A Phase III randomized, open-label study comparing GSK2118436 to DTIC in previously untreated subjects with BRAF mutation positive advanced (Stage III) or metastatic (Stage IV) melanoma (BRF113683)

Published: 17-12-2010
Last updated: 04-05-2024

Primary: superiority of GSK2118436 over DTIC with respect to progression-free survival for subjects with BRAF mutation positive metastatic melanoma.Secondary: overall survival, best overall response, duration of response, non-melanoma skin lesions,...

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

Summary

ID

NL-OMON44057

Source
ToetsingOnline

Brief title
BRF113683

Condition

- Skin neoplasms malignant and unspecified

Synonym
melanoma

Research involving

Human

Sponsors and support

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

Intervention

Keyword: BRAF mutation, GSK2118436, melanoma, metastatic

Outcome measures

Primary outcome

Progression-free survival

Secondary outcome

Overall survival, best overall response, duration of response, non-melanoma

skin lesions, second malignancies, further validation of a BRAF mutation assay,

quality of life, safety, tolerability, PK, translational research.

Study description

Background summary

Cutaneous melanoma is the most aggressive form of skin cancers. The current standard of care (dacarbazine [DTIC]) is not optimal, since the median progression-free survival is approximately 2 months, and the median overall survival is approximately 7 months. The need for novel agents for this disease is therefore evident.
The RAS/RAF/MEK/ERK pathway is a critical proliferation pathway in many human cancers. This pathway can be activated by alterations in specific proteins, including BRAF. BRAF mutations have been identified at a high frequency in specific cancers, including approximately 50-60% of melanoma. The frequency of this activating mutation and the pathway addiction to which it leads makes mutated BRAF an extremely attractive target. GSK2118436 has demonstrated suppression of phosphorylated ERK (pERK) in tumor cell lines, demonstrated anti-proliferative activity against multiple BRAF mutant tumor cell lines, and achieved biomarker suppression and tumor regression in BRAF mutant xenograft models. In subjects with mutant BRAF melanomas, 9/15 had an objective tumor

response by RECIST at first restaging (8-9 weeks) at doses of 150 mg BID and higher.

Study objective

Primary: superiority of GSK2118436 over DTIC with respect to progression-free survival for subjects with BRAF mutation positive metastatic melanoma.
Secondary: overall survival, best overall response, duration of response, non-melanoma skin lesions, second malignancies, further validation of a BRAF mutation assay, quality of life, safety, tolerability, PK, translational research.

Study design

Open-label, randomized Phase III study comparing intravenous DTIC with the oral GSK2118436. Subjects will be screened for BRAF mutation V600 E. Only BRAF mutation positive patients will be eligible. Subjects will receive either intravenous DTIC 1000mg/m2 every 3 weeks or GSK2118436 150 mg twice daily. Treatment until disease progression or severe toxicity.
Subjects on the DTIC arm will be allowed to receive GSK2118436 after initial progression, and will be followed for response, progression, survival, and further anti-cancer therapy.
Approx. 200 patients.
IDMC.

Intervention

Treatment with DTIC or GSK2118436.

Study burden and risks

Risk: adverse events of study treatment.
Burden: Most test/procedures would be performed during regular care as well. No extra visits.
Extra tests/procedures: approx. 10 ml blood extra per occasion (extra safety tests, PK, biomarkers), echocardiogram every 6 weeks, ECG every 3-6 weeks, quality of life questionnaire 5x in 1st 15 weeks, 1x when study ends.
Optional substudies: pharmacogentics (10 ml blood), biomarkers (tumour tissue (extra biopsy)) after discontinuation of study treatment, biopsy in case of non-melanoma skin lesions.

Contacts

Public

GlaxoSmithKline

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Subjects with histologically confirmed advanced or metastatic melanoma
* Treatment naïve for metastatic disease (with the exception of IL-2, which will be allowed).
* BRAF V600 mutation positive.
* Measurable disease.
* 18 years and above.
* ECOG Performance Status 0-1.
* Females of childbearing potential: double barrier method of contraception.

Exclusion criteria

* Previous treatment for metastatic melanoma, including treatment with BRAF or MEK inhibitor.
* Known ocular or primary mucosal melanoma.
* Currently receiving cancer therapy.
* Any major surgery, radiotherapy, or immunotherapy within the last 4 weeks.

* Evidence of active CNS disease.
* Pregnancy or breastfeeding

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2011
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	DTIC
Generic name:	dacarbazine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	GSK2118436
Generic name:	GSK2118436

Ethics review

Approved WMO

Date:	17-12-2010
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	03-03-2011
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	17-05-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	08-09-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-03-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-03-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	02-04-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-06-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-06-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	07-08-2012
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	07-06-2013
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Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-04-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	08-08-2014

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Approved WMO Date:	12-08-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	04-02-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	11-03-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
Other	clinicaltrials.gov. Registratienummer NCT01227889.
EudraCT	EUCTR2009-015298-11-NL
CCMO	NL34853.031.10