A Phase 1b/3, Multicenter, Trial of Talimogene Laherparepvec in Combination With Pembrolizumab (MK-3475) for Treatment of Unresectable, Stage IIIB to IVM1c Melanoma (MASTERKEY-265)

Published: 03-02-2016
Last updated: 20-04-2024

Primary Objectives:To evaluate the efficacy of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab, as assessed by progression free survival (PFS) (response evaluation by blinded independent central review using modified...

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

Summary

ID

NL-OMON50729

Source
ToetsingOnline

Brief title
20110265 MASTERKEY

Condition

- Skin neoplasms malignant and unspecified

Synonym
1) Unresectable 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: - Combination Therapy Talimogene Laherparepvec/Placebo - Pembrolizumab, - Melanoma, - Phase1b/3, - Randomised

Outcome measures

Primary outcome

PFS (response evaluation by blinded independent central review assessed using

modified RECIST 1.1) (PFS1) and OS

Secondary outcome

- iCRR by blinded independent central review using modified irRC-RECIST

- iPFS by blinded independent central review using modified irRC-RECIST (PFS2)

- OS in subjects excluding stage IVM1c per CRF

- ORR (CR+PR), BOR, DRR, DOR, and DCR (response evaluation by blinded

independent central review assessed using modified RECIST 1.1 and iORR (iCR +

iPR), iBOR, iDRR, iDOR, and iDCR (response evaluation by blinded independent

central review assessed using modified irRC-RECIST)

Incidence of treatment-emergent and treatment-related AEs (all AEs, grade >= 3

AEs, serious

adverse events, fatal AEs, and AEs defined as events of interest), and abnormal

laboratory

tests

-Changes in EORTC QLQ-C30 GHS/QoL subscale

Study description

Background summary

It's expected that talimogene laherparepvec and PD-1 blockade likely play complementary roles in regulating adaptive immunity. Talimogene laherparepvec likely augments dendritic cell-mediated tumor antigen presentation through local expression of GM-CSF and local antigen release by direct tumor lysis. Pembrolizumab prevents T-cell exhaustion in peripheral tissues. The combination of an agent that increases tumor-specific immune activation with one that blocks inhibitory T-cell checkpoints could produce greater antitumor activity than either agent alone. It's expected that talimogene laherparepvec in combination with pembrolizumab will be safe and well tolerated and that talimogene laherparepvec in combination with pembrolizumab compared to pembrolizumab alone will improve PFS and will improve OS.

Study objective

Primary Objectives:
To evaluate the efficacy of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab, as assessed by progression free survival (PFS) (response evaluation by blinded independent central review using modified Response Evaluation Criteria in Solid Tumors 1.1 [RECIST]) and overall survival (OS).

Secondary Objectives:
To evaluate the efficacy of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab, as assessed by:
- Complete response rate (iCRR) by blinded independent central assessed modified immune-related response criteria simulating response evaluation criteria in solid tumors (modified irRC-RECIST)
-iPFS by blinded independent central assessed modified irRC-RECIST
-OS in subjects excluding stage IVM1c per case report form (CRF) ORR, BOR, DRR, DOR, DCR (response evaluation by blinded independent central review assessed modified RECIST 1.1 and irRC-RECIST)
-To evaluate the safety of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab, as assessed by incidence of treatment-emergent and treatment-related AEs and abnormal laboratory tests.
-To evaluate patient reported outcomes (PRO) in phase 3 as assessed by the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) Global Health Status/Quality of Life

(GHS/QoL) subscale.

Study design

This is a multicenter, double-blind, placebo-controlled, randomized trial to evaluate the efficacy, as assessed by PFS and OS of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab in subjects with unresectable, stage IIIB to IVM1c melanoma. Approximately 660 subjects will be randomized 1:1 to receive the following:
• Arm 1: talimogene laherparepvec plus pembrolizumab
• Arm 2: placebo plus pembrolizumab
Randomization will be stratified by stage of disease: less advanced stages (IIIB, IIIC, and IVM1a) versus more advanced stages (IVM1b and IVM1c) and by prior BRAF inhibitor therapy: no prior BRAF inhibitor versus BRAF inhibitor with or without MEK inhibitor.
Subjects will be treated with talimogene laherparepvec in combination with pembrolizumab (arm 1) or placebo in combination with pembrolizumab (arm 2) until 24 months from the date of the first dose of pembrolizumab or end of treatment for other reasons as described in Section 3.1.1.1, whichever occurs first.

Intervention

Amgen Investigational Product Dosage and Administration:
Talimogene laherparepvec or placebo will be administered by intralesional injection into injectable cutaneous, subcutaneous, and nodal lesions with or without image ultrasound guidance. Investigational product must not be administered into visceral organ metastases. See Section 6.2.1. for additional information regarding dosage and administration information.

The initial dose of double-blind treatment is up to 4.0 mL of 106 PFU/mL talimogene laherparepvec or placebo (talimogene laherparepvec formulation excipients as described in the Talimogene Laherparepvec Investigator*s Brochure). The second dose up to 4.0 mL of 108 PFU/mL talimogene laherparepvec or placebo should be administered 21 (+3) days after the initial dose. Subsequent doses up to 4.0 mL of 108 PFU/mL talimogene laherparepvec or placebo should be given every 2 weeks (± 3) days until week 9 and every 3 weeks (± 3) days thereafter. When double-blind treatment and pembrolizumab are administered on the same day, double-blind treatment must be administered first.

Non-Amgen Investigational Product Dosage and Administration:

Pembrolizumab at a dose of 200 mg will be administered intravenously every 3 weeks (±3 days). the second dose of pembrolizumab will be administered 21 (+3) days after the initial dose.
See Section 6.2.2 or additional information regarding dosage and administration

of pembrolizumab.

Study burden and risks

RISKS:
Adverse events related to talimogene laherparepvec en pembrolizumab. The patient will be checked for adverse events during the hospital visits.

BURDEN:
Maximal study duration is 2 years + 60 month FU survival.

Contacts

Public
Amgen

Minervum 7061
Breda 4817ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male or female age >= 18 years with histologically confirmed diagnosis of melanoma and stage IIIB to IVM1c for whom surgery is not recommended. Subjects must have measurable disease and be a candidate for intralesional therapy administration into cutaneous, subcutaneous, or nodal lesions. Subjects must have ECOG performance status of 0 or 1, and adequate hematologic, hepatic, renal, and coagulation function.
• Subjects with serine/threonine protein kinase B-Raf V600 (BRAFV600) wild-type tumors must not have received any prior systemic anticancer treatment consisting of chemotherapy, immunotherapy, or targeted therapy given in a non-adjuvant setting for unresectable stage IIIB to IVM1c melanoma. Subjects with BRAFV600 mutated tumors who have received prior BRAF inhibitor therapy either alone or in combination with MEK inhibitor as their only prior systemic therapy are eligible for the phase 3 of this study.
• Subjects with BRAFV600 mutant melanoma or unknown BRAFV600 mutation status who have not received a BRAF inhibitor are also eligible for the phase 3 of this study as first-line treatment if they meet the following criteria: lactate dehydrogenase (LDH) < upper limit of normal (ULN), no clinically significant tumor related symptoms, and absence of rapidly progressing metastatic melanoma.
• Subjects (BRAF mutant, wildtype and UNK) who received prior adjuvant therapy for melanoma will not be excluded with the exception that prior adjuvant therapy with inhibitors of PD-1 or PD-L1 is not allowed. However, if the subject received adjuvant therapy, the subject must have completed therapy at least 28 days prior to enrollment.
• Subjects must have a tumor sample (archival sample or newly obtained biopsy) that is adequate for PD-L1 assessment prior to randomization.

Exclusion criteria

• Subjects must not have clinically active cerebral metastases and/or carcinomatous meningitis. Subjects with up to 3 cerebral metastases may be enrolled, provided that all lesions have been adequately treated with stereotactic radiation therapy, craniotomy, or Gamma Knife therapy, with no evidence of progression, and not requiring steroids, for at least 2 months prior to enrollment.
Carcinomatous meningitis is excluded regardless of clinical stability
• Subjects must not have primary uveal or mucosal melanoma, history or evidence of melanoma associated with immunodeficiency states or history of other malignancy within the past 3 years with the exceptions of the prior malignancies noted in Section 4.1.3.
• Subjects may not have been previously treated with T-VEC, any other oncolytic virus, pembrolizumab, or any other inhibitor of PD-1, PD-L1, or programmed cell

death ligand 2 (PD-L2).
• Prior treatment with other immunotherapies is allowed only in the adjuvant setting.
• Subjects must not have history or evidence of symptomatic autoimmune glomerulonephritis, vasculitis, other symptomatic autoimmune disease, documented history of autoimmune disease or syndrome requiring systemic treatment in the past 2 years except vitiligo or resolved childhood asthma/atopy, or evidence of clinically significant immunosuppression.
• Subjects must not have active herpetic skin lesions or prior complications of herpetic infection and must not require intermittent or chronic treatment with an antiherpetic drug, other than intermittent topical use.
For a full list of eligibility criteria please refer to Section 4.1.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-08-2017
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	Imlygic

Generic name:	Talimogene Laherparepvec
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-02-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-02-2017
Application type:	First submission
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:	26-04-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-06-2017

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:	26-06-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-07-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-10-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-12-2017
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	03-01-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-01-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-04-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-06-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-06-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-01-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	22-07-2019
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	07-08-2019
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)
Approved WMO Date:	22-11-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-01-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-01-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-02-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-03-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	21-04-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-06-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-10-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-11-2020
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	EUCTR2014-000185-22-NL
ClinicalTrials.gov	NCT02263508
CCMO	NL54270.000.16

Study results

Results posted: 30-09-2021

Summary results
Trial ended prematurely

First publication
02-07-2021