Trial record **1 of 1** for: IMCgp100-201

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Phase 1b/2 Study of the Combination of IMCgp100 With Durvalumab and/or Tremelimumab in Cutaneous Melanoma

ClinicalTrials.gov Identifier: NCT02535078

Recruitment Status: Recruiting
First Posted: August 28, 2015
Last Update Posted: April 27, 2018

See **Contacts and Locations**

Sponsor:
Immunocore Ltd

Collaborator:
MedImmune LLC

Information provided by (Responsible Party):
Immunocore Ltd

Study Details | **Tabular View** | **No Results Posted** | Disclaimer | How to Read a Study Record

Study Description

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Brief Summary:

This study is a Phase Ib/II, multi-center, open-label study of IMCgp100 as a single agent and in combination with durvalumab (MEDI4736) and/or tremelimumab in metastatic cutaneous melanoma. The purpose of this study is to characterize the safety, tolerability, pharmacokinetics (PK), pharmacodynamics, and anti-tumor activity of IMCgp100 in combination with durvalumab (MEDI4736, programmed death-ligand 1 [PD-L1] inhibitor), tremelimumab (CLTA-4 inhibitor), and the combination of durvalumab with tremelimumab compared to single-agent IMCgp100 alone. The study will enroll patients who have metastatic melanoma that is refractory to treatment with an anti-PD-1 inhibitor as well as patients naive to therapy in the metastatic setting.

Recent biologic evidence indicates that optimal responses to programmed cell death-1 (PD-1) directed therapy require the presence of CD8+ T cells in the tumor microenvironment and thus therapies such as IMCgp100 that recruit these effector cells to the tumor may overcome pre-existing resistance to checkpoint blockade. This emerging biology of checkpoint inhibitor resistance suggests the combination of IMCgp100 with checkpoint inhibition may have enhanced activity in patients with pre-existing resistance.

Condition or disease	Intervention/treatment	Phase
Malignant Melanoma	Drug: IMCgp100 Drug: durvalumab Drug: tremelimumab	Phase 1 Phase 2

Study Design

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Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	225 participants
Allocation:	Randomized
Intervention Model:	Crossover Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase Ib/II Open-label, Multi-center Study of the Safety and Efficacy of IMCgp100 in Combination With Durvalumab (MEDI4736) or Tremelimumab or the Combination of Durvalumab and Tremelimumab in Patients With Advanced Melanoma
Study Start Date:	November 2015
Estimated Primary Completion Date:	November 2018
Estimated Study Completion Date:	November 2019

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Melanoma

Drug Information available for: Durvalumab

Genetic and Rare Diseases Information Center resources: Melanoma, Familial Neuroendocrine Tumor Neuroepithelioma

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment

Experimental: Arm 1 IMCgp100 with durvalumab (MEDI4736)	Drug: IMCgp100 soluble gp100-specific T cell receptor with anti-CD3 scFV Drug: durvalumab anti-PD-L1 monoclonal antibody Other Name: MEDI4736
Experimental: Arm 2 IMCgp100 with tremelimumab	Drug: IMCgp100 soluble gp100-specific T cell receptor with anti-CD3 scFV Drug: tremelimumab anti-CTLA-4 monoclonal antibody
Experimental: Arm 3 IMCgp100 with durvalumab (MEDI4736) and tremelimumab	Drug: IMCgp100 soluble gp100-specific T cell receptor with anti-CD3 scFV Drug: durvalumab anti-PD-L1 monoclonal antibody Other Name: MEDI4736 Drug: tremelimumab anti-CTLA-4 monoclonal antibody
Experimental: Arm 4 IMCgp100 (single agent)	Drug: IMCgp100 soluble gp100-specific T cell receptor with anti-CD3 scFV

Outcome Measures

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Primary Outcome Measures :

1. Progression-free survival [Time Frame: 12 months]

Secondary Outcome Measures :

1. Objective response rate [Time Frame: 12 months]
2. Overall survival [Time Frame: 2 years]

Eligibility Criteria

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Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Age ≥ 18 years
2. Written informed consent must be obtained from all patients prior to any study procedures
3. Patients with advanced melanoma defined as unresectable stage III or metastatic stage IV disease. Patients with acral or mucosal melanoma or patients with unknown primary melanoma are acceptable in Phase 1b but are excluded from Phase II. Patients with uveal melanoma are excluded from the study.
4. Phase II PD-1/PD-L1 refractory subsets: Patients with confirmed disease progression within 1 year following initiation of PD-1/PD-L1 inhibitor therapy (patients must have received at least 2 doses of the PD-1/PD-L1 inhibitor). No prior cytotoxic therapy in the advanced setting is permitted. BRAF inhibition therapy is acceptable before immunotherapy where clinically indicated. CTLA-4-inhibition therapy is acceptable as a prior line of therapy or in combination with anti-PD-1 therapy.
5. Phase II IMT naive cohorts: Patients have not received systemic cytotoxic or immune-based therapy for advanced melanoma. BRAF and/or MEK inhibition therapy is acceptable before immunotherapy where clinically indicated. Other systemic cytotoxic or targeted therapy in the advanced setting is not permitted in this subset
6. Phase Ib: no restriction on prior therapy
7. HLA-A*0201 positive by Central Assay
8. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
9. Life expectancy of at least 3 months
10. Phase II cohorts only: patients must have measurable disease according to RECIST v.1.1 criteria. Patients enrolled in Ph Ib cohorts must have evaluable disease
11. Phase II cohorts only: Patients must have a site of disease amenable to biopsy, and be a candidate for tumor biopsy according to the treating institution's guidelines. Phase Ib patients need not have disease accessible to biopsy
12. Those receiving prior immunotherapy must meet all of the following conditions:
    - Must not have experienced an immune-related adverse event (irAE) where the irAE was the reason for permanent discontinuation of prior immunotherapy in the most recent prior treatment regimen
    - All irAEs while receiving prior immunotherapy must have resolved to ≤ grade 1 or Baseline prior to Screening for this study. Must not have experienced a ≥ grade 3 immune-related AE within the past 16 weeks or any grade 4 life- threatening irAE (regardless of duration) or neurologic or ocular AE of any grade while receiving prior immunotherapy (NOTE: Subjects with endocrine AE of any grade are permitted to enroll if they are stably maintained on appropriate replacement therapy, but must have no history of adrenal crisis and be asymptomatic)
    - Patients currently receiving chronic corticosteroid treatment (longer than 8 weeks duration) for management of pre-existing adverse events, or patients with a history of chronic corticosteroid treatment longer than 8 weeks' duration for AEs within 6 months of Screening are excluded

Exclusion Criteria:

1. Presence of untreated or symptomatic central nervous system metastases, or central nervous system metastases that currently require local therapy (such as radiotherapy or surgery), or require doses of corticosteroids within the prior 4 weeks
2. History of severe hypersensitivity reactions to other mAbs
3. History of treatment-related interstitial lung disease/pneumonitis
4. Patient with any out-of-range laboratory values defined as:
    - Serum creatinine ≥ 1.5 x ULN and/or creatinine clearance (calculated using Cockcroft-Gault formula, or measured) < 50 mL/min
    - Total bilirubin > 1.5 x ULN, except for patients with Gilbert's syndrome who are excluded if total bilirubin > 3.0 x ULN or direct bilirubin > 1.5 x ULN
    - Alanine aminotransferase (ALT) > 3 x ULN
    - Aspartate aminotransferase (AST) > 3 x ULN
    - Absolute neutrophil count (ANC) < 1.0 x 10^9/L
    - Absolute lymphocyte count < 0.5 x 10^9/L
    - Platelet count < 75 x 10^9/L
    - Hemoglobin (Hgb) < 8 g/dL
    - Potassium, magnesium, corrected calcium or phosphate abnormality of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) > grade 1
5. Clinically significant cardiac disease or impaired cardiac function, including any of the following:
    - Clinically significant and/or uncontrolled heart disease such as congestive heart failure (New York Heart Association [NYHA] grade ≥ 2), uncontrolled hypertension or clinically significant arrhythmia currently requiring medical treatment
    - QTcF >470 msec on screening ECG or congenital long QT syndrome
    - Acute myocardial infarction or unstable angina pectoris < 6 months prior to Screening
6. Active autoimmune disease or a documented history of autoimmune disease within 3 years before Screening (or as indicated below), including the following:
    - A documented history of inflammatory bowel disease (ulcerative colitis or Crohn's disease, within three years)
    - Patients with vitiligo, alopecia, managed hypothyroidism (on stable replacement doses), psoriasis, resolved childhood asthma/atopy, well-controlled asthma and type I diabetes mellitus are NOT excluded
7. Recent (< 12 months) active diverticulitis
8. Active infection requiring systemic antibiotic therapy. Patients requiring systemic antibiotics for infection must have completed therapy before Screening is initiated
9. Known history of human immunodeficiency virus (HIV) infection. Testing for HIV status is not necessary unless clinically indicated
10. Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, currently requiring medical intervention, per institutional protocol. Testing for HBV or HCV status is not necessary unless clinically indicated or the patient has a history of HBV or HCV infection requiring treatment with currently an unknown status. History of treated hepatitis is not exclusionary
11. Malignant disease, other than that being treated in this study. Exceptions to this exclusion include the following: malignancies that were treated curatively and have not recurred within 2 years after completion of treatment; completely resected basal cell and squamous cell skin cancers; any malignancy considered to be indolent and that has never required therapy; and completely resected carcinoma in situ of any type

12. Any medical condition that would, in the investigator's judgment, prevent the patient's participation in the clinical study due to safety concerns, compliance with clinical study procedures or interpretation of study results
13. Systemic anti-cancer therapy within 2 weeks of the first dose of study treatment. For cytotoxic agents that have major delayed toxicity and any prior immunotherapy approach, 4 weeks is indicated as washout period
14. Presence of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) ≥ grade 2 toxicity (except alopecia, peripheral neuropathy and ototoxicity, which are excluded if ≥ NCI CTCAE grade 3) due to prior cancer therapy
15. Chronic systemic corticosteroid use (ie, prednisone > 10 mg QD or the equivalent of longer duration than 8 weeks for any medical condition) or history of chronic corticosteroid use (longer than 8 weeks duration) within the past 6 months; treatment for well-controlled and asymptomatic adrenal insufficiency is permitted, but replacement dosing is limited to prednisone ≤ 10 mg QD or the equivalent, and patients must have no history of adrenal crisis. Local steroid therapies (eg, otic, ophthalmic, intra-articular or inhaled medications) are acceptable
16. Use of any live vaccines against infectious diseases within 4 weeks of initiation of study treatment. Non-live vaccination (eg, influenza) are permitted anytime during treatment
17. Major surgery as defined by the investigator within 2 weeks of the first dose of study treatment (minimally invasive procedures such as bronchoscopy, tumor biopsy, insertion of a central venous access device, and insertion of a feeding tube are not considered major surgery)
18. Radiotherapy within 2 weeks of the first dose of study drug, with the exception of palliative radiotherapy to a limited field, such as for the treatment of bone pain or a focally painful tumor mass
19. Use of hematopoietic colony-stimulating growth factors (eg, G-CSF, GMCSF, M-CSF) ≤ 2 weeks prior start or study drug. Patients must have completed therapy at least 2 weeks before the screening period begins with any hematopoietic colony-stimulating growth factors. An erythroid stimulating agent is allowed as long as it was initiated at least 2 weeks prior to the first dose of study treatment and the patient is not red blood cell transfusion dependent
20. Pregnant or lactating women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test
21. Women of child-bearing potential who are sexually active with a non-sterilized male partner, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective contraception from screening throughout study treatment, and must agree to continue using such precautions for 6 months after the final dose of investigational product; cessation of birth control after this point should be discussed with a responsible physician. Highly effective methods include the following:
    - Total abstinence from sexual relations for the duration of the treatment when applicable to the lifestyle of the patient. Periodic abstinence (eg, calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception
    - Female sterilization (have had surgical bilateral oophorectomy with or without hysterectomy) or tubal ligation at least 6 weeks before taking study treatment. In case of oophorectomy alone, this applies only when the reproductive status of the woman has been confirmed by follow up hormone level assessment
    - Male sterilization (at least 6 months prior to Screening). For female patients on the study the vasectomized male partner should be the sole partner for that patient
    - The combination of any 2 of the following methods when both are used simultaneously:
        1. Use of oral, injected, or implanted hormonal methods of contraception or other forms of hormonal contraception that have comparable efficacy (failure rate <1%), for example hormone vaginal ring or transdermal hormone contraception
        2. Placement of an intrauterine device or intrauterine system
        3. Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps)

when used with spermicidal foam, gel, film, cream, or used of a spermicidal vaginal suppository Women of child-bearing potential must have a negative serum pregnancy test at Screening. Otherwise, female patients must be post-menopausal (no menstrual period for at least 12 months prior to Screening), or surgically sterile.

22. Male patients must be surgically sterile or use double barrier contraception method from enrollment through treatment and for 6 months following administration of the last dose of study drug.

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT02535078***

Contacts

Contact: Christina M Coughlin, MD, PhD 484-534-5261 christina.coughlin@immunocore.com

Show 24 Study Locations

Sponsors and Collaborators

Immunocore Ltd

MedImmune LLC

More Information

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Responsible Party:	Immunocore Ltd
ClinicalTrials.gov Identifier:	NCT02535078 History of Changes
Other Study ID Numbers:	**IMCgp100-201**
First Posted:	August 28, 2015 Key Record Dates
Last Update Posted:	April 27, 2018
Last Verified:	April 2018

Additional relevant MeSH terms:

Melanoma
Neuroendocrine Tumors
Neuroectodermal Tumors
Neoplasms, Germ Cell and Embryonal
Neoplasms by Histologic Type
Neoplasms
Neoplasms, Nerve Tissue
Nevi and Melanomas
Antibodies, Monoclonal
Tremelimumab
Immunologic Factors
Physiological Effects of Drugs
Antineoplastic Agents