Trial record **1 of 1** for: IMCgp100-102

Previous Study | Return to List | Next Study

A Study of the Intra-Patient Escalation Dosing Regimen With IMCgp100 in Patients With Advanced Uveal Melanoma

ClinicalTrials.gov Identifier: NCT02570308

Recruitment Status: Recruiting
First Posted: October 7, 2015
Last Update Posted: June 29, 2018

See Contacts and Locations

Sponsor:
Immunocore Ltd

Information provided by (Responsible Party):
Immunocore Ltd

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

Study Description

Go to

Brief Summary:

IMCgp100-102 is a Phase I study of the weekly intra-patient escalation dose regimen with IMCgp100 as a single agent in patients with metastatic uveal melanoma (mUM). According to this regimen, all patients in the trial will receive 2 weekly doses of IMCgp100 at a dose level below the identified weekly recommended Phase II dose (RP2D-QW) and then a dose escalation will commence at the third weekly dose at C1D15. The Phase I testing of the intra-patient escalation dosing regimen is designed to achieve a higher exposure and maximal plasma concentration of IMCgp100 after doses at Cycle 1 Day 15 (C1D15) and thereafter .

Condition or disease	Intervention/treatment	Phase
Uveal Melanoma	Drug: IMCgp100	Phase 1 Phase 2

Detailed Description:

This is a Phase I clinical study of IMCgp100 in patients with advanced melanoma. In the Phase I FIH study of IMCgp100 in advanced melanoma, a dose escalation was conducted with IMCgp100 administered on a weekly

basis (Middleton, 2015). In this study, the MTD when IMCgp100 is administered on a weekly basis was declared at 600 ng/kg. With a data cut off of 18 August 2015, it was observed that DLT of grade 3 (n=3) and grade 4 (n=1) hypotension in the weekly dosing cohort was observed with the first dose in this trial. Based on observed safety and the PK profile, a flat dosing regimen was implemented across the program and the RP2D of the RP2D-QW was identified as 50 mcg QW.

In this same FIH study, several patients with metastatic uveal melanoma were treated in the weekly dosing regimen at the MTD dose level (600 ng/kg) and as well at the dose level above MTD, 900 ng/kg (n=5, data cut off 18 August 2015). Based on review of the observed objective responses in the Phase I trial in UM as well as objective responses noted in cutaneous melanoma, it was noted that patients with larger diameters of disease burden (both cutaneous and UM) experienced objective tumor responses at the higher overall exposures to IMCgp100. The intra-patient dose escalation study design is based on 2 observations in the clinic: (1) objective partial and minor tumor responses in patients with higher tumor burdens were generally observed at the higher absolute doses in the Phase I trial and (2) the occurrences of more severe toxicity leading to dose limitation were limited to the first 2 weeks of dosing on C1D1 and C1D8. Based on these 2 observations, it is hypothesized that an increased exposure to drug in the weeks following the occurrence of the more severe toxicity (at the first 2 doses) may lead to an enhanced tumor response in a setting of an unfavorable tumor microenvironment such as UM.

This is a Phase I study of IMCgp100 administered on a weekly basis with an intra-patient escalation dosing regimen. The intra-patient escalation occurs at the third weekly dose on Cycle 1 Day 15 (C1D15). According to this regimen, all patients in the trial will receive 2 weekly doses of IMCgp100 at a dose level below the identified weekly recommended Phase II dose (RP2D-QW) and then a dose escalation will commence at the third weekly dose at C1D15 with the goal to achieve a long-term dosing regimen at a dose higher than that identified for the straight weekly dosing regimen (RP2D-QW). The dose escalation will identify the RP2D-IE.

The Phase I portion of the study will be a standard 3+3 dose escalation design. After the dose escalation portion is complete and the recommended Phase II dose of the intra-patient escalation dose regimen (RP2D-IE) is identified, 2 expansion cohorts in metastatic uveal melanoma will be completed. The cohorts will enroll patients with metastatic uveal melanoma and are defined based on prior therapy The expansion portion will enroll approximately 150 patients.

Study Design

Go to

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	150 participants
Allocation:	Non-Randomized
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase I/II Open-label, Multi-center Study of the Safety and Efficacy of IMCgp100 Using the Intra-patient Escalation Dosing Regimen in Patients With Advanced Uveal Melanoma
Study Start Date:	February 2016
Estimated Primary Completion Date:	September 2019

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Melanoma

Genetic and Rare Diseases Information Center resources:
Intraocular Melanoma Neuroendocrine Tumor
Neuroepithelioma Uveal Diseases

U.S. FDA Resources

Arms and Interventions

Go to

Arm	Intervention/treatment
Experimental: Dose escalation Dose escalation cohorts of the intra-patient escalation regimen	Drug: IMCgp100 Bispecific soluble HLA-A2 restricted gp100-specific TCR fused to anti-CD3
Experimental: Dose expansion Dose expansion cohort with the recommended phase 2 dose of the intra-patient dose escalation regimen	Drug: IMCgp100 Bispecific soluble HLA-A2 restricted gp100-specific TCR fused to anti-CD3

Outcome Measures

Go to

Primary Outcome Measures:

1. Phase 1 Recommended phase 2 dose of the intra-patient escalation regimen (RP2D-IE) [Time Frame: 2 years]
2. 2. Phase 2: Objective response rate by RECIST 1.1 assessed by independent central review [Time Frame: 2 years]

Secondary Outcome Measures:

1. Objective response rate (Phase 1) [Time Frame: 2 years]
2. Progression free survival [Time Frame: 2 years]
3. Overall survival [Time Frame: 2 years]
4. Duration of response [Time Frame: 2 years]
5. Time to response [Time Frame: 2 years]
6. Minor response rate [Time Frame: 2 years]
7. Number of treatment dose interruptions and reductions [Time Frame: 2 years]
8. Area under the plasma concentration-time curve (AUC) [Time Frame: 2 years]
9. Area under the plasma concentration-time curve (AUC) [Time Frame: 3 weeks]
10. The maximum observed plasma drug concentration after single dose administration (Cmax) [Time Frame: 2 years]
11. The time to reach maximum plasma concentration (Tmax) [Time Frame: 3 weeks]
12. The elimination half-life (t1/2) [Time Frame: 3 weeks]

13. Incidence of anti-IMCgp100 antibody formation [Time Frame: 2 years]

Eligibility Criteria

Go to

Information from the National Library of Medicine

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. Male or female patients age ≥ 18 years of age at the time of informed consent
2. Ability to provide and understand written informed consent prior to any study procedures
3. Histologically or cytologically confirmed diagnosis of metastatic uveal melanoma (mUM)
4. Surgically sterile patients or patients of child-bearing potential who agree to use highly effective methods of contraception during study dosing and for 6 months after last dose of study drug
5. Life expectancy of >3 months as estimated by the investigator
6. Human leukocyte antigen (HLA)-A2 positive
7. ECOG Performance Status of 0 or 1 at Screening
8. Patients must have disease (measurable or non-measurable acceptable) according to Response Evaluation Criteria In Solid Tumors (RECIST) v.1.1 criteria
9. Patients in Phase 2 expansion cohort A will have experienced disease progression with 1 systemic treatment containing a checkpoint inhibitor. Any prior liver directed therapy is acceptable.
10. Patients in Phase 2 expansion cohort B will have experienced disease progression with 1 or 2 prior lines of therapy, including up to 1 prior line of liver-directed therapy

Exclusion Criteria:

1. Presence of symptomatic or untreated central nervous system (CNS) metastases, or CNS metastases that require doses of corticosteroids within the prior 3 weeks to Study Day 1. Asymptomatic and adequately treated CNS metastases are not exclusionary
2. History of severe hypersensitivity reactions to other biologic drugs or monoclonal antibodies
3. Patient with any out-of-range laboratory values defined as:
   - Serum creatinine > 1.5 x upper limit of normal (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
   - ALT > 3 x ULN
   - AST > 3 x ULN

- Absolute neutrophil count < 1.0 x 10^9/L
- Absolute lymphocyte count < 0.5 x 10^9/L (Phase 1 and Phase 2 Cohort A); absolute lymphocyte count < 1.0 x 10^9/L (Phase 2 Cohort B)
- Platelet count < 75 x 10^9/L
- Hemoglobin < 8 g/dL
- Potassium, magnesium, corrected calcium or phosphate abnormality of National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) > grade 1

4. 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 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
5. Active infection requiring systemic antibiotic therapy. Patients requiring systemic antibiotics for infection must have completed therapy before Screening
6. Known history of HIV infection. Testing for HIV status is not necessary unless clinically indicated
7. Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection 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
8. Patients receiving systemic treatment with systemic steroid therapy or any other immunosuppressive medication at any dose level that would interfere with the action of the study drugs in the opinion of the investigator
9. 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 prior to study 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
10. 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
11. Systemic anti-cancer therapy within 2 weeks of the first dose of study treatment. For cytotoxic or immunotherapy agents that can present with major delayed toxicity (eg, anti-CTLA-4), 4 weeks is indicated as washout period
12. Presence of NCI CTCAE ≥ grade 2 toxicity (except alopecia, peripheral neuropathy and ototoxicity, which are excluded if ≥ NCI CTCAE grade 3) due to prior cancer therapy
13. Chronic systemic corticosteroid use (ie, prednisone > 10 mg QD or the equivalent); 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
14. Major surgery within 2 weeks of the first dose of study drug (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 and are not exclusionary)
15. 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
16. Use of hematopoietic colony-stimulating growth factors (eg, G-CSF, GMCSF, M-CSF) ≤ 2 weeks prior to start of 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

17. Pregnant, likely to become pregnant, or lactating women (where pregnancy is defined as the state of a female after conception and until the termination of gestation)
18. Patients with adrenal insufficiency or patients currently requiring chronic, systemic corticosteroid therapy at any dose for longer than 2 weeks. Local steroid therapies (eg, otic, ophthalmic, intraarticular, or inhaled medications) are acceptable
19. Patients may not have been included in any prior IMCgp100 trial, regardless of treatment cohort

Contacts and Locations

Go to

Information from the National Library of Medicine

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): ***NCT02570308***

Contacts

Contact: Rachael Easton, MD, PhD 484-534-5261 rachael.easton@immunocore.com

Contact: Rachael Johnson 484-534-5261 rachael.johnson@immunocore.com

Locations

United States, California

The Angeles Clinic and Research Institute - W LA Office — **Recruiting**
Los Angeles, California, United States, 90025
Contact: Omid Hamid, MD
Contact 3102302121
Principal Investigator: Omid Hamid, MD

United States, Colorado

University of Colorado Denver Anschutz Medical Campus — **Recruiting**
Aurora, Colorado, United States, 80045
Contact: Matthew Rioth, MD 720-848-7135
Principal Investigator: Matthew Rioth, MD

United States, Florida

University of Miami Hospital Clinics/Sylvester Comprehensive Cancer Center — **Recruiting**
Miami, Florida, United States, 33136
Contact: Lynn Feun, MD 305-243-6606
Principal Investigator: Lynn Feun, MD

H. Lee Moffitt Cancer Center and Research Institute, Inc — **Recruiting**
Tampa, Florida, United States, 33612-9497
Contact: Zeynep Eroglu, MD
Contact 8137458581
Principal Investigator: Zeynep Eroglu, MD

United States, Illinois

The University of Chicago Medical Center — **Recruiting**
Chicago, Illinois, United States, 60637
Contact: Jason Luke, MD 773-702-8222
Principal Investigator: Jason Luke, MD

United States, Missouri

Washington University, School of Medicine — **Recruiting**
Saint Louis, Missouri, United States, 63110
Contact: Melissa Meredith 314-362-4140
Principal Investigator: Leonel Hernandez-Aya, MD

United States, New York

Columbia University Medical Center - The New York Presbyterian Hospital — **Recruiting**
New York, New York, United States, 10032
Contact: Richard Carvajal, MD 212-639-5096
Principal Investigator: Richard Carvajal, MD

United States, Pennsylvania

Thomas Jefferson University Medical Oncology Clinic — **Recruiting**
Philadelphia, Pennsylvania, United States, 19107
Contact: Tracy Newhall 215-503-7488
Principal Investigator: Takami Sato, MD

United States, Tennessee

Vanderbilt University Medical Center — **Recruiting**
Nashville, Tennessee, United States, 37232
Contact: Douglas Johnson, MD
Contact 6159368422
Principal Investigator: Douglas Johnson, MD

Canada, Ontario

Princess Margaret Cancer Center — **Recruiting**
Toronto, Ontario, Canada, M5G2M9
Contact: Marcus Butler, MD (416) 946-2000
Principal Investigator: Marcus Butler, MD

United Kingdom

The Clatterbridge Cancer Centre — **Recruiting**
Wirral, Merseyside, United Kingdom, CH63 4JY
Contact: Maria Maguire +441513341155
Principal Investigator: Joseph Sacco, MD

Mount Vernon Cancer Centre — **Recruiting**
Northwood, Middlesex, United Kingdom, HA6 2RN
Contact: Joanna Pascal +441923844763
Principal Investigator: Paul Nathan, MD

Sponsors and Collaborators

Immunocore Ltd

More Information

Go to

Responsible Party: Immunocore Ltd

ClinicalTrials.gov Identifier:	NCT02570308	History of Changes
Other Study ID Numbers:	**IMCgp100-102**	
First Posted:	October 7, 2015	Key Record Dates
Last Update Posted:	June 29, 2018	
Last Verified:	June 2018	

Additional relevant MeSH terms:

Melanoma
Uveal Neoplasms
Neuroendocrine Tumors
Neuroectodermal Tumors
Neoplasms, Germ Cell and Embryonal
Neoplasms by Histologic Type
Neoplasms
Neoplasms, Nerve Tissue
Nevi and Melanomas
Eye Neoplasms
Neoplasms by Site
Eye Diseases
Uveal Diseases