PRECLINICAL EVALUATION OF ISB 1442, A FIRST-IN-CLASS CD38 AND CD47 BISPECIFIC ANTIBODY INNATE CELL MODULATOR FOR THE TREATMENT OF AML AND T-ALL

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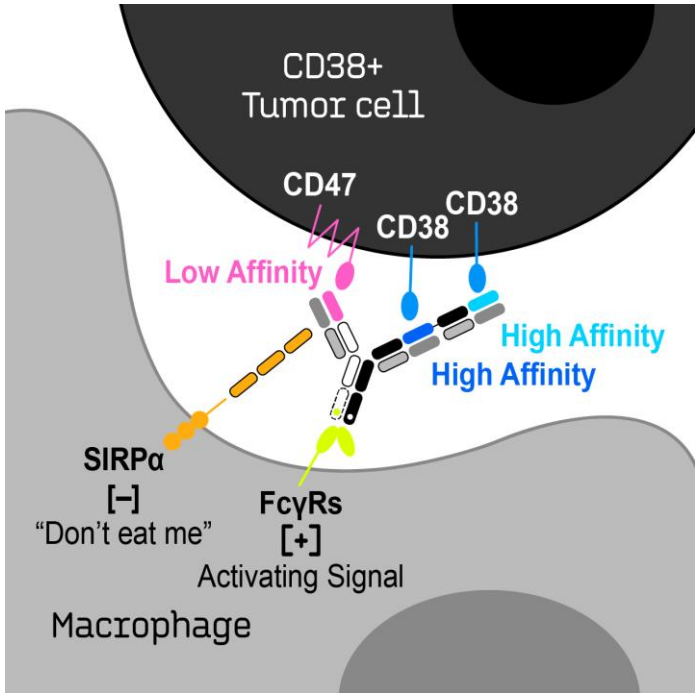
ISB 1442 Redirects Myeloid Cells to CD38+ Tumors and Overcomes Mechanisms of Resistance to Daratumumab

ISB 1442 (CD38 X CD47) BISPECIFIC ANTIBODY	BEAT® 2.0



KEY ATTRIBUTES

- Two arms drive binding to distinct CD38 epitopes on tumor cells
  - + No functional competition with daratumumab
- One arm blocks CD47-SIRPa binding on tumor cells to enhance ADCP
  - + Increased phagocytosis by blocking CD47 "don't eat me" signal
  - + CD47 is over-expressed by hematologic tumors and associated with worse prognosis
  - + Reduced potential for antigen sink with lower-affinity Fab binding to CD47 expressed on healthy cells
- Potent ADCC and CDC based on
  - + Optimized affinity, epitope, architecture/avidity and Fc engineering
- Optimized tolerability
  - + Low potential for adverse effects on red blood cells (RBC) such as hemagglutination, platelet aggregation

*BEAT®: **B**ispecific **E**ngagement of **A**ntibodies based on the **T**CR*

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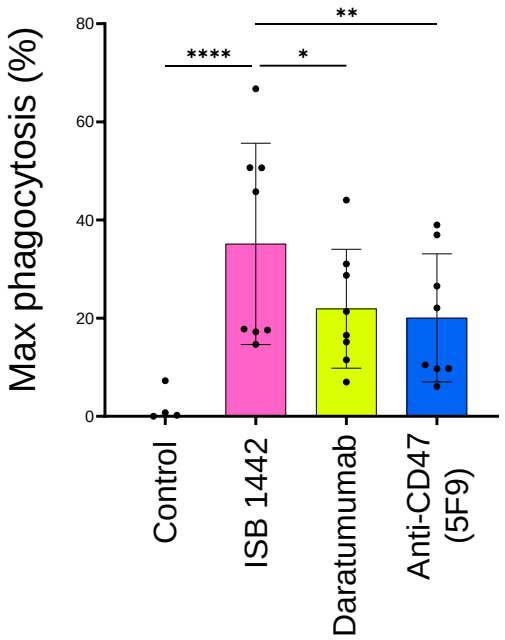
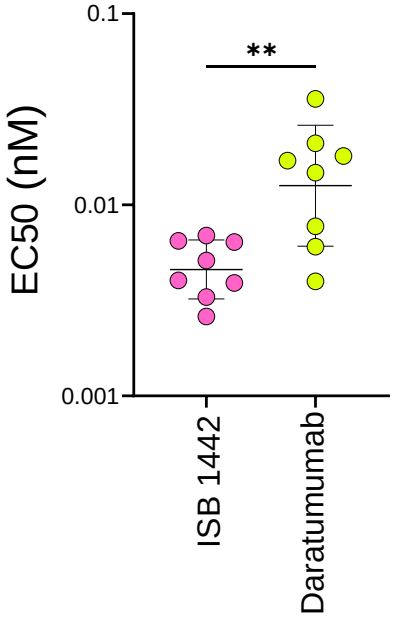
ISB 1442 Shows Higher Potency Against AML Cell Lines Compared to Anti-CD38 and Anti-CD47 Mono-Targeting Antibodies

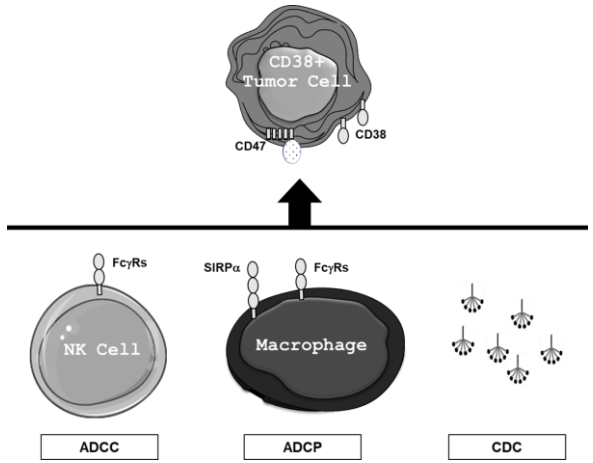
Antibody Dependent Cell Phagocytosis (ADCP)

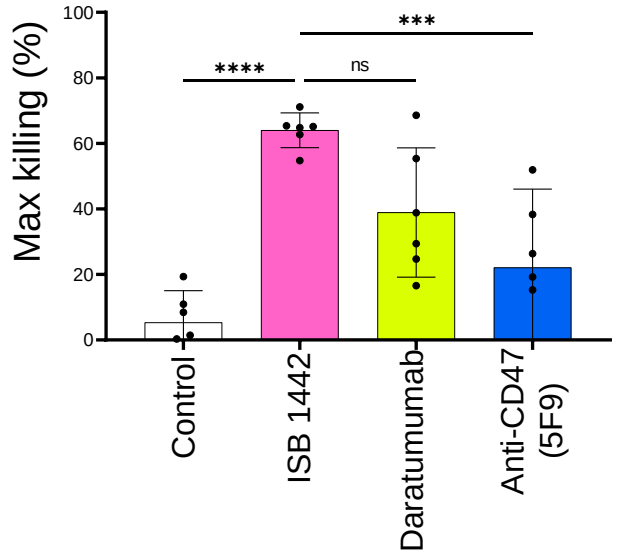


Antibody Dependent Cell Cytotoxicity (ADCC)



Multiple Mechanisms Of Action Of Killing (MMoAK)





P < 0.05
** P < 0.01,
*** P < 0.001
**** P < 0.0001

Statistics: Not Significant (NS)
AML: Acute Myeloid Leukemia
Cell used: MOLM-13 ($CD38^{INT}$ $CD47^{LOW}$)

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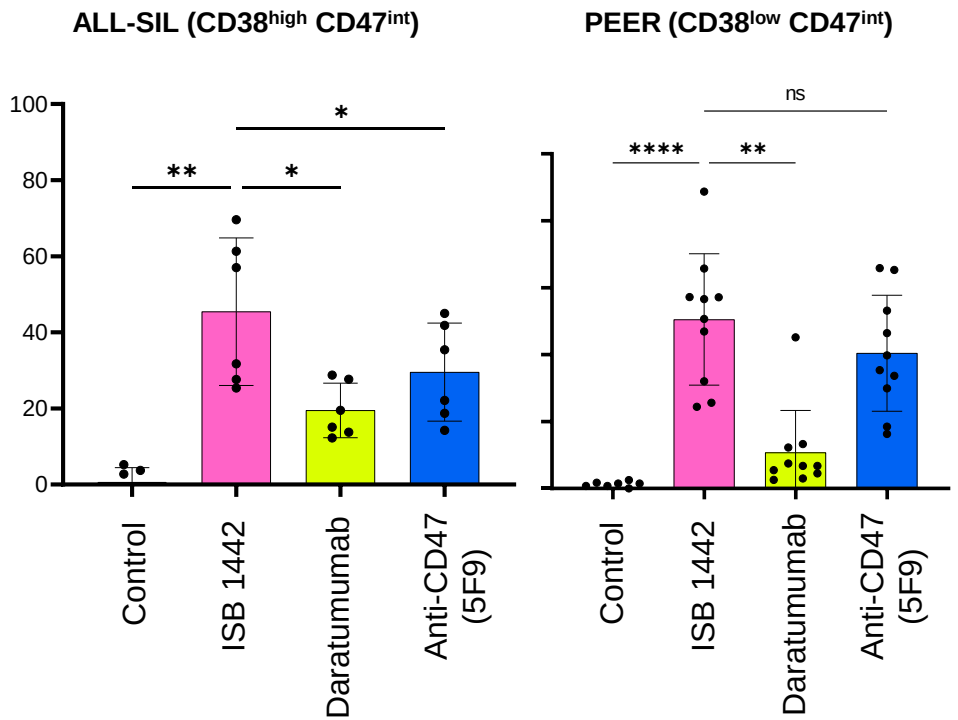
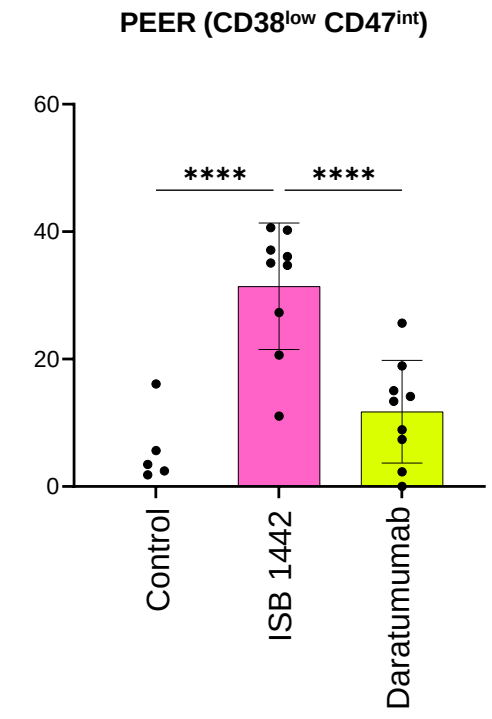
ISB 1442 Induces Higher Phagocytosis and Higher NK Cell Killing of T-ALL Cell Lines with Intermediate or Low CD38 Expression as Compared to Daratumumab

Antibody Dependent Cell Phagocytosis (ADCP)



Antibody Dependent Cell Cytotoxicity (ADCC)



P < 0.05
** P < 0.01
*** P < 0.001
**** P < 0.0001

Statistics: Not Significant(NS)
T-ALL: T-Cell Acute Lymphoblastic Leukemia

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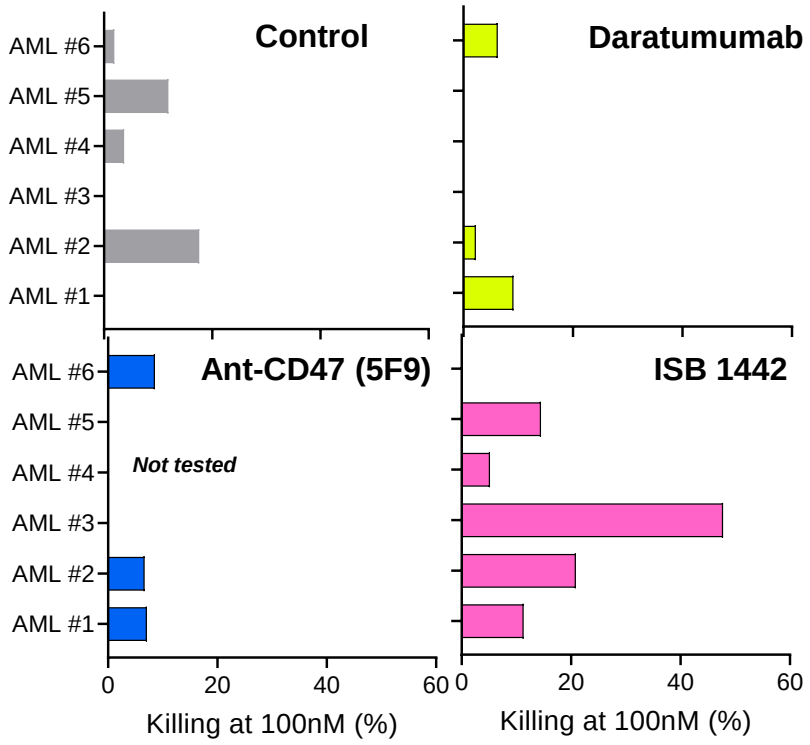
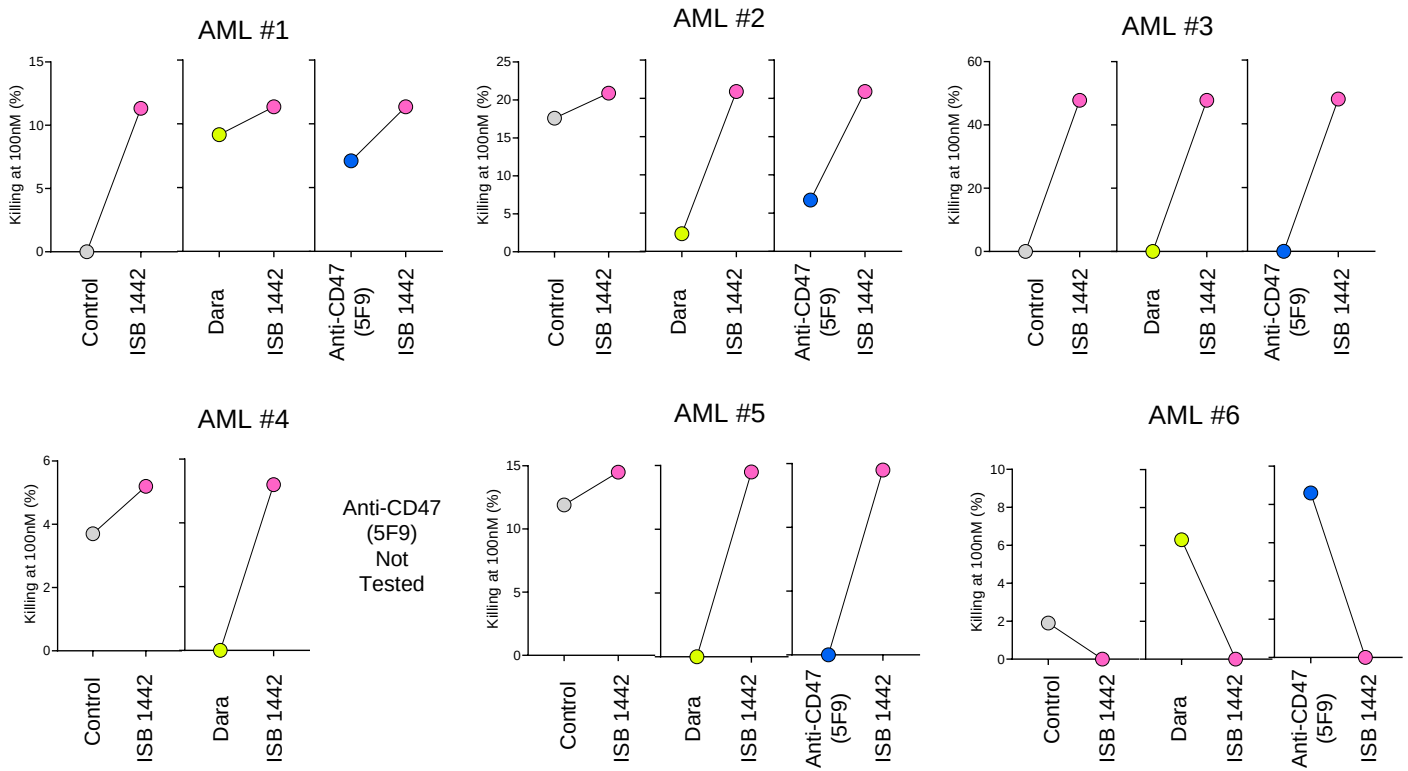
ISB 1442 Showed More Frequent Killing of AML Blasts and a Trend of Higher Potency as Compared to Monospecific Anti-CD38 Daratumumab or Anti-CD47 (5F9) in AML Bone Marrow Aspirates

Killing of AML Blasts



Potency Compared to Anti-CD38 or Anti-CD47 Monospecifics



DARA: Daratumumab

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Conclusions

- ISB1442 induces killing of AML and T-ALL cell lines in multiple *in vitro* assays, including ADCP and ADCC
- ISB 1442 shows superior activity to daratumumab in AML and T-ALL cell lines having intermediate or low CD38 expression
- In AML bone marrow aspirates where direct killing was detectable, ISB 1442 showed more frequent killing of AML blasts and a trend of higher potency as compared to monospecific anti-CD38 daratumumab or anti-CD47 (5F9)