Melanoma Margins Trial-II: 1cm v 2cm Wide Surgical Excision Margins for AJCC Stage II Primary Cutaneous Melanoma (MelMarT-II)

Published: 08-02-2021
Last updated: 20-06-2024

This study will determine whether there is a difference in disease free survival for patients treated with either a 1cm excision margin or 2cm margin for clinical stage II (pT2b-pT4b) primary cutaneous melanoma (AJCC 8th edition, Table 1). The study…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Skin and subcutaneous tissue therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON54102

Source
ToetsingOnline

Brief title
MelMarT-II

Condition

- Skin and subcutaneous tissue therapeutic procedures

Synonym
disease free survival, Excision margin

Research involving
Human

Sponsors and support

Primary sponsor: Melanoma and Skin Cancer Trials Limited, Melbourne Australia

Source(s) of monetary or material Support: Geen subsidie

Intervention

Keyword: Disease free survival, Margin, Melanoma, Wide local excision

Outcome measures

Primary outcome

1. Disease-Free Survival: Time from randomisation until the first clinically, histologically or radiologically confirmed recurrence of melanoma at any body site, or death from any cause.

Secondary outcome

1. Local recurrence: time from randomisation to any clinically, histologically or radiologically confirmed local recurrence of melanoma including satellite lesions and in transit metastases between the primary site and the regional draining lymph nodes

2. Distant Disease-free survival: time from randomisation to any clinically, histologically or radiologically confirmed distant recurrence of melanoma

3. Melanoma specific survival: Time from randomisation to death due to melanoma

4. Overall Survival: time from randomisation to death from any cause.

5. QoL and neuropathic pain assessments at baseline, 3, 6, 12 and 24 and at melanoma recurrence.

6. Surgery related adverse events up to 30 days from the date of surgery.

7. Adverse events within 1 year

8. Health economic evaluation resource utilisation and cost-utility analysis

Study description

Background summary

A wide, radical excision to remove the entire primary tumour, to prevent spread and local recurrence is a classic surgical teaching. In primary melanoma, a secondary wider excision around the original biopsy scar is advocated to reduce risk of local recurrence and improve patient outcomes. Surprisingly, the detail of the wide excision is still highly controversial. Surgical margins vary significantly worldwide, from 1cm to 3cm, translating into large excision defects from 2cm to 6cm across. The management of patients with intermediate and high-risk primaries is particularly speculative. There is a growing concern internationally amongst surgeons that the excess morbidity caused by the larger excision defects, including increased hospital stay, complications and need for reconstructive surgery, coupled with prolonged rehabilitation and increased risk of chronic pain is not justifiable. Many surgeons suspect that 1cm is ample. An appropriately designed trial of adequate size is clearly needed to unify international guidance and to benefit the large and increasing numbers of melanoma patients worldwide.

Study objective

This study will determine whether there is a difference in disease free survival for patients treated with either a 1cm excision margin or 2cm margin for clinical stage II (pT2b-pT4b) primary cutaneous melanoma (AJCC 8th edition, Table 1). The study is designed to be able to prove or disprove that there is no difference in risk of melanoma recurrence between the two groups of patients. This study is designed to show that the risk of long-term pain associated with surgery can be reduced. If the study achieves its primary objective and demonstrates safety with a narrower margin, then we will also be able to determine how much of an impact the narrower excision has on patients in terms of improved quality of life and reduced side effects from the surgery and melanoma disease. This trial will also evaluate and determine the economic impact of narrower excision margins on the health services and society in general.

Study design

This is a randomised, controlled, multi-centre, non-inferiority, internationally recruiting, phase III clinical trial.

Intervention

Once determined as being eligible, patients will be randomised 1:1 to either a 1 cm excision margin or a 2 cm excision margin, in combination with a staging

sentinel lymph node biopsy.

Study burden and risks

Time associated with filling out questionnaires

Contacts

Public
Melanoma and Skin Cancer Trials Limited, Melbourne Australia

St Kilda Road 553
Melbourne VIC 3004
AU
Scientific
Melanoma and Skin Cancer Trials Limited, Melbourne Australia

St Kilda Road 553
Melbourne VIC 3004
AU

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients must have a stage II primary invasive cutaneous melanoma with Breslow thickness 2.01mm to 4mm or >4mm with or without ulceration (pT3a-pT4b, AJCC 8th edition) as determined by
diagnostic biopsy (narrow excision, incision or punch biopsy) and

subsequent histopathological analysis.
2. Must have a primary melanoma that is cutaneous (including head, neck, trunk, extremity, scalp, palm or sole).
3. An uninterrupted 2cm margin must be technically feasible around biopsy scar or primary melanoma.
4. Surgical intervention (which refers to SLNB and WLE as these are both to be done on the same day), must be completed within 120 days of the original diagnosis.
5. Patients must be 18 years or older at time of consent.
6. Patient must be able to give informed consent and comply with the treatment protocol and follow-up plan.
7. Life expectancy of at least 5 years from the time of diagnosis, not considering the melanoma in question, as determined by the PI.
8. Patients must have an ECOG performance score between 0 and 1 at screening.
9. A survivor of prior cancer is eligible provided that ALL of the following criteria are met and documented:
o The patient has undergone potentially curative therapy for all prior malignancies,
o There has been no evidence of recurrence of any prior malignancies for at least FIVE years (with the exception if successfully treated uterine/cervical or non-melanoma skin cancers
(SCCs/BCCs with no evidence of recurrence), and
o The patient is deemed by their treating physician to be at low risk of recurrence from previous malignancies.

Exclusion criteria

1. Uncertain diagnosis of melanoma i.e. so-called *melanocytic lesion of unknown malignant potential*.
2. Patient has already undergone wide local excision at the site of the primary index lesion.
3. Patient unable or ineligible to undergo staging sentinel lymph node biopsy of the primary index lesion.
4. Desmoplastic or neurotropic melanoma: with any patient where pathology determines melanoma as PURE desmoplastic (as per WHO definition of >90% desmoplasia),
they are not eligible for this study. However other melanomas with less than 90% desmoplasia or mixed subtypes are eligible unless there is neurotropism present (peri
neural invasion). Neurotropism in any type of melanoma is an exclusion. Peri-neural invasion does not include entrapment of nerves within the main primary tumour
mass*.
5. Microsatellitosis as per AJCC 8th edition definition
6. Subungual melanoma

7. Patient has already undergone a local flap reconstruction of the defect after excision
of the primary and determination of an accurate excision margin is impossible.
8. History of previous or concurrent (i.e., second primary) invasive melanoma.
9. Melanoma located distal to the metacarpophalangeal joint; on the tip of the nose; the eyelids or on the ear; genitalia, perineum or anus; mucous membranes or internal
viscera.
10. Physical, clinical, radiographic or pathologic evidence of satellite, in-transit, regional, or distant metastatic melanoma.
11. Patient has undergone surgery on a separate occasion to clear the lymph nodes of the probable draining lymphatic field, including sentinel lymph node biopsy, of the
index melanoma.
12. Any additional solid tumour or hematologic malignancy during the past 5 years (with exception of non-melanoma skin cancers (T1 skin lesions of squamous cell
carcinoma (SCCs), basal cell carcinoma (BCC*s)), or uterine/cervical cancer).
13. Melanoma-related operative procedures not corresponding to criteria described in the protocol.
14. Planned adjuvant radiotherapy to the primary melanoma site after Wide Local Excision is not permitted as part of the protocol and any patients given this treatment would
be excluded from the study.
15. History of organ transplantation.
16. Oral or parenteral immunosuppressive agents (not topical or inhaled steroids) at enrolment or within 6 months prior to enrolment.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-09-2021
Enrollment:	1000
Type:	Actual

Ethics review

Approved WMO Date:	08-02-2021
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	09-03-2021
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	29-09-2021
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	13-06-2022
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	15-03-2023
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	23-05-2023

Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	22-08-2023
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	25-09-2023
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	08-03-2024
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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
ClinicalTrials.gov	NCT03860883
CCMO	NL75543.096.21