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

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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)

Schema

**Untreated advanced ccRCC**

**Any IMDC**

**ECOG 0-2**

**Adjuvant IO allowed (>12mths)**

**N=25**

**Study drugs:** Avelumab 800mg iv q14days, axitinib 5mg po bid, palbociclib 75mg d8-28.
**Cycle length:** 28 days

- **Enrollment**
  - C1
  - C2
  - C3
  - C4
  - C5
  - C6
  - C7
  - C8
  - C9
  - C10
  - C11
  - C12

- **Radiology assessments (R):** Imaging every 2 months until month 4, then every 3 months
- **Research biopsy (RBx):** Optional – prior to C1 and C3, and at progression
- **Research blood draws (B):** Every 3 months, starting at C1

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

**PROGRESSION TOXICITY WITHDRAWAL**
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