Use of cabozantinib for previous treated metastatic renal cell carcinoma: Initial outcomes and toxicities in a single UK Centre

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Introduction
Cabozantinib, a multi-tyrosine kinase inhibitor is now recommended by NICE for the treatment of advanced renal cell carcinoma after vascular endothelial growth factor (VEGF) targeted therapy. In this large, randomized, open-label phase II trial METEOR(1), Cabozantinib was compared with Everolimus as a second line therapy following progression on VEGF targeted therapy and showed a significant improvement in progression free survival. Cabozantinib became available for use in Velindre Cancer Centre, Cardiff, South Wales, via an Early Access Scheme in January 2017 followed by NICE approval in July 2017.

Aims
To determine the outcomes, including dosage and toxicities, treatment response and survival of patients treated with Cabozantinib at Velindre Cancer Centre

Methods and Materials
Patients who received cabozantinib from December 2016 to September 2017 were included, with retrospective analysis of electronic patient records to collect data on demographics (age, gender, performance status), dosage, toxicities and outcomes. Progression Free Survival (PFS) and overall survival (OS) were calculated by Kaplan Meier Analysis using SPSS.

Results: Patient demographics and characteristics
Data was collected on a total of 28 patients who received cabozantinib in the period specified with a median age of 71 (age range 53 to 87). Most patients were WHO Performance Status 1 (57%).

The median dose used was 40mg and the mean length of time on treatment was 7 months. Patients were followed up for a median of 7.25 months. These results were compared with those in the METEOR study as demonstrated in graphs 1 and 2, and tables 1 and 2.

Results: Toxicities
Due to discrepancies in reporting unable to accurately grade toxicities based on Table 3: List of toxicities experienced by patients in VCC versus METEOR

Results: Discussion
Differences in patient population impacting on PFS / OS data
- Older cohort compared with trial (median age 63 years versus 71 years)
- Worse PS than in trial (68% vs 57%)

Stable significant proportion patients requiring dose reduction, especially if started at 60mg
- This despite a lower average dose used in our cohort of patients compared with the VCC cohort when compared with the METEOR study

Conclusions
Initial outcomes found may reflect a shorter follow up period, and an older patient population with worse performance status and more heavily pre-treated cohort when compared with the METEOR study (1). However, further analysis with larger patient population and longer follow up is needed.

Table 1: Comparison of patient demographics and characteristics between Velindre Cancer Centre cohort and Cabozantinib arm of METEOR Study (1)

Table 3: List of toxicities experienced by patients in VCC versus METEOR

Table 2: Comparison of details of treatment and follow up in Velindre Cancer Centre versus the METEOR Cabozantinib treatment arm

Discussion
- • 22 patients had adverse events with 11 patients requiring a dose reduction on cabozantinib
- The most common toxicities included diarrhoea and fatigue

Results: Limitations
- Short median follow up
- Definition of progressive disease sometimes made clinically rather than radiologically
- Lack of data on smoking, MSKCC prognostication
- Censorship data based on CANISC / chemocare database
- Lack of data on staging, MSKCC prognostication
- Definition of progressive disease sometimes made clinically rather than radiologically
- Lack of data on smoking, MSKCC prognostication
- Censorship data based on CANISC / chemocare database
- Problems of toxicity assessment from retrospective case notes

Table 2: Comparison of details of treatment and follow up in Velindre Cancer Centre versus the METEOR Cabozantinib treatment arm

Table 3: List of toxicities experienced by patients in VCC versus METEOR

References

Graph 1: Comparison of patient ages in VCC and METEOR (1) study groups

Graph 2: Comparison of previous lines of treatment in VCC and METEOR Study (1) groups

Graph 3: Overall survival experience of 28 patients on Cabozantinib

Graph 4: Kaplan Meier Graph depicting overall survival of cabozantinib in VCC

Graph 5: Overall survival and Progression Free Survival

Table 1: Comparison of patient demographics and characteristics between Velindre Cancer Centre cohort and Cabozantinib arm of METEOR Study (1)