A phase 2 study to determine the pathological response to neoadjuvant nivolumab & relatlimab in high risk stage II cutaneous melanoma (NeoReNi II)

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Background

- Patients diagnosed with stage II melanoma account for ~50% of those who develop metastatic disease[1] and have a melanoma-specific mortality rate of 12% to 25% at 10 years[2].
- Stage IIB/C have a worse prognosis than stage IIIA melanomas, and stage IIC shares the same prognosis as stage IIIB melanomas[2].
- Adjuvant treatment with anti-PD-1 therapy improves recurrence free survival (RFS) in resected stage IIB/C melanoma, with a risk reduction of 35% for adjuvant pembrolizumab[3] and 58% for adjuvant nivolumab[4] at median follow-up of 14.4 months and 15.8 months, respectively.
- Emerging phase II evidence suggests improved event-free survival (EFS) for patients with resectable stage III/IV melanoma who receive neoadjuvant, plus adjuvant, anti-PD-1 monotherapy compared with those receiving adjuvant anti-PD-1 monotherapy alone (72% vs. 49% at 2-years)[5].
- Using International Neoadjuvant Melanoma Consortium (INMC) pathological response criteria[6], major pathological response (≤10% viable tumour) correlates with a low risk of recurrence in resectable stage III melanoma[7].
- The neoadjuvant setting provides an opportunity to gain early insight into response, enables feedback to patients regarding individual response and prognosis, offers the ability to personalize subsequent management, and supports the collection of translational specimens to explore mechanisms of response and resistance[8].

INMC Response Criteria[6]

	Viable Tumour (%)
Major Pathological Response	
Pathological complete response (pCR)	0%
Near-pathological complete response (near-pCR)	≤10%
Non-Major Pathological Response	
Pathological partial response (pPR)	>10% - ≤50%
Pathological no response (pNR)	>50%

Objectives

Primary Objectives

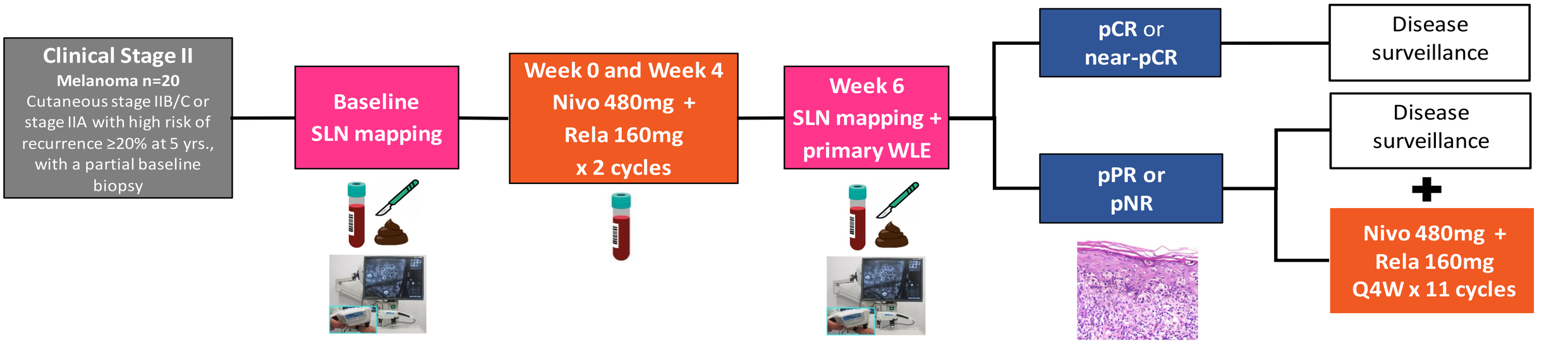
- Rate of pCR at week 6 resection in the sentinel lymph node (SLN) and wide local excision (WLE) specimens.
- Feasibility of neoadjuvant therapy in a stage II cutaneous melanoma population.

Secondary Objectives

- RFS, EFS, distant metastasis-free survival (DMFS), and OS.
- Assess safety and tolerability.
- Describe surgical outcomes.
- Describe changes in the primary melanoma using in vivo reflectance confocal microscopy and dermoscopy.
- Rate of SLN positivity, and changes in lymphatic mapping.
- Quality of life (QoL).
- Tissue, blood and stool biomarker analyses.

Study Design

The aim of the NeoReNi II trial is to determine whether combination PD-1 blockade with nivolumab (nivo), plus lymphocyte-activation 3 (LAG3) checkpoint inhibition with relatnimab (rela), will achieve a high rate of pathological response and manageable toxicity in patients with stage II primary melanoma.



Key Eligibility Criteria

Inclusion Criteria

- Patients ≥18 years of age.
- Histologically confirmed AJCC (8th ed.) clinical stage IIA (T2b, T3a), IIB (T3b, T4a), or IIC (T4b) cutaneous primary melanoma, with residual disease at study entry following a partial biopsy.
- Estimated ≥ 20% risk of recurrence at 5 years, according to the Melanoma Institute Australia stage II risk calculator (melanomarisk.org.au), for patients with stage IIA disease at study entry.

Exclusion Criteria

- Clinical or radiographic evidence of nodal, intransit, or satellite metastases.
- Previous treatment with any systemic anti-cancer therapy.

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- Patient recruitment is ongoing at MIA.

Clinicaltrials.gov identifier: NCT05418972

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