Trial in Progress: Phase II Trial of Alternative Cabozantinib Dosing Schedule in Metastatic Renal Cell Carcinoma

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Background/Rationale

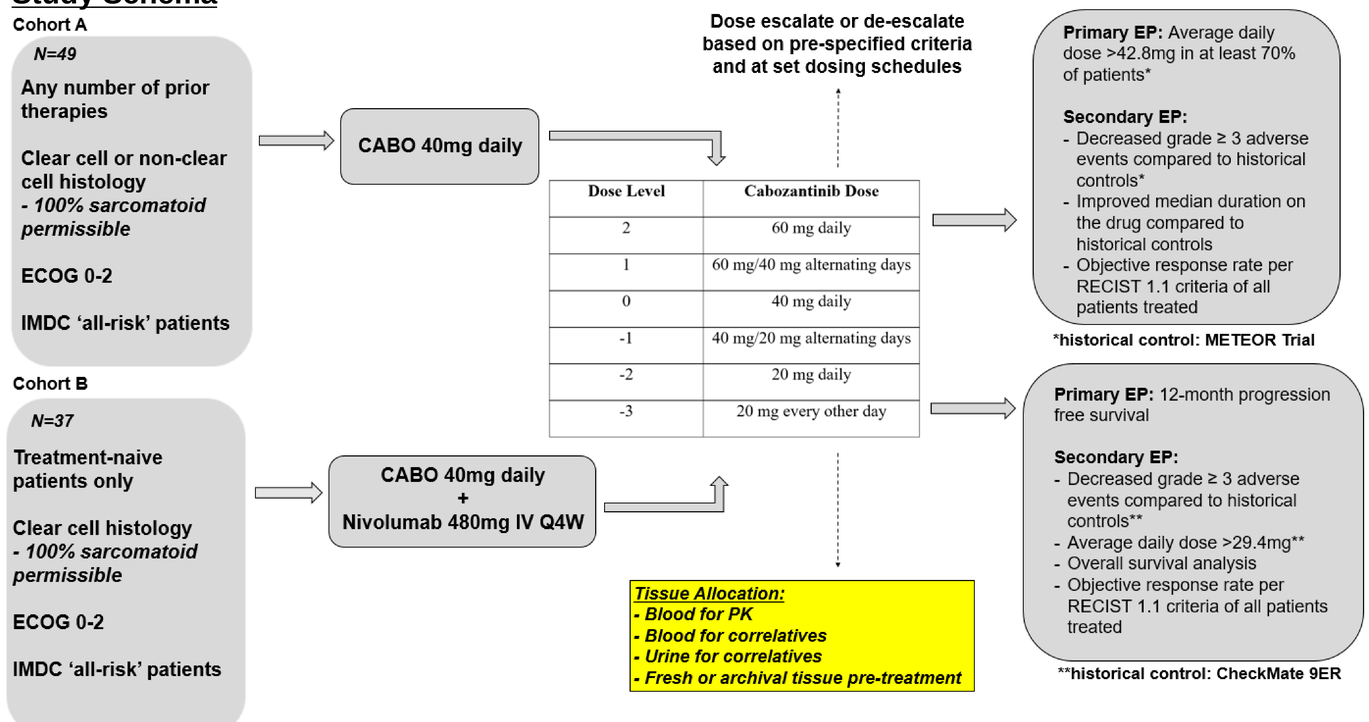
- Tolerability to Cabozantinib (CABO) is a challenge, as efficacy is limited by toxicity.
- Most adverse events (AE) can be mitigated with dose reductions and treatment breaks, thus optimal usage of CABO is dependent upon balancing the AEs and tolerability to maximize efficacy
- **We seek to test if an alternative dosing strategy could increase average daily drug exposure to ultimately improve efficacy and minimize toxicity**

Study Design

- Multi-site, single arm phase II trial of CABO that includes two cohorts.
  - **Cohort A (n=49)**: Any line of therapy treated with CABO monotherapy
    - Dose escalate or deescalate based on pre-specified criteria
    - Adjustments in 10 mg average daily dosing increments by utilizing alternate day dosing schedules (e.g 60 mg/40 mg every other day) rather than decreasing by 20 mg
    - The maximum dose of CABO is 60 mg daily, minimum 20 mg every other day
    - The median daily dose in the METEOR trial, 42.8 mg, will serve as the historical control
  - **Cohort B (n=37)**: Treatment-naïve patients treated with alternatively dosed CABO in combination with fixed-dose nivolumab
    - Combination therapy with the same CABO dosing schema as in cohort A
    - The median daily dose in the CheckMate 9ER trial, 29.4mg, will serve as historical control

***Importance of this study*: Optimization of CABO delivery through an alternative dosing strategy may allow for greater drug exposure while decreasing AE's. This study has the potential to improve treatment efficacy, survival, and minimize toxicity thereby improving patient quality of life.**

Study Schema



Proposed correlative Studies: Explore soluble serum **biomarker** profiles as **predictive** tools for treatment response.
- Blood collection at baseline, C2D1, C4D1, and at the time of progression/end of treatment
- Plan to assay for dynamic changes in soluble markers of angiogenesis (MET, AXL, Tie-2, VEGFR1/sFlt-1, and VEGFR2)
- Correlate markers to treatment response and survival to predict treatment sensitivity and resistance

NCT05263050
Current Status:
The study is currently enrolling