A Randomized Phase 3 Study of Tasisulam Administered as an Intravenous Infusion on Day 1 of a 28-Day Cycle vs. Paclitaxel as Second-Line Treatment in Patients with Metastatic Melanoma

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

Summary

ID

NL-OMON34807

Source
ToetsingOnline

Brief title
tasisulam study H8K-MC-JZAO

Condition

- Skin neoplasms malignant and unspecified

Synonym
Metastatic Melanoma

Research involving

Human

Sponsors and support

Primary sponsor: Eli Lilly
Source(s) of monetary or material Support: Eli Lilly (sponsor van de studie)

Intervention

Keyword: Melanoma, Second-line treatment, Tasisulam

Outcome measures

Primary outcome

See Objective of the study: Primairy objectives.

Secondary outcome

See Objective of the study: Secondairy objectives.

Study description

Background summary

Metastatic melanoma has remained a challenging clinical problem for over 3 decades,
with first-line treatment dacarbazine/temozolomide being little better than best supportive
care. In addition, despite numerous clinical studies, no agent has been shown to improve
the survival of patients failing front-line treatment. Although Study JZAF is still in
progress, the response rate and number of tasisulam doses patients have received are
encouraging, particularly since there were no limits imposed on the number of prior
immuno-based treatments, pre-treatment LDH, or the presence or absence of visceral
metastases. A recent meta-analysis of cooperative group trials in metastatic melanoma
from 1975 to 2005 suggested that a 6-month PFS rate of 15% and a 1-year overall survival rate of 25% were reasonable benchmarks for success for a Phase 2 study (Korn

et al. 2008). The activity of tasisulam observed in second-line metastatic melanoma
patients in Study JZAF provides rationale for further study for this novel anti-cancer
agent in metastatic melanoma patients who have failed first-line dacarbazine or temozolomide.

Study objective

The primary objective of this study is to compare the overall survival (OS) of patients who
have received one prior regimen of dacarbazine or temozolomide-based chemotherapy for metastatic
melanoma when treated with either tasisulam or paclitaxel.

The secondary objectives of the study are the following:
To compare the following between treatment arms:
• time-to-event efficacy variables, including:
• progression-free survival (PFS)
• duration of response (DoR)
• deterioration in the FACT-M TOI score
• objective tumor response rate
• therapeutic benefit rate (TBR)
• measures of relative safety, including quantitative and qualitative laboratory and non-laboratory toxicities
•health outcome measures, including the quality-adjusted life years (QALYs) gained, time to worsening of health related quality of life (TWQ), and measures of the patient*s well-being and symptoms.
Translational Research (TR):
• to evaluate the treatment-specific and treatment-independent effects of BRAF and c-Kit mutational status on measures of clinical efficacy, including OS, PFS, DoR, and response
• to evaluate the treatment-specific effects of genetic markers, including but not limited to DMET genes such as CYP2C19 and CYP2C9, on measures of clinical efficacy and toxicity.
• to assess other exploratory biomarkers relevant to tasisulam and paclitaxel
• to assess other exploratory biomarkers relevant to the disease state of melanoma
• to assess the association between other exploratory biomarkers and clinical outcome.

Study design

Study Design: This is a randomized, open-label, 2-arm, multicenter, Phase 3 investigation of tasisulam
versus paclitaxel after 1 previous systemic treatment with a dacarbazine or

temozolomide-based regimen for metastatic melanoma. Tasisulam will be administered as a 2-hour intravenous (IV) infusion on Day 1 of a 28-day cycle. Paclitaxel will be administered as a 1-hour IV infusion on Days 1, 8, & 15 of a 28-day cycle.
Approximately 800 patients are planned to be enrolled into the study world-wide and the study will remain
open until approximately 600 events (deaths from any cause) have been observed. Patients will be
randomized 1:1 to either tasisulam or paclitaxel treatment. Appropriate efficacy measures will be recorded
every other cycle until progression, and upon discontinuation of treatment, with the exception of physically
assessed lesion measurements which will be repeated every cycle before tasisulam or paclitaxel
administration and at discontinuation of treatment as appropriate.

Intervention

This is a randomized study with 2 arms to compare tasisulam versus paclitaxel after 1 previous systemic treatment with a dacarbazine or temozolomide-based regimen for metastatic melanoma.
Tasisulam will be administered as a 2-hour intravenous (IV) infusion on Day 1 of a 28-day cycle. Paclitaxel will be administered as a 1-hour IV infusion on Days 1, 8, & 15 of a 28-day cycle

Study burden and risks

Side effects tasisulam / paclitaxel -> see question E9
Study procedures: blood, ECG, CT or MRI scans, see 'study schedule', protocol pages 74 t/m 77 and question E6.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Histologic and/or cytologic diagnosis of malignant melanoma that is metastatic (Stage IV); measurable disease as defined by the Response Evaluation Criteria in Solid Tumors (RECIST 1.0); at least 18 years of age; performance status of 0 to 1 on the Eastern Cooperative Oncology Group (ECOG) Scale; have progressed after 1 previous systemic treatment containing dacarbazine or temozolomide for metastatic melanoma; have discontinued all previous therapies for cancer, including chemotherapy, radiotherapy, immunotherapy, or other investigational therapy for at least 30 days (6 weeks for mitomycin-C or nitrosoureas) before study enrollment and recovered from the acute effects of therapy (except alopecia).

Exclusion criteria

Have received >= 2 previous cytotoxic-based treatment regimens for metastatic melanoma. An immunotherapy or antibody based regimen [including vaccination-based treatments], or single agent treatment with a targeted agent (e.g.BRAF or c-Kit inhibitor, are not counted as a prior treatment regimen for determining study eligibility unless either was combined with a chemotherapeutic drug); have documented active central nervous system or leptomeningeal metastasis (brain metastasis) at the time of study entry; currently receiving warfarin; have primary ocular or mucosal melanoma; any previous treatment with paclitaxel or a paclitaxel-containing regimen for metastatic melanoma

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2010
Enrollment:	25
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Taxol
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tasisulam
Generic name:	unknown at this moment

Ethics review

Approved WMO Date:	10-12-2009
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-12-2009
Application type:	First submission

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-02-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-05-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	28-07-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-09-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-11-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-12-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-12-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-12-2010
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	12-01-2011
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-01-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-07-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	De studie zal binnenkort geregistreerd worden op de internet site: www.clinicaltrials.gov.
EudraCT	EUCTR2009-014591-21-NL
CCMO	NL30148.028.09