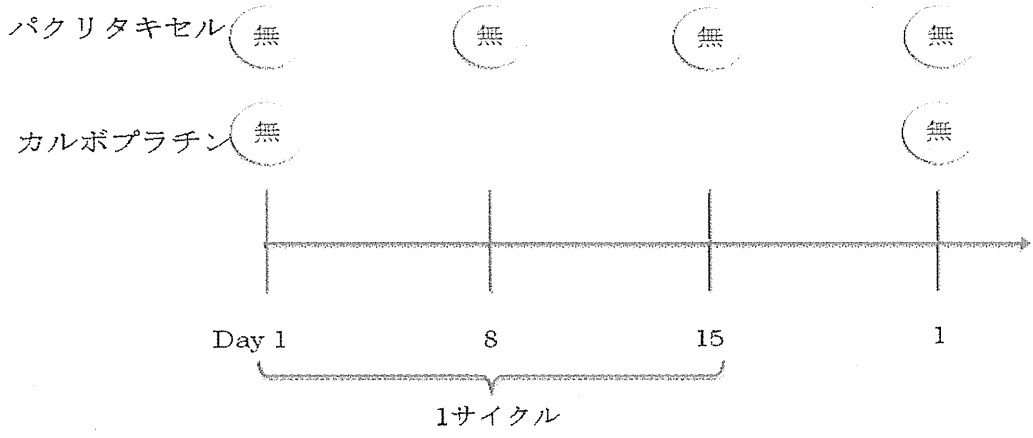
【治療法Ⅱ：パクリタキセル毎週静脈投与＋カルボプラチン腹腔内投与の場合の薬剤費】



【患者さんの費用負担の内訳】

	ポート挿入費用(手術時)	カルボプラチン薬剤費	パクリタキセル薬剤費
治療法①：パクリタキセル毎週静脈投与＋カルボプラチン静脈内投与の場合	不要	保険診療	費用負担なし (無償提供される薬剤を使用)
治療法②：パクリタキセル毎週静脈投与＋カルボプラチン腹腔内投与の場合	保険診療	費用負担なし (無償提供される薬剤を使用)	費用負担なし (無償提供される薬剤を使用)

□副作用や事故が起きたときの対応について

治療は慎重に進めますが、試験の期間中または終了後にこの治療に関連した健康被害が生じる可能性があります。この臨床試験によって身体や精神に障害がおきた場合、それに対する金銭的な補償は、抗がん剤の効果を調べる他の臨床試験と同様に原則として行なわれません。ただし、何らかの障害が起きた場合には、すみやかに適切な処置と治療をもって対応させて頂きます。その際の医療費の負担は健康保険診療内で患者さんの一部負担となります。

なお、本試験は臨床試験保険（賠償保険）に加入しております。この保険は、試験を実施する手順が記載されている試験実施計画書の内容に不備があったた

めに起こった健康障害等が補償の対象となります。また、試験の期間中だけでなく、試験治療が終了した後でもこの試験に関係すると疑われる健康障害が生じた時は担当医師にご相談ください。

□試験に参加する患者さんへのお願い

試験の期間中は、この治療法の正しい評価とあなた自身の安全のためにも必要な検査にご協力ください。また、試験期間中に体調に異常を感じた時には出来るだけ早めに試験担当の医師の診察をお受けください。やむを得ず他の病院にかかられるときには、試験に参加していることを伝えていただくとともに当院の担当医師にもご連絡ください。また、現在他の薬（市販薬、サプリメントを含む）を飲まれている場合は、必ず担当医師にお知らせください。

この臨床試験に関することでご質問がありましたら、いつでも遠慮なく担当医師にお尋ねください。

□腹腔リザーバーポート挿入した患者さんへのお願い

極まれに空港のゲートなどの金属探知機にかかる可能性があります。そのため、診断書とポートキットに一緒に入っているポートが留置されていることを示すカードの携帯をお薦めいたします。

なお、ポートを挿入している間にレントゲン/MRI/CT 等の検査を実施する場合、安全に実施していただけますのでご安心下さい。

□この臨床試験の倫理的な審査について

この臨床試験は、多くの医学専門家によって十分に検討されたものです。さらに、病院内の臨床試験審査委員会において、患者さんの権利と健康を守ることへの配慮がなされていることが確認され、承認を得ています。臨床試験に関わる職員も、患者さんの人権を守ることを意識して対応致します。もし、患者としての人権に関して何かお尋ねになりたいことがありましたら、下記までご連絡下さい。

なお、平成 21 年 4 月以降開催される臨床試験審査委員会の手順書、委員名簿、委員会の議事録要旨などはすべて公開されることになりましたので、お知りになりたい場合はお問い合わせ下さい。なお、これらの情報につきましては、当院ホームページにも掲載していますのでご参照ください。

この臨床試験を審査した委員会

- 名称：　埼玉医科大学国際医療センター病院アイアールビー
- 設置者：　病院長　小山勇
- 所在地：　埼玉県日高市山根　1397-1
- ホームページアドレス：　http://www.saitama-med.ac.jp/kokusai/

この臨床試験の責任医師の連絡先は、次のとおりです。

試験責任医師

- 氏名：　藤原　恵一
- 連絡先（所属）：　婦人科腫瘍科　(職名)　教授
- 電話番号：　042-984-4111

また、この試験に関する不満や苦情などについても、この試験に直接関与していない中立的な立場にある者がお伺いしますので、いつでも下記の「患者さ担当」にお気軽にご相談下さい。

患者さん担当

担当者名：　石井　正幸
所属：　臨床試験支援センター　(職名)　次長
電話番号：　042-984-4523

口研究資金と利益相反について

この臨床試験は、平成 21 年度厚生労働科学研究費補助金(主任研究者：埼玉医科大学国際医療センター　藤原恵一)を主たる研究資金とし、また会議費やモニタリング費用などの研究経費の一部については GOTIC（一般社団法人　北関東婦人科がん臨床試験コンソーシアム）および JGOG（婦人科悪性腫瘍研究機構)より資金提供を受けています。GOTIC および JGOG は、いずれも企業から目的を限定しない寄付金や教育研修費などの資金提供を受けています。

厚生労働科学研究費は主任研究者が所属する組織の事務担当者のもとに適切に管理されます。

埼玉医科大学国際医療センターでは、この臨床試験に係るすべての医師がこの試験を行うことによって個人的な利益に結びつく可能性のある状態（これを利益相反といいます。たとえば、研究者がこの試験に関係のある製薬企業の高額の株式保有や多額の寄付金などを得ている状態をいいます。）にないことを確認しています。また、藤原班の班員およびこの臨床試験のデータ管理に係る iPocc コーディネーティングセンター（北里大学臨床薬理研究所）の担当者、

およびすべての研究実施施設の医師は、「本試験に係る利益相反」について所属機関の規定に則り、利益相反審査委員会または倫理審査委員会などの審査を受けています。さらに、この試験の結果を公表する際には、発表者となる全ての研究者の利益相反について、「この試験の結果が研究者の個人的な利益に結びつく状況にないか」という観点から、GOTIC および JGOG の COI 委員会において事前に審査が行われます。

□試験内容の公開

試験を広く一般に公開することを目的に本試験は臨床試験登録＝UMIN（University Hospital Medical Information Network）：http://www.umin.ac.jp/ctr/index-j.htm および clinical.gov： http://clinicaltrials.gov/ に登録をしています。試験の内容や進捗状況、結果等について誰でもウェブより確認することが可能です。

□おわりに

この臨床試験に参加するか否かは、あなたの自由な意思にお任せします。何かわからないことがありましたらいつでも遠慮なく担当医にお尋ね下さい。

ゆっくりと考えた上で、この臨床試験に参加して頂ける場合には、次ページの同意書に署名と日付を記入して担当医師にお渡し下さい。あなたの控え用として同意書のコピーをお渡しいたします。この説明書をよく読んで頂き、試験に参加して頂けるかどうかご検討頂ければ幸いです。

同意書

埼玉医科大学国際医療センター　病院長　殿

説明年月日：平成　　年　　月　　日

説明した医師

科名　婦人科腫瘍科

医師名(署名)

私は自分自身の意思によって「上皮性卵巣癌、卵管癌、腹膜原発癌に対するPaclitaxel毎週点滴静注＋Carboplatin3週毎点滴静注投与とPaclitaxel毎週点滴静注＋Carboplatin3週毎腹腔内投与のランダム化第II/III相試験」に参加することに同意します。

これは口頭と文書により以下の項目について詳しい説明を受け納得した上で、私自身がこの臨床試験へ参加することに同意するものです。

1. 試験の目的
2. この臨床試験に参加する予定の患者数と試験期間
3. この臨床試験の背景
4. 具体的な治療の方法
   （腹腔内投与群になった場合は 腹腔用リザーバーポートを設置すること）
5. 予想される副作用
6. 他の治療法の有無および内容
7. 同意しない場合でも不利益を受けないこと
8. 同意した場合でもいつでもこれを撤回できること
9. 試験に関する情報提供が行われること
10. 個人情報の保護に関すること
11. 費用の負担は、保険を使用する部分と使用しない部分があること
12. 副作用や事故が起きた時の対応、補償について
13. この臨床試験の倫理的な審査について
14. 研究資金と利益相反について
15. その他

上記項目について、担当医師から詳細な説明を受け理解し納得しましたので、この臨床試験に参加して治療をうけることに同意します。

なお、私は『この試験における費用の調査』には、

□　参加します

□　参加しません　(ただし、費用の調査以外はこの試験に参加します)

年　月　日

患者さん氏名(自署)　　日付（同意年月日）

年　月　日

代諾者（又は法的代理人）氏名　　日付（同意年月日）　患者との関係

＊[必要時のみ記載] (自署)

上記の試験について私が十分に説明を行ない、同意が得られたことを確認し、説明書ならびに同意書の写しをお渡ししました。

年　月　日

担当医師名(自署)　　日付（手交日）

同意説明文書例

英語版

iPocc Trial

IntraPeritoneal therapy for Ovarian Cancer with Carboplatin

GOTIC-001 / JGOG3019

A RANDOMIZED PHASE II/ III TRIAL OF INTRAVENOUS (IV) PACLITAXEL WEEKLY PLUS IV CARBOPLATIN ONCE EVERY 3 WEEKS VERSUS IV PACLITAXEL WEEKLY PLUS INTRAPERITONEAL (IP) CARBOPLATIN ONCE EVERY 3 WEEKS IN WOMEN WITH EPITHELIAL OVARIAN, FALLOPIAN TUBE OR PRIMARY PERITONEAL CANCER

Patient Information Sheet

Introduction

At Saitama Medical University International Medical Center, we conduct experimental treatments called clinical trials with the purpose of providing you with the latest forms of treatment. "Clinical trial" refers to research conducted with the cooperation of patients in order to find out if the new treatments or drugs are effective against certain diseases. It is essential for the advancement of disease treatment that information and data are obtained by means of clinical trials. All of the drugs and treatments we are currently using are results of accumulated clinical trials.

In a clinical trial, the effects and safety of the new treatment are investigated with the consent of the patients while strictly adhering to the protocol. The clinical study we are asking you to participate in investigates which administration methods are effective if one of the two drugs in the combined anticancer drug therapy, which has already been in use for patients with ovarian cancer is changed from intravenous to peritoneal administration. It is not known at present which of these routes are more effective.

This is an international trial, GCIG (Gynecologic Cancer Intergroup). In Japan, this trial is conducted by a research organization called GOTIC (Gynecologic Oncology Trial and Investigation Consortium), who specializes in the research on gynecologic cancer, in cooperation with JGOG (Japanese Gynecologic Oncology Group).

Saitama Medical University International Medical Center: Gynecologic Oncology is conducting this clinical trial as an institution which has been given participation approval.

This clinical study is called the iPocc study.

Regarding the participation in this study

We are giving explanations on this clinical study and asking you to consider participating in this study since your condition fits the criteria for patients who participate in this clinical study. You are free to decide whether to participate in this study or not. You may consult other medical professionals. Your decision not to participate in this study does not affect the relationship with your treating doctor or result in disadvantages such as not being able to undergo treatments. In addition, you are free to cancel the participation in the clinical study after the study has started.

Regarding consent

Please decide voluntarily whether to participate in this study or not, after being given sufficient explanation of the clinical study from your treating physician and having fully understood this explanation. You may consult your family and friends. Please take time in considering this matter.

Objectives of this clinical study

This clinical study involves 2 types of treatments (both treatments use the same drugs, however the administration route is different with intravenous or peritoneal administration) using 2 types of drugs called paclitaxel and carboplatin and aims to compare the effects and the adverse effects of these treatments in patients who are diagnosed with stage II, III, and IV epithelial ovarian cancer; fallopian tube cancer; or primary peritoneal cancer in order to investigate which treatments are better for the patients. The details of the study are explained later.

The following explanations apply to patients with ovarian cancer; however, epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer are all very similar in nature. Peritoneal cancer occurs in the peritoneum and fallopian tube cancer occurs from the epithelium of the fallopian tube, however these disorders have the same etiology as the epithelial ovarian cancer. It is known that chemotherapy (therapy using anti-cancer drugs), which is effective in ovarian cancer, is also effective in these types of cancer.

If you have been diagnosed with fallopian tube cancer or primary peritoneal cancer, replace the words "ovarian cancer" with "fallopian tube cancer" or "primary peritoneal cancer" while reading this information.

Estimated number of patients who participate in the study and the planned study period

This clinical study started in May 2010 in Japan. Approximately 746 patients with the same condition as you will be participating in the study. The treatment period will vary for each patient; however, it will be about 5 to 7 months. There is a follow-up period of about 3 years set aside after the treatment for regular observation of the patient conditions.

Background of this clinical study

As early diagnosis methods have not been established for ovarian cancer and symptoms are difficult to detect in the early stage, 60% or more of the

patients diagnosed with the disorder already have cancer spread across their abdomen. For this reason, ovarian cancer is considered one of the cancers that are relatively difficult to treat.

The standard treatment (which is considered the best treatment at present) for advanced ovarian cancer involves surgical removal of the tumor followed by the administration of anti-cancer drugs. Usually, two types of drugs, paclitaxel and carboplatin are administered as intravenous drip every 3-4 weeks for approximately 6 times. However in reality, more than half of the patients experience a recurrence of the cancer after this treatment, and development a more effective treatment is in urgent need.

In 2008, the result of a Japanese clinical study was reported that compared (i) traditional treatment involving intravenous drip of paclitaxel and carboplatin every 3 weeks, and (ii) new treatment where a relatively small dose of paclitaxel is administered intravenously every week and carboplatin is administered by intravenous drip every 3 weeks. The results showed improved prognosis in patients who had undergone the new treatment (ii). This finding has gotten attention globally.

Ovarian cancer often spreads to the whole of the abdominal cavity (the abdomen). For this reason, the method of administering anti-cancer drugs into the abdominal cavity was developed a few decades ago. This method is expected to be highly effective, as it involves application of a much higher concentration of anti-cancer drugs compared to intravenous administration directly to the tumor. Also, the adverse reaction in this treatment are expected to be lighter compared to intravenous administration where the anti-cancer drugs only take effect after spreading to the whole body.

In the last 10 years or so, a large number of patients with ovarian cancer from Europe and the United States have participated in a number of clinical studies on the peritoneal administration of anti-cancer drugs. The results have demonstrated that risk of death in patients with ovarian cancer is decreased by 21.6% for peritoneal administration of anti-cancer drugs when compared with intravenous administration. The findings are attracting major attention. From the results of clinical studies that have been conducted up to now, the treatment method considered most effective is (iii) 3-weekly intravenous administration of paclitaxel and 3-weekly peritoneal administration of cisplatin (platinum preparation in the same group as carboplatin) and paclitaxel. However, this treatment is associated with strong adverse reactions, such as nausea, vomiting, or abdominal pain, and

because of this a treatment with less adverse reactions is being investigated currently. Of the newly investigated treatments, combination therapy of intravenous paclitaxel and peritoneal carboplatin is one of the therapies with the high expectations. A number of small-scale clinical studies have been conducted for this treatment in Japan already, and satisfactory results have been reported, along with a small incidence of adverse effects. However, at present it is not known whether intravenous administration or peritoneal administration is more beneficial.

Therefore, in order to establish a more effective chemotherapy with fewer adverse reactions, we have planned this clinical study to compare the following:

Treatment I:

Weekly intravenous drip of paclitaxel with relatively small dose, combined with 3-weekly intravenous drip of carboplatin

Treatment II:

Weekly intravenous drip of paclitaxel with relatively small dose, combined with 3-weekly peritoneal administration of carboplatin

Specific details regarding this clinical study

1. Drugs used

In this clinical study, the patients will be treated with 2 drugs, paclitaxel and carboplatin, which are both used widely across the world for treating ovarian cancer. These drugs are also used widely for other types of cancer.

2. Requirements and procedures before the start of the study treatment

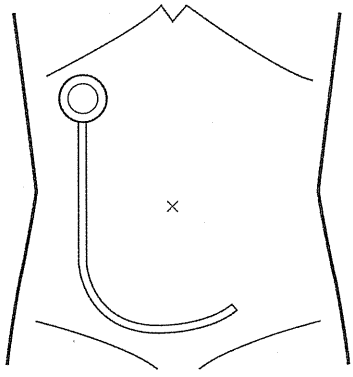
If you agree to participate in the study, we will conduct examination such as blood tests and ECG before the surgery to check if your current condition is suitable for this study. In some cases, we may use the results of examinations that have been conducted before your consent is obtained for study participation. If we find from the examination results that you are not suitable for participation in this study, your participation will be cancelled even if you agreed to participate. This will also apply to cases where the surgery results indicate that you are not suitable for participating in this study. In these cases, your treating physician will explain other treatments that are considered the best for you.

If you are participating in this study, a decision must be made during (or after) the surgery as to whether carboplatin is administered intravenously

or via the abdomen. The type of treatment you will undergo will be determined not by yourself or your treating physician, but by neutral means using a computer (called randomization) in order to eliminate bias at a third party institution (Kitasato University Research Center for Clinical Pharmacology, Clinical Trial Coordinating Center: iPocc Trial Center, 5-9-1 Shirokane, Minato-ku, Tokyo Japan). The patients will be allocated so that the conditions of the patients (stage, tumor size, etc.) in the treatment groups will be uniform to the extent possible, in order to compare the two treatment types. You may question why the patients or the treating physicians cannot make choices on the treatment method used; however, this method is adopted in clinical studies worldwide as being the best method of investigating what types of treatment are most effective or beneficial.

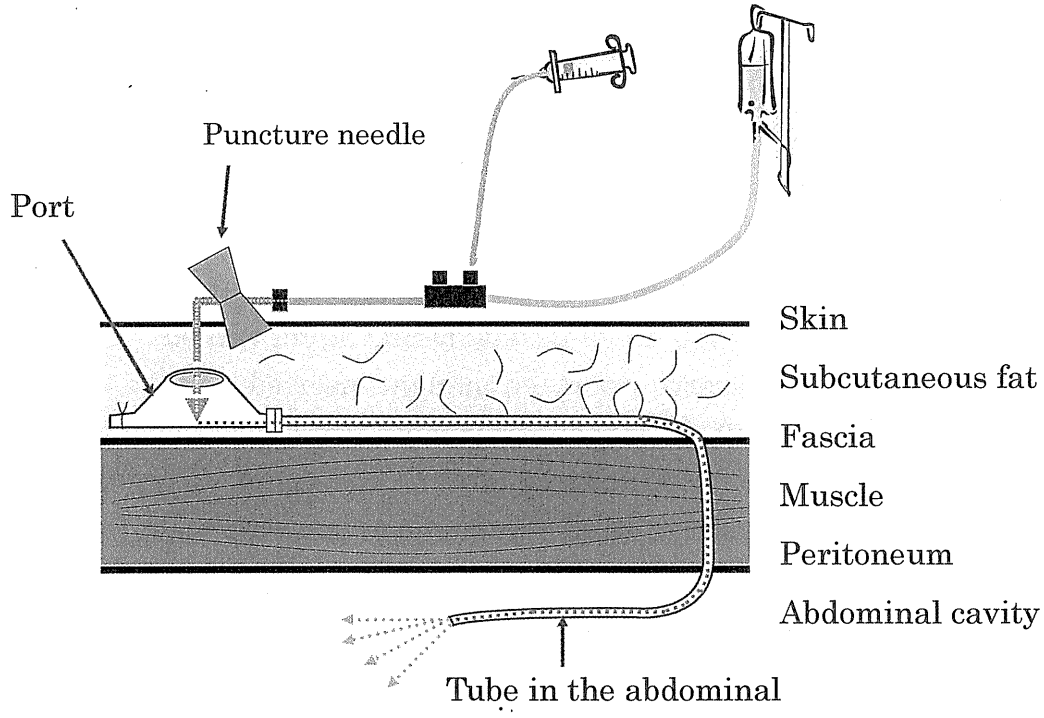
In order to administer anti-cancer drugs into the abdominal cavity, the peritoneal reservoir port becomes necessary. The peritoneal reservoir port is the equipment for administering anti-cancer drugs into your abdomen, and is implanted under the skin of the abdomen (please refer to the figure below). In this figure, the equipment is implanted in the right upper abdomen; however, in actual practice, it will be placed in a location considered optimal for the patient. Some patients may experience some discomfort in the location where the peritoneal reservoir port is implanted. However, the implant does not usually cause pain or impact daily activities such as having a bath. The equipment will be removed from the body if the implanted reservoir does not function properly, cause infections, or if all scheduled study treatment has been completed. Because the implanted equipment usually does not have a special impact on life, there is no need to remove the equipment if you do not wish to have it removed.

Peritoneal reservoir port in the abdomen



A part of the equipment implanted under the skin (the circular part) enables multiple injections. Carboplatin is injected into the abdomen from here.

Carboplatin will travel through the tube and spread to whole of the abdomen. The injected Carboplatin will be naturally absorbed by the body over approximately 24 hours and removed from the abdomen.



Whether Carboplatin is administered intravenously or via the peritoneum will be determined during laparotomy. The reason for this is that the clinical study involves stage II, III, and IV patients, and the stages of the ovarian cancer cannot be diagnosed without laparotomy. The peritoneal reservoir port will be implanted during the surgery only in patients who

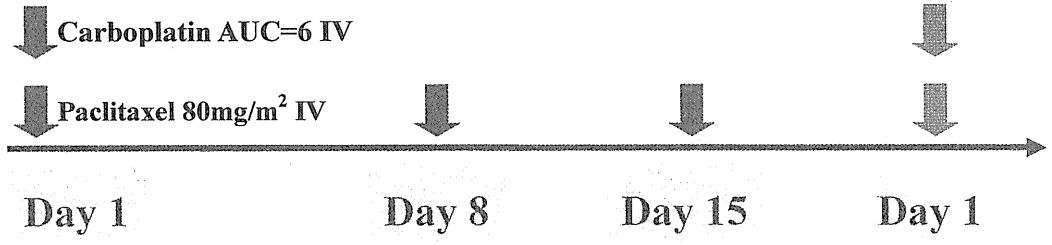
were allocated to peritoneal Carboplatin administration by randomization. Implant of peritoneal reservoir port will not be conducted for patients who are allocated to intravenous carboplatin administration.

In some patient, placement of the IP port may be performed after surgery.

3. Study treatment methods

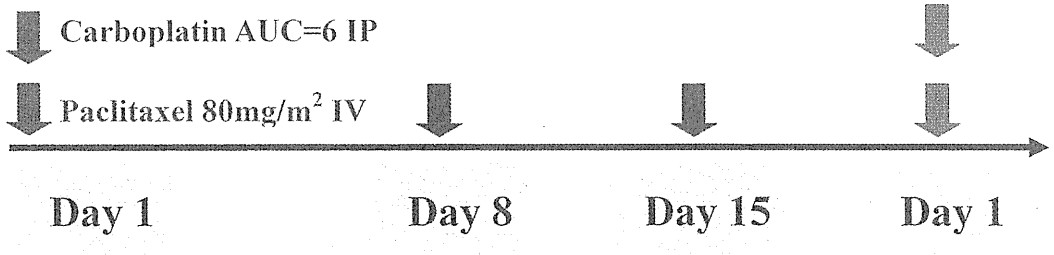
Treatment method (i): For intravenous administration of carboplatin

On day 1, paclitaxel is administered as an intravenous drip over 1 hour, then carboplatin is administered as an intravenous drip. Following this, on days 8 and 15, paclitaxel is administered as an intravenous drip over 1 hour. Three weeks of treatment are set as 1 cycle and this treatment is repeated for 6-8 cycles.



Treatment method (ii): For peritoneal administration of carboplatin

On day 1, paclitaxel is administered as an intravenous drip over 1 hour, and at the same time 1000-1500 mL of normal saline liquid will be administered through the reservoir port (equipment inserted into the abdomen during the surgery). After the intravenous drip of paclitaxel is complete, carboplatin will be administered into the abdominal cavity. The dose of carboplatin is the same as when administered intravenously. Following this, on days 8 and 15, paclitaxel is administered as an intravenous drip over 1 hour. Three weeks of treatment is set as 1 cycle, and this treatment is repeated for 6-8 cycles.



As described above, the only difference between the two treatments is whether carboplatin is administered as an intravenous drip or into the abdominal cavity. Depending on the occurrence of adverse reactions, the dose may be reduced or the interval of administration may be prolonged in the following treatment. If strong adverse reactions appear or the administration interval is excessively large, this treatment may be discontinued.

There are cases where patients experience nausea or allergic reactions. These will be prevented by the use of antiemetics or steroids before paclitaxel administration. Furthermore, if the tumor could not be completely removed in the surgery, another surgery may be performed after 3-5 cycles of chemotherapy. If this is the case, further 1-3 cycles of chemotherapy will be added following the surgery, resulting in a total of 6-8 treatment cycles.

4. What is being investigated in this clinical study?

The first point we want to find out in this study is which group of the patients who received (i) the combination of weekly intravenous infusion of paclitaxel and 3-weekly intravenous infusion of carboplatin, or (ii) the combination of weekly intravenous infusion of paclitaxel and 3-weekly peritoneal administration of carboplatin live longer periods without a progression of a disease of recurrence of cancer.

We will also investigate the survival period of the patients after treatment, the effect of the treatment to reduce the tumor size if tumors remain after surgery, as well as the rates of patients who have completed the treatment as scheduled and the types and severity of adverse reactions. Furthermore, we will investigate the patient's quality of life (QOL) and the cost incurred from treatment.

QOL survey will be conducted before the initial treatment, after 3 cycles of protocol treatment (or 9 weeks after the date of treatment commencement), after 6 cycles of protocol treatment (or 18 weeks after starting treatment), 36 weeks after starting treatment, 60 weeks after starting treatment, and 84 weeks after starting treatment. We ask all patients who participate in this study to fill in the QOL survey. Specifically, you will be handed the survey sheet by the QOL staff of the hospital you are attending, so please answer the questions, then hand it back to the QOL staff.

In this clinical study, the cost involved in the study will be investigated, and compared between the group being administered carboplatin intravenously and the group being administered carboplatin via the peritoneum. Regardless of the group you are allocated in, you will be asked to report the cost you pay at hospitals and pharmacies, as well as other costs such as travelling costs to the hospital.

If you are able to cooperate in this cost study, information such as the type of your insurance and amounts of hospital payments need to be send to the iPocc Trial Coordinating Center for this clinical study. In addition, you will be asked to cooperate in the regular survey on your personal payments such as pharmacies payments and traveling costs to the hospital. These data will be accumulated at the iPocc Trial Coordinating Center (Kitasato University Research Center for Clinical Pharmacology, 5-9-1 Shirokane, Minato-ku, Tokyo, Japan).

Please make your own decision on whether you will participate in the cost study for this clinical study.

If you decide to participate in this study, various examinations and symptom observations will be conducted regularly. This includes physical examination by a doctor, blood tests, urine test, imaging examinations such as CT and MRI, as well as a survey of the quality of life (QOL). All of these examinations are conducted to investigate the effects and safety of these treatments. In regards to examinations other than the QOL survey, these are conducted during normal treatments as required, even if you do not participate in this clinical study. You may find that you will undergo blood tests or imaging examinations slightly more often in the clinical studies, since these examinations are conducted more often in case adverse effects occur. After the completion of the clinical study, long-term follow-up observations need to be conducted regularly, as after the general cancer treatment.

This study is for the patients with epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer in the tissues excised by surgery. For this reason, we will submit a thin slice of this cancer tissue on a slide and specialists of the Central Pathology Committee will once again confirm the diagnosis.

5. If the study is discontinued

If you are unable to continue the study due to adverse reactions or other disorders, your participation in the study will be discontinued. If the study is discontinued due to adverse reactions, regular examinations and observations will be conducted until it disappears. Also, appropriate treatments for the adverse effects will be provided as required. The chemotherapy tumor may not work as expected, and the tumor may grow during the treatment. The study will be discontinued in such cases, and other appropriate treatments will be provided.

Expected adverse reactions

Cancer cells have disordered functions in regulating cell growth and are characteristic in that they have faster growth compared to healthy cells. Anti-cancer cells attack the cancer cells using this characteristic as the target; however, some healthy cells grow fast, and adverse effects occur from the effect of anti-cancer drugs on these cells. Typical examples are the hematopoietic cells in the bone marrow and the cells at the hair root. There is a wide variety on how adverse effects appear for individual patient, and it is impossible to predict beforehand what adverse effects are experienced by each patient.

Therefore, the treatment is carried out carefully while observing the conditions of the patients. The main adverse reactions that are generally expected to occur are as follows:

♦Reduced blood cells, such as white blood cells and neutrophils:
If the decrease of white blood cells (or neutrophils) appears strongly, the patients may be injected with drugs to increase white blood cells (neutrophils) (G-CSF preparation). The decrease in white blood cells (or neutrophils) may accompany fever or result in an increased risk of infections. Please contact immediately if you experience change of physical conditions (especially fever) during the treatment period. We will use antibiotics in case an infection occurs.

♦Anemia or decreased platelets:
If anemia becomes severe, you become more likely to experience a feeling of heaviness, fatigue, and lightheadedness. Also, since platelets have a blood-clotting function, a decrease in the platelets results in bleeding more easily. If this symptom is severe, transfusions may be required.

♦Hair loss:

Although this varies with individuals, some patients may lose so much hair that they need to wear wigs. The hair will grow back after the treatment has ended.

♦Loss of appetite, general malaise, hot flushes, nausea, and vomiting are expected to occur. These symptoms disappear after stopping the medication; however, nausea and vomiting can be relieved using drugs.

♦In addition, changed liver functions and decreased kidney functions may occur.

♦It is known that treatment with anti-cancer drugs increases the risk of developing secondary cancer, such as acute leukemia.

In addition, muscle aches and joint pain may occur as adverse effects of paclitaxel. These adverse reactions can be treated with painkillers. Also, numbness may occur in the tips of the fingers and toes. Chinese medicine with (*Goshajinkigan* and *Shakuyakukanzoutou*) may be used for numbness; however, if these symptoms affect your daily activities, Paclitaxel may be discontinued. These adverse effects are observed relatively often. Furthermore, the following adverse effects may occur, though these have lower incidences: hives, allergic reactions, abnormal pulse such as arrhythmia, diarrhea, stomatitis, changed taste sensation, headache, increased neutral fat in blood, mood changes, skin disorders (if the drug solution leaked from the blood vessels during administration), changes in visual sensation (blurring, etc.), cerebral edema, convulsions, etc. In addition, although the incidence is unknown there is a chance of interstitial pneumonia occurring. Interstitial pneumonia is inflammation of lungs caused by various drugs, and it is often treatment-resistant and may lead to death. We will observe carefully for symptoms such as breathing difficulty and coughs during the study period.

The adverse reactions of carboplatin, which are observed relatively often, are decreased white blood cells and neutrophils, and anemia. Other possible adverse effects are as follows: allergic reactions, loss of appetite, diarrhea, constipation, nausea, abdominal pain, skin rash, changed taste sensation, changed visual sensation, hand/food numbness, convulsion, ringing of the ears, decreased hearing, hearing loss, fever, decreased kidney or liver function, stomatitis, etc. In addition, interstitial pneumonia may occur though the incidence is not high.

As adverse reactions of combination therapy of intravenous paclitaxel and peritoneal carboplatin, abdominal pain may be experienced from the stimulation of inserting drugs into the abdomen. The symptoms can be suppressed using painkillers; however, if the symptoms are severe, the treatment may be changed. Also, though these are very rare, peritonitis or holes in intestinal tract may occur from implanting the peritoneal reservoir port. Appropriate actions will be carried out immediately in such cases. Other possible adverse reactions include those listed before in regards to the individual drugs.

Adverse reactions specific to peritoneal administration include the followings. In order to repeatedly administer the drugs via the abdomen, a device called a reservoir port will be implanted under the skin. This will be implanted only in patients allocated to the peritoneal administration group of this study immediately before the completion of the initial surgery. The technique is not difficult; however, it may occasionally result in hematoma. In addition, the ascites, or biological saline liquid or drugs which have been injected into the abdominal cavity, may flow back into the port. If Carboplatin flows back into the subcutaneous layer or leaks from the port, there may be needed to take actions such as steroid administration, however, such cases becoming serious matters are very rare.

Since reservoir ports are implanted in the subcutaneous fat, the section of implant sticks a little. You may experience discomfort or mild pain; however, these usually subside with time. When inserting injection needles to the port, this is conducted carefully; however, it may cause infection. If it is not appropriate to leave the port inside the body, such as in the case of severe pain in the port location and infection, the port will be removed.

There are cases where the intestinal tract becomes adhered around the catheter at the end of the reservoir port, disabling peritoneal injection. It is extremely rare that surgery is required for adhesion around the catheter; however, peritoneal administration will be discontinued nonetheless. Also, there is a possibility that hole (perforation) will form in the intestines or the sutured sections of vagina from the tip of catheter coming in contact with the location of surgery, but this is rare. If this occurs, peritoneal administration will be discontinued, and if required laparotomy will be conducted to repair the perforated location.

The reservoir port is made of materials that do not cause problems if the device is left in the body permanently in most cases. However, this can be removed after the study treatment. The device is removed usually under