Adjuvant peginterferon alfa-2b for 2 years vs Observation in patients with an ulcerated primary cutaneous melanoma with T(2-4)bN0M0: a randomized phase III trial of the EORTC Melanoma Group.

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To prospectively assess the efficacy, toxicity, quality of life with peginterferon alfa-2b as compared to observation after adequate surgery for ulcerated primary cutaneous melanomas with T(2-4)bN0M0

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

Summary

ID

NL-OMON43578

Source
ToetsingOnline

Brief title
Adjuvant Pegylated Interferon in Ulcerated Melanoma

Condition

- Skin neoplasms malignant and unspecified

Synonym
skin cancer melanoma

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: Educational Grant from pharmaceutical company,Merck Sharp & Dohme (MSD)

Intervention

Keyword: Adjuvant, Melanoma, peginterferon alfa-2b, Ulceration

Outcome measures

Primary outcome

Primary endpoint:

Relapse-free survival (RFS) will be assessed by physical, US/CT/MRI and /or

biopsy

Secondary outcome

Secondary endpoints:

Overall survival (OS)

Distant metastases-free survival (DMFS) will be assessed by imaging and/or

biopsy

Quality of life will be assessed by QLQ-C30 version 3

Study description

Background summary

The main purpose of this study is to determine whether post-operative adjuvant therapy for two years with Peginterferon alfa-2b improves relapse-free survival

(RFS) as compared to observation (no treatment will be given for your cancer). The other objectives are to assess safety, distant metastasis free survival, overall survival and quality of life.
It has been shown in some previous studies that patients who have ulcerated melanoma tend to relapse faster when compared to their non ulcerated counterparts and this also reflected in the overall survival of the patients.
The biological characteristics of ulcerated cancers are quite different in that their immune response is different and moreover it has been demonstrated that lymph nodes of these melanomas have much more suppressed immune cell counts along with different white blood cell populations.
Interferon * has been the most studied drug in the adjuvant setting and has been evaluated in a number of trials and is the most promising agent at present. peginterferon alfa-2b is pegylated interferon in which the PEG (polyethylene glycol) protects the interferon from faster breakdown in the body thereby increasing the time the drug stays in the body. This essentially means that less amount peginterferon alfa-2b will have the same benefit as compared to high dose normal interferon.
peginterferon alfa-2b is approved by US Food and Drug Administration to treat patients of melanoma whose cancer has been removed surgically but their lymph nodes have been invaded by melanoma. This above mentioned approval was given based on a study conducted by EORTC.

Study objective

To prospectively assess the efficacy, toxicity, quality of life with peginterferon alfa-2b as compared to observation after adequate surgery for ulcerated primary cutaneous melanomas with T(2-4)bN0M0

Study design

This is a multicenter randomized phase III trial.

A total of 1200 patients with ulcerated primary cutaneous melanoma T(2-4)b N0M0 will be randomized within 12 weeks after definitive surgery into two equal-sized arms (approximately 600 patients each):

ARM A: Peginterferon alfa-2b subcutaneous injection at 3.0 *g/kg, weekly for 2 years or until relapse of disease.

ARM B: OBSERVATION

Treatment will be administered unless there is relapse of the disease, unacceptable toxicity, patient's refusal, patient's best interest to stop according to treating physician.

Intervention

Peginterferon alfa-2b is administered by subcutaneous injection at a dose of 3.0 *g/kg.

Acetaminophen (500-1000 mg) will be given in the clinic 30 minutes prior to receiving the first dose of peginterferon alfa-2b. Subjects should be observed for 1-2 hours after the first dose. Acetaminophen (500-650 mg PO q 4-6 hours) should be continued as needed, and should not exceed 3000 mg/day.

Patients who are deemed competent to self administer the subcutaneous injections of peginterferon alfa-2b will be instructed and may do so.

Patients in ARM A:Peginterferon alfa-2b will receive peginterferon alfa-2b (3.0 *g/kg), weekly for 2 years or until relapse of the disease, unacceptable toxicity, patient's refusal, patient's best interest to stop according to treating physician.

Study burden and risks

Patients may have side effects while on the study.

Side effects may be mild or very serious. Many side effects go away soon after taking the peginterferon alfa-2b. In some cases, side effects can be serious, long lasting, or may never go away.
Risks and side effects related to the peginterferon alfa-2b include those which are:

Likely
* Fatigue
* Loss of appetite, weight loss, taste alterations
* Depression

Less Likely
* Flu-like symptoms: Fever, chills, rigors
* Muscle aches, joint aches, headaches
* Nausea, vomiting, diarrhea
* Increase in heart rate (less common: irregular heartbeat)
* Mood alterations
* Rash (localized at injection site or diffuse)
* Abnormality in liver enzymes and bilirubin
* Alteration in kidney function (rare: kidney failure)
* Alteration in blood counts

Reproductive risks: Patients should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. Patients need to use birth control while on this study.

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

- Subjects must have histologically documented ulcerated primary cutaneous melanoma with a Breslow thickness of more than 1mm that has been excised radically 3 months prior to randomization. Excision margins of at least 1 cm are required. In the head and neck areas and in case of locations distally on extremities narrower margins are acceptable as long as they are radical.;Subjects must undergo Sentinel Node staging after the excision of the primary, and this must be done within the time frame of 3 months between the date of final excision of the primary and the date of randomization.;- Subjects must have an ECOG performance status of 0 or 1.;- Subjects must be between 18-70 years old.;- Subjects must have adequate hepatic, renal and bone marrow function as defined by the following parameters obtained within 120 hours prior to initiation of study treatment;- Subject must give informed consent according to ICH-GCP or national/local policy

Exclusion criteria

- Subjects suffering from a mucous membrane melanoma or ocular melanoma;- Subjects who have evidence of (non-)regional lymph node metastases or intransit metastases (even if they have been resected);- Subjects whose disease cannot be completely surgically resected;- Subjects who have not recovered from the effects of recent surgery;- Subjects with a history of prior malignancy within the past 5 years other than surgically cured non-melanoma skin cancer or cervical carcinoma in situ;- Subjects who have severe cardiovascular disease, i.e., arrhythmias requiring chronic treatment, congestive heart failure (NYHA Class III or IV) or symptomatic ischemic heart disease;- Subjects with thyroid dysfunction not responsive to therapy;- Subjects with uncontrolled diabetes mellitus;- Subjects suffering from an active autoimmune disease;- Subjects with active and/or uncontrolled infection, including active hepatitis;- Subjects who have a history of seropositivity for HIV;- Subjects who have a history of neuropsychiatric disorder requiring hospitalization;- Subjects who are known to be actively abusing alcohol or drugs;- Subjects who are pregnant, lactating, or of reproductive potential and not practicing an effective means of contraception;- Subjects with a medical condition requiring chronic systemic corticosteroids;- Subjects who have received any experimental therapy within 30 days prior to randomization in this study;- Subjects who have received any prior chemotherapy, immunotherapy, hormonal or radiation therapy for melanoma;- Subjects who have previously received interferon-alpha for any reason;- Subject having history of epilepsy or other major central nervous system disease;- Subject having eyes disorders

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-08-2015
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cylatron, Powder for Injection (200 mcg strength)
Generic name:	peginterferon alfa-2b
Product type:	Medicine
Brand name:	Cylatron, Powder for Injection (300 mcg strength)
Generic name:	peginterferon alfa-2b
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	22-04-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-07-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-08-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	11-11-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-12-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-01-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2009-010273-20-NL
ClinicalTrials.gov	NCT01502696
CCMO	NL42514.078.12