Multimeric IgM antibodies targeting DR5 are potent and rapid inducers of tumor cell apoptosis and cell death in vitro and in vivo
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**Abstract No. 3050 AACR Annual Meeting 2019, March 29-April 3, Atlanta, GA**

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**Background**

- Tumor necrosis factor receptor (TNFR) superfamily death receptor DR5 requires multimerization to induce apoptosis and tumor cytotoxicity.
- While agonistic antibodies targeting DR5 have demonstrated evidence of preclinical efficacy, limited clinical efficacy was observed likely due to insufficient receptor crosslinking in the tumor microenvironment.
- We have developed a novel multivalent anti-DR5 IgM antibody that effectively clusters the receptor and compares its functional activity to the corresponding IgG antibody.

**IgM Antibody Efficiently Clusters DR5**

**IgM Induces Apoptosis More Rapidly Than IgG**

**Anti-DR5 IgM Is Efficacious in IgG Sensitive and Resistant Xenograft Models**

**Summary**

- Anti-DRS IgM demonstrates a more rapid and greater magnitude of apoptotic induction compared to IgG.
- Anti-DRS IgM is 100-10,000 fold more potent than IgG at inducing cytotoxicity in solid and hematologic tumor cell lines in vitro.
- Anti-DRS IgM is efficacious in IgG sensitive and resistant tumor models, solid tumor and hematologic models, large tumors up to 600 mm³ in volume, as well as colorectal PDX models in vivo.
- Combining anti-DRS IgM with Kras induced durable tumor regression and increased tumor shrinkage in the colorectal xenograft model, combining with Gemcitabine resulted in an additive effect in BEPAC pancreatic model.
- These data demonstrate that targeting DR5 with IgM is superior to IgG and supports the development of anti-DRS IgM to treat solid and hematologic cancers.