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The Anti-Tumor Activity of IGM-8444, an Agonistic Death Receptor 5 (DR5) IgM Antibody, is Sensitized in Combination with Chemotherapy and Bcl-2 Inhibitors in NHL and AML

ASH Annual Meeting

December 5-8, 2020

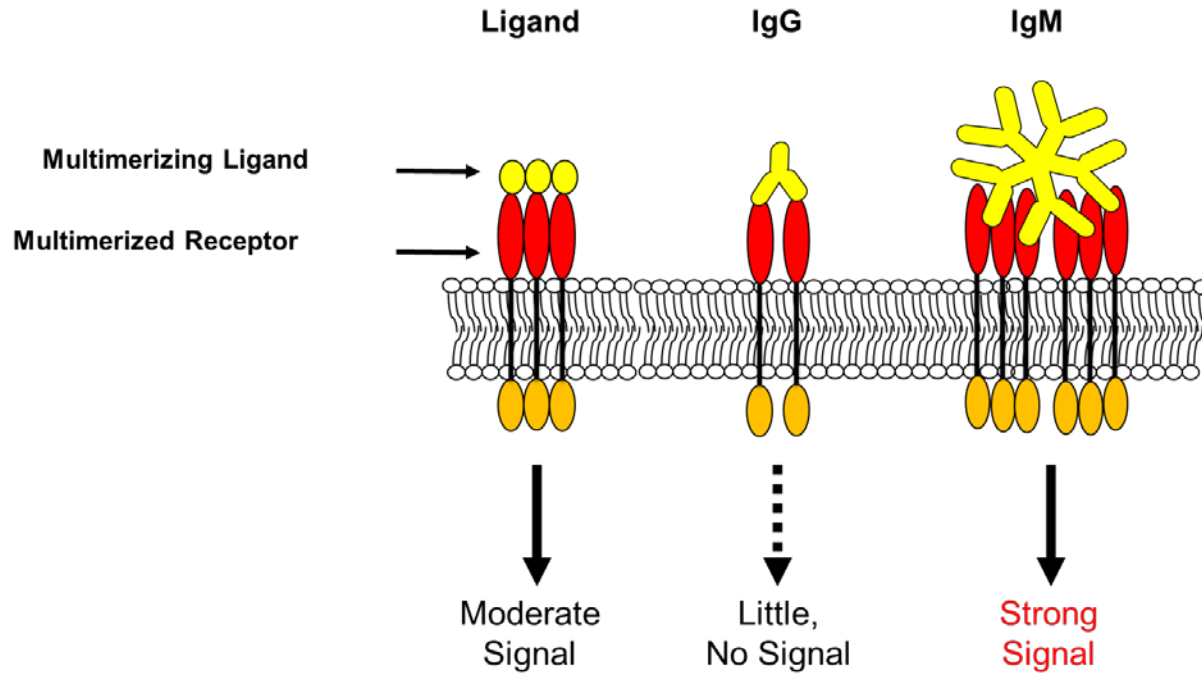
Beatrice T. Wang, Thomas J. Matthew, Ling Wang, Tasnim Kothambawala, Susan E. Calhoun, Xingjie Chen, Poonam Yakkundi, Rodnie A. Rosete, Hope Lancero, Maya F. Kotturi, Eric W. Humke, Angus M. Sinclair, Bruce A. Keyt

Disclosures

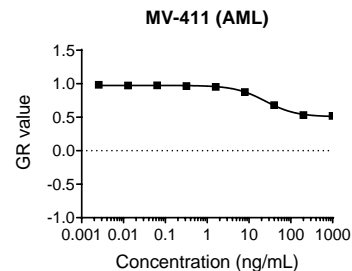
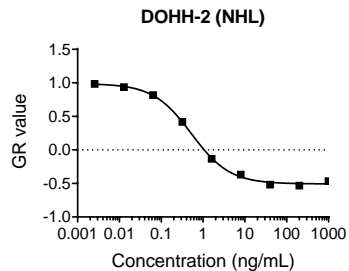
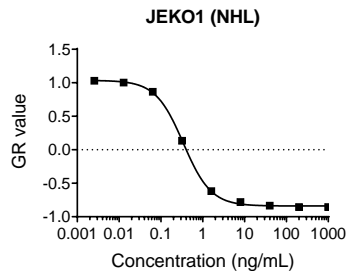
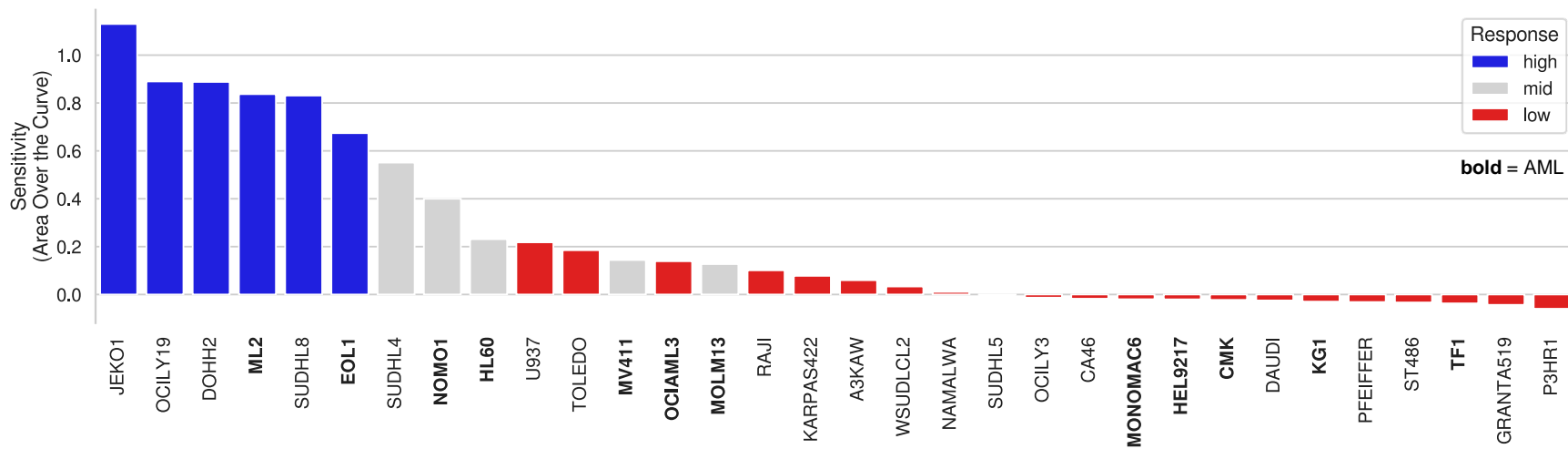
- I am an employee and stockholder of IGM Biosciences, Inc.



Multimeric IgM Antibodies Enhance TNFRSF Signaling

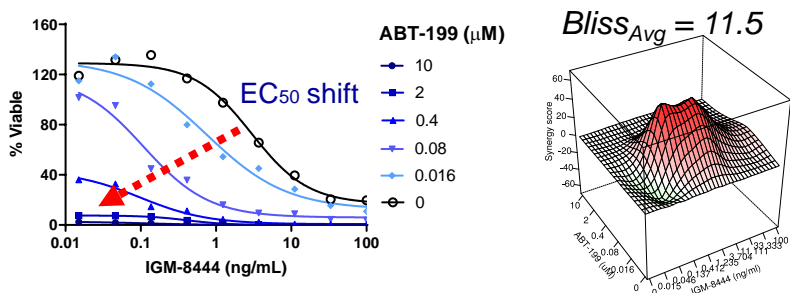


IGM-8444 Potency on NHL and AML Cell Lines

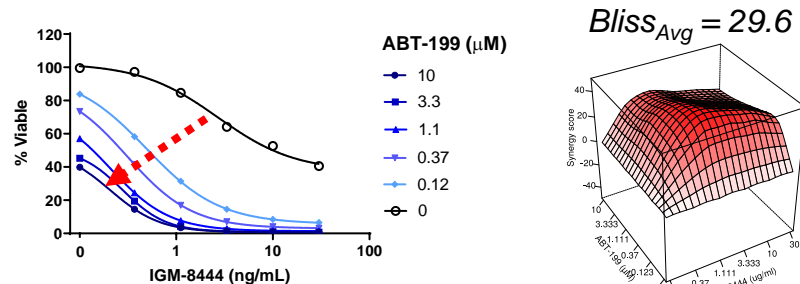


IGM-8444 Synergistic Combinations in NHL Cell Lines

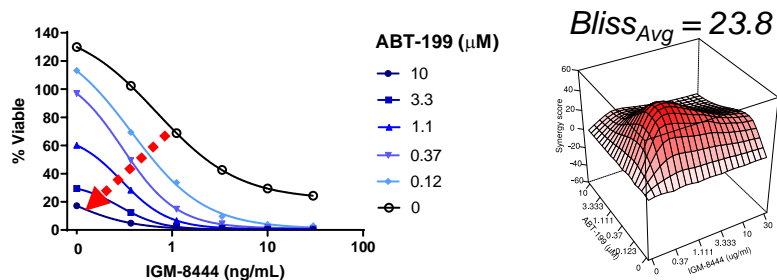
ABT-199 in DOHH-2 cells



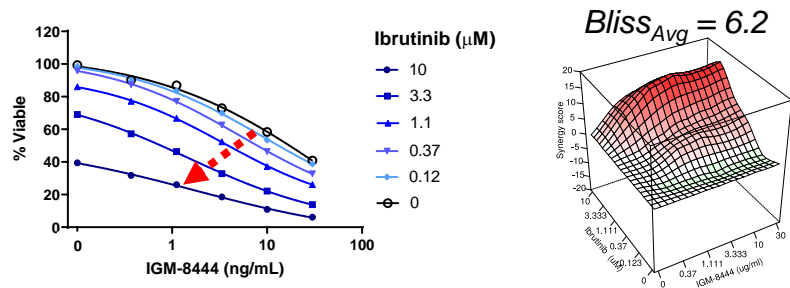
ABT-199 in WSU-DLCL2 cells



ABT-199 in Karpas-422 cells

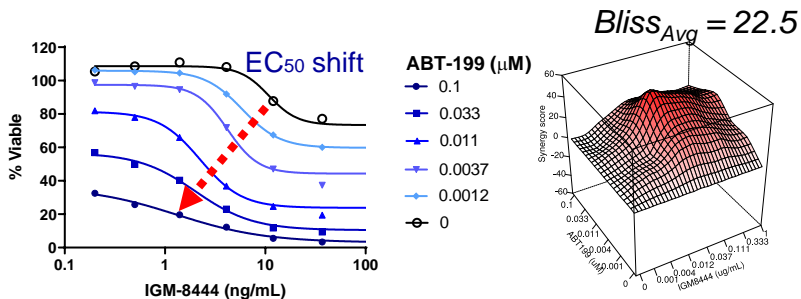


Ibrutinib in U-937 cells

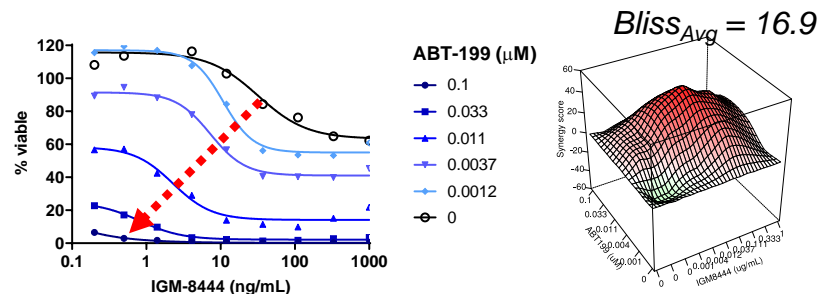


IGM-8444 Synergistic Combinations in AML Cell Lines

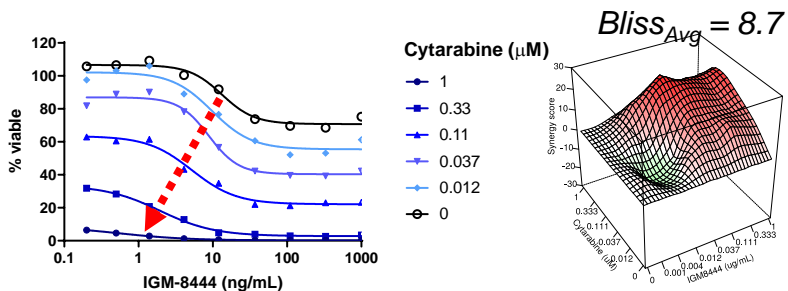
ABT-199 in MV-411 cells



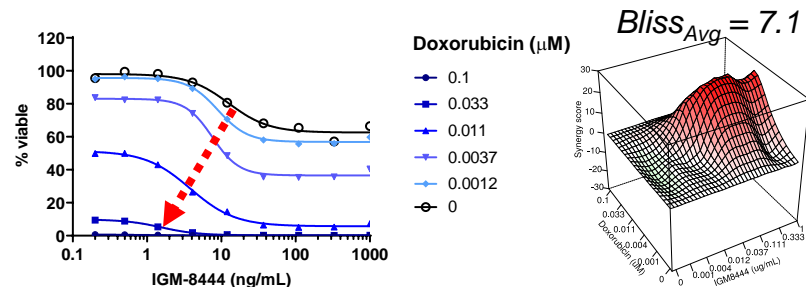
ABT-199 in Molm-13 cells



Cytarabine in MV-411 cells

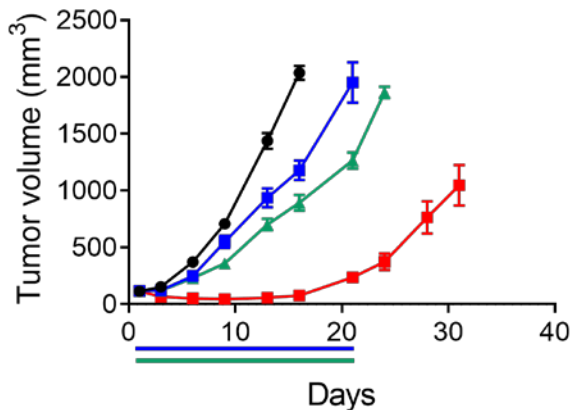


Doxorubicin in MV-411 cells



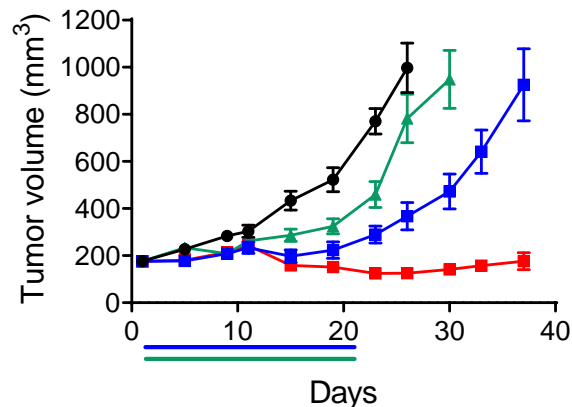
IGM-8444 Combinations Enhance Anti-Tumor Efficacy

**DOHH-2 NHL Model:
ABT-199 combination**



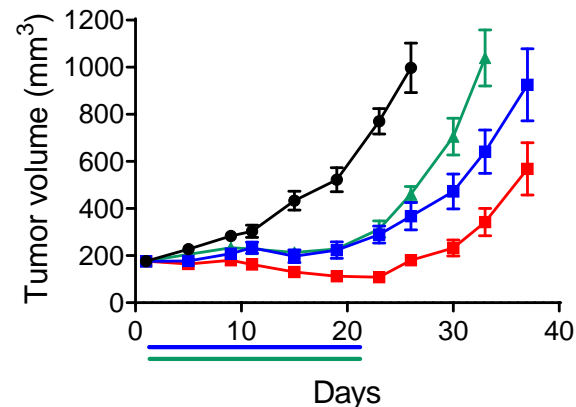
- Vehicle (i.v., Q2Dx11)
- IGM-8444 (5 mg/kg i.v. Q2Dx11)
- ▲ ABT-199 (100 mg/kg p.o. QDx21)
- IGM-8444 + ABT-199

**MV-411 AML Model:
ABT-199 Combination**



- Vehicle (i.v., Q2Dx11)
- IGM-8444 (5 mg/kg i.v. Q2Dx11)
- ▲ ABT-199 (100 mg/kg p.o. QDx21)
- IGM-8444 + ABT-199

**MV-411 AML Model:
Cytarabine Combination**

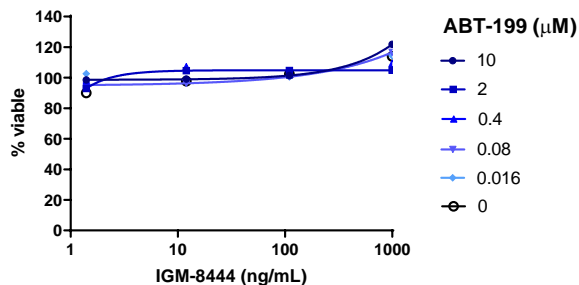


- Vehicle (i.v., Q2Dx11)
- IGM-8444 (5 mg/kg i.v. Q2Dx11)
- ▲ Cytarabine (12.5 mg/kg i.p. QDx21)
- IGM-8444 + Cytarabine

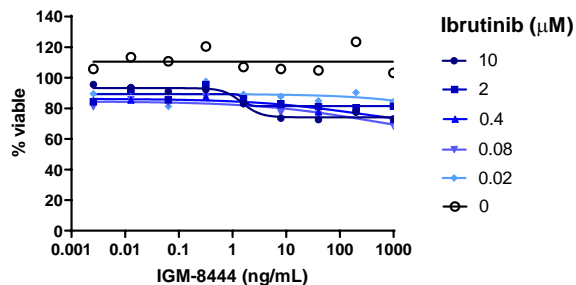


Combinations are Safe on Human Hepatocytes In Vitro

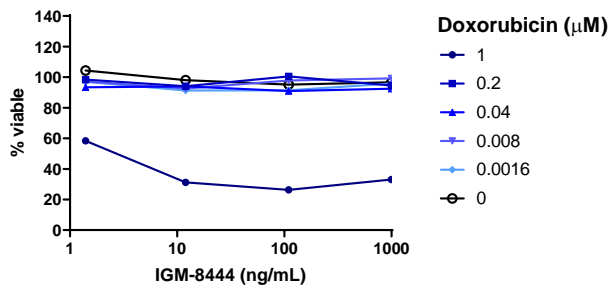
IGM-8444 + ABT-199



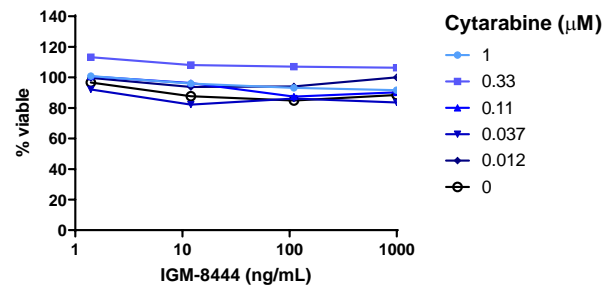
IGM-8444 + Ibrutinib



IGM-8444 + Doxorubicin

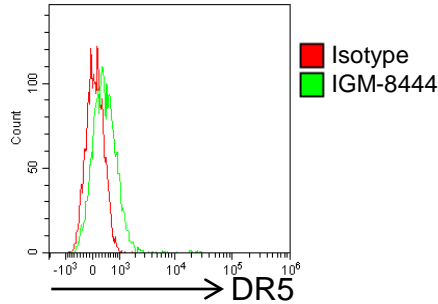


IGM-8444 + Cytarabine

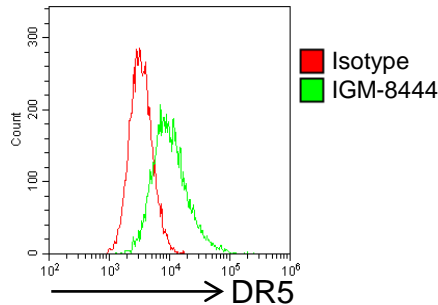


No IGM-8444 Induced Cytotoxicity of Human Monocytes

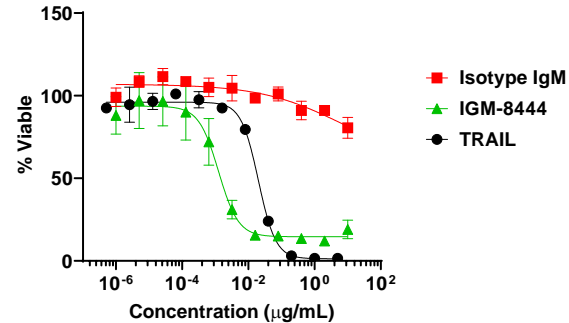
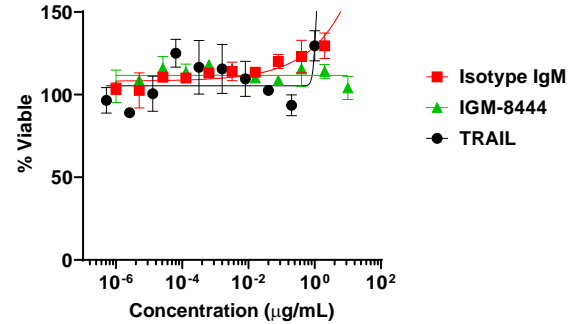
Human Monocytes



Colo205



24-hour cytotoxicity assay



Summary and Conclusions

- IGM-8444 shows potency across a panel of NHL and AML cell lines
- Combinations of IGM-8444 with standard of care chemotherapy and targeted agents enhance tumor cytotoxicity both *in vitro* and *in vivo* in NHL and AML models
- IGM-8444 does not kill primary human hepatocytes *in vitro* either as a single agent or in combination with agents that synergistically kill tumor cells
- IGM-8444 also does not kill human monocytes which express low levels of DR5
- IGM-8444 is currently being evaluated in a Phase 1 study as a single agent and in combination with chemotherapy-based regimens in patients with solid cancers and NHL

