The anti-CD47 antibody SRF231 increases anti-tumor activity of standard care chemotherapy in platinum-resistant PDX models of ovarian cancer

Background

CD47 is a type I integral membrane protein expressed on multiple human tumors, including ovarian cancer, and modulates cell processes such as cell migration, adhesion, T-cell function, and cell death via interaction with multiple ligands. Interaction of CD47 with SIRPa expressed on myeloid cells results in an inhibitory “don’t eat me” signal that prevents phagocytosis of CD47-expressing cancer cells. Enhancement of the anti-tumor activity of chemotherapy has also been reported with CD47 antagonists. We investigated the effects of combining SRF231, an investigational fully human IgG4 anti-CD47 antibody, with chemotherapy in models of human ovarian cancer.

Methods

- Expression of CD47 in 8 established platinum-resistant PDX models of ovarian cancer was measured by immunohistochemistry with the anti-CD47 antibody SP279.
- SRF231-mediated phagocytosis of ovarian cancer cell lines was assessed using a macrophage coculture system.
- In vitro tumor cell death in the presence of immobilized SRF231 with either doxorubicin or platinum was assessed by an Annexin V assay.
- The activity of SRF231 combined with doxorubicin in vivo was compared to isotype control, SRF231, or doxorubicin monotherapy in an ovarian cancer subtype-matched xenograft model, OVCAR3.
- Additionally, the activity of SRF231 combined with platinum was compared to isotype control, SRF231, or platinum monotherapy in two luciferase-expressing intraperitoneal PDX ovarian cancer models, as measured by bioluminescent imaging.

Results

Several human ovarian cell lines are susceptible to SRF231-mediated phagocytosis

SRF231 cooperativity with oxaliplatin or doxorubicin leads to enhanced tumor cell death

SRF231 with doxorubicin leads to enhanced anti-tumor activity in the OVCAR3 model

Conclusions

- Anti-CD47 directed therapy with SRF231, a fully human antibody, demonstrated the ability to significantly increase the anti-tumor activity of standard chemotherapies in xenograft and platinum-resistant PDX models of ovarian cancer.
- Further exploration of combining anti-CD47 and platinum regimens in ovarian cancer is warranted.
- Please refer to poster #2196 for more on SRF231 combinations.