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 people with advanced nccRCC, and N + I is active in people 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 (papillary), Xp11 translocation, collecting duct, and unclassified histological subtypes.
• Sample size: UNISON is powered to distinguish a clinically non-relevant objective tumour response rate (OTRR) for N alone in Part 1, and for I + N in Part 2

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

6. TRIAL SCHEMA

Part 1: N 240mg q2w

PD (often >8-12 weeks)

SD → max. 12m if PD...

Part 1: N 240mg + I 240mg q2w

PR/CR → max. 12m if PD...

PD < 12m

Benefit? continue N 240mg q2w until consent withdrawal, 12m total, unacceptable toxicity, death; treatment beyond 12m or progression with discussion with TMC

Part 2: 48/48 as at 31 Jan 2020

If PD...

3. Background

7. ELIGIBILITY

Adequate organ function
Prior treatment with VEGF-TKIs permitted

Inclusion criteria
Exclusion criteria

8. STUDY PROGRESS

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

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