KCRS22 Kidney Cancer Research Summit

APART – A Phase 2 trial of Axitinib, Palbociclib and Avelumab as Renal Cell Carcinoma Therapy

Praful Ravi

Wanling Xie, Wenxin Xu, David Braun, Stephanie Berg, Gretchen Gignac, Christian Thomas, David McDermott, Toni Choueiri, Bradley McGregor

Dana-Farber Cancer Institute, Boston

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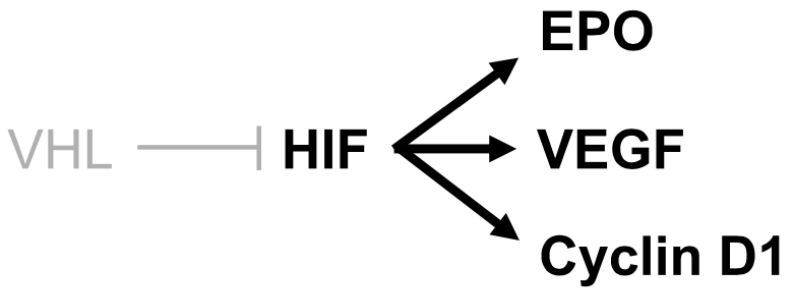
Background

- New targets beyond TKI and IO are needed in RCC

- Cell cycle pathway
  - CDKN2A inactivation in 16% of metastatic RCC
  - Loss of 9p in 40% of localized RCC



Ricketts et al, Cell Rep 2018; El-Mokadem et al, Br J Cancer 2014; Ravi et al, Cancer J 2020

Rationale

- Why combine IO with CDK4/6i?
  - Pre-clinical evidence of synergism between IO and CDK4/6i
  - CDK4/6i → upregulation of PD-L1
  - Genomic aberrations in CDK pathway associated with IO resistance in melanoma

- Axitinib + avelumab + palbociclib
  - Phase 1/2 trial in NSCLC
  - MTD: avelumab 10mg/kg q2w, axitinib 5mg bid, palbociclib 75mg d8-28
    - No DLTs at this dose
  - Key G3/4: cytopenia (>20%), hypertension (20%), diarrhea (7%)
  - 27% with PR (10/15 had prior IO, 14/15 had ≥1 prior line of therapy)

Goel et al, Nature 2017; Zhang et al, Nature 2010; Yu et al, CCR 2019; Solomon et al, Cancer Med 2022

Schema

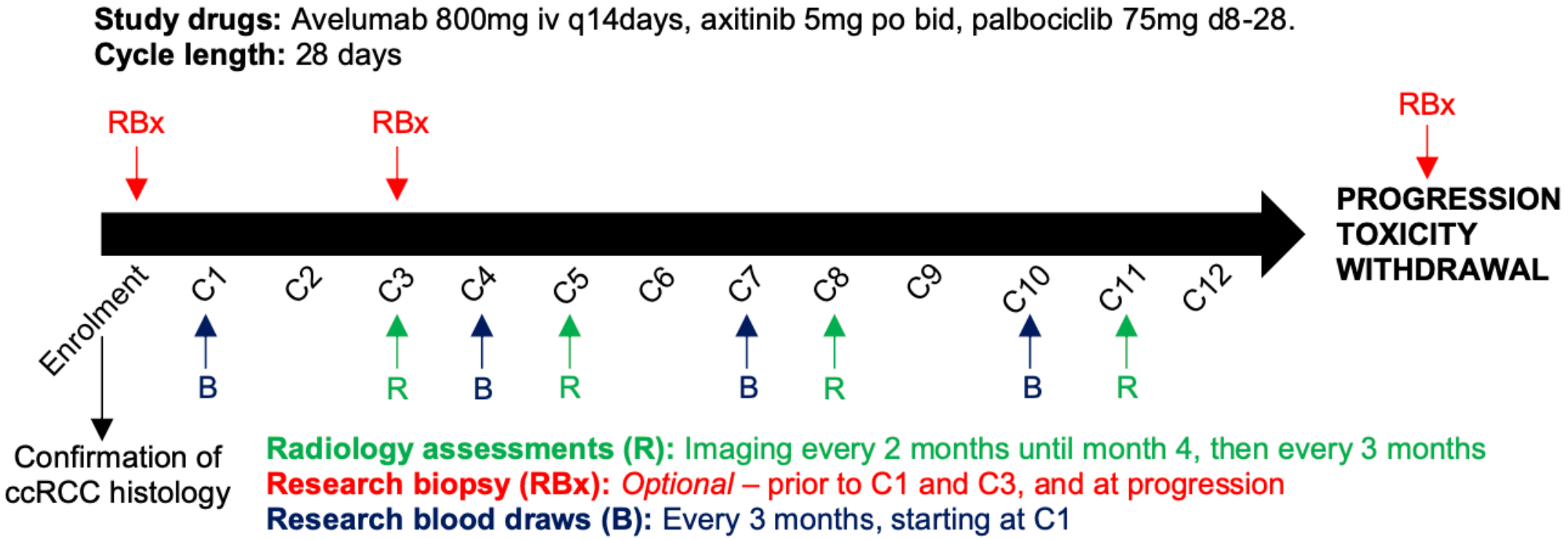
Untreated advanced ccRCC

Any IMDC

ECOG 0-2

Adjuvant IO allowed (>12mths)

N=25



Research blood – serum TK1 (liquid biomarker of cell cycle activity)
Research biopsies – expression of ERVs (associated with IO response)

Endpoints

- Primary
  - ORR of avelumab/axitinib/palbociclib in untreated advanced ccRCC
    - 85% power to detect improvement in ORR from 50% to 75%, one-sided alpha = 0.05
- Secondary
  - Safety of combination in ccRCC
  - Rate of CR + deep PR (≥80% reduction)
  - PFS, OS
- Exploratory
  - Immunologic and biologic correlates of response/resistance to therapy

Trial status – opened Sep 2022 and accruing patients across 4 sites