A Phase 2 study to determine the pathological response to neoadjuvant nivolumab (nivo) and relatlimab (rela) in stage I to III resectable Merkel Cell Carcinoma (Neo-MCC)

M. Gonzalez[1], A.C.J. Van Akkooi[1,2,5], S. Ch'ng[1,2,4,5,6], K.F. Shannon[1,2,4,5,6], A.J. Spillane[1,3,4], J. Stretch[1,2,4,5], M.A. Rtshiladze[1], T. Pennington[1,4,5], D. Coker[1,2,4,5] , R.P.M. Saw[1,2,4,5], R. Kapoor[3], E. Hsiao[3,7], R.V. Rawson[1,5], M. Osorio[1], A.M. Menzies[1,2,3,4], S. Lo[1,2], R.A. Scolyer[1,2,5], A.Hong[1,2,4,5,6] G.V. Long[1,2,3,4] , I. Pires da Silva[1,2,8]

1. Melanoma Institute Australia, 2. The University of Sydney, 3. Royal North Shore Hospital, 4. Sydney Mater Hospital, 5. Royal Prince Alfred Hospital, 6. Chris O'Brien Lifehouse, 7. I-Med Radiology, 8. Blacktown Hospital

Background

The Neo-MCC trial will examine whether combination PD-1 blockade plus lymphocyte-activation 3 (LAG3) checkpoint inhibition will achieve a high rate of pathological complete response with manageable toxicity in patients with resectable stage I-III MCC.

- Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine cancer of the skin with viral and sun related etiologies, and an overall mortality rate twice that observed in cutaneous melanoma (33% vs 15%)[1].
- The 5-year disease specific survival is 60% to 87% for those presenting with local disease, 39% to 62% for nodal disease, and 11% to 20% for metastatic disease[1].
- In melanoma, using International Neoadjuvant Melanoma Consortium (INMC) pathological response criteria[2], a major pathological response to neoadjuvant immunotherapy (≤10% viable tumor) correlates with low risk of recurrence in resectable stage III macroscopic disease [3] and improved event free survival (EFS) when immunotherapy is given neoadjuvantly compared to adjuvant treatment[4].
- In a study of neoadjuvant anti-PD1 monotherapy with nivolumab (CheckMate 358), in patients with resectable IIA-IV MCC (N=36), 47.2% of patients achieved a pathological complete response (pCR)[5].
- 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.

INMC Response Criteria[2]

	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 non-response (pNR)	>50%

Objectives

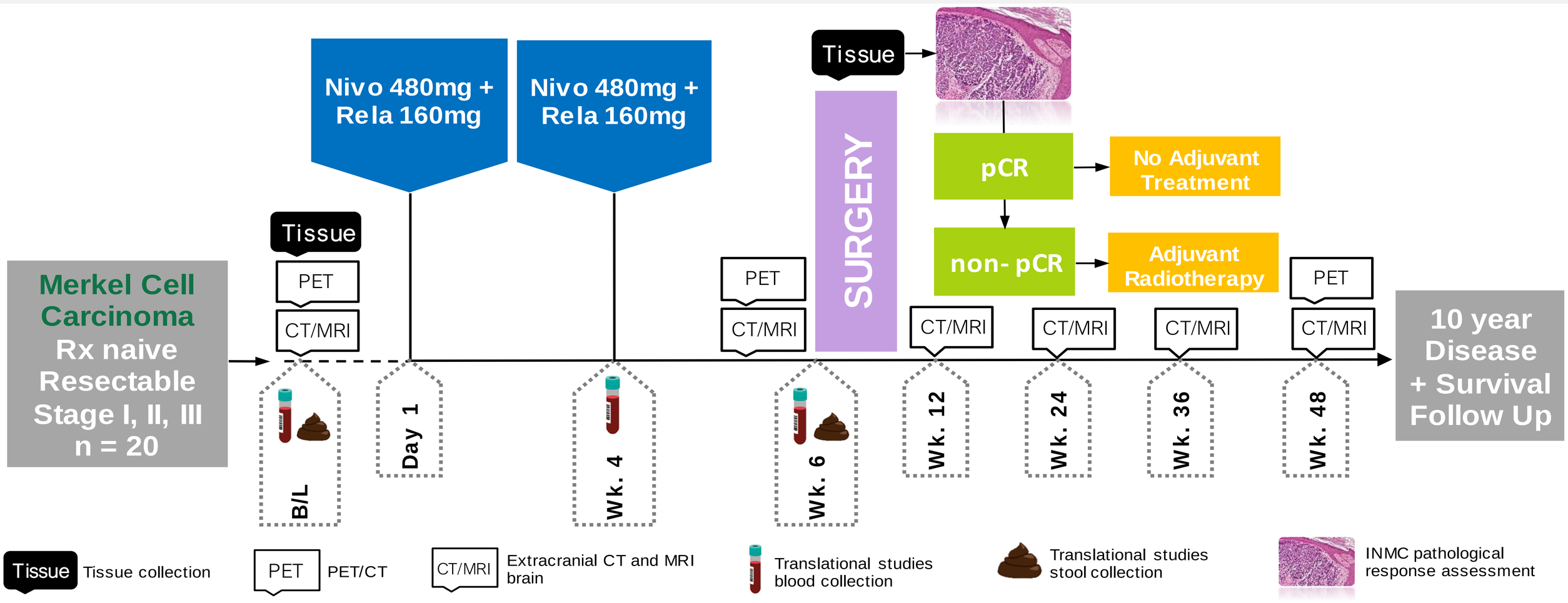
Primary Objective

- Rate of pCR at resection after neoadjuvant therapy using INMC response criteria.

Secondary Objectives

- Rate of near-pCR, pPR, and pNR.
- RECIST objective response rate (ORR).
- PERCIST metabolic response rate.
- Recurrence free survival (RFS).
- Event free survival (EFS).
- Overall survival (OS).
- Assess safety and tolerability.
- Describe surgical outcomes.
- Quality of life (QoL).
- Tissue, blood and stool biomarker analyses.
- Compare primary and secondary objectives against CheckMate 358.

Study Design



Key Eligibility Criteria

Inclusion Criteria

- Patients ≥18 years of age.
- Histologically confirmed, resectable, clinical stage I (≥ 10 mm), IIA, IIB or III MCC
- In-transit metastases are permitted if they are completely resectable.
- Measurable disease according to RECIST version 1.1 criteria.

Exclusion Criteria

- Clinical or radiographic evidence of distant metastasis.
- Prior anti-PD-1, CTLA-4, PDL-1 or LAG3 antibody exposure, or other experimental local or systemic drug therapy.
- Active autoimmune disease.

Acknowledgements

- Trial sponsored by Melanoma Institute Australia.
- Nivolumab and relatlimab supplied by BMS.
- Patient recruitment is ongoing at Melanoma Institute Australia.

Clinicaltrials.gov identifier: NCT06151236

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