UNICAB: Cabozantinib In Locally Advanced Or Metastatic Non-Clear Cell Renal Cell Carcinoma Post Immunotherapy or in those Unsuitable For Immunotherapy (ANZUP 1802)

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1. Background

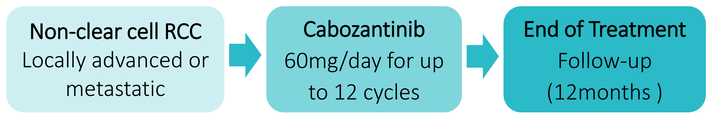
- Non-clear cell renal cell carcinomas (nccRCC) exhibit diverse biology and therapeutic responses
- Immune checkpoint immunotherapy (ICI) benefits some people with nccRCC, however many tumours progress on therapy
- We sought to assess Cabozantinib (C) in people with nccRCC who are refractory to ICI, or in whom ICI treatment is contraindicated

2. Methods

- To be eligible for enrolment, participants (pts) required a histological diagnosis of nccRCC (making up >50% of the tumor sample), advanced/metastatic disease on imaging, ECOG PS < 2 and either prior treatment with ICI or contraindication to treatment with ICI.
- Eligible pts started C at 60mg daily with dose modifications as per the investigator brochure.
- Clinical assessments cycles were 28 days and radiological assessment occurred every 8 weeks for 12 months.
- Pts experiencing durable benefit continued C on an access program

3. Trial Schema

Open label, single-arm, multi-centre, phase 2 trial



Primary Objectives
- ORR (RECIST 1.1)

Secondary Objectives
- Safety and Toxicity (CTCAE v5.0), Progression-Free Survival (PFS), Overall Survival (OS)

4. Study Outcomes

- Recruitment was influenced by the COVID 19 pandemic and enrolment was ceased after 35 pt recruited (March 2019-December 2022): 2 pt were ineligible (brain metastases, concurrent CYP3A4 inducer) and 2 pt did not start treatment (clinician decision, pt withdrawal)
- Median age was 64 with predominantly (61%) males enrolled (Table 1)
- 24 pts had received prior ICI; mostly Nivolumab monotherapy (17) or anti-PD1-antibodies in combination with other agents (e.g. anti-CTLA4, anti-TIGIT) including pts from the ANZUP UNISON clinical trial

5. Participant Experience

- 90% of pts required dose reduction, most often due to fatigue, hypertension, diarrhoea or hand-foot syndrome (with no new safety signals observed)
- Dose delays occurred due to adverse events in 16/31 (52%)
- The median dose of C administered was 40mg/day (mean 46mg, range 24-60mg)
- 12 pts completed 12 months of treatment and continued C via access program
- Treatment cessation occurred for: unacceptable toxicity (3), disease progression (4) and death (2)

6. Results

- ORR was 22.6%, all responders had prior exposure but were refractory to ICI (ORR 29% 7/24); no responses were observed in pts where ICI were contraindicated (0/7)
- Duration of therapy was similar in pts refractory to ICI, as in pts in whom ICI were contraindicated (11 (2-12) vs 5 (3-12)) months

7. Conclusions

- Cabozantinib is an active treatment for people with nccRCC refractory to prior treatment with ICI
- Tumour responses were not seen in pts where ICI were contraindicated in this small cohort, but the duration of therapy was similar
- Further follow-up will further determine duration of response and OS
- The optimal sequencing of ICI +/- tyrosine kinase inhibitors such as cabozantinib in nccRCC remains unclear

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Table 1. Participant Characteristics and Outcomes

	All pt (n=31)
Age (median) (years)	64 (22-83)
Gender at birth	Male:Female 61%:39%
Stage (AJCC 8th)	Stage IV - 42%
Prior ICI exposure	24/31
Histology	Papillary type 2 (10), chromophobe (7), papillary type 1 (4), Xp11 translocation (3), other histologies (7)
Median duration of therapy (months, range)	9 (2-12)
Treatment Related Adverse Events	Grade 1: 1/31 Grade 2: 11/31 Grade 3: 18/31 Grade 4 : 1/31
Tumour RECIST response rate	7/31: 22.6% (95% CI 9.6-41.1)
Median dose of cabozantinib	40mg/day

Study Progress

Enrolment: March 2019 – December 2022
Total study sites: 13
Enrolment: 33
Median Follow-up: 9 months

ClinicalTrials.gov identifier: NCT03685448

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research trials outcomes

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