Inguinal or Ilio-inguinal Lymphadenectomy for Patients With Metastatic Melanoma to Groin Lymph Nodes and no Evidence of Pelvic Disease on PET/CT Scan - A Randomised Phase III Trial (EAGLE FM)

Published: 05-04-2016
Last updated: 19-04-2024

This study aims to provide a more rational evidence base for appropriate management for metastatic melanoma in the groin LNs, through assessing the effect of the addition of ipsilateral pelvic lymphadenectomy on patient disease-free survival (DFS),...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Spleen, lymphatic and reticuloendothelial system disorders
Study type	Interventional

Summary

ID

NL-OMON43637

Source
ToetsingOnline

Brief title
Evaluation of Groin Lymphadenectomy Extent For Metastatic Melanoma EAGLE FM

Condition

- Spleen, lymphatic and reticuloendothelial system disorders
- Metastases
- Skin and subcutaneous tissue therapeutic procedures

Synonym
metastases of melanoma in the lymph nodes of the groin

Research involving
Human

Sponsors and support

Primary sponsor: Australia and New Zealand Melanoma Trials Group
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Groin, Lymph node metastasis, Lymphadenectomy, Melanoma

Outcome measures

Primary outcome

The primary endpoint of the study will be the DFS following lymphadenectomy,

assessed after 60 months of follow-up.

Secondary outcome

1. OS

2. DDFS

3. Regional Recurrence-Free Survival

4. Morbidity differences between IL and I-IL in a balanced cohort with

microscopic and macroscopic nodal disease. This includes lymphoedema, wound

complications (wound infections, dehiscence/necrosis, and seroma) chronic pain,

and restriction in mobility

5. QOL evaluation in respect to surgery, or other morbidities.

6. Sensitivity / specificity and PPV and NPV of PET / CT and CT scan for pelvic

disease

7. Resource use and utility based QOL at 60 months, reported as an incremental

cost-effectiveness ratio (ICER) of I-IL compared to IL alone.

8. Provide a resource of tissue and blood for evaluation of biological markers

predictive of outcome in resected stage III disease

Study description

Background summary

Currently the standard treatment for melanoma patients presenting with microscopic (subclinical) nodal metastasis identified by SNB or macroscopic (palpable) metastasis in groin LNs includes a completion or therapeutic lymphadenectomy.
The Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand advocate inguinal (superficial) groin lymphadenectomy (IL) in the presence of proven nodal melanoma and suggest the addition of ipsilateral iliac and obturator lymphadenectomy (ilio-inguinal lymphadenectomy, I-IL) if there is radiological evidence of pelvic LN metastases on imaging, gross inguinal clinical involvement or >= 3 inguinal nodes involved, or if there are clinically suspicious LNs high in the groin (Australian Cancer Network Melanoma Guidelines Revision Working Party 2008). The National Comprehensive Cancer Network (NCCN) recommends considering I-IL in similar circumstances and also recommends it if there is a positive node of Cloquet (National Comprehensive Cancer Network 2009). These recommendations are based on expert opinion, not high level evidence. Another contemporary rationale for I-IL is for patients in whom an inguinal sentinel node (SN) was biopsied and found to be positive but a pelvic SN identified on the lymphoscintigram was not removed at the time of the SNB procedure. Similarly, van der Ploeg et al used the presence of second tier LNs in the pelvis on the original lymphoscintigram to recommend I-IL after a SNB was positive, whereas those patients with inguinal second tier nodes had an IL (van der Ploeg, Kroon et al. 2009). Despite the various guidelines and promoted management strategies, the frequency I-IL is performed compared to IL varies from surgeon to surgeon, as well as from melanoma unit to melanoma unit. The reason for this is surgeon or unit preference rather than any high level evidence that is available. A recent international online survey of melanoma surgeons from 25 countries demonstrated a virtual 3 way split on management strategy when the surgeons were offered the same clinical scenario of involved inguinal LNs. About 36% surgeons would do an IL, 30% would do an I-IL and 34% would vary depending on the exact patient and disease characteristics on an individual basis (Pasquali, Spillane et al. 2012).

Spread of metastatic melanoma to the groin lymph nodes (LN) is a common event for patients with melanoma. In melanoma treatment centres around the world, patients without demonstrated pelvic LN disease receive 1 of 3 strategies of management in relatively equal proportions (Pasquali, Spillane et al. 2012):
i. Inguinal Lymphadenectomy (IL)
ii. Ilio-inguinal Lymphadenectomy (I-IL)

iii. Variable use of either IL or I-IL surgery.
Some larger melanoma centres have an institutional policy that all patients have either IL or I-IL for metastatic inguinal node involvement. Nearly all centres would agree that patients with pelvic LN involvement without distant metastatic disease should have I-IL

Study objective

This study aims to provide a more rational evidence base for appropriate management for metastatic melanoma in the groin LNs, through assessing the effect of the addition of ipsilateral pelvic lymphadenectomy on patient disease-free survival (DFS), distant disease-free survival (DDFS), overall survival (OS), morbidity, and quality of life. In addition, the study will clarify the reliability of PET (Positron Emission Tomography) / CT (Computed Tomography) scans for staging pelvic LNs, clarify morbidity differences between the operations in a balanced cohort, evaluate any health economic benefits of I-IL over IL and provide a tissue and serum resource to be used to identify biological markers of recurrence and progression after inguinal metastases.

Study design

This is an international, multi-centre, phase III, non-inferiority, prospective, randomised clinical trial.

Intervention

Inguinal or Ilio-inguinal Lymphadenectomy for patients with metastatic melanoma to groin lymph nodes and no evidence of pelvic disease on PET/CT Scan

Cytologically or histologically confirmed metastatic melanoma in inguinal lymph node (H&E & IHC); Specifically no evidence of pelvic node involvement or distant spread of melanoma on PET / CT staging scans; All eligibility criteria met
Consent and Randomise to Groin Lymphadenectomy
*Arm 1: Inguinal Lymphadenectomy
*Arm 2: Ilio-inguinal Lymphadenectomy

Study burden and risks

n.v.t.

Contacts

Public

Australia and New Zealand Melanoma Trials Group

The Poche Centre Level 1, Rocklands Rd 40
North Sydney NSW 2060
AU
Scientific
Australia and New Zealand Melanoma Trials Group

The Poche Centre Level 1, Rocklands Rd 40
North Sydney NSW 2060
AU

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients may be included in the study if they meet ALL of the following criteria:
1. Must be 15 and above.
2. Have primary cutaneous melanoma or if the patient presents with stage III melanoma with no known primary tumour then a thorough search for the primary should be documented (including perineal and perianal areas).
3. Life expectancy of at least 10 years from the time of diagnosis, not considering the melanoma in question, as determined by the PI.
4. Must have one or multiple inguinal node(s) involved, histologically or cytologically proven as metastatic melanoma. This can can be detected:
* At the time of diagnosis;
* Or by Ultrasound detection;
* Or later after relapse when no Sentinel Node Biopsy (SNB) was performed at the time of primary tumour management;
* Or as a result of SNB;

* Or at the time of regional recurrence after *false negative* SNB;
5. Absent distant disease clinically and on PET/CT scan. (Patients must have NO further distant disease or visceral metastases).
6. ECOG performance status must be between 0 to 2 at randomisation.
7. Whole body PET/CT scan, specifically stating there is NO evidence of pelvic lymph node involvement prior to randomisation and CT Brain or MRI Brain. Scans must be performed within 4 weeks of randomisation.
8. Able to provide written, informed consent.
9. Willing to return to the centre for follow up examinations and procedures, as outlined in the protocol.
10. All patients must be randomised and undergo lymphadenectomy surgery no more than 90 days following diagnosis of inguinal LN involvement.

Exclusion criteria

Patients will be excluded from the study for ANY of the following reasons:
1. Distant metastatic disease on clinical examination or staging imaging (whole body PET/CT scan and CT or MRI brain scan). Scans must be performed within 4 weeks of randomisation.
2. Pelvic LN involvement on SNB or PET/CT scan suggestive of metastatic disease in the pelvis - criteria for diagnosis include normal size or enlarged lymph nodes (> 1 cm) with increased FDG activity on PET (SUV >3). If there are enlarged, necrotic lymph nodes FDG activity on PET is not required to be present. If unsure central review facilitated by the Trial Coordinating Centre should be sought.
3. Bilateral inguinal lymph node involvement.
4. Patients with a history of major pelvic surgery and / or regional radiotherapy at any time in the past.
5. Requiring planned radiotherapy following surgery due to macroscopic, bulky and matted nodes.
6. Unfit for General Anaesthesia.
7. Melanoma-related operative procedures not corresponding to criteria described in the protocol.
8. Patients with prior cancers, except:
* those with a thin <=1 mm, regionally unrelated melanoma > 5 years ago.
* those with a good prognosis regionally unrelated cancer (>90% probability of 10 years disease specific survival).
* other cancers diagnosed more than five years ago with no evidence of disease recurrence within this time.
* successfully treated basal cell and squamous cell skin carcinoma.
* carcinoma in-situ of the cervix.
9. A medical or psychiatric condition that compromises ability to give informed consent or complete the protocol.
10. Positive urine pregnancy test for women of childbearing potential (+/-7 days of randomisation onto the trial).
The patient treatment history (including adjuvant systemic therapy clinical trial participation) will be recorded at the first study visit and as appropriate throughout the duration of the

study. Patients can receive treatment using neoadjuvant therapies prior to and during this trial.

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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2015
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	05-04-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-07-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NCT02166788
CCMO	NL53224.042.15