec 2013	Updated leukapheresis and sipuleucel-T risks sections, and infusion section to align with IB, edition 19.
Interruptions (globally)	
Were there any global interruptions to the trial? No	
Limitations and caveats	
Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.	
None reported	

2 October 2014
EMA/240810/2013

European Medicines Agency policy on publication of clinical data for medicinal products for human use

POLICY/0070
Status: Adopted
Effective date: 1 January 2015
Review date: No later than June 2016
Supersedes: Not applicable

1. Introduction and purpose

The aim of the European Medicines Agency ('the Agency') is to protect and foster public health. Transparency is a key consideration for the Agency in delivering its service to patients and society.

Although the Agency since its creation has launched several initiatives to increase transparency of information on medicinal products, there is growing demand from stakeholders for additional transparency, not only about the Agency's deliberations and actions, but also about the clinical data on which regulatory decisions are based. The Agency is committed to continuously extend its approach to transparency and has, therefore, taken the initiative to develop a policy on publication of clinical data, in accordance with article 80 of Regulation (EC) No 726/2004[1]. Consultations with a broad range of stakeholders and European Union (EU) bodies have taken place in drafting this policy. It should be noted that this policy is without prejudice to Regulation (EC) No 1049/2001[2], and, therefore, it does not replace the existing 'Policy on access to documents (related to medicinal products for human and veterinary use)' (POLICY/0043) (EMA/110196/2006), which came into effect in December 2010. Moreover, the provisions of this policy are not intended in any manner to limit the application or the rights given by Regulation (EC) No. 1049/2001. Any natural or legal person may continue to submit a request for access to documents to the Agency independently of the proactive publication mechanisms established by this policy.

[1] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
[2] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents.

This policy is also without prejudice to Regulation (EU) No 536/2014[3].

2. Scope

The scope of the policy relates to clinical data, composed of clinical reports and individual patient data (IPD), submitted under the centralised marketing authorisation procedure after the effective date (see chapter 4.3. for further information), either using the common technical document (CTD) format or another format:

- as part of a marketing authorisation application (MAA);
- or as part of a post-authorisation procedure for an existing centrally authorised medicinal product;
- or as part of a procedure under Article 58 of Regulation (EC) No 726/2004;
- or submitted by a third party in the context of a MAA or a post-authorisation procedure for an existing centrally authorised medicinal product;
- or requested by the Agency/ submitted by the applicant/marketing authorisation holder (MAH) as additional clinical data in the context of the scientific assessment process for the aforementioned situations.

The following clinical data are not covered by the scope of the policy:

- Clinical data held by the Agency for applications submitted under the centralised procedure before 1 January 2015, and for extension of indication applications and line extension applications submitted before 1 July 2015.
- Clinical data (either data provided to the Agency before 1 January 2015 or data not yet held by the Agency) submitted to the Agency for non-centrally authorised products.

These clinical data continue to be made available to external requesters on a reactive basis in accordance with the aforementioned Agency's policy on access to documents.

In addition, the following clinical data are not covered by the scope of the policy:

- Clinical data that are not held by the Agency, even if they concern a medicinal product that has been authorised by the Agency (e.g. clinical trials on an authorised product conducted by independent investigators and not submitted to the Agency).
- Pharmacovigilance data based on individual case safety reports (ICSRs). Access by third parties to ICSR data is addressed in the Agency's 'EudraVigilance access policy for medicines for human use' (EMA/759287/2009 corr.).

3. Definitions

For the purpose of this policy the following definitions apply:

- **Applicant/MAH:**

Applicant/MAH shall mean the natural or legal person(s) or organisation(s) that submitted the clinical reports to the Agency in the context of applications in support of centralised marketing authorisations (MAs)/post-authorisation submissions for existing centrally authorised medicinal products, as well as

[3] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

any person(s) or organisation(s) who own(s) copyright or other intellectual property rights in the clinical reports.

- **Clinical data:**

Clinical data shall mean the clinical reports and IPD.

- **Clinical reports:**

Clinical reports shall mean the clinical overviews (generally submitted in module 2.5) and clinical summaries (generally submitted in module 2.7) and the clinical study reports (generally submitted in module 5, "CSR"), together with appendices to the CSRs no. 16.1.1 (protocol and protocol amendments), 16.1.2 (sample case report form) and 16.1.9 (documentation of statistical methods).

- **Clinical study:**

Clinical study shall mean any investigation in relation to humans intended to:

- discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products;
- identify any adverse reactions to one or more medicinal products; or
- study the absorption, distribution, metabolism and excretion of one or more medicinal products;

with the objective of ascertaining the safety or efficacy of those medicinal products.

- **Commercially confidential information (CCI):**

CCI shall mean any information contained in the clinical reports submitted to the Agency by the applicant/MAH that is not in the public domain or publicly available and where disclosure may undermine the legitimate economic interest of the applicant/MAH.

- **Individual patient data (IPD):**

IPD shall mean the individual data separately recorded for each participant in a clinical study.

- **Personal data:**

Personal data shall mean any information relating to an identified or identifiable natural person ('data subject'); an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to their physical, physiological, mental, economic, cultural or social identity (Article 2(a) of Regulation (EC) No 45/2001).

4. Policy statement

The following aspects are addressed in this policy:

- Objectives of the policy.
- Characteristics of the policy.
- Date of coming into effect of the policy.

4.1. Objectives of the policy

The main objectives of the policy by making clinical data available proactively, are to enable

- public scrutiny,

- and application of new knowledge in future research,

all this in the interest of public health.

A high degree of transparency will take regulatory decision-making one step closer to EU citizens, and promote better-informed use of medicines. In addition, the Agency takes the view that access to clinical data will benefit public health in future. The policy has the potential to make medicine development more efficient by establishing a level playing field that allows all medicine developers to learn from past successes and failures. Furthermore, it will enable the wider scientific community to make use of detailed clinical data to develop new knowledge in the interest of public health. Access to clinical data will allow third parties to verify the original analysis and conclusions, to conduct further analyses, and to examine the regulatory authority's positions and challenge them where appropriate.

The Agency also takes the view that transparency should be mutually respected. Those who perform secondary analysis of clinical data, published in accordance with this policy, must be held to the same standard of transparency as those who generate clinical data in the first place. Hence, all secondary analyses are expected to also be in the public domain and accessible for further scrutiny by the scientific community. In addition, those who perform secondary analysis of clinical data published in accordance with this policy, are encouraged to provide the Agency with a copy of any article resulting from such secondary analysis before publication, in particular in those circumstances where the secondary analysis might result in the need for regulatory action to protect public health. This is a critical consideration in view of the Agency's role and responsibilities for a timely review of all available information which might have an impact on the benefit/risk ratio of centrally authorised products.

The Agency cannot guarantee that all secondary data analyses that are enabled by the policy will be conducted and reported to the highest possible scientific standard; this is not possible with a truly open approach.

Allowing external parties access to clinical data held by the Agency will directly or indirectly affect different stakeholders' rights, interests and values. In developing this policy the Agency had to consider a number of competing principles which needed to be carefully balanced in order to best ensure the overarching, long-term goal of protecting and fostering public health. These principles, as well as the Agency's positions and views, are described below:

- **Protecting personal data:**

The protection of personal data is enshrined in EU legislation; it is a fundamental right of EU citizens. The policy has to ensure adequate personal data protection; it must be fully compliant with applicable regulations in the EU, in particular Regulation (EC) No 45/2001 and Directive 95/46/EC. There are ways and means to anonymise data and protect patients from retroactive identification. Yet, the Agency is primarily concerned that emerging technologies for data mining and database linkage will increase the potential for unlawful retroactive patient identification. The Agency, therefore, takes a guarded approach to the sharing of patient-level data, which is done to enable legitimate learning from sharing patient-level data while preventing rare but potentially damaging instances of patient identification. Furthermore, patients' informed consent should be respected. The secondary analysis of personal data will have to be fully compatible with the individual privacy of clinical trial participants and data protection.

- **Protecting commercially confidential information (CCI):**

The Agency respects and will not divulge CCI. In general, however, clinical data cannot be considered CCI. The Agency acknowledges that there are limited circumstances where information could constitute CCI.

- **Protecting the Agency's and the European Commission's deliberations and decision-making process:**

Regulators have a legal mandate to evaluate medicines. In doing so, they should only focus on the science and the best interests of patients. The decision-making process should be protected against external pressures from whatever direction. Once a decision has been reached, this consideration no longer applies.

- **Ensuring future investment in pharmaceutical research and development (R&D):**

Sustained and extensive pharmaceutical research activity is a precondition for future improvements in public health. The policy has no intention to negatively impact on the incentives to invest in future pharmaceutical R&D. It is designed to guard against unintended consequences, e.g. breaches of intellectual property rights that might disincentivise future investment in R&D.

4.2. Characteristics of the policy

The main characteristics of the policy are:

- Introduction of a publication process for clinical reports.
- Management of CCI in clinical reports.
- Methods for balancing the protection of patients' privacy whilst retaining scientific value of the data.
- Stepwise implementation of the policy.

4.2.1. Introduction of a publication process for clinical reports

The introduction of a publication process for clinical reports is based on 2 pillars:

- Terms of use (ToU) which govern the access to and use of clinical reports.
- A user-friendly technical tool allowing access to such clinical reports.

The ToU provide more information in relation to the access to the information contained in the clinical reports and the intended use of such information. Two sets of ToU are available, depending on the intended use of the information contained in the clinical reports, as described below:

- **Clinical reports available on-screen for any user, with a simple and limited registration process:**

The main characteristics are:

Registration process:

- Obtaining a user ID/password.
- Accepting the ToU.

ToU for general information purposes (see annex 1):

- Intended use is for general information and non-commercial purposes, including non-commercial research purposes.
- Clinical reports are made available in a "view-on-screen-only" mode.
- Clinical reports will be made available in a searchable format and will be permanently available.

- **Downloadable clinical reports available to identified users:**

The main characteristics are:

Registration process:

- Obtaining a user ID/password.
- Accepting the ToU.
- Providing the Agency with elements concerning the identity of the user (i.e. name, date of birth, passport or ID card number, expiry date of the document; for juridical persons, the affiliation and position within the organisation of the user should also be provided).

ToU for academic and other non-commercial research purposes (see annex 2):

- Intended use is for academic and non-commercial research purposes.
- Clinical reports can be downloaded, saved and printed.
- Clinical reports will be made available in a searchable format and will be permanently available.

Common to the two sets of ToU are the following elements:

- No attempt shall be made to re-identify the trial subjects or other individuals from the information.
- The clinical reports may not be used to support a MAA/ extensions or variations to a MA nor to make any unfair commercial use of the clinical reports.
- A watermark is applied to the published information to emphasise the prohibition of its use for commercial purposes.
- The Agency accepts no responsibility for the user's compliance with the ToU.

4.2.2. Management of CCI in clinical reports

Although generally the information contained in clinical reports should not be considered CCI, the Agency acknowledges that in limited circumstances the clinical reports could contain CCI, and could, therefore, be subject to redaction prior to publication. Where redaction of CCI is proposed by the applicant/MAH, a consultation with the applicant/MAH will be undertaken, following scrutiny by the Agency of the proposed redaction, including the justification provided by the applicant/MAH, as to whether the definition of CCI applies (see annexes 3 and 4).

4.2.2.1. Redaction principles

The clinical reports that will be published in accordance with this policy shall only be subject to redactions when needed to protect those specific elements which qualify as CCI that should not be released. This complements the aforementioned use controls that will need to be accepted by recipients of the documents in order to protect the originator against misuse of the data as a whole. This covers information that is not in the public domain or publicly available and where disclosure may undermine the economic or competitive position of the applicant/MAH. In this regard, the assessment of this information will take into account the justification provided by the applicant/MAH with regard to various factors, including the nature of the product concerned, the competitive situation of the

therapeutic market in question, the approval status in other jurisdictions, the novelty of the clinical development, and new developments by the same company.

In general, as already mentioned, most of the information in clinical reports would not be considered CCI. There, are, however, limited circumstances where the clinical reports could contain CCI.

The information referred to in annex 3, which is contained in the sections of the clinical reports, may be considered CCI and, therefore, may have to be redacted as per the aforementioned redaction principles, after assessment by the Agency of the justification provided by the applicant/MAH. The same rules regarding CCI and the redaction principles will apply to the same information presented in other formats or other sections in the documents submitted by the applicant/MAH to the Agency.

If justification for additional redaction going beyond the list in annex 3 has been provided by the applicant/MAH, and agreed upon by the Agency, the Agency will then proceed with the publication of the so redacted clinical reports. The Agency will, once further experience with the implementation of the policy has been obtained, undertake first a consultation with all relevant stakeholders in order to explore if the outcome of the individual case(s) should exceptionally lead to a revision of the redaction principles.

4.2.2.2. Process for publication of clinical reports

The process for publication of clinical reports is described in annex 4. This process foresees in consultation with the applicant/MAH in case the Agency disagrees with the redaction proposed by the applicant/MAH.

4.2.3. Methods for balancing the protection of patient's privacy whilst retaining scientific value of the data

Protection of patients' identity is of crucial importance. In order to achieve this objective both identification and re-identification of patients need to be avoided. Particular challenges in this respect are continuous developments in the field of technologies relating to data mining and database linkage, as well as specific scenarios to be considered in the area of medicine regulation, for instance the situation of rare diseases. In deciding on the most optimal approach (anonymisation versus pseudonymisation) the Agency will take due account of recent developments, e.g. the work undertaken by the network of EU Data Protection Authorities on anonymisation techniques[4], and subsequently discuss with stakeholders (e.g. patients' organisations, academia, pharmaceutical industry) to agree on the best way forward.

4.2.4. Stepwise implementation of the policy

The implementation of the policy will be undertaken in a stepwise manner:

- In a first phase, the publication of clinical data will relate to clinical reports only.
- In a second phase, the Agency will review various aspects in relation to IPD, including finding the most appropriate way to make IPD available, the latter in compliance with privacy and data protection laws[5].

[4] Opinion 05/2014 on anonymisation techniques, adopted on 10 April 2014 by the Article 29 Data Protection Working Party.
[5] The Agency will notify the European Data Protection Supervisor (EDPS) accordingly.

4.2.4.1. First phase: publication of clinical reports

The publication of clinical reports will be in accordance with the arrangements described in chapters 4.2.1., 4.2.2. and 4.2.3. of the policy.

In addition, the following principles will apply as regards the timing of publication:

The timing of publication takes into account the need to protect the Agency's and the European Commission's deliberations and decision-making process. In order not to undermine such decision-making process the Agency will only publish clinical data once the concerned procedure has been finalised. In practical terms this means:

- following the European Commission Decision granting or refusing the MA/post-authorisation submission outcome; or
- following the scientific committee Opinion if there is no subsequent European Commission Decision; or
- following the scientific committee conclusion if there is no Opinion; or
- following receipt of the applicant's/MAH's letter notifying the withdrawal of the MAA/post-authorisation submission.

The process described in chapter 4.2.2.2. for publication of clinical reports, including where necessary interaction with the applicant/MAH, will start following the adoption of the scientific committee Opinion/conclusion or the receipt of the withdrawal letter, as referred to above.

4.2.4.2. Second phase: reviewing various aspects in relation to IPD

Before IPD can be made available, there is a need to first clarify:

- the submission of IPD for subsequent scientific review by the Agency, and
- how to best provide access to such IPD, including the conditions to be fulfilled.

It is important to emphasise in this regard that the Agency will not request applicants/MAHs to submit IPD for the sole purpose of publication of IPD.

The Agency will first undertake a targeted public consultation with all concerned stakeholders on the various aspects in relation to IPD to provide clarification. Subsequently, in consultation with the Agency's Management Board, the policy will be amended to reflect the outcome of this targeted public consultation.

4.3. Date of coming into effect of the policy

For the coming into effect of the policy a stepwise approach will be applied.

The effective date will be 1 January 2015 for any new MAAs, and Article 58 applications submitted as from the effective date onwards.

The effective date will be 1 July 2015 for extension of indication applications and line extension applications relating to existing centrally authorised medicinal products submitted as from the effective date onwards. For all other post-authorisation procedures relating to existing centrally authorised medicinal products where supporting clinical reports have been submitted, the effective date will be determined in 2015.

5. Related documents

Further information on the development and implementation of the policy is provided in a Q&A document[6].

6. Changes since last revision

Not applicable, new policy.

The policy will be revised, as appropriate taking into account the experience obtained, not later than 18 months after coming into effect.

London, 2 October 2014

Signature on file

Guido Rasi
Executive Director

[6] Q&A on the European Medicines Agency policy on publication of clinical data for medicinal products for human use (EMA/357536/2014).

Annex 1

Terms of Use for general information purposes

These Terms of Use ("***Terms***") govern the access and use of clinical data, as defined in chapter 3. of the EMA policy on publication of clinical data, Policy 0070 ("***Policy***"), that are made available to *Users* via such *Policy*. By accepting these *Terms* and upon being granted access to the *Clinical Reports*, you agree to be bound by these *Terms*. Please read them carefully.

1. Definitions

In these *Terms* the terms below have the following meaning:

"**EMA**" means the European Medicines Agency.

"**Clinical Reports**" means the clinical overviews (module 2.5), the clinical summaries (module 2.7) and the clinical study reports (module 5, "CSR"), together with appendixes to the CSRs no. 16.1.1, 16.1.2 and 16.1.9 which are accessible via the *EMA* website as a result of the implementation of the *Policy*.

"Applicant/MAH" means the natural or legal person(s) or organisation(s) that submitted the *Clinical Reports* to the *EMA* in the context of applications in support of centralised marketing authorisations/post-authorisation submissions under Regulation (EC) No 726/2004, as well as any person(s) or organisation(s) who own(s) copyright or other intellectual property rights in the *Clinical Reports*.

"**User**" means the natural or legal person or organisation who, having registered with the *EMA* website in connection with the implementation of the *Policy*, receives access to the *Clinical Reports*.

2. Access to the *Clinical Reports* under the *Policy*

The *User* acknowledges that the *Clinical Reports* are protected by copyright or other intellectual property rights of the *Applicant/MAH* and can be considered commercially valuable when used for commercial and regulatory purposes.

The *User* acknowledges that the *Clinical Reports* will be made available to the *User* on the *EMA* website in a "view-on-screen-only" mode, after completing the registration process. The *User* agrees that the *User* is not permitted to download, save, edit, photograph, print, distribute or transfer the *Clinical Reports*. The *User* agrees not to access the *Clinical Reports* using a method other than the interface provided by the *EMA*, or remove, bypass, circumvent, neutralise or modify any technological protection measures which apply to the *Clinical Reports*.

3. Use of the *Clinical Reports*

The *User* agrees to use the *Clinical Reports* according to these *Terms* and, in particular, that:

a) The *User* may use the *Clinical Reports* for general information and non-commercial purposes, including non-commercial research purposes, subject to these *Terms*.

b) The *User* is not granted any intellectual property or other commercial rights in relation to the *Clinical Reports* other than as expressly set out in these *Terms*.

When using the *Clinical Reports*, the *User* shall:

a) acknowledge that its source is the *Applicant/MAH*;

b) not use it in a way that suggests that the *Applicant/MAH* endorses the *User's* use of the *Clinical Reports* for any other purpose than general information and non-commercial purposes, including non-commercial research purposes;

c) ensure that the use of the *Clinical Reports* comply at all times with applicable law;

d) not misrepresent the source of the *Clinical Reports*;

e) not seek to re-identify the trial subjects or other individuals from the *Clinical Reports* in breach of applicable privacy laws.

The *User* may not:

- use the *Clinical Reports* to support an application to obtain a marketing authorisation and any extensions or variations thereof for a product anywhere in the world;
- share the *User's* username, password or other account details with a third party or otherwise provide a third party with access to the *User's* account;
- make any unfair commercial use of the *Clinical Reports*.

If the *User* fails to accurately complete the registration process, comply with these conditions, or uses the *Clinical Reports* in breach of these *Terms*, the rights to access and use the *Clinical Reports* will be revoked.

4. Warranties and liability

Without prejudice to any obligation of the *Applicants/MAHs* in accordance with the Union legislation:

- The *EMA* and the *Applicant/MAH* exclude all representations, warranties, obligations and liabilities in relation to the *Clinical Reports* as accessible via the *EMA* website to the maximum extent permitted by law;
- Neither the *EMA* nor the *Applicant/MAH* are liable for any errors or omissions in the *Clinical Reports* as provided via the *EMA* website and shall not be liable for any loss, injury or damage of any kind caused by its use.
- The Agency accepts no responsibility for the *User's* compliance with the *Terms*.

5. Third party rights

The restrictions and conditions and the warranty and liability provisions of these *Terms* are also made for the benefit of any and all *Applicants/MAHs* and, accordingly, each such *Applicant/MAH* may in its own right enforce these *Terms* in accordance with the provisions of the Contracts (Rights of Third Parties) Act 1999.

6. Governing law

These *Terms* and any dispute or claim arising out of or in connection with them or their subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

7. Jurisdiction

The courts of England and Wales shall have non-exclusive jurisdiction to settle any dispute or claim arising out of or in connection with these *Terms* or their subject matter or formation (including non-contractual disputes or claims).

Annex 2

Terms of Use for academic and other non-commercial research purposes

These Terms of Use ("***Terms***") govern the access and use for academic and non-commercial research purposes of clinical data, as defined in chapter 3. of the EMA policy on publication of clinical data, Policy 0070 ("***Policy***"), that are made available to *Users* via such *Policy*. By accepting these *Terms* and upon being granted access to the *Clinical Reports*, you agree to be bound by these *Terms*. Please read them carefully.

1. Definitions

In these *Terms* the terms below have the following meaning:

"**EMA**" means the European Medicines Agency.

"**Clinical Reports**" means the clinical overviews (module 2.5), the clinical summaries (module 2.7) and the clinical study reports (module 5, "CSR"), together with appendixes to the CSRs no. 16.1.1, 16.1.2 and 16.1.9 which are accessible via the *EMA* website as a result of the implementation of the *Policy*.

"Applicant / MAH" means the natural or legal person(s) or organisation(s) that submitted the *Clinical Reports* to the *EMA* in the context of applications in support of centralised marketing authorisations/post-authorisation submissions under Regulation (EC) No 726/2004, as well as any person(s) or organisation(s) who own(s) copyright or other intellectual property rights in the *Clinical Reports*.

"**User**" means the natural or legal person or organisation who, having registered with the *EMA's* website in connection with the implementation of the Policy, receives in electronic format a copy of the *Clinical Reports*.

2. Access to the *Clinical Reports* under the *Policy*

The *User* acknowledges that the *Clinical Reports* are protected by copyright or other intellectual property rights of the *Applicant/MAH* and can be considered commercially valuable when used for commercial and regulatory purposes.

The *User* acknowledges that the *Clinical Reports* will be made available to the *User* in electronic format for academic and non-commercial research purposes. Before being granted access to the *Clinical Reports* in electronic format, the *User* shall provide the EMA with:

- An e-mail address,
- A place of address in the European Union; in the event that the *User* does not have a place of address in the European Union and wishes to avail itself of the services of a third party resident or domiciled in the European Union, such third party shall be considered *User* for the purposes of these *Terms* and shall comply with all the terms hereof,

- Elements concerning the identity of the user (i.e. name, date of birth, passport or ID card number, expiry date of the document; for juridical persons, the affiliation and position within the organisation of the user should also be provided).

3. Use of the *Clinical Reports*

The *User* agrees to use the *Clinical Reports* according to these *Terms* and, in particular, that:

a) The *User* may use the *Clinical Reports* solely for academic and non-commercial research purposes, subject to these *Terms*.

b) The *User* is not granted any intellectual property or other commercial rights in relation to the *Clinical Reports* other than as expressly set out in these *Terms*.

The *User* may not:

- use the *Clinical Reports* to support an application to obtain a marketing authorisation and any extensions or variations thereof for a product anywhere in the world;
- share the *User's* username, password or other account details with a third party or otherwise provide a third party with access to the *User's* account;
- make any unfair commercial use of the *Clinical Reports*;
- seek to re-identify the trial subjects or other individuals from the *Clinical Reports* in breach of applicable privacy laws.

For the avoidance of doubt, the *User* is permitted to download, save and print the *Clinical Reports*, subject to these *Terms*.

If the *User* fails to accurately complete the registration process, comply with these conditions, or uses the *Clinical Reports* in breach of these *Terms*, the rights to access and use the *Clinical Reports* will be revoked.

4. Warranties and liability

Without prejudice to any obligation of the *Applicants/MAHs* in accordance with the Union legislation:

- The *EMA* and the *Applicant/MAH* exclude all representations, warranties, obligations and liabilities in relation to the *Clinical Reports* as made accessible to the *Users* to the maximum extent permitted by law;
- Neither the *EMA* nor the *Applicant/MAH* are liable for any errors or omissions in the *Clinical Reports* as made accessible to the *Users* and shall not be liable for any loss, injury or damage of any kind caused by its use.
- The Agency accepts no responsibility for the *User's* compliance with the *Terms*.

5. Third party rights

The restrictions and conditions and the warranty and liability provisions of these *Terms* are also made for the benefit of any and all *Applicants/MAHs* and, accordingly, each such *Applicant/MAH* may in its own right enforce these *Terms* in accordance with the provisions of the Contracts (Rights of Third Parties) Act 1999.

6. Governing law

These *Terms* and any dispute or claim arising out of or in connection with them or their subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the law of England and Wales.

7. Jurisdiction

The courts of England and Wales shall have non-exclusive jurisdiction to settle any dispute or claim arising out of or in connection with these *Terms* or their subject matter or formation (including non-contractual disputes or claims).

Annex 3

Information contained in the sections of the clinical reports that may be considered CCI

The information contained in the clinical reports that may be considered CCI and the reference to the relevant sections is provided in the table below. Guidance described in column 2 advises what should be discussed in case of information that may be considered CCI.

Title	Information that may be considered CCI	Justification for redaction
Elements relating to clinical trials and contained in "The common technical document for the registration of pharmaceuticals for human use" (from ICH harmonised tripartite guideline, Module 2 and 5)		
Product Development Rationale *Information expected to be found in section 2.5.1 of the clinical overview as per ICH M4(R3) guideline*	• "Describe the clinical development programme of the medicinal product, including ongoing and planned clinical studies and the basis for the decision to submit the application at this point in the programme…." • "Regulatory guidance and advice from outside the EU should be identified, with discussion of how that advice was implemented." • "Formal advice documents (e.g., official meeting minutes, official guidance, letters from non EU regulatory authorities) should be referenced…."	• Information for planned clinical studies may include "exploratory endpoints" that are not intended to yield data in support of the then-current approval of a use or indication, but could provide clues to potential uses and indications for competitors. • Regulatory advice from outside the EU is typically non-public and includes agreements with regulators on study design, strategies for organisation and presentation of findings, and other aspects of the regulatory process that competitors could copy. • Same justification as above.
Overview of Biopharmaceutics *Information expected to be found in section 2.5.2 of the clinical overview as per ICH M4(R3) guideline*	• Detailed assay information/quantitative composition/lot numbers	• As the Biopharmaceutical Summary Documents (2.7.1) are considered CCI, this section may contain some overlapping information.
Overview of Clinical Pharmacology *Information expected to be found in section 2.5.3 of the clinical overview as per ICH*	• Stereochemistry issues.	• Competitors could gain a detailed understanding of the stereoisomers and three-dimensionality of the molecule.

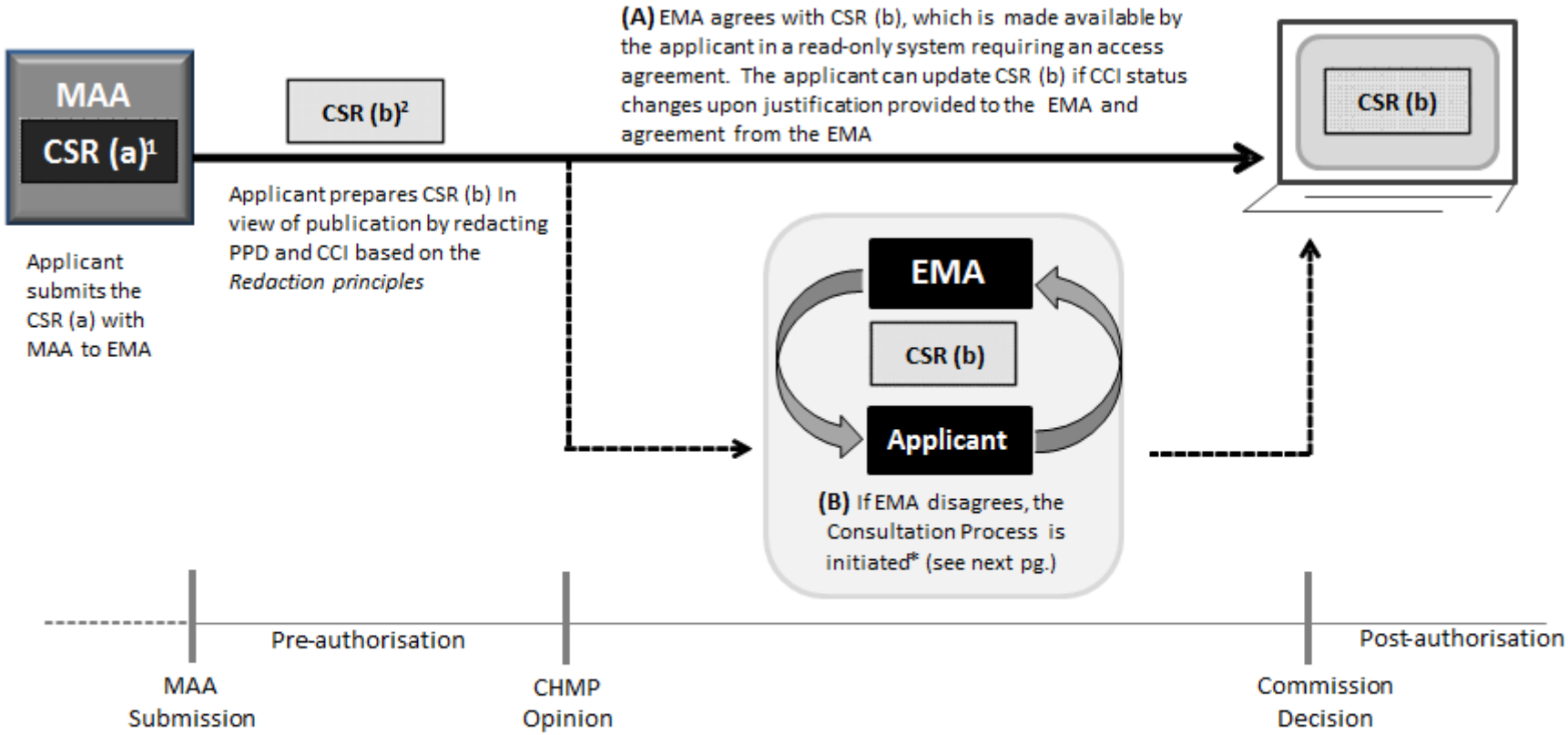
Title	Information that may be considered CCI	Justification for redaction
M4(R3) guideline		
Benefits and Risks Conclusions *Information expected to be found in section 2.5.6 of the clinical overview as per ICH M4(R3) guideline*	• Implications of any deviations from non EU regulatory advice or guidelines.	• The company may include justifications for any deviation from regulatory advice or guidance outside of the EU jurisdiction, a competitor may have an unwarranted new perception of the regulatory risk associated with a certain regulatory strategy.
Summary of Biopharmaceutic Studies and Associated Analytical Methods *Information expected to be found in section 2.7.1 of the clinical summary as per ICH M4(R3) guideline*	• Information about specifications on company assays.	• This section may contain CCI in the form of details and specifications on assays developed by the company. The information may bring significant advantages to competitors if published.
Summary of Clinical Pharmacology Studies *Information expected to be found in section 2.7.2 of the clinical summary as per ICH M4(R3) guideline*	• Information about specifications on company assays and immunogenicity assays.	• This section may contain CCI in the form of details and specifications on assays developed by the company. The information may bring significant advantages to competitors if published.
Reports of Biopharmaceutic Studies *Information expected to be found in section 5.3of module 5 "Clinical study reports" as per ICH M4(R3) guideline*	• Information about specifications on company assays by which the results of the studies (e.g. Bioavailability, In Vitro – In Vivo Correlation) are obtained. • Information about company innovative bioassays/analytical methods.	• This section may contain CCI in the form of details and specifications on assays developed by the company. The information may bring significant advantages to competitors if published.

Title	Information that may be considered CCI	Justification for redaction
Structure and content of clinical study reports (CSRs) (from ICH harmonised tripartite guideline, E3)		
Introduction *Information expected to be found in section 7 of the clinical study reports as per ICH E3 guideline*	• Development of the protocol or any other agreements/meetings between the sponsor/company and non EU regulatory authorities that are relevant to the particular study, should be identified or described.	• May contain non-public information that the sponsor agreed in another jurisdiction outside of the EU.
Study Objectives (including Exploratory Endpoints and Efficacy and Safety Variables) *Information expected to be found in sections 8 and 9.5 of the clinical study reports as per ICH E3 guideline*	• Statements/descriptions relating to objectives that are not supportive of a label claim and they were not taken into consideration in the overall benefit/risk evaluation. This includes the definition of efficacy and safety variables collected and analysed in support of exploratory objectives.	• The exploratory study objectives could be used by a competitor to gain insights into additional future study plans and/or indications for the product. For example, in some trials for a new anti-inflammatory medicinal product, an exploratory lipid profile was included, investigating the lipid metabolism in patients treated with the product, to inform future studies rather than to support the MAA. The results of these analyses were included in the CSRs submitted to the EMA in the course of the MAA procedure. • Alternatively the exploratory objectives may include biomarkers that could be used as 'hypothesis generating' for future studies. At that stage there would not be enough information to file patent applications on these objectives until some data are available from clinical and non-clinical studies. Disclosing these exploratory objectives may preclude obtaining patents that would cover biomarkers/diagnostics themselves, as well as method of use patents directed to

Title	Information that may be considered CCI	Justification for redaction
		patient subpopulations.
Determination of Sample Size *Information expected to be found in section 9.7.2 of the clinical study reports and appendix 16.1.9 as per ICH E3 guideline*	• Analysis of the information that drives the sample size calculation (e.g. estimates of endpoint variability, measurement precision, screening and retention rates).	• The sample size per se is not considered CCI. However there may be occasions when the intellectual consideration that goes into the analysis of the information that drives the sample size calculation (e.g. estimates of endpoint variability, measurement precision, screening and retention rates) is considered CCI.
Method of PK/PD determination *Information expected to be found in section 9.5.4 of the clinical study reports as per ICH E3 guideline*	• CCI on analytical methods.	• This section may have proprietary information on how analyses are performed.

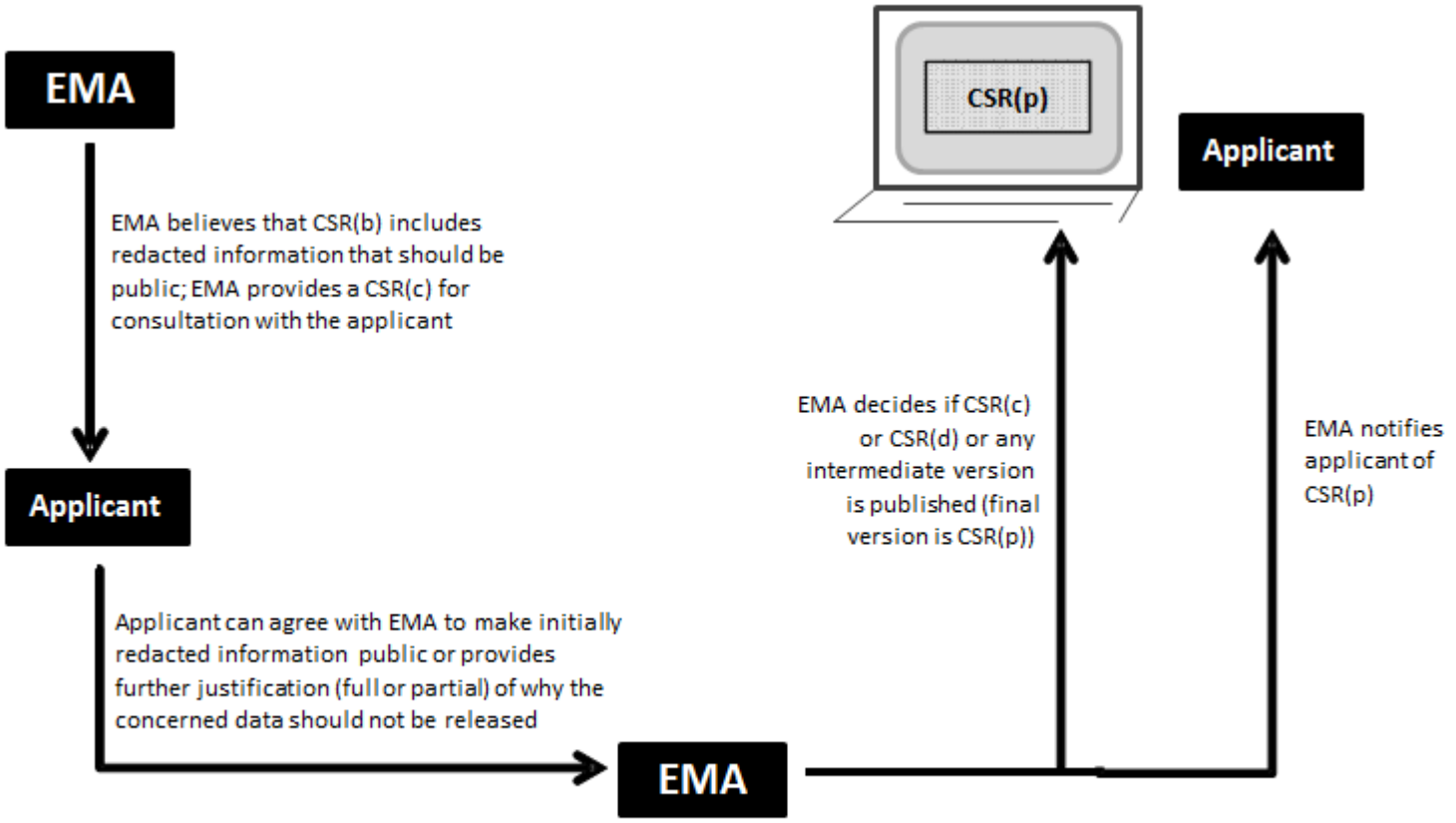
Annex 4

Process for publication of clinical reports (scenario: MAA)



1. CSR (a) = CSR in accordance with EMA guidance (1995 and 2004)
2. CSR (b) = CSR available under the EMA policy

*Consultation process



* Consultation process to be concluded within Decision making process timelines – exact timing still to be determined.