OMIT trial: omitting therapeutic lymph node dissection in patients with stage IIIB/C melanoma and major pathological response in the index lymph node after neoadjudvant immunotherapy

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To investigate whether TLND can be safely omitted in patients with macroscopic resectable stage III (B/C/D) melanoma achieving an MPR within the ILN upon neoadjuvant treatment with nivolumab in combination with ipilimumab.

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

Summary

ID

NL-OMON57418

Source
ToetsingOnline

Brief title
OMIT Trial

Condition

- Skin neoplasms malignant and unspecified
- Skin and subcutaneous tissue therapeutic procedures

Synonym
lymph node dissection, melanoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Erasmus MC Foundation

Intervention

Keyword: major pathology response, Melanoma, neoadjuvant immunotherapy, omitting lymph node dissection

Outcome measures

Primary outcome

The two coprimary endpoints are 2-year LRFS and 2-year DMFS

Secondary outcome

• To evaluate the HR-QoL from baseline to follow-up visits.

• To describe the rates of pathological complete response (pCR), near-pCR,

pathologic partial response (pPR), and pathologic non-response (pNR) in the ILN.

• To describe surgical morbidity

• To describe Concordance between radiological response and pathological

response (pCR, pPR, pNR) in the ILN.

• To describe the proportion of patients (eventually) undergoing TLND

stratified by MPR and non-MPR status.

• To describe melanoma specific survival and overall survival.

• To describe surgical adverse events (AEs) and neoadjuvant immunotherapy AEs

Study description

Background summary

Two randomized trials, NADINA and SWOG-1801, have demonstrated that neoadjuvant treatment with anti-PD1 improves event-free survival in patients with

macroscopic resectable stage III melanoma. In these studies, therapeutic lymph node dissection (TLND) was standard of care, showing that patients achieving a major pathological response (MPR, i.e., <=10% residual viable tumor bed) have an excellent outcome (EFS and DMFS). The PRADO trial indicated that the MPR definition can also be revealed from an surrogate lymph node response, the index lymph node (ILN), allowing sparing the extensive surgery in MPR patients. In these MPR patients the distant metastasis free survival (DMFS) was 100% after 1 year and 98% after 2 years, and recurrence-free survival (RFS) was 95% after 1 year and 93% after 2 years. Given that TLND is associated with morbidity and has a significant impact on health-related quality of life (HR-QoL) and healthcare costs, this study aims to prospectively investigate the safety of omitting TLND in patients who have a MPR within the ILN after neoadjuvant immunotherapy.

Study objective

To investigate whether TLND can be safely omitted in patients with macroscopic resectable stage III (B/C/D) melanoma achieving an MPR within the ILN upon neoadjuvant treatment with nivolumab in combination with ipilimumab.

Study design

This study is a prospective, single-arm phase 2 nationwide multicenter trial

Intervention

Performing an Index node (ILN) procedure and if patients achieve a MPR in the index node, the TLND will be omitted

Study burden and risks

Participants will be treated according to standard of care neoadjuvant immunotherapy and lymph node dissection after marking the largest LN metastasis, the and ILN. The study inherent burden includes additional follow-up visits, blood draws, and imaging as compared to SoC. An additional burden is the double surgery intervention for non-MPR patients (ILN followed by TLND), while patients achieving an MPR might benefit from the less extensive surgery burden as compared to SoC (TLND) as as shown in PRADO to improve their QoL. Another risk is a potential increase in local recurrence when omitting the TLND in MPR patients, although current data suggest that this risk is small (7% at 2 years) in patients who achieve a MPR. Additionally, if local recurrence does occur, a TLND can still be performed, resulting in a DMFS of 98% at 2 yearsfor MPR patients.
Potential benefits from participating in this trial would be avoiding an extensive and potentially morbid surgery (TLND) in MPR patients, without

increase of DMFS, but potentially significantly improved quality of life

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Patients must be eligible for neoadjuvant treatment
• Patients must be 16 years of age or older.
• Patients must have a histologically confirmed diagnosis of macroscopic resectable stage III melanoma (stage III B/C/D) with one or more macroscopic lymph node metastase defined as either one:
o a palpable node, confirmed as melanoma by pathology;
o a non-palpable but enlarged lymph node according to RECISTv1.1 (at least 15 mm in short axis), confirmed as melanoma by pathology;

o a PET scan positive lymph node of any size confirmed as melanoma by pathology;
• The patient must have a measurable tumor burden that qualifies (according to clinical practice) for neoadjuvant therapy with immune checkpoint inhibitors
• Patients in whom ILN marking is feasible
• Written informed consent

Exclusion criteria

• Uveal/ocular or mucosal melanoma
• in-transit metastases only (without cytological or histological proven lymph node involvement)
• Melanoma located in the head and neck region, where performing two surgeries is deemed to result in significant morbidity
• Patients with (history of) distant metastasis (stage IV melanoma).
• Presence of more than 3 in-transit metastases

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025
Enrollment:	213
Type:	Anticipated

Ethics review

Approved WMO

Date:	14-04-2025
Application type:	First submission
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
ClinicalTrials.gov	NCT06754904
CCMO	NL88017.078.24