SRF231, a fully human CD47 antibody, potentiates the effects of opsonizing antibodies and cytotoxic chemotherapies in preclinical cancer models

Kshama A. Doshi, Matthew Rausch, Caroline M. Armet, Li Zhang, Alison M. Paterson, Benjamin H. Lee, Vito J. Palombella, Pamela M. Holland, Marisa O. Peluso
Surface Oncology, Inc., Cambridge, MA, USA

**Background**

- CD47, often referred to as a “Don’t Eat Me” signal, is widely expressed on tumor cells and an important checkpoint of the innate immune response
- Several unique anti-CD47 molecules are currently being evaluated in the clinic to antagonize the CD47 axis in cancer
- SRF231 is a high-affinity, CD47-targeting antibody that blocks the SIRPα/CD47 interaction and induces Fc-FcR interactions, thereby potentiating phagocytic cell death
- SRF231 also potentiates combinatorial activity of agents known to provide additional “Eat Me” signals to tumor cells (such as:
  - Opsonizing hIgG containing antibodies that enhance Fc-FcR interactions
  - Chemotherapies that trigger cell death induction pathways

**Results**

**Figure 1:** SRF231 Potentiates Phagocytosis Induced by Opsonizing Agents, Elotuzumab (anti-SLAMF7), or Daratumumab (anti-CD38) in Multiple Myeloma

**Figure 2:** SRF231 Potentiates Cell Death Induced by Cisplatin In Vitro

**Figure 3:** SRF231 Potentiates the Effects of Opsonizing Antibodies and Chemotherapy In Vitro

**Figure 4:** Enhanced Antitumor Activity Observed with SRF231 +/- Elotuzumab in Disseminated MM.13 Multiple Myeloma Xenograft Model

**Figure 5:** Enhanced Antitumor Activity Observed with SRF231 +/- Daratumumab in H929 Xenograft Model

**Figure 6:** SRF231 Administration Enhances Survival in the A549 Lung Orthotopic Xenograft Model

**Figure 7:** Chemotherapy Combined with SRF231 Leads to Enhanced Antitumor Activity in H-175 (EGFR Mutant) Lung Xenograft Model

**Conclusions**

- The anti-CD47 mAb, SRF231, demonstrates both single-agent and combinatorial activity with opsonizing antibodies and cytotoxic chemotherapies in vivo in preclinical hematologic and solid tumor cancer models
- As a single agent, SRF231:
  - Was highly potent in the disseminated MM.13 multiple myeloma xenograft model, and a dose-dependent survival benefit was seen with dosing regimens as low as 3 µg/mouse, qe 3
  - Extended survival in the orthotopic A549 lung xenograft model
- In combination with opsonizing antibodies or cell death-inducing chemotherapies, SRF231:
  - Potentiates the activity of data (anti-CD38) and anti-SLAMF7 in multiple myeloma xenograft models, with either single- or multi-dose administration of SRF231, leading to enhanced CRs and overall survival
  - Enhanced antitumor activity trending towards extended survival and increased survival benefit in the H-175 lung xenograft model in combination with docetaxel
  - Please refer to poster #2196 for more on SRF231 combinations

*Presented at AACR 2020*