#CT053

MERLIN_001: A prospective registry study of a primary melanoma gene-signature to predict sentinel node (SN) status and determine its prognostic value for more accurate staging of SN-negative melanoma patients

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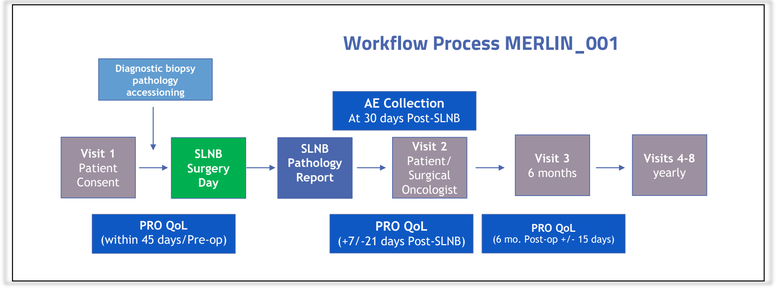
Introduction

- Sentinel lymph node biopsy (SLNB) provides important staging and prognostic information that guides surveillance and adjuvant systemic therapy decisions for melanoma patients [1]
- Guidelines recommend surgeons “discuss and consider” SLNB for cutaneous melanoma (CM) patients with 5-10% risk of having clinically occult nodal metastases and “recommend” SLNB for CM patients with > 10% risk [2]
- Approximately 85% of CM patients undergoing SLNB surgery do not have nodal metastasis [3]
- SLNB surgery carries costs and potential for complications such as seroma, infections and lymphedema [3]
- Furthermore, SN-negative CM patients still have a risk of recurrence and may be candidates for adjuvant therapy, therefore new techniques to identify SN-negative patients at highest risk of recurrence are clearly needed [4,5]
- CP-GEP, a model combining clinicopathological features (CP) and gene expression profile (GEP) of the primary tumor can potentially identify CM patients with a low risk of having nodal metastasis [6]
- The CP-GEP model has been clinically validated in multi-center retrospective studies both in EU and in the US as well as in a Dutch prospective study during the Covid-19 pandemic [7-10]
- The current study aims to validate the CP-GEP model in a prospective multi-center registry study across the US



Scheme 1. Workflow process for the MERLIN_001 Study. Abbreviations: **PRO QoL**: Patient Related Outcomes, Quality of Life; **AE**: Adverse Events.

Study Objectives

1) Determine predictive capability of CP-GEP model to identify primary cutaneous melanoma patients who can safely forgo SLNB.
2) Determine prognostic value to predict recurrence of melanoma after a negative SLNB.

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#NCT04759781

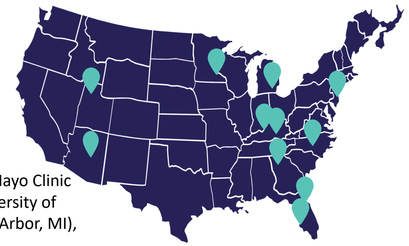

Figure 1. Sites participating the MERLIN_001 Study: Mayo Clinic (Rochester, MN; Scottsdale, AZ; Jacksonville, FL), University of Louisville (Louisville, KY), University of Michigan (Ann Arbor, MI), Emory University (Atlanta GA), University of Kentucky (Lexington, KY), Memorial Sloan Kettering Cancer Center (New York, NY), University of Utah (Salt Lake City, UT), Duke University (Durham, NC), and Moffitt Cancer Center (Tampa, FL).

Methods and Materials

Study design

- Multi-center, non-interventional clinical study with a consortium of surgical oncologists
- Prospectively validate the CP-GEP model in clinics across the US
- Results will be blinded to both patients and clinicians
- See Scheme 1 for the workflow process

Study population

- Newly diagnosed pT1b-pT3 cN0M0 primary cutaneous melanoma patients who are elected to undergo SLNB

Target # patients

- 2,340 patients with cutaneous melanoma

Enrollment Period

- 2 years (1st patient enrolled on 1st Sept, 2021)

References

1) Gershenwald et al 2017 CA Canc. J. Clin.
2) Swetter et al 2018 JAAD
3) Morton et al 2014 New Eng. J. Med.
4) Whiteman et al 2015 J. Inv. Dermatol.
5) Luke et al 2022 Lancet
6) Bellomo et al 2020 JCO P.O.
7) Mulder et al 2021 Br. J. Dermatol.
8) Yousaf et al 2021 Int. J. Dermatol.
9) Johansson et al 2021 Eur. J. Surg. Oncol.
10) Stassen et al 2022 EADO oral presentation

Inclusion Criteria

- Newly diagnosed melanoma:
  - pT1b-pT3 (BT ≤4.0 mm) cN0M0
  - pT1a (BT <0.8 mm) with adverse features (e.g. very high mitotic index (≥2/mm^2), young age (<40 years), lymphovascular invasion, combination of these factors)
- Male or female, ≥ 18 years
- Elected to undergo SLN biopsy per treating physician’s recommendation

Exclusion Criteria

- Melanoma pathology report & diagnostic biopsy tissue unobtainable
- Regional and distant metastatic disease clinically present
- Any prior or concurrent primary invasive melanoma potentially draining to the same lymph node basin
- Documented prior history of primary invasive melanoma of T1b or greater at any site within last 5 years before current diagnosis
- Previous surgery in draining lymph node basin of current primary melanoma
- Ocular, vulvar, perianal, and mucosal melanoma and melanocytic tumors of uncertain malignant potential (MELTUMP) or atypical Spitz tumors

Enrollment & Analysis Plan

- Enrollment of patients started in September 2021 and is ongoing
- As of March 2023, 931 patients have been enrolled, representing 57% of the targeted number of patients with a successful SLNB and CP-GEP test result
- Performance metrics for CP-GEP will be evaluated (SLNB reduction rate, NPV, PPV, sensitivity, specificity)
- Patient stratification based on risk of recurrence (RFS, DMSF, OS) will be assessed on five-year outcome data
- Additional analyses will be performed using collected data

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