4) 内田恵理子，古田美玲，菊池裕，窪崎敦隆，遊佐精一，宮原美知子，佐々木裕子，小原有弘，大谷梓，松山晃文，大倉華雪，山口照英：細胞基材に対するマイコプラズマ否定試験のPCR法の見直しに関する研究．医薬品医療機器レギュラトリーサイエンス、印刷中
5) 山口照英：バイオ医薬品の効率的製造に向けた世界動向と規制状況．BioIndustry, 30, 47-54 (2013)
6) 山口照英：再生医療の安全性確保法と薬事法改正、レギュラトリーサイエンス学会誌（RSMP）、vol.4, No.3, 237－247(2014)
7) Maeda,D., Yamaguchi,T., Ishiduka,K., Takekita,T., Sato,D.：Regulatory Frameworks for Gene and Cell Therapies in Japan. in "Reguratory Aspects of Gene Therapy and Cell Therapy Products in Japan." Springer, Serbian,M. & Galli,M.C. eds., in press
8) Hashii,N., Nakazawa,S., Tada,M., Yamaguchi,T.： Analysis of aggregation-prone regions in monoclonal antibody by hydrogen/deuterium exchange mass spectrometry. J. Pharma. Sci. in press
9) 内田恵理子，古田美玲，菊池裕，窪崎敦隆，遊佐精一，宮原美知子，佐々木裕子，小原有弘，大谷梓，松山晃文，大倉華雪，山口照英：日本薬局方参考情報収載マイコプラズマ否定試験のPCR法改正のための共同研究、マイコプラズマ学会雑誌（印刷中）
10) 内田恵理子，古田美玲，菊池裕，窪崎敦隆，遊佐精一，宮原美知子，佐々木裕子，小原有弘，大谷梓，松山晃文，大倉華雪，山口照英：細胞基材に対するマイコプラズマ否定試験のPCR法の見直しに関する研究、医薬品医療機器レギュラトリーサイエンス 45 (5), 442-451 (2014)

G-2 学会発表

1) Kishioka,Y, Sakurai,K, Yamaguchi,T.: Current Situation of Japanese Biosimilar Regulation. APEC International Symposium **Soul Korea,** (2013)

H. 知的財産権の出願・登録状況

H-1 特許取得 なし

H-2 実用新案登録 なし

H-3 その他 なし

図．1　製品群別のがんワクチンプロトコール数

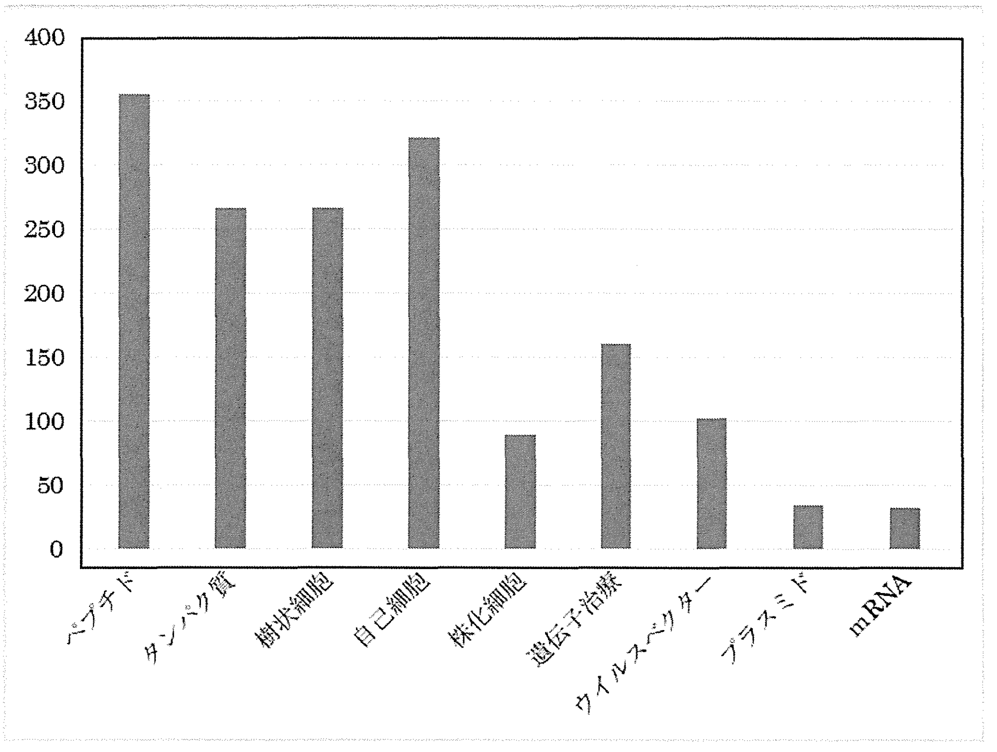

図２．Treg 細胞とその機能分子

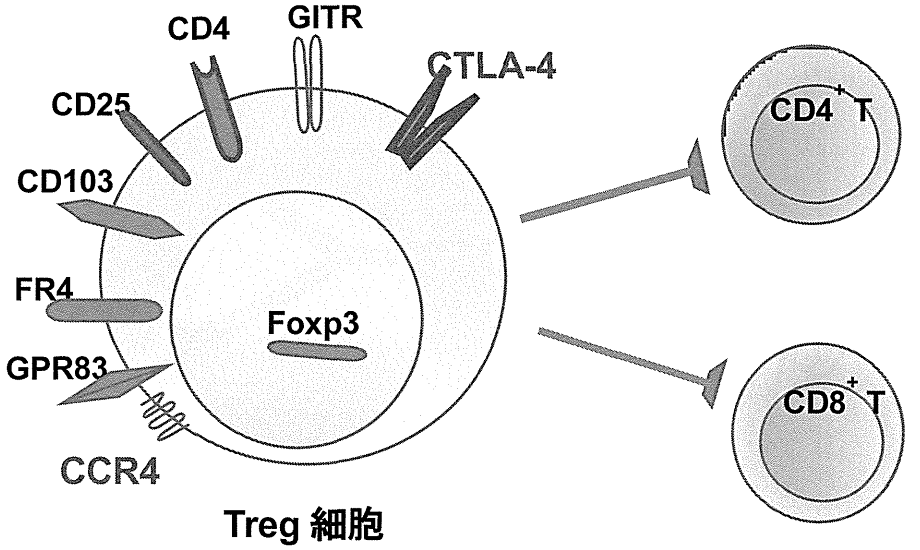

図 3.樹状細胞のクロスプレゼンテーションと CTL 活性化

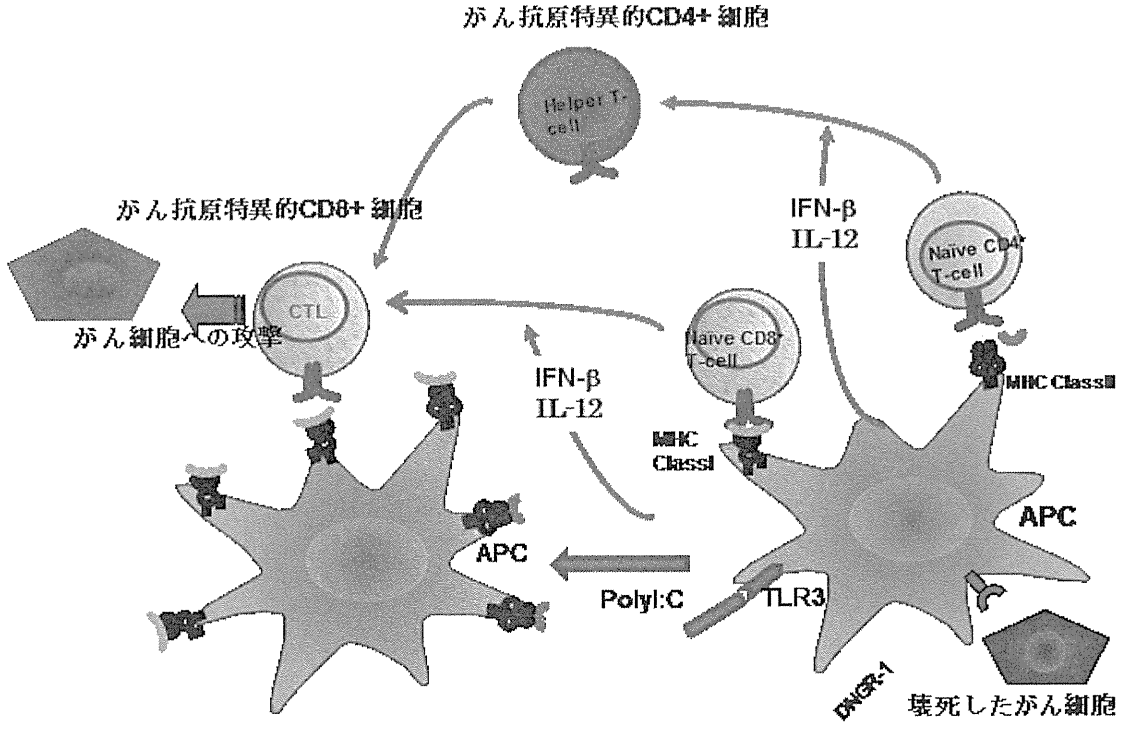

図 4. イディオタイプネットワーク仮説

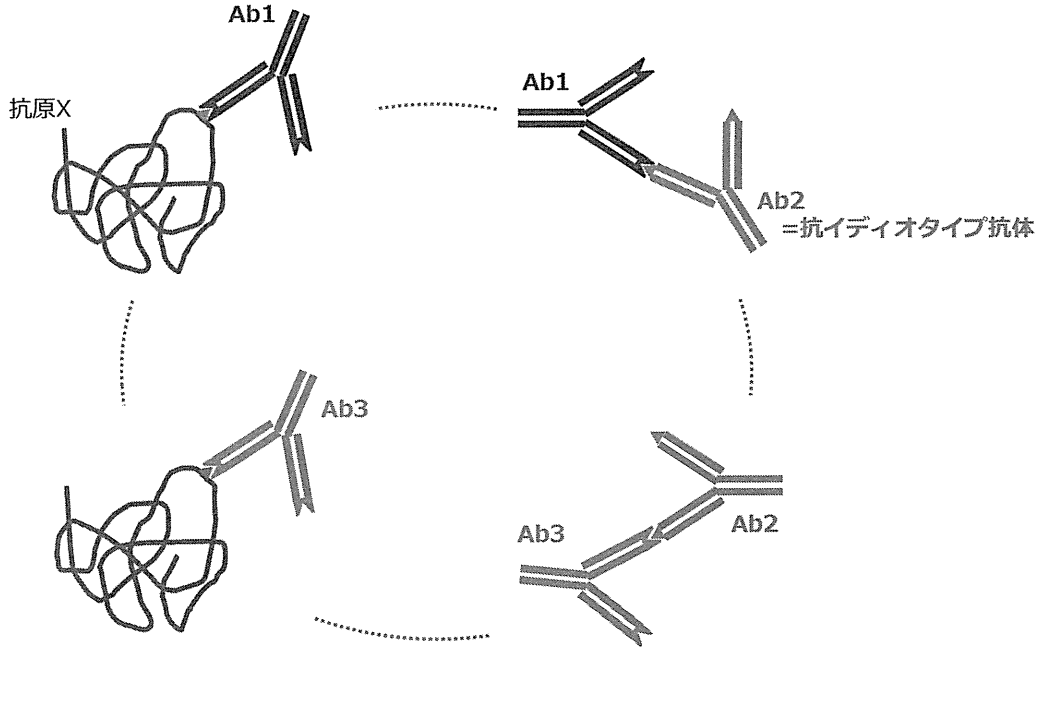

表1．がんワクチンキーポイント

- がんをワクチンで治療するという戦略が多くの難題を提起しているが、最近の成果から臨床的な有効性を示せる結果が出つつある
- がん免疫に関する理解、特に腫瘍微小環境の性質やダイナミズムの理解が進んだ
- 多くの臨床研究からは従来のがん治療とワクチンの作用がどのように異なるのか十分な情報が得られていないが、腫瘍微小環境において働くがんによる免疫抑制機構が重要な作用をしていることが明らかにされつつある
- 活性化免疫療法に対してベネフィットのある患者を選択するためのがんワクチンバイオマーカー開発が望まれている
- 臨床試験の結果から有効性が期待されるのはがんが進行していない患者集団である可能性が示唆されている
- 将来の戦略として腫瘍特異的な免疫応答を最適化するために腫瘍微小環境を制御する方法を開発するべきである

表2．がんワクチンに用いられる抗原

共通抗原
- がん精巣抗原；BAGE、GAGE、MAGE、NY-ESO-1
- 分化抗原：CEA、gp100、Melan-A、PSA、Tyrosinase
- Overexpressed antigen：HER2、hTERT、p53、survivin

特殊抗原
- Oncogene-associated antigens: β-catenin-m、HSP70-2/m、KRAS Shared antigens with unique mutations
- Glycans: GM2, MUC1

アジュバント
- Cytokine/endogenous immunmodulators: GM-CSF、IL12
- Microbes and microbial derivatives：BCG、CpG、Detox、MPL、polyI:C
- Mineral salts：Alum
- Oil emulsions or surfactants：ASO2、MF59、Montanide™ ISA-51、QS21
- Particulates：ASO4、polyactide co-glycolide、virosomes
- Viral vector：Adenovirus、vaccinia、fowlpox

表３．がん細胞が作り出す宿主免疫を抑制する物質とその作用機作

- キヌレニン：トリプトファンの代謝酵素であるインドールアミン2, 3-ジオキシゲナーゼ(IDO)がT細胞およびNK細胞の増殖を抑制するがその作用を介在しているのがキヌレニンとされる。
- アデノシン：抗炎症性T細胞反応を媒介し、Treg細胞による免疫抑制の主要メカニズムの一つと考えられている
- PGE2：肺癌などの悪性腫瘍で非常に高レベルに産生され、免疫機能をもつTreg細胞を活性化し、癌に対する患者の免疫力を弱めると考えられている
- TGFβ：T細胞の活性化、増幅、分化を阻害し、CTLや樹状細胞の活性を阻害、さらにレギュラトリーT細胞の分化を誘導する。
- VEGFA：腫瘍由来の血管新生因子であるVEGF-AとVEGF受容体の相互作用により、免疫チェック分子を誘導する重要な要素と想定されている。抗VEGF-A阻害と抗PD-1阻害抗体による併用療法によりがんの免疫抑制解除と抗腫瘍効果が発揮される報告がある。

1) Opitz CA, et al.: An endogenous tumour-promoting ligand of the human aryl hydrocarbon receptor. Nature 478, 197–203. (2011)
2) KM, Gao W, et al. Adenosine generation catalyzed by CD39 and CD73 expressed on regulatory T cells mediates immune suppression. J Exp Med. 204, 1257-1265. (2007)
3) Mizumoto N, Kumamoto T, Robson SC, et al. CD39 is the dominant Langerhans cell-associated ecto-NTPDase: modulatory roles in inflammation and immune responsiveness. Nat Med.;8:358-365. (2002)
4) Baratelli F et al.; Prostaglandin E2 induces FOXP3 gene expression and T regulatory cell function in human CD4+ T cells. J Immunol. 2005 Aug 1;175(3):1483-90.
5) Sharma S et al.: Tumor cyclooxygenase-2/prostaglandin E2-dependent promotion of FOXP3 expression and CD4+ CD25+ T regulatory cell activities in lung cancer. Cancer Res. 2005 Jun 15;65(12):5211-20
6) Walker,M.R. et al.: Induction of FoxP3 and acquisition of T regulatory activity by stimulated human CD4+. J Clin. Invest. 112, 1437-1443 (2003)
7) Voron T et al.: VEGF-A modulates expression of inhibitory checkpoints on CD8+ T cells in tumors. J Exp Med. Feb 9;212(2):139-48. (2015)

表４．臨床試験成績

免疫治療	抗原	アジュバント 免疫制御因子	対象患者	被験者数	臨床データ	論文
前立腺がん						
ワクシニアウイルスベクター と fowlpox ベクター	PSA	GM-CSF + co-stimulators	Metastatic, castration-resistant prostate cancer	125	**臨床効果** OS: 25.1 mo vs. 16.6 mo (HR 0.56; P=0.0061) PFS: 3.8 mo vs. 3.7 mo (HR 0.88; P=0.60) **免疫応答** No detectable antibody responses to PSA	Kantoff, P. W. et al. *J. Clin. Oncol.* **28**, 1099-1105 (2010). NCT01322490
アデノウイルスベクター	PSA	Vector	Recurrent/hormone-refractory prostate cancer	44	**臨床効果** Increase in PSA doubling time in 64% of patients **免疫応答** T cell response: 100% (recurrent disease) and 67% (hormone-refractory disease) of patients	Lubaroff, D. M. et al. *Cancer Res.* **72**, Abstr 2692 (2012).
mRNA: CV9103/9104, CureVac®	PSA + PSCA + PSMA + STEAP1	mRNA	Metastatic, castration-resistant prostate cancer	38	**臨床効果** Prolonged stabilization of PSA levels for individual patients **免疫応答** T cell response: 79% of patients, 58% with multiepitope responses	Kübler, H. et al. *J. Clin. Oncol.* **29** suppl., Abstr 4535 (2011).
乳がん						
Peptide: nelipepimut-S (E75), NeuVax™	HER2	GM-CSF	High-risk breast cancer, in remission after standard treatment	182	**臨床効果** 2-yr DFS:	Mittendorf, E. A. et al. *Cancer.* **118**, 2594-2602 (2012).

					Overall: 94.3% vs. 86.8% (P=0.08) Low HER2-expressing tumours: 94.0% vs. 79.4% (P=0.04) High HER2-expressing tumours: 90.3% vs. 83.3% (P=0.44)	NCT01479244
Peptide: GP2	HER2	GM-CSF	High-risk breast cancer, in remission after standard treatment	172	**臨床効果** Recurrence rate: 4.3% vs. 11.6% (P=0.41) **免疫応答** DTH: 21.5 vs. 6.0 mm (P<0.01)	Trappey, F. et al. *J. Clin. Oncol.* **31**, Abstr 3005 (2013).
肺がん						
Peptide: CIMAvax EGF	EGFR	Montanide ISA51 + CYC	Stage IIIB/IV NSCLC, after chemotherapy	80	**臨床効果** OS: Overall (vaccine vs. control): 6.5 mo vs. 5.3 mo (P=0.098) Good vs. poor immune responders: 11.7 mo vs. 3.6 mo (P=0.002) Good immune responders vs. control: 11.7 mo vs. 5.3 mo (P=0.0024) **免疫応答** Good antibody response in 51% of patients	Neninger Vinageras E. et al. *J Clin Oncol.* **26**, 1452-1458 (2008). NCT01444118
Peptide: GV1001	Telomerase	GM-CSF	Unresectable stage III NSCLC; after chemoradiotherapy	23	**臨床効果** OS: 28.8 mo PFS: Overall: 11.7 mo; Immune responders vs. non-responders: 12.2 mo vs. 6.0 mo (P=0.20) **免疫応答**	Brunsvig, P. F. et al. *Clin. Cancer Res.* **17**, 6847-6857 (2011). NCT01579188

					T cell response: 16/23 patients (69.6%)	
Viral vector (vaccinia): TG4010	MUC1	Vector + IL-2	Stage IV NSCLC, with chemotherapy	148	**臨床効果** 6-mo PFS: 43.2% vs. 35.1% (P=0.307) OS: 10.7 mo vs. 10.3 mo (P=0.59) TTP: 5.9 mo vs. 5.2 mo (P=0.070) ORR: 41.9% vs. 28.4% (P=0.082) Outcomes worse than control in subset of patients with high levels of activated natural killer cells. **免疫応答** No significant differences between study arms in cellular responses to MUC1	Quoix, E. et al. *Lancet Oncol.* **12**, 1125-1133 (2011). NCT01383148
Allogeneic tumour cell: belagenpumatucel-L, Lucanix™	Tumour cell	Anti-TGF-β	Stage II–IV NSCLC; after front-line chemotherapy	75	**臨床効果** OS: 14.4 mo; longer survival with higher (19.1 mo) vs. low (8.3 mo; P=0.0186) dose immunization	Nemunaitis, J. et al. *J. Clin. Oncol.* **24**, 4721-4730 (2006). NCT00676507
Allogeneic tumour cell: tergenpumatucel-L, HyperAcute® Lung	Tumour cell	αGT	Stage IIIB/IV NSCLC; progressive or relapsed after chemotherapy	28	**臨床効果** OS: Overall: 11.3 mo IFNγ responders vs. non-responders: 21.9 mo vs. 5.5 mo (P<0.001) **免疫応答** Increased IFNγ responses in 61% of patients	Morris, J. C. et al. *J. Clin. Oncol.* **30** suppl, Abstr 2571 (2012). NCT01774578
Anti-idiotype: racotumomab	Idiotype	Alum	Stage IIIB/IV NSCLC; after primary treatment	176	**臨床効果** OS: 8.3 mo vs. 6.3 mo (P=0.02)	Macías, A. et al. *Ann. Oncol.* **23** suppl 9, Abstr 1238PD (2012).

						NCT014604722
メラノーマ						
Peptide	survivin	Montanide ISA51 + CYC	Metastatic, treatment-refractory stage IV melanoma	61	**臨床効果** OS: Overall: 9.1 mo Immune responders vs. non-responders: 19.6 mo vs. 8.6 mo; P=0.0077) PFS: Overall: 2.8 mo **免疫応答** T cell responses in 13/41 (32%) patients	Becker, J. C. et al. *Cancer Immunol. Immunother.* **61**, 2091-2103 (2012).
Peptide	gp100 + MART-1 + tyrosinase	GM-CSF + Montanide ISA51	Metastatic melanoma	22	**臨床効果** OS: 13.4 mo PFS: 1.9 mo **Immunologic** T cell responses in 9/20 (45%) patients	Tarhini, A. A. et al. *J. Immunother.* **35**, 359-366 (2012).
Dendritic cell	gp100 + MAGE-A1, A2, A3 + MART-1 + tyrosinase	KLH	Metastatic melanoma	24	**臨床効果** OS: Overall: 13.6 mo (vs. 7.3 mo matched controls) Immune responders vs. non-responders: 21.9 mo vs. 8.1 mo **免疫応答** T cell responses in 18/24 (75%) patients; multiepitope responses in 13/24 (54%) patients	Oshita, C. et al. *Oncol. Rep.* **28**, 1131-1138 (2012).
Dendritic cell	gp100 + tyrosinase	KLH	Stage III/IV melanoma	33	**臨床効果**	Aarntzen, E. H. et al. *Cancer Res.* **73**, 19-29

表５　バイオ医薬品の原薬において設定される規格及び試験方法の項目の例

項目	内容
名称	一般的名称(JAN)、国際一般的名称(INN)及び販売名。
構造式	アミノ酸配列並びにジスルフィド結合や糖鎖修飾などの翻訳後修飾の情報を記載する。
分子式及び分子量	その分子式及び分子量を記載する。糖鎖など不均一な修飾を含む場合には、タンパク質部分の分子式及び分子量を記載する。
基原	本質(由来、分類、構造、物性、活性など)を記載する。
含量規格	含量、濃度又は比活性を記載する。
性状	物理的状態(例えば、固体、液体)及び色を定性的に規定する。
確認試験	有効成分などをその特性に基づいて確認するための試験。分子構造上の特徴、特有な性質に基づき設定する。 例)理化学試験:ペプチドマッピング、質量分析;生物学的試験:生物活性;免疫学的試験:ウエスタンブロット法、ELISA
示性値	安定性、有効性及び安全性に関与する物理的化学的性質等を設定する。
不均一性	翻訳後修飾や構造の不均一性の恒常性を評価する。 例)糖鎖不均一性:糖鎖分析、グライコフォーム分析、単糖分析
純度と不純物の試験	純度を規定するための試験。混在物の種類及びその存在量を測定する。 純度は一般に複数の方法にて評価される。 不純物の規格値は、それぞれ個別に及び／または総量で適切に設定する。 例)サイズ排除クロマトグラフィー、イオン交換クロマトグラフィー、SDS-PAGE
定量法	成分の含量、力価などを物理的化学的または生物学的方法によって測定する。 力価:生物学的性質に基づく生物活性(バイオアッセイ、結合性、細胞応答性) 物質量:タンパク質含量
標準物質	試験において標準として用いる物質であり、適切な品質であることが必要である。バイオ医薬品では、定量法での使用以外に、確認試験や糖鎖試験で用いられる場合がある。

6　臨床試験が実施された抗イディオタイプ抗体を有効成分とするがんワクチン

抗イディオタイプ抗体ワクチン	模倣する抗原	適応	臨床試験
Racotumomab(1E10)	NeuGcGM3	Breast Cancer	Phase I
		NSCLC	Phase III (NCT01460472)
TriGem (4B5)	GD2	Melanoma	Phase I/II (NCT00004184)
MK2-23	HMW-MAA	Melanoma	Phase I/II
BR3E4	EpCam	Colorectal Cancer	Phase I
3H1（CeaVac)	CEA	Colorectal Cancer	Phase III
105AD7	CD55	Colorectal Cancer	Phase I/II (NCT00007826)
11D10（TriAb)	HMGF	Colorectal Cancer	Phase II (NCT00033748) *3H1 との併用
Abagovomab	CA-125	Ovarian Cancer	Phase II/III (NCT00418574)

Ladjemi MZ. *Front Oncol*. 2:158 (2012)、https://clinicaltrials.gov を参考に作成

Status	資料1. NIH Clinical Study Protocol		
Completed	NY-ESO-1 Plasmid DNA (pPJV7611) Cancer Vaccine		NY-ESO-1NY-ESO-1 Plasmid DNA (pPJV7611)
	Conditions:	Prostate Cancer; Bladder Cancer; Non-Small Cell Lung Cancer; Esophageal Cancer; Sarcoma	
	Intervention:	Biological: NY-ESO-1 plasmid DNA Cancer Vaccine 2005	
	Primary Outcome: estimate the safety of NY-ESO-1 Plasmid DNA (pPJV7611) Cancer Vaccine given by PMED in patients with tumor type known to express NY-ESO-1 or LAGE-1 using frequency, severity, and duration of treatment-related adverse effects as endpoints. **Secondary Outcome**: evaluate NY-ESO-1 specific cellular and humoral immunity by determination of: a)NY-ESO-1 specific antibody,NY-ESO-1 specific CD8+ and CD4+ cells and b) delayed-type-hypersensitivity[DTH]) induced by NY-ESO-1 Plasmid DNA (pPJV7611) Eligible patients with tumor type known to express NY-ESO-1 or LAGE-1 antigen will be assigned to cohorts. NY-ESO-1 Plasmid DNA (pPJV7611) Cancer Vaccine will be administered by PMED at a pressure of 500 psi using the XR-1 Powderject delivery device. The 4 microgram dosage of NY-ESO-1 will be administered as 4 X 1 microgram PMEDs in close proximity. Similarly, the 8 microgram dosage will be administered as 8 X 1 microgram PMEDs. The third cohort of patients will receive the 8 microgram dosage as a cluster dosage of 4 doses (day 1, 3, 5, 8) as 2 X 1 microgram PMEDs per day. **Blood samples will be obtained at baseline, 2 weeks after each vaccination, prior to the second and third vaccination, and 4 weeks after the third vaccination** for the assessment of clinical hematology, biochemistry measurements and immunology responses. Patients will be evaluated for toxicity throughout the study. DTH testing will be performed with NY-ESO-1 protein in all patients, with NY-ESO-1b peptide inHLA-A2+ patients and with NY-ESO-1 DP4 peptide in HLA-DP4+ patients at baseline and at the 2-week visit following the first and third vaccinations. NY-ESO-1 and/or LAGE-1 specific antibodies will be assessed in all patients byELISA using recombinant NY-ESO-1 protein. NY-ESO-1 specific CD4+ and CD8+ T cells will be assessed in all patients by tetramer and/or ELISPOT assays **(cross-presentation)**.		
Active, not recruiting	Vaccine Maintenance Treatment for Non-Small Cell Lung Cancer		gene-modified lung cancer cells (sugar chain)HAL-1, HAL-2, HAL-3 (遺伝子改変がん細胞)
	Condition:	Carcinoma, Non-Small-Cell Lung	
	Intervention:	Biological: HyperAcute-Lung Cancer Vaccine 2007	
	Primary Outcome: To determine the response rate of the administration of HyperAcute® Lung (HAL) Cancer Vaccine cells by injection into subjects with stage IIIB (pleural effusion) or stage IV non-small cell lung carcinoma who have been treated with first line platinum-dou [Time Frame: 4 months] **Secondary Outcome:** To conduct correlative scientific studies of subject samples to determine the mechanism of any observed antitumor effect. In these studies human humoral and cellular immune responses to HAL cells will be evaluated. [Time Frame: while on study] In this project, we have put a mouse gene into human lung cancer cells that produces these abnormal sugar patterns and stimulates the immune system to attack the lung cancer. This strategy works well to kill human other cancer cells in the laboratory, but it needs to be tried in lung cancer patients to see if it will be effective and to determine if such a treatment causes any side effects. We propose to test this new treatment in subjects with non-small cell lung cancer to see if it can stop, slow or destroy tumors in these subjects. Subjects will be injected with an anti-tumor vaccine consisting of a mixture of three types of dead human lung cancer cells that have been genetically altered to express the mouse gene responsible for making this abnormal sugar-protein on the cells.		
Completed	A Cancer Vaccine (CG8123) Given With and Without Cyclophosphamide for Advanced Stage Non-Small Cell Lung Cancer (NSCLC)		GM-CSF Gene-Modified Autologous Tumor Vaccine (CG8123) Trastuzumab + Cyclophosphamide
	Conditions:	Lung Cancer; Carcinoma, Non-Small-Cell Lung	
	Interventions:	Biological: CG8123; Drug: Cyclophosphamide 2004	

	The main purpose of this research study is to determine if a vaccine made from a patient's lung cancer tumor cells will be effective in making the cancer shrink or disappear. The vaccine will be given by itself to some patients, while other patients will get the vaccine with cyclophosphamide (a type of chemotherapy). Studies in animals and other cancer vaccine trials suggest that cyclophosphamide may make tumor vaccines more potent. This study will try to determine if vaccine given with or without this chemotherapy is effective in destroying lung cancer cells. Additionally, the study will collect information on vaccine safety, both with and without chemotherapy, and whether the vaccine improves lung cancer-related symptoms (e.g., shortness of breath). Tumors from surgical resection will be processed and made into a vaccine. Prior to treatment, patients will be randomized equally to one of two treatment groups, Cohort A and Cohort B. Patients in Cohort A will be treated with CG8123 vaccine only and patients in Cohort B will be treated with CG8123 vaccine plus a single dose of cyclophosphamide administered one day prior to the first, third, and fifth vaccine treatments. Patients will receive intradermal (beneath the skin) vaccine injections every two weeks for up to eight weeks, for a total of up to five vaccine treatments. The duration of this study, including active follow up, is approximately	
Active, not recruiting	Trastuzumab, Cyclophosphamide, and an Allogeneic GM-CSF-secreting Breast Tumor Vaccine for the Treatment of HER-2/Neu-Overexpressing Metastatic Breast Cancer Condition: Breast Neoplasms 2006 Interventions: Biological: Allogeneic GM-CSF-secreting breast cancer vaccine; Drug: Trastuzumab; Drug: Cyclophosphamide 2006	allogeneic GM-CSF-secreting whole breast cancer cells(遺伝子改変細胞) re-evaluating disease status with tumor markers and RECIST criteria for 30 days. Immunological response [30 days after
	Purpose This is a feasibility study to examine **combination therapy with Trastuzumab (T), Cyclophosphamide (CY), and an allogeneic GM-CSF-secreting whole cell breast cancer vaccine** in patients with Stage IV **HER-2/neu-overexpressing breast cancer**. The main purposes of this study are to test the safety, clinical benefit, and bioactivity of vaccine therapy in combination with Cyclophosphamide and Trastuzumab in patients with HER-2/neu-overexpressing Stage IV breast cancer. This study will also to test whether the Cyclophosphamide can eliminate the suppressive influence of regulatory T cells, and whether Trastuzumab can increase antigen processing and presentation. These drug activities may make the immune system react better and enhance the effects of the vaccine in treating breast cancer. The vaccine consists of two irradiated allogeneic mammary carcinoma cell lines genetically modified to secrete human granulocyte-macrophage colony stimulating factor (GM-CSF). This open label, single arm study is designed to recruit up to 40 subjects to identify 20 research subjects with HER-2/neu-overexpressing Stage IV breast cancer eligible for study treatment. **Primary:** Safety will be evaluated by assessing toxicity related to the vaccine, CY, Trastuzumab, cardiac dysfunction, and the**potential induction of autoimmunity.** [30 days] . /Clinical benefit will be assessed by re-evaluating disease status with tumor markers and RECIST criteria, or with full evaluation upon the development of new symptoms. [Time Frame: Until 30 days after intervention] **Secondary:** Immunological response [Time Frame: Until 30 days after intervention]	
Completed	Dose Escalation and Efficacy Trial of GVAX® Prostate Cancer Vaccine Condition: Prostate Cancer Intervention: Biological: Immunotherapy allogeneic GM-CSF secreting cellular vaccine 2005	allogeneic GM-CSF secreting cellular vaccine cells
Active, not recruiting	Vaccine Study for Surgically Resected Pancreatic Cancer Condition: Pancreatic Cancer Intervention: Biological: HyperAcute(R)-Pancreatic Cancer Vaccine 2007	HAPa-1 and HAPa-2 cancer cell **vaccine** components (DFS) at one (1) year. OS.

		Primary: The primary objective of this Phase II trial is to assess disease-free survival (DFS) at one (1) year following initiation of treatment as the primary endpoint of the study in subjects treated with the HyperAcute®-Pancreatic Cancer Vaccine [Time Frame: one year] **Secondary:** We will use overall survival and adverse events rates as secondary endpoints. Unfortunately, despite the best clinical efforts and breakthroughs in biotechnology, most patients diagnosed with pancreatic cancer continue to die from their disease in a very short period of time. The primary reason for this is the short progression time of the disease; in fact, most patients with pancreatic cancer have symptoms at the time of the diagnosis. Moreover, lack of any single agent or procedure to have any significant impact on long term survival rates further contributes to poor prognostic outcomes observed with this disease. These reasons are the major causes of cancer progression that are usually discussed when considering treatment options for patients with disease that continues to grow and spread. However, another important part of the body should be considered-- the immune system. Scientists have clearly shown that pancreatic cancer cells as well as other cancer cells produce a number of abnormal proteins or abnormal amounts of certain proteins not found in normal cells. Normally one would expect a patient to develop an immune response against these abnormal proteins found in their cancer and attack them much the way we would fight off an infection from a foreign bacteria or virus. However, for reasons that scientists do not fully understand, the immune system fails to respond to these abnormal proteins and does not attack the cancer cells. This human clinical trial proposes a new way to make the immune system recognize the cancer and encourage it to attack the cancer cells	
Active, not recruiting		Low Dose Vaccine Study for Surgically Resected Pancreatic Cancer	HyperAcute(R)-Pancreatic Cancer cells vaccine HAPa-1 and HAPa-2 vaccine components. (DFS) at one (1) year. OS
	Condition:	Pancreatic Cancer	
	Intervention:	Biological: HyperAcute(R)-Pancreatic Cancer Vaccine 2008	
		Primary: The primary objective of this Phase II trial is to assess disease-free survival (DFS) at one (1) year following initiation of treatment as the primary endpoint of the study in subjects treated with the HyperAcute®-Pancreatic Cancer Vaccine [Time Frame: One year] **Secondary:** We will use overall survival and adverse events rates as secondary endpoints. In this project, we propose to put a mouse gene into human pancreatic cancer cells that produces these abnormal sugar patterns and stimulates the immune system to attack the pancreatic cancer. This strategy works well to kill other human cancer cells in the laboratory, but it needs to be tried in pancreatic cancer patients to see if it will be effective. We propose to test this new treatment in patients with pancreatic cancer who have undergone tumor resection to see if it can stop or slow recurrence of tumors in these patients. Patients will be injected with an anti-tumor vaccine consisting of a mixture of two types of dead human pancreatic cancer cells that have been genetically altered to express the mouse gene responsible for making this abnormal sugar-protein on the cells.	
Recruiting		Cancer Vaccine Study for Unresectable Stage III Non-small Cell Lung Cancer	Stimuvax: L-BLP25 or BLP25 Liposome Vaccine. 糖たんぱく質抗原MUC1 Merck.
	Condition:	Non-small Cell Lung Cancer	
	Interventions:	Biological: Stimuvax; Biological: Placebo 2006	

	Survival duration of all randomized subjects by treatment arm [Time Frame: Interim analysis at 353 + 529 events (deaths); Final analysis at 705 events (deaths. Time To Symptom Progression (TTSP) One-, 2- 3-year survival **Primary:** To compare survival duration of all randomized subjects by treatment arm [Time Frame: Interim analysis at 353 + 529 events (deaths); Final analysis at 705 events (deaths) **Secondary**: To compare all randomized subjects by treatment arm for: Time To Symptom Progression (TTSP) as measured by the Lung Cancer Symptom Scale (LCSS) [Time Frame: Interim analysis at 353 + 529 events (deaths); Final analysis at 705 events (deaths)] Time To Progression (TTP) as determined by the investigator [Time Frame: Interim analysis at 353 + 529 events (deaths); Final analysis at 705 events (deaths)] **One-, two- and three-year survival [Time Frame: Analyzed at 1, 2, & 3 years post treatment onset] [Designated as safety issue: No]** Safety	
Not yet recruiting	Experimental Therapeutic Cancer Vaccine Created In-situ in Patients With Stage II-Stage IV Cancer Conditions: Solid Tumors Stage II, Stage III and Stage IV; Breast Cancer; Colorectal Cancer; Prostate Cancer; Melanoma; Ovarian Cancer; Sarcoma; Non-small Cell Lung Cancer Interventions: Biological: AlloStim; Procedure: Cryoablation 2010	AlloStim: cancer cells. 探索：
	tumor-specific CTL killer cells in the circulation.anti-tumor effect of AlloStimTM administration. [Time Frame: 1 year. immunological response[90 days] This is a Phase I/II clinical study to investigate the optimal protocol and indication for creating a personalized anti-tumor vaccine within the body of patients with cancer. The aim of the study is to evaluate the safety of administration and anti-tumor effect of a vaccine protocol that has three separate steps. Cancer patients generally present with an immune response to cancer biased to a Th2 response, while a Th1 response is considered necessary for mediating anti-tumor immunity. The first step of the study consists of multiple intradermal priming doses of AlloStimTM. The aim of this step is to create Th1 immunity to the alloantigens in AlloStimTM, thus increasing the number of Th1 cells in circulation. The second step of the protocol involves the cryoablation of a selected tumor lesion followed by an intratumoral AlloStimTM injection. The aim of this step is to generate tumor-specific CTL killer cells in the circulation. The final step is an intravenous infusion of AlloStimTM. The aim of this step is to activate circulating Th1 cells, killer cells, and natural killer cells. The further aim of this step is to create an inflammatory environment that can break-down the ability of the tumor to avoid an anti-tumor immune response. In patients with partial responses and recurrence of disease, additional intravenous "booster" infusions are utilized to reactivate the circulating immune cells.	
Completed	Prime-Boost Dose Scheduling Trial for Human GM-CSF Gene Transduced Irradiated Prostate Allogeneic Cancer Vaccine (Allogeneic Prostate GVAX®) in Patients With Hormone-Refractory Prostate Cancer Condition: Prostate Cancer Intervention: Biological: Immunotherapy allogeneic GM-CSF secreting cellular vaccine 2005	Immunotherapy allogeneic GM-CSF secreting cellular vaccine: Human GM-CSF Gene Transduced Irradiated Prostate Allogeneic Cancer Vaccine
	The objective of this study is to evaluate the safety and efficacy of a prime-boost dose schedule of Human GM-CSF Gene Transduced Irradiated Prostate Allogeneic Cancer Vaccine (Allogeneic Prostate GVAX®) as measured by standard toxicity evaluation, changes in PSA, and tumor responses. Additional objectives are to measure the time to PSA and/or clinical disease progression as well as local and systemic immune responses to the vaccine.	
Recruiting	Vaccine Therapy With or Without Cyclophosphamide in Treating Patients Undergoing Chemotherapy and Radiation Therapy for Stage I or Stage II Pancreatic Cancer That Can Be Removed by Surgery Condition: Pancreatic Cancer Interventions: Biological: GVAX pancreatic cancer vaccine; Drug: cyclophosphamide 2008	GVAX pancreatic cancer vaccine: GM-CSF Secreting Allogeneic Pancreatic Cancer cells

	Immune response [Time Frame: Unknown] . OS＋PFS. RATIONALE: Vaccines made from gene-modified tumor cells may help the body build an effective immune response to kill pancreatic cancer cells. Drugs used in chemotherapy, such as cyclophosphamide, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. Giving vaccine therapy together with cyclophosphamide may kill more tumor cells. It is not yet known whether vaccine therapy is more effective with or without cyclophosphamide in treating patients with pancreatic cancer. PURPOSE: This randomized clinical trial is studying the side effects of vaccine therapy and to see how well it works when given with or without cyclophosphamide in treating patients undergoing chemotherapy and radiation therapy for stage I or stage II pancreatic cancer that can be removed by surgery.	
Recruiting	A Clinical Study to Assess Safety and Efficacy of a Tumor Vaccine in Patients With Advanced Renal Cell Carcinoma (ASET) Condition: Stage IV Renal Cell Cancer Intervention: Biological: MGN1601 2010	MGN1601：Genetically Modified Allogeneic (Human) Tumor Cells
	Autoimmune effects [(12 w), extension phase (120 w) plus 5 years follow-up] the presence of MIDGE vectors. immune response (8 w, 120w) Primary: Assessment of safety profile of MGN1601 [Time Frame: Treatment phase (12 weeks), extension phase (120 weeks, if applicable), plus 5 years follow-up] Secondary : Assessment of potential autoimmune effects of MGN1601 [Time Frame: Treatment phase (12 weeks), extension phase (120 weeks, if applicable) plus 5 years follow-up (if applicable)]. /Assessment of the presence of MIDGE vectors [Time Frame: Treatment phase (12 weeks)] . / Assessment of the immune response to MGN1601 [Time Frame: Treatment phase (12 weeks), extension phase (120 weeks, if applicable)] . /Evaluation of clinical and radiological response to MGN1601 [Time Frame: Treatment phase (12 weeks), extension phase (120 weeks, if applicable) plus 5 years follow-up]	
Recruiting	Phase I Study To Test The Safety of TVAX Immunotherapy As A Treatment For Recurrent Grade III/IV Gliomas Conditions: Glioma; High Grade Astrocytoma; Glioblastoma Multiforme Intervention: Biological: Cancer vaccine plus immune adjuvant, plus activated white blood cells 2010	Cancer vaccine plus immune adjuvant, plus activated white blood cells.
	Primary: Relative toxicity [Time Frame: 8 weeks]. /To determine the relative toxicity (safety) of vaccinating recurrent grade III/IV glioma patients four times with live, attenuated cancer cells combined with granulocyte-macrophage colony-stimulating factor (GM-CSF). Toxicity will be assessed following delivery of each treatment. **Secondary:** Potency [Time Frame: 8 weeks]. /The potency of the modified vaccination regimen will be assessed by measuring immune responses following each vaccination. The study is designed to determine whether vaccinating recurrent grade III/IV glioma subjects four times with attenuated cancer cells stimulates more powerful immune responses than vaccinating subjects twice. Clinical effects also will be measured to determine whether the treatment causes the cancer to regress.	
Active, not recruiting	Safety and Efficacy Trial of a RNActive®-Derived Prostate Cancer Vaccine in Hormone Refractory Disease Condition: Hormonal Refractory Prostate Cancer Intervention: Biological: CV9103 2009	CV9103：a RNActive®-Derived Prostate cancer
	vrecommended dose for exploration in the phase II part [Time Frame: 6-9 months] Immunotherapy of prostate cancer is a promising approach for the treatment of advanced or recurrent forms of prostate cancer. Recently, immunotherapy of prostate cancer has been facilitated by the identification of a number of prostate specific antigens that are expressed in healthy and tumor prostate tissues. For prostatectomized patients, such antigens offer ideal targets for immunotherapy as they are only present in tumor but not in healthy tissue. The use of prostate specific antigens in a cancer vaccine is one attractive option for cancer immunotherapy.	
Terminated	Trial of Melaxin Cancer Vaccine Plus Bacillus Calmette-Guerin (BCG) to Treat Malignant Melanoma	Melaxin (autologous dendritoma vaccine) and

<table>
<tr><td></td><td>Condition:</td><td>Melanoma</td><td rowspan="2">BCG, the professional antigen-presenting cell, the dendritic cell</td></tr>
<tr><td></td><td>Intervention:</td><td>Biological: Melaxin (autologous dendritoma vaccine) and BCG 2009</td></tr>
<tr><td></td><td colspan="3">Primary: Adverse events and clinical laboratory results [6 weeks] Secondary: Tumor response as measured using the RECIST criteria
Chemotherapy and immunotherapy are the main therapies for metastatic melanoma with the hope of prolonging survival. The ideal immunotherapy would consist of the professional antigen-presenting cell, the dendritic cell, with the entire repertoire of tumor antigens inside. The best way to achieve this is by creating an autologous hybrid fusion cell of the dendritic cell and tumor cell. In this study, melanoma tumor tissue surgically removed from the patient will be disassociated into single cells, irradiated and fused to dendritic cells produced by culturing the patient's blood monocytes. Prior to the electrofusion procedure, the tumor cells are stained red and the dendritic cells are stained green. After fusion, the uniquely colored fused cells, or dendritomas, are separated from the unfused cells by use of a fluorescence activated cell sorter. This highly purified population is then divided into 4 doses containing 250,000 dendritomas each and frozen. Each dose is thawed, diluted to 1 ml with Sterile Saline for Injection containing 5% human serum albumin and administered subcutaneously over a lymph node bed to the patient once every 4 weeks. A separate injection of BCG is administered in the same area within 10 minutes of the dendritoma injection. The safety and efficacy of the therapy wil be evaluated in 25 patients.</td></tr>
<tr><td rowspan="3">Recruiting</td><td colspan="2"><u>Cyclophosphamide and Vaccine Therapy With or Without Trastuzumab in Treating Patients With Metastatic Breast Cancer</u></td><td rowspan="3">allogeneic GM-CSF-secreting breast cancer cells, Cyclophosphamide GM-CSF, Sargramostim, Trastuzumab</td></tr>
<tr><td>Condition:</td><td>Breast Cancer 2009</td></tr>
<tr><td>Interventions:</td><td>Biological: allogeneic GM-CSF-secreting breast cancer vaccine; Biological: trastuzumab; Drug:</td></tr>
<tr><td></td><td colspan="3">PFS(無増悪生存期間), PD: peripheral CD4+CD25+ regulatory T cells CTL/ELISPOT, T cell memory pool,, Immune priming in in-vivo vaccine-site biopsies
Primary: To evaluate the safety of cyclophosphamide-modulated vaccination with vs without trastuzumab in patients that does not overexpress HER-2/neu.
To compare the clinical benefit of cyclophosphamide-modulated vaccination with vs without trastuzumab in these patients.
To measure HER-2/neu-specific CD4+ and CD8+ T-cell immunity by delayed-type hypersensitivity (DTH) and ELISPOT.
To measure the pharmacodynamics of CD4+CD25+ regulatory T cells by flow cytometry.
Secondary: To assess the impact of trastuzumab on immune priming in vivo by immunohistochemistry of vaccine-site biopsies at day +3 and day +7 of courses 1 and 3 on the two study arms, comparing cellular infiltrates to those seen in previous preclinical and clinical models.
To measure hTERT-specific CD8+ T-cell immunity by ELISPOT.
To characterize the peripheral-memory T-cell pool.
Tertiary: To determine baseline and change in vaccine site-draining lymph node immunohistology and gene expression profile.
To develop the tandem tetramer/CD107a cytotoxicity assay for HER-2/neu-specific CD8+ T cells.
To measure novel T-cell responses induced by trastuzumab and cyclophosphamide-modulated vaccination.
OUTLINE: Patients are randomized to 1 of 2 treatment arms.
Arm I: Patients receive cyclophosphamide IV over 30 minutes on day -1 and allogeneic GM-CSF-secreting breast cancer vaccine intradermally on day 0. Courses repeat every 4-6 weeks for 3 courses in the absence of disease progression or unacceptable toxicity. Patients then receive a fourth vaccination at 6-8 months.
Arm II: Patients receive cyclophosphamide and the vaccine as in arm I and trastuzumab IV over 30-90 minutes on day -1. Courses repeat every 4-6 weeks for 3 courses in the absence of disease progression or unacceptable toxicity. Patients then receive a fourth vaccination at 6-8 months.</td></tr>
<tr><td rowspan="3">Recruiting</td><td colspan="2"><u>Trial of an RNActive®-Derived Cancer Vaccine in Stage IIIB/IV Non Small Cell Lung Cancer (NSCLC)</u></td><td rowspan="3">CV9201: mRNAs (drug product components) encoding antigens that are overexpressed or exclusively expressed in NSCLC cells.</td></tr>
<tr><td>Condition:</td><td>Non Small Cell Lung Cancer</td></tr>
<tr><td>Intervention:</td><td>Biological: CV9201 2009</td></tr>
</table>

	Primary: Phase I: Determination of the recommended dose (RD) for exploration in the phase IIa part of the study [Time Frame: During the first 2-3 month of Phase I] [Phase II: Assessment of safety and tolerability of the treatment regimen [Time Frame: Complete duration of Phase II] Medical Need: Lung cancer is the leading cause of cancer mortality in developed countries; about 87% of lung cancers are of the NSCLC type. Patients with more advanced but non-metastatic disease (IIIA or IIIB) usually undergo chemotherapy and/or radiation therapy, with or without secondary surgical resection. Patients with progression after chemotherapy and/or radiotherapy may receive second-line treatment with targeted therapies. Despite these aggressive treatments, only about 5% of patients with metastatic disease survive for 5 or more years. Given these dismal statistics, it is clear that new therapeutic approaches for treatment of NSCLC are urgently needed. Potential Benefits: CV9201 is an mRNA-based vaccine for the treatment of human NSCLC that is based on CureVac's RNActive® technology. As an mRNA-based vaccine, CV9201 features several advantages over other approaches: it is highly specific, there is no restriction to the patient's MHC genotype, and it does not need to cross the nuclear membrane to be active. Finally, in the absence of reverse transcriptase, RNA can not be integrated into the genome.	
Not yet recruiting	Safety Study of Peptide Cancer Vaccine To Treat HLA-A*24-positive Advanced Small Cell Lung Cancer Condition: Small Cell Lung Cancer Intervention: Biological: HLA-A*2402-restricted CDCA1 and KIF20A peptides 2010	HLA-A*2402-restricted CDCA1 and KIF20A peptides. PD:
	PD: Peptides specific CTL, Antigen cascade, Regulatory T cells, Cancer antigens and HLA levels. Efficacy: OS **Detailed Description:** We previously identified three novel HLA-A*2402-restricted epitope peptides, which were derived from two cancer-testis antigens, CDCA1 and KIF20A, as targets for cancer vaccination against lung cancer. In this phase I trial, we examine using a combination of these two peptides the safety, immunogenicity, and antitumor effect of vaccine treatment for HLA-A*2402-positive advanced small cell lung cancer patients who failed to standard therapy.	
Recruiting	Cancer Vaccine Study for Stage III, Unresectable, Non-small Cell Lung Cancer (NSCLC) in the Asian Population Condition: Non-small Cell Lung Cancer 2009 Interventions: Biological: L-BLP25 or BLP25 liposome vaccine (Stimuvax); Biological: Placebo	L-BLP25 or BLP25 liposome vaccine (Stimuvax) Efficacy: OST
	Primary: Overall Survival Time [Time Frame: , Dec 2009, until cut-off date expected Sept 2014]. /Time from randomization to death. Patients without event are censored at the date of last contact, or date lost to follow-up **Secondary**: Safety - Adverse Events. /Time to Symptom Progression (TTSP) . /Time from randomization to symptomatic progression. Symptomatic progression is defined as an increase (worsening) of the ASBI (The Average Symptomatic Burden Index i.e., the mean of the six major lung cancer specific symptom scores of the LCSS subject scale). Worsening is defined as a 10% increase in the scale breadth from the baseline score. /Time to Progression (TTP) [Time Frame: Dec 2009, until the cut-off date expected Sept 2014]. /Time from randomization to the radiological confirmation of progression performed according to Response Evaluation Criteria In Solid Tumors (RECIST). If radiological confirmation cannot be obtained but a subject is withdrawn from trial treatment due to PD, TTP will be measured from the date of randomization to the date of discontinuation of trial treatment. TTP of subjects without PD at the time of analysis will be censored at the time of last contact. Progression Free Survival (PFS) Time [Time Frame:Dec 2009, until the cut-off date expected Sept 2014]. /Time from randomization to PD as determined by the investigator or death. PFS time for subjects without an event will be censored as of the date of last contact. /Time to Treatment Failure /Time from randomization to discontinuation of trial treatment for any reason as reported by the investigator. For subjects still receiving treatment at the time of analysis, the time between the date of randomization and the last date of treatment will be used as a censored observation in the analysis. Subjects who have missed two consecutive scheduled doses will be considered as treatment failures and the TTF will be calculated from the date of randomization to the date of their first missed treatment.	
Not yet recruiting	Safety Study of Peptide Cancer Vaccine To Treat HLA-A*02-positive Advanced Non-small Cell Lung Cancer	HLA-A*0201 or HLA-A*0206-restricted URLC10 peptides

	Condition:	Non-small Cell Lung Cancer	URLC10 peptides
	Intervention:	Biological: HLA-A*0201 or HLA-A*0206-restricted URLC10 peptides 2010	
	Primary: Evaluation of safety (NCI CTCAE version3) and tolerability (maximum tolerated dose, MTD and dose limiting toxicity, DLT) as well as adverse effects of vaccination therapy, and determination of the recommended dose for next phase trial. [Time Frame: 2 months] **Secondary**: Immunological responses: Peptides specific CTL, Antigen cascade, Regulatory T cells, Cancer antigens and HLA levels. [Time Frame: 2 months] Evaluation of clinical efficacy: Objective response rate (RECIST1.1), Tumor markers, Overall survival, Progression free survival. [Time Frame: 2 months We previously identified three novel HLA-A*0201 or HLA-A*0206-restricted epitope peptides, which were derived from a cancer-testis antigen, URLC10, as targets for cancer vaccination against lung cancer. In this phase I trial, we examine using a combination of these three peptides the safety, immunogenicity, and antitumor effect of vaccine treatment for HHLA-A*0201 or HLA-A*0206-positive advanced non-small cell lung cancer patients who failed to standard therapy.		
Not yet recruiting	Safety Study of Peptide Cancer Vaccine To Treat HLA-A*24-positive Advanced Non-small Cell Lung Cancer		HLA-A*2402restricted URLC10 , CDCA1, and KIF20A peptides
	Condition:	Non-small Cell Lung Cancer	
	Intervention:	Biological: HLA-A*2402restricted URLC10, CDCA1, and KIF20A peptides 2010	
	Peptides specific CTL, Antigen cascade, **Regulatory T cells**, **Cancer antigens and HLA levels**. /Tumor markers, **OS**, **PFS**. We previously identified three novel HLA-A*2402-restricted epitope peptides, which were derived from three cancer-testis antigens, URLC10, CDCA1, and KIF20A, as targets for cancer vaccination against lung cancer. In this phase I trial, we examine using a combination of these three peptides the safety, immunogenicity, and antitumor effect of vaccine treatment for HLA-A*2402-positive advanced non-small cell lung cancer patients who failed to standard therapy. ARM1: Experimental: URLC10-CDCA1-KIF20A 1mg Patients will be vaccinated once a week for four weeks of a treatment cycle. On each vaccination day, the HLA-A*2402-restricted URLC10 peptide (1mg), CDCA1 peptide (1mg) and KIF20A peptide(1mg) mixed with Montanide ISA 51 will be administered by subcutaneous injection. Escalating doses of every peptide will be administered by subcutaneous injection on days 1, 8, 15 and 22 of each treatment cycle. Planned doses of peptides are 1.0mg, 2.0mg and 3.0mg. ARM2: perimental: URLC10-CDCA1-KIF20A 2mg Patients will be vaccinated once a week for four weeks of a treatment cycle. On each vaccination day, the HLA-A*2402-restricted URLC10 peptide (2mg), CDCA1 peptide (2mg) and KIF20A peptide(2mg) mixed with Montanide ISA 51 will be administered by subcutaneous injection. Escalating doses of every peptide will be administered by subcutaneous injection on days 1, 8, 15 and 22 of each treatment cycle. Planned doses of peptides are 1.0mg, 2.0mg and 3.0mg. ARM3: Experimental: URLC10-CDCA1-KIF20A 3mg Patients will be vaccinated once a week for four weeks of a treatment cycle. On each vaccination day, the HLA-A*2402-restricted URLC10 peptide (3mg), CDCA1 peptide (3mg) and KIF20A peptide(3mg) mixed with Montanide ISA 51 will be administered by subcutaneous injection. Escalating doses of every peptide will be administered by subcutaneous injection on days 1, 8, 15 and 22 of each treatment cycle. Planned doses of peptides are 1.0mg, 2.0mg and 3.0mg.		
Completed	The Use of Dendritic Cell/Tumor Fusions as a Novel Tumor Vaccine in Patients With Multiple Myeloma		Dendritic Cell Tumor Fusion Vaccine. tumor specific cellular and humoral immunity with GM-CSF
	Condition:	Multiple Myeloma	
	Intervention:	Biological: Dendritic Cell Tumor Fusion Vaccine	

	Detailed Description: To create the study vaccine, cells will be removed from the participants tumor and fused (mixed) with powerful immune system stimulating cells (dendritic cells) obtained from the participants blood. /Not everyone who participates in this study will be receiving the same amount of study vaccine. A small group of people will be enrolled into the study and given a certain dose. If they tolerate it well, the next group of people enrolled will receive a higher dose. This will continue until the highest dose level tolerated is determined. /Once the screening tests are completed and it is determined the participant is eligible, they will undergo some baseline procedures. In an effort to make the study vaccine, tumor cells and dendritic cells will be collected from the participant. Tumor cells may be collected from bone marrow or from a collection of tumor cells called a plasmacytoma. A decision will be made based upon the location of the cancer. A bone marrow aspiration/biopsy will be performed during the following time points: at screening, prior to the first vaccination, and at 1 month, 3 months, and 6 months after the final study vaccination. These will be used to assess and follow the participants multiple myeloma. Leukapheresis will be performed to obtain dendritic cells. This procedure takes 2 to 4 hours to and involves the collection of a large number of white blood cells. Dendritic cells will be generated in the laboratory from white blood cells. If not enough white blood cells are collected, the participant may be asked to return to the clinic for an additional leukapheresis procedure. Before each vaccine is administered (weeks 0, 3, 6) the following study tests and procedures will be performed: skin test; blood test, physical exam and 24-hour urine collection. A physical exam and blood tests will be performed on the weeks when the participant does not receive the vaccine (weeks 1,2,4,5,7,8). The study schedule will consist of a fixed dose of the fused (mixed) cell vaccine under the skin every 3 weeks. Each study vaccine will be accompanied by an injection of GM-CSF. Participants will receive 2 or more vaccines depending upon the total number of fusion cells made, the dose the participant is assigned to receive and their response to the study vaccine. Follow-up after the vaccine treatment is completed will consist of the following: blood collection (1, 3 and 6 months after final study vaccination); bone marrow aspiration/biopsy (1, 3 and 6 months after final study vaccination); physical exam (1, 2, 3, 4, 5 and 6 months after final study vaccination); radiologic tumor assessment (1, 3 and 6 months after final study vaccination.	
Active, not recruiting	<u>Vaccine Therapy in Treating Patients With Stage IIIB or Stage IV Bronchoalveolar Lung Cancer</u> Condition: Lung Cancer Intervention: Biological: GVAX lung cancer vaccine 2003	GVAX lung cancer cell vaccine. Autologous Cancer Vaccine. OS + PFS.
	Determine the progression-free and overall survival of patients with selected stage IIIB or stage IV bronchoalveolar carcinoma treated with GVAX lung cancer vaccine. Determine the response rate (confirmed and unconfirmed and complete and partial) in patients treated with this vaccine. Determine the frequency and severity of toxic effects of this vaccine in these patients. Determine the functional status of patients treated with this vaccine. Correlate systemic biologic activity (i.e., antigen-specific antitumor and systemic cytokine responses) with clinical outcome in patients treated with this vaccine. OUTLINE: This is a multicenter study. Patients are stratified according to prior systemic cancer therapy for bronchoalveolar carcinoma (BAC) (yes vs no) and pattern of BAC (diffuse vs nodular). After successful vaccine manufacturing from tumor tissue procured, patients receive GVAX lung cancer vaccine intradermally (ID) (6-7 injections per vaccination) on weeks 1, 3, 5, 7, and 9 for a total of 5 vaccinations. Treatment continues in the absence of disease progression or unacceptable toxicity. Quality of life is assessed at baseline and at weeks 9, 13, and 21.	
Active, not recruiting	<u>Vaccine Therapy With or Without Cyclophosphamide and Doxorubicin in Women With Stage IV Breast Cancer</u> Condition: Breast Cancer Interventions: Biological: allogeneic GM-CSF-secreting breast cancer vaccine; Drug: cyclophosphamide; Drug: doxorubicin hydrochloride 2004	allogeneic GM-CSF-secreting breast cancer vaccine.