A Phase 2, Multicenter, Open-label, Single-arm Trial to Evaluate the Correlation Between Objective Response Rate and Baseline Intratumoral CD8+ Cell Density in Subjects With Unresected Stage IIIB to IVM1c Melanoma Treated With Talimogene Laherparepvec

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43786

Source
ToetsingOnline

Brief title
20120325

Condition

- Skin neoplasms malignant and unspecified

Synonym
1) Unresected stage IIIB to IVM1c melanoma; 2) Unremoved melanoma (type of skin cancer)

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: Biomarker, Phase 2, Talimogene Laherparepvec, Unresected Stage IIIB to IVM1c Melanoma

Outcome measures

Primary outcome

To explore the correlation between baseline intratumoral CD8+ cell density and

objective response rate (ORR) in subjects with unresected stage IIIB to IVM1c

melanoma treated with talimogene laherparepvec

Secondary outcome

- to explore the correlation between baseline intratumoral CD8+ cell density

and durable response rate (DRR), duration of response (DOR), and changes in

tumor burden

- to explore the correlation between changes in intratumoral CD8+ cell density

during treatment and ORR, DRR, DOR, and changes in tumor burden

- to evaluate ORR, DOR, time to treatment failure (TTF), DRR, OS, and change in

tumor burden during treatment

- to evaluate the safety and tolerability of talimogene laherparepvec

Study description

Background summary

In this study talimogene laherparepvec is studied. Talimogene laherparepvec is a modified form of herpes simplex virus (HSV) type-1. The virus* genes were modified so that it produces human granulocyte macrophage colony-stimulating factor (GM-CSF). It multiplies and grows in tumor cells. Talimogene laherparepvec is designed to work in two complementary ways. It directly destroys cells in the tumor into which it is injected, and it activates the body*s own immune fighting cells to destroy the tumor cells throughout the body. Intralesional injection of talimogene laherparepvec has been approved by the United States Food and Drug Administration (FDA) for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery. The European Union regulatory authority is currently assessing an application for approval.
A total of about 110 people are expected to participate in this study. Amgen Inc. is funding this clinical study.

Study objective

In this study, we explore the correlation between baseline intratumoral CD8+ cell density and objective response rate (ORR) as well as other biomarker parameters in subjects with unresected stage IIIB to IVM1c melanoma treated with talimogene laherparepvec. In addition, safety and tolerability of talimogene laherparepvec is examined.

Study design

This phase 2 study is performed in several hospitals within and outside the European Union. Patients start the study after signing the Informed Consent with the screenings phase. When the patient is eligible the patient starts with the treatment phase. The first dose of talimogene laherparepvec is administered in cycle 1; treatment cycle 2 will be 3 weeks thereafter. Subsequent doses will be given every 2 weeks. The duration of the treatment will depend on how the patient*s disease responds to talimogene laherparepvec, or how the study treatment is tolerated.
Subjects will be followed for safety 30 days after the last dose of talimogene laherparepvec
and for survival every 3 months for up to approximately 24 months after the last subject is enrolled.
Blood and tumor tissue samples will be collected and tumor biopsies will be performed.
Samples will be analyzed to explore if intratumoral CD8+ cell density at baseline
and its change during treatment is correlated with the objective response rate in subjects with
unresected stage IIIB-IVM1c melanoma

Intervention

Patients will receive several doses of Talimogene laherparepvec. The initial dose is up to 4.0 mL of 10^6 PFU/mL. Subsequent doses of are up to 4.0 mL of 10^8 PFU/mL. The second dose up to 4.0 mL of 10^8 PFU/mL should be administered 21 (+5) days after the initial dose. Subsequent doses up to 4.0 mL of 10^8 PFU/mL should be given every 14 (± 3) days

Study burden and risks

Risk: Adverse events of the study medication talimogene laherparepvec. During the visits to the hospital the subjects will be monitored for adverse events.
Burden: Maximum study duration is about 28-32 months

Contacts

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Amgen

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Subject has provided informed consent prior to initiation of any study-specific activities/procedures ;- Male or female age * 18 years at the time of informed consent;- Histologically confirmed diagnosis of melanoma;- Subject with stage IIIB to IVM1c melanoma for whom surgery is not
recommended;- Subject who is treatment naïve or had received prior treatment for melanoma. Any systemic treatment for melanoma must have been completed at least 28 days prior to enrollment;- Candidate for intralesional therapy (ie, disease is appropriate for direct injection or through the use of ultrasound guidance) defined as one of the following:;-at least 1 injectable cutaneous, subcutaneous, or nodal melanoma lesion * 10 mm in longest diameter, or;- multiple injectable melanoma lesions that in aggregate have a longest diameter of * 10 mm;- Measurable disease defined as one or more of the following:;- at least 1 melanoma lesion that can be accurately and serially measured in at least 2 dimensions and for which the greatest diameter is * 10 mm as measured by contrast-enhanced or spiral computed tomography (CT) scan, magnetic resonance imaging (MRI), or ultrasound for nodal/soft tissue disease (including lymph nodes);- at least 1 * 10 mm superficial cutaneous or subcutaneous melanoma lesion as measured by calipers;- multiple superficial melanoma lesions which in aggregate have a total diameter of * 10 mm;- Serum lactate dehydrogenase (LDH) levels * 1.5 X upper limit of normal (ULN) within 28 days prior to enrollment ;- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (see Appendix E);- Adequate organ function determined within 28 days prior to enrollment, defined as follows:;- absolute neutrophil count * 1500/mm3;- platelet count * 75,000/mm3;- hemoglobin * 8 g/dL without need for hematopoietic growth factor or transfusion support;- serum creatinine * 1.5 x ULN ;- serum bilirubin * 1.5 x ULN;- aspartate amino transferase (AST) * 2.5 x ULN;- alanine amino transferase (ALT) * 2.5 x ULN;- alkaline phosphatase * 2.5 x ULN;- serum albumin * 2.5 g/dL;- prothrombin time (PT) * 1.5 x ULN (or international normalization ratio [INR] * 1.3)*;- partial thromboplastin time (PTT) * 1.5 x ULN

Exclusion criteria

- Clinically active cerebral metastases. Subjects with up to 3 (neurological performance status of 0) cerebral metastases may be enrolled, provided that all lesions have been adequately treated with stereotactic radiation therapy (including Gamma Knife) or resection, with no evidence of progression and have not required steroids for at least two months prior to enrollment.;- Greater than 3 visceral metastases (this does not include lung metastases or nodal metastases associated with visceral organs). For subjects with 3 visceral metastases, no lesion > 3 cm and liver lesions must be stable for at least 1 month prior to enrollment.;- Bone metastases;- Primary ocular or mucosal melanoma;- History or evidence of symptomatic autoimmune pneumonitis, glomerulonephritis, vasculitis, or other symptomatic autoimmune disease;- Evidence of clinically significant immunosuppression such as the following:;* primary immunodeficiency state such as Severe Combined Immunodeficiency Disease;*concurrent opportunistic infection;*receiving systemic immunosuppressive therapy (> 2 weeks), including oral steroid doses > 10 mg/day of prednisone or equivalent during the

2 monthsprior to enrollment;- Active herpetic skin lesions or prior complications of HSV-1 infection (eg, herpetic keratitis or encephalitis);- Requires intermittent or chronic systemic (intravenous or oral) treatment with an antiherpetic drug (eg, acyclovir), other than intermittent topical use;- Previous treatment with talimogene laherparepvec;- Currently receiving treatment with another investigational device or drug study, or less than 28 days since ending treatment with another investigational device or drug study(s);- Other investigational procedures while participating in this study are excluded;- Known to have acute or chronic active hepatitis B infection;- Known to have acute or chronic active hepatitis C infection;- Known to have human immunodeficiency virus infection;- History of other malignancy within the past 3 years with the following exceptions:;* malignancy treated with curative intent and with no known active disease present for * 3 years before enrollment and felt to be at low risk for recurrence by the treating physician
* adequately treated non-melanoma skin cancer without evidence of disease
* adequately treated cervical carcinoma in situ without evidence of disease
* adequately treated breast ductal carcinoma in situ without evidence of disease
*prostatic intraepithelial neoplasia without evidence of prostate cancer
*adequately treated urothelial papillary noninvasive carcinoma or carcinoma in situ;- Subject has known sensitivity to any of the products or components to be administered during dosing;- Subject likely to not be available to complete all protocol required study visits or procedures, and/or to comply with all required study procedures to the best of the subject*s and investigator*s knowledge;- History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above) that, in the opinion of the investigator or Amgen medical monitor, if consulted, would pose a risk to subject safety or interfere with the study evaluation, procedures, or completion;- Subject previously has entered this study;- Female subject is pregnant or breast-feeding, or planning to become pregnant during study treatment and through 3 months after the last dose of talimogene laherparepvec;- Female subject of childbearing potential who is unwilling to use acceptable method(s) of effective contraception during study treatment and through 3 months after the last dose of talimogene laherparepvec;- Sexually active subjects and their partners unwilling to use male or female latex condom to avoid potential viral transmission during sexual contact while on treatment and within 30 days after treatment with talimogene laherparepvec.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-06-2016
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	Not yet available
Generic name:	Talimogene Laherparepvec

Ethics review

Approved WMO Date:	24-06-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-12-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-01-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-02-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	09-08-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-09-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-11-2016
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-03-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-06-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-06-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-06-2018
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-12-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-03-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-07-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-005552-15-NL
ClinicalTrials.gov	NCT02366195
CCMO	NL51482.000.15

Study results

Results posted: 17-11-2021

First publication
10-06-2021