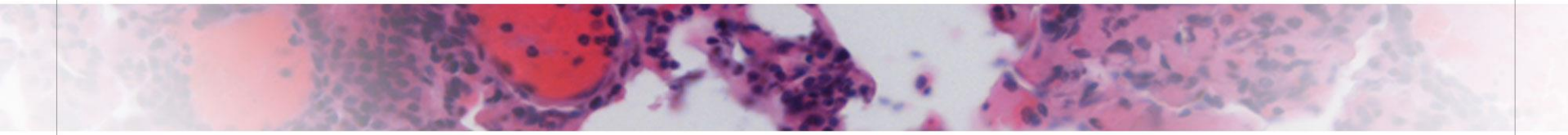
American Society *of* Hematology
Helping hematologists conquer blood diseases worldwide



MP0533: A CD3 Engager DARPin Targeting CD33, CD123 & CD70 for the Treatment of AML and MDS

Matteo Bianchi, Christian Reichen, Stefanie Fischer, Yvonne Grübler, Aline Eggenschwiler, Rajlakshmi Marpakwar, Thamar Looser, Patricia Spitzli, Christel Herzog, Denis Villemagne, Yvonne Kaufmann, Alienor Auge, Martin Hänggi, Waleed Ali, Tamara Lekishvili, Teresa Frasconi, Stephan Wullschleger, Christof Zitt, Marco Franchini, Amelie Croset, Randall Watson, Vladimir Kirkin, Ursina Luethi, Adrian F. Ochsenbein, Carsten Riether, Daniel Steiner, Nicolas Leupin, **Anne Goubier**

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- **Need to cure the disease by eliminating all LSCs and blasts**
  - 50% of patients relapse in 12-18 months

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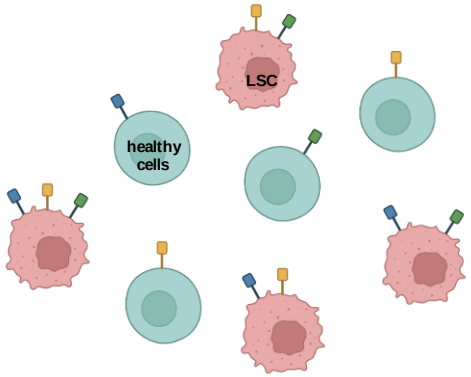

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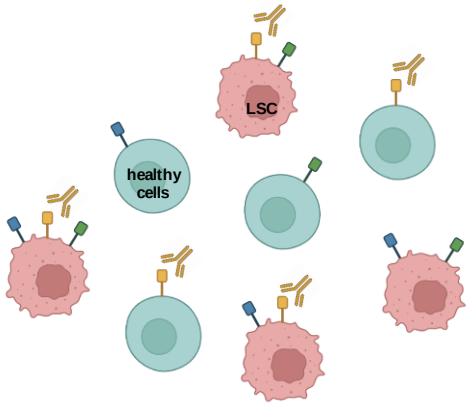

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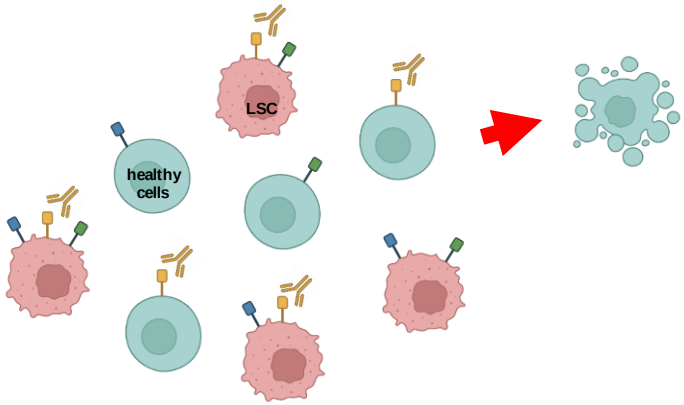

Mono-targeting agents also kill healthy cells

→ **Adverse Events, DLT**

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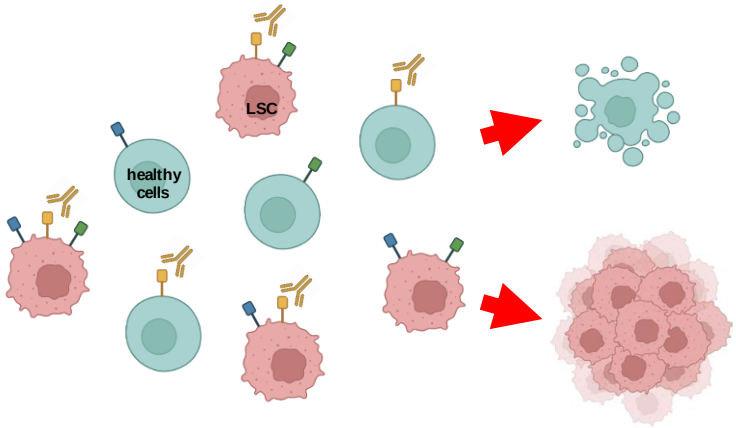

Mono-targeting agents also kill healthy cells

→ **Adverse Events, DLT**

Mono-targeting agents might not kill all LSCs and blasts

→ **Clonal selection and Recurrence of disease**

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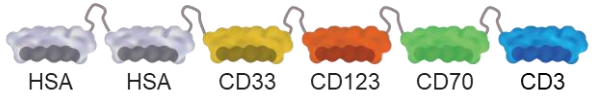
Our Approach: a Trispecific CD3 Engager DARPin



MP0533

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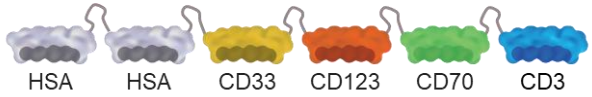

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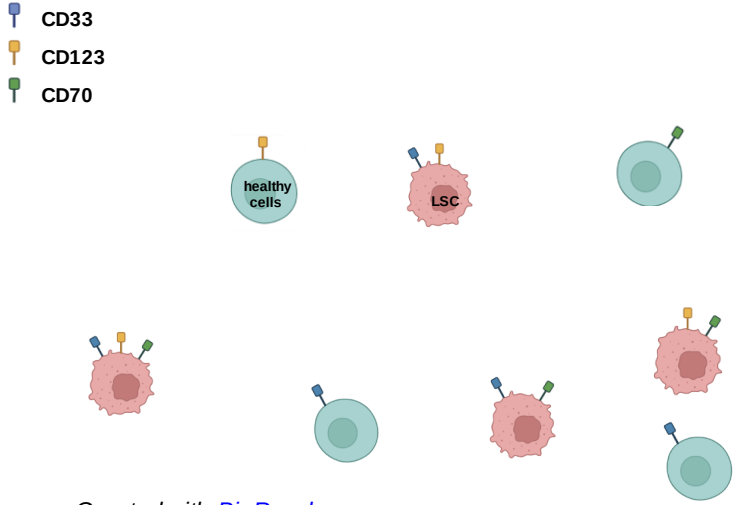

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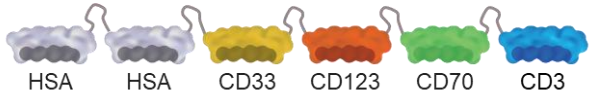

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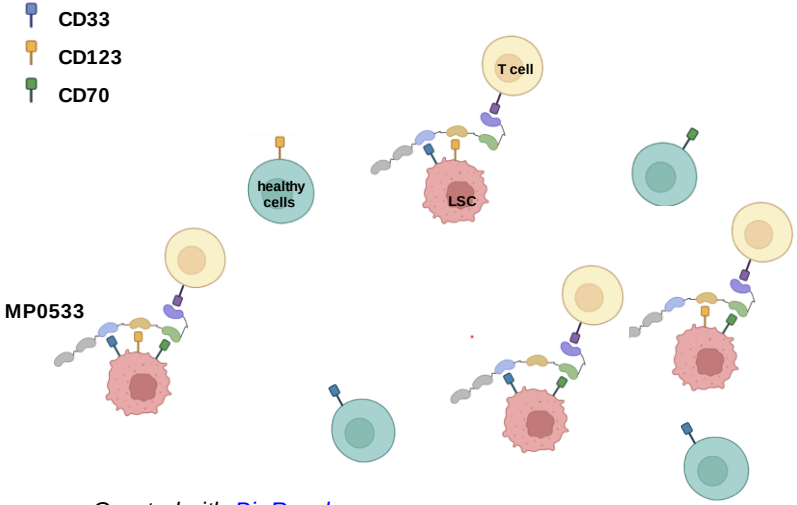

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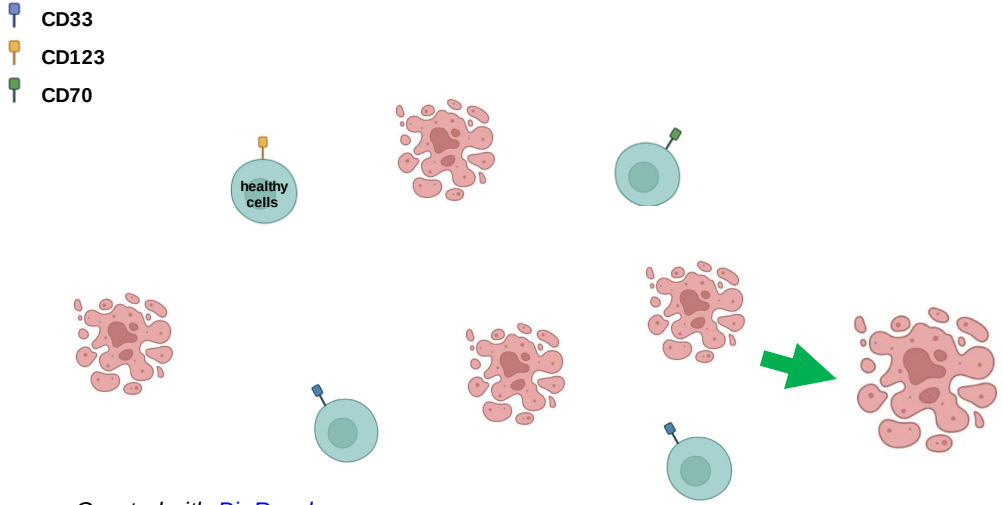

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MP0533 has the potential to kill all AML cells despite Ag heterogeneity

→ Long term disease control

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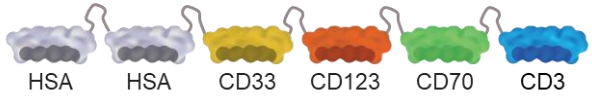

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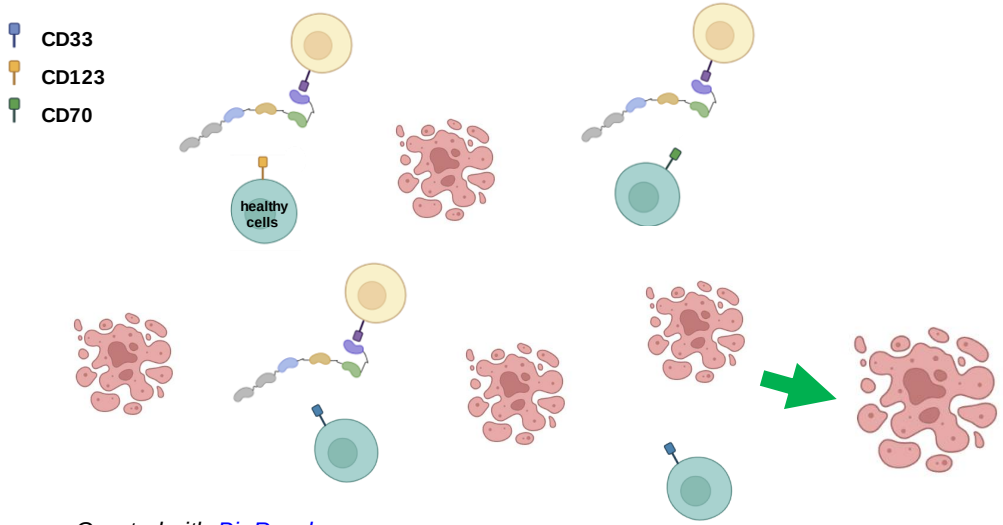

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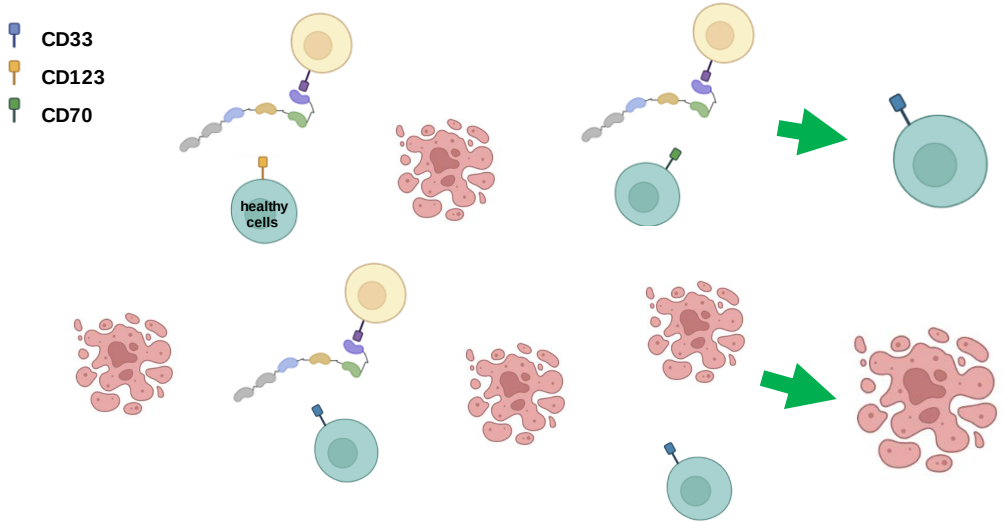

MP0533 should preserve healthy cells

→ **Therapeutic Window**

MP0533 has the potential to kill all AML cells despite Ag heterogeneity

→ **Long term disease control**

MP0533: a Unique DARPin Solution for AML Patients

- Ensures **long term control of the disease** by eliminating LSCs
- **Controls tumor heterogeneity** by targeting multiple Ag
- **Increases the therapeutic window**: optimal dose levels for efficacy
  - Limited killing of healthy HSCs
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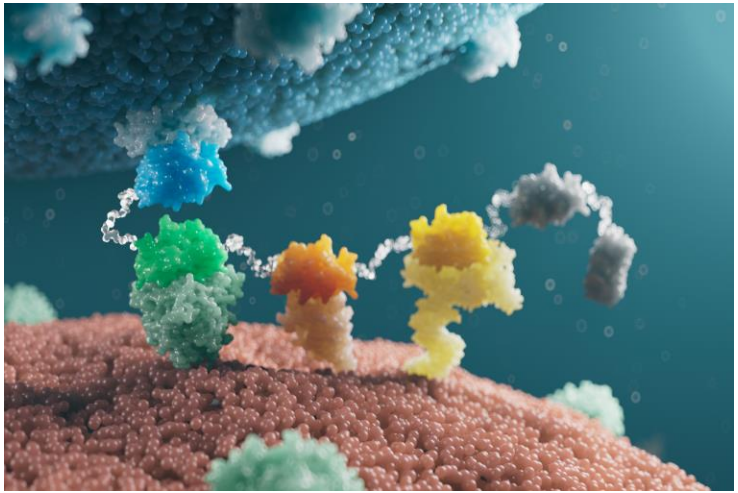


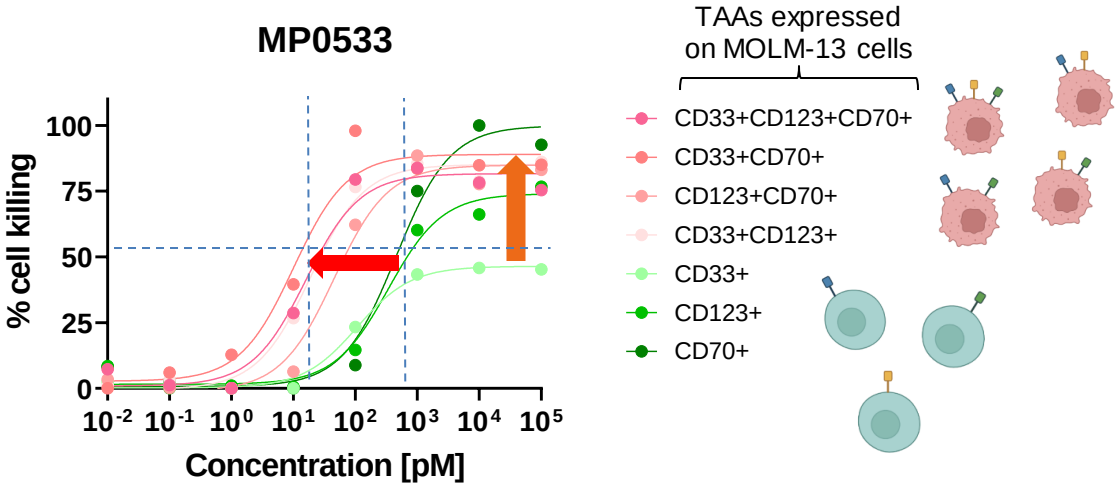
MP0533 Induces Specific Killing of AML Cells Expressing 2 or 3 TAAs

MOLM-13 cells WT
or KO for CD70, CD33 and/or CD123
+ Healthy donor T cells (E:T = 5:1)

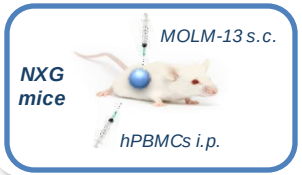
MP0533 or controls

48 hours

Tumor cell killing
T cell activation



MP0533 Shows *in vivo* anti-Tumor Efficacy without Systemic Toxicity



HuPBMCs — Day -2

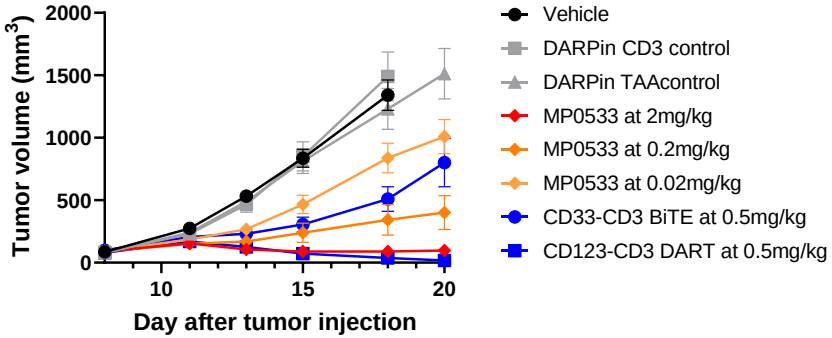
MOLM-13 s.c. — Day 0

Treatment Start — Day 8

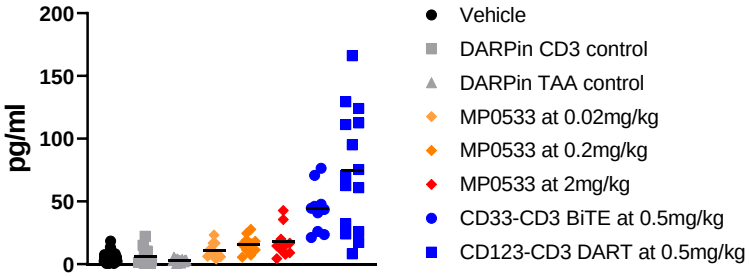
MP0533 3 times per week for 2 weeks (6 injections)

CD33-BiTE or CD123-DART daily for 2 weeks (14 injections)

MOLM-13 tumor growth



TNFα in serum



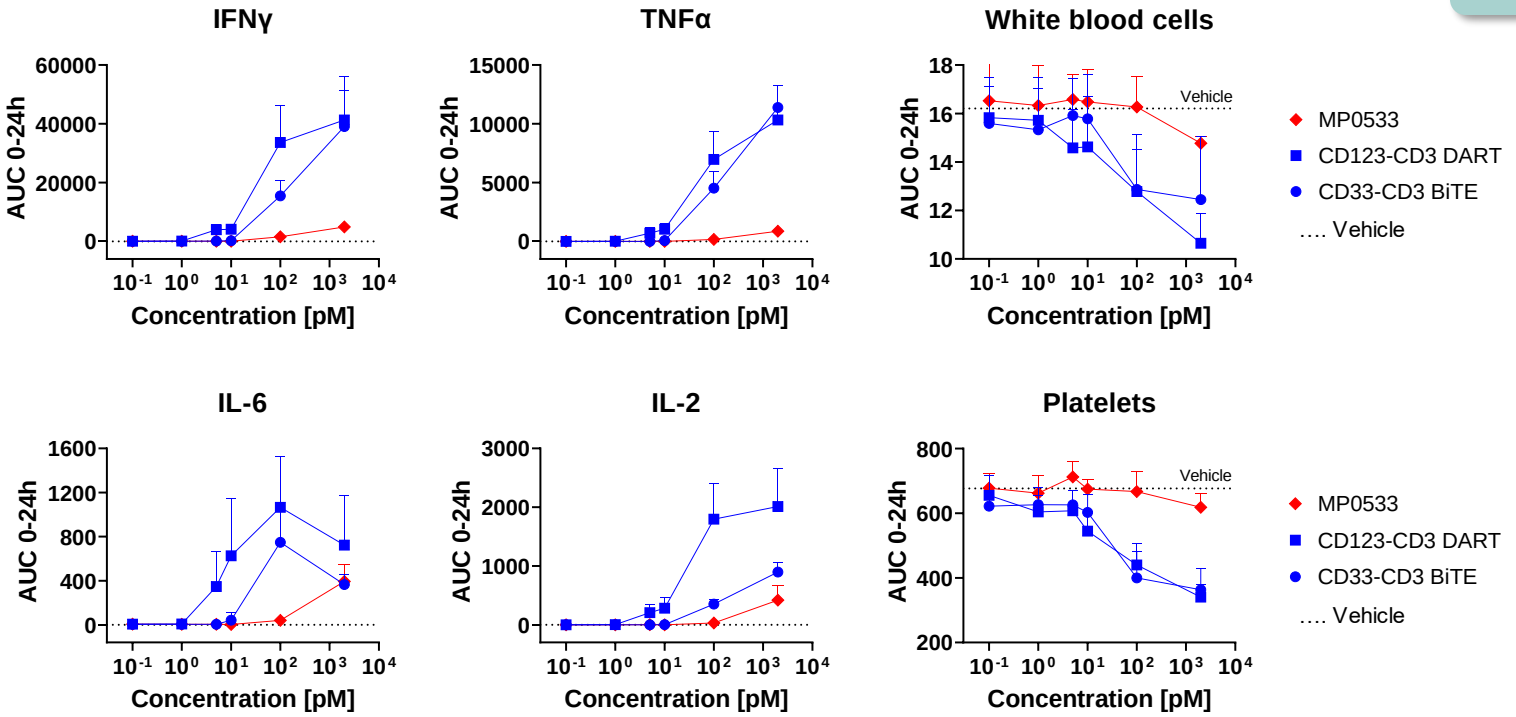
Efficacy

Safety

MP0533 Demonstrates Reduced Cytokine Release and Hemotoxicity

As compared to CD123-CD3 DART and CD33-CD3 BiTE

Safety

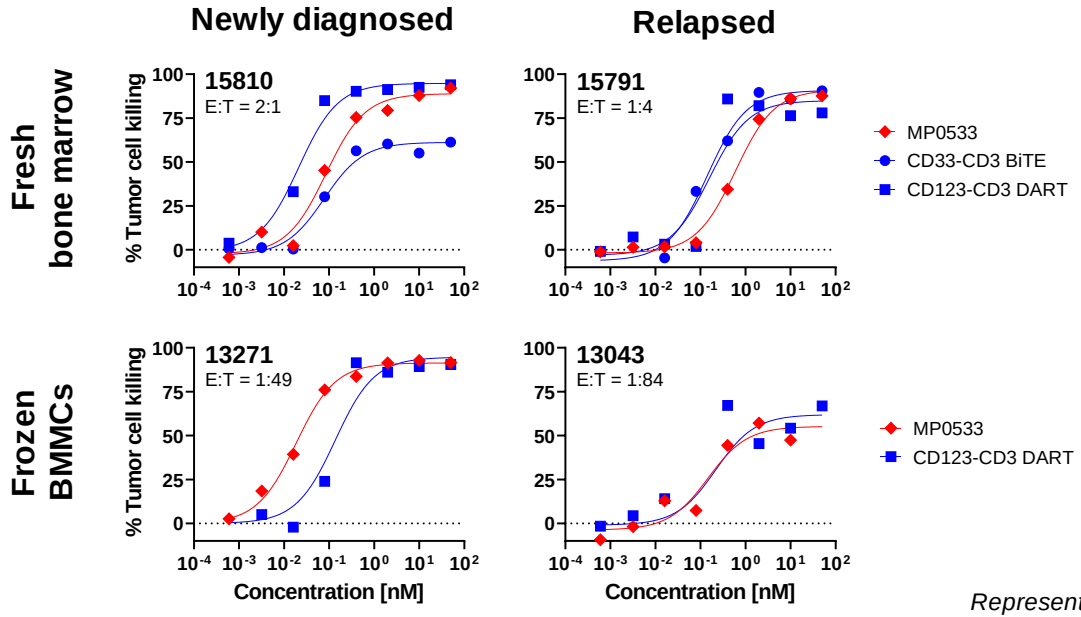


MP0533 Induces AML Killing by Patients' Own Intra-tumoral T Cells

Despite lower frequency and expected lower quality of T cells

Efficacy

Primary AML samples (no addition of healthy T cells) → *MP0533 or controls*, 5 days → Tumor cell killing



Representative of 10 patients

MP0533 Shows Preferential Killing of CD34+ LSCs over HSC

Larger therapeutic window as compared to CD123-CD3 DART and CD33-CD3 BiTE

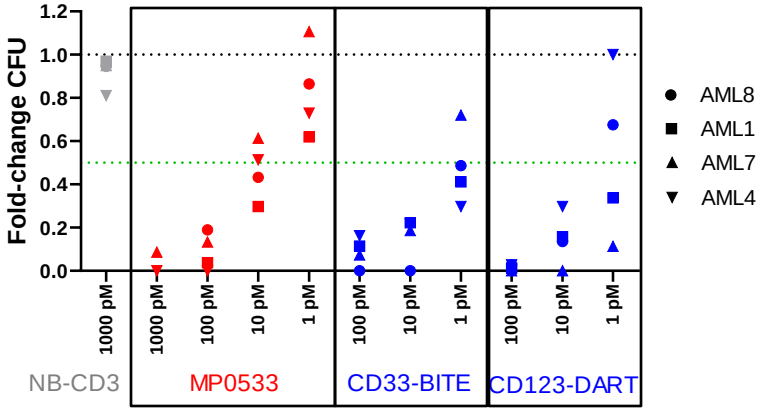
Sorted CD34+ LSC or HSC
+ Healthy donor T cells (E:T = 1:1)

MP0533 or controls

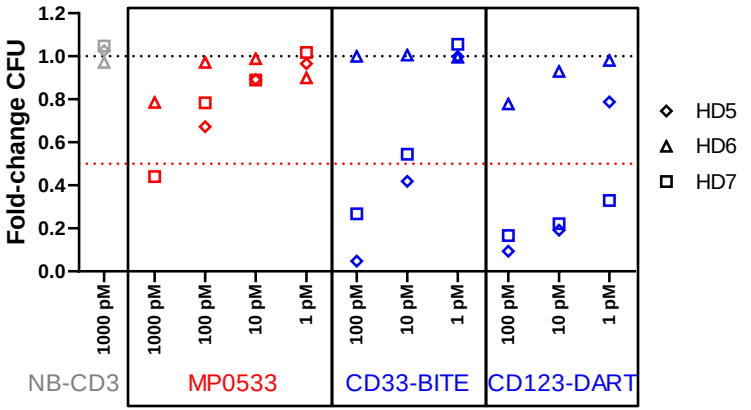
14 days colony forming assay

Counting of Colony Forming Units (CFU)

Allogeneic killing of **AML CD34+ LSC**



Allogeneic killing of **healthy donor CD34+ HSC**



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*NB = Non-Binding to TAAs

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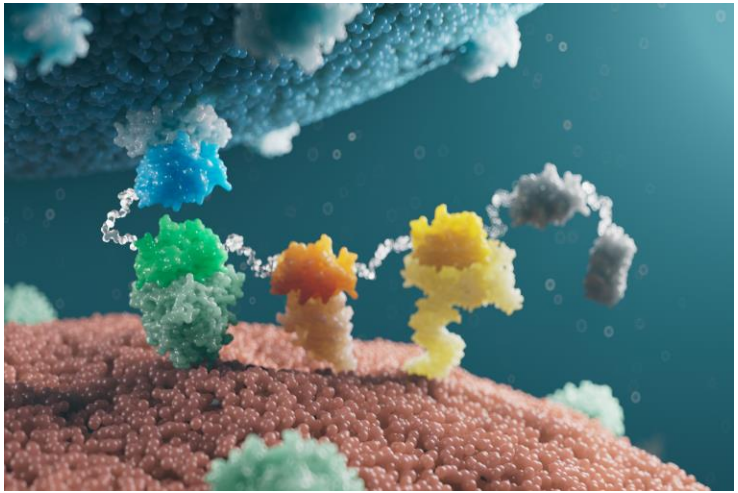

Phase 1, open-label, multicenter dose-escalation study in patients with relapsed/refractory AML and higher-risk MDS- **Opening this week**

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Daniel Steiner
Amelie Croset
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Kenneth Crook
Keith Dawson
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