UNISON: Nivolumab (N) then ipilimumab + nivolumab (I + N) in advanced non clear cell renal cell carcinoma (nccRCC) (ANZUP 1602)

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1. BACKGROUND

- Rare variant or non-clear cell renal cell carcinoma (nccRCC) account for ~20% of advanced kidney cancer and mortality
- Vascular endothelial growth factor (VEGF)-tyrosine kinase inhibitors (TKIs) elicit modest, often brief responses in people with nccRCC
- Immune checkpoint inhibitors (ICI) such as nivolumab (N) and ipilimumab (I) are active against many cancers including clear cell renal cell carcinoma
- People with rare variant nccRCC have been excluded from frontline trials despite having a more aggressive disease course and poorer prognosis compared to those with clear cell renal cell carcinoma

2. HYPOTHESES

- N is active in people with advanced nccRCC, and N + I is active in people with advanced nccRCC refractory to N alone

3. AIM

- To determine the activity and safety of N in participants with advanced nccRCC, and the activity and safety of N + I in participants with advanced nccRCC refractory to N alone

4. STUDY DESIGN

- **Design:** Open label, single-arm, 2-part sequential, multi-centre, phase 2 trial
- **Target population:** Participants aged ≥18 years with metastatic or locally advanced unresectable rare variant nccRCC, including but not limited to:
  - Papillary (type 1/2)
  - Chromophobe
  - Sarcomatoid (pure)
  - Xp11 translocation
  - collecting duct, and
  - unclassified histological subtypes.
- **Sample size:** UNISON is powered to distinguish a clinically non-relevant objective tumour response rate (OTRR) of 15% in people taking combination ICI whose cancers are refractory to single-agent PD1, versus a clinically-relevant OTRR of 30% at 5% level of significance with 80% power
- 85 participants were to be recruited in Part 1, on the assumption that ~55% of those entering Part 1 will be eligible for inclusion in Part 2 (n = 48)

5. OBJECTIVES

Primary

- OTRR for N alone in Part 1, and for I + N in Part 2

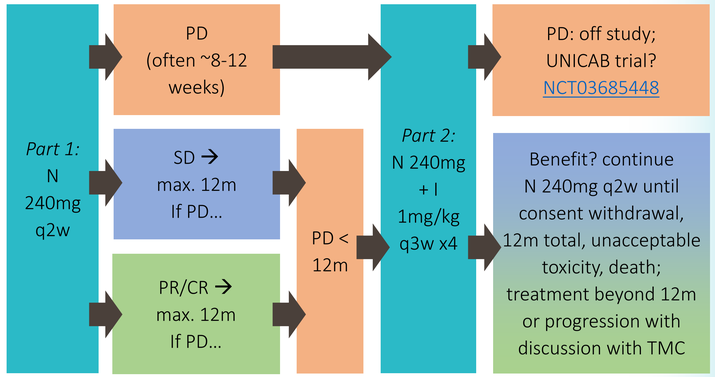
Secondary

- Duration of objective tumour response
- Progression free survival
- Immune-related tumour response rate and disease control rate
- Overall survival
- Frequency and severity of adverse events (incl. irAEs)
- Frequency of treatment delays and discontinuation due to toxicity
- Time to treatment discontinuation

Tertiary

- Association between clinical outcomes and biomarkers

6. TRIAL SCHEMA

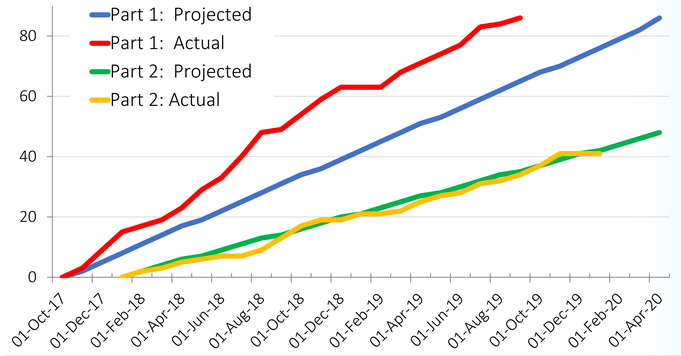


7. ELIGIBILITY

Inclusion criteria	Exclusion criteria
• Adequate organ function • Prior treatment with VEGF-TKIs permitted	• Predominant clear cell histology of >50% • Prior checkpoint inhibitor

8. STUDY PROGRESS

- **Enrolment opened:** November 2017
- **Total study sites:** 19
- **Current enrolment in Part 1:** 86
- **Participants treated with I + N in Part 2:** 41/48 as at 31 Jan 2020



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Website: www.anzup.org.au
For trial enquiries: Contact.Bact@petermac.org

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research trials outcomes

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