**Background**

Renal Cell Carcinoma and CXCR4

- Approximately 70% of sporadic clear cell renal cell carcinoma (RCC) patients have a loss of VHL gene function that drives tumor angiogenesis by increasing VEGF receptor expression.

- A number of fynicrein linear inhibitors (TSIs) that target the VEGF pathway have been approved for RCC, including sunitinib, although most patients eventually relapse through angiogenic escape.

- Multiple mechanisms implicates the CXCL12/CXCR4 chemokine signaling axis in contributing to the lack of efficacy of tumor angiogenesis inhibitors.

- CXCR4 is expressed by human tumors, including clear cell RCC, melanoma, and ovarian cancer.

- Immune suppression and enhanced tumor infiltration by myeloid-derived suppressor cells (MDSC) and T regulatory cells (Treg) are critical issues for RCC patients.

**Study Objectives**

- Evaluate the safety and tolerability of mavorixafor in combination with axitinib in patients with advanced clear cell RCC.

- Assess the clinical activity of mavorixafor + axitinib in patients with advanced RCC with prior treatment failure by RECIST v1.1 criteria.

**Study Design**

- Figure 3: Dose Escalation and Expansion Phases

- Phase 1: Dose Escalation (N = 12)
  - mavorixafor 100 mg QD + axitinib 5 mg BID
  - mavorixafor 200 mg QD + axitinib 5 mg BID
  - mavorixafor 400 mg QD + axitinib 5 mg BID

- Phase 2: Expansion (N = 55)
  - mavorixafor 600 mg QD + axitinib 5 mg BID
  - (n = 6)

- This is a Phase 1/2, multi-center, open-label study of mavorixafor in combination with axitinib in patients with histologically confirmed advanced RCC who have received at least one prior systemic therapy.

- Safety analysis included 111 patients that were treated with mavorixafor 200 mg QD or 113 patients that were treated with mavorixafor 400 mg QD and axitinib 5 mg BID.

- Treatment responses were assessed using RECIST v1.1 every 4 weeks from Day 1 for 8 weeks and then every 12 weeks thereafter by blinded, independent central review.

**Mavorixafor Increases Tumor Immune Cell Infiltration and Activation**

- This increase in tumor immune cell infiltration, as well as the increase in tumor immune activity, demonstrated greater than the activity for mavorixafor alone.

**Patient Disposition**

- Table 1: Mavorixafor + Axitinib (N = 65)

- Safety:
  - Adverse Events (≥ Grade 3) and Grade 4 Data Cut-off: August 27, 2019

**Future Directions**

- Given the encouraging mPFS noted in this heavily pretreated advanced RCC patient population, mavorixafor + axitinib may have potential as a new treatment option for patients with advanced RCC.

**Acknowledgments**

- The authors would like to thank the patients and their families, investigators, co-investigators, and the study teams at each of the participating centers. This clinical study is sponsored by X4 Pharmaceuticals. Medical editorial support provided by Tim Henion and John Welle of Acumen Medical Communications and funded by X4 Pharmaceuticals. Axitinib is provided by Pfizer Inc. through an innovative research collaboration agreement.

**References**


