CD47 pruning is only observed on RBCs and combination therapy.

Liu et al. (1) established that red blood cell (RBC) phagocytosis is protective for RBCs in the context of continued anti-CD47 antibody therapy.

Methods

- CD47 receptor occupancy analysis was performed on patient peripheral blood and bone marrow samples from NCT02216409 (solid tumor) and NCT02678338 (AML) trials.
- Flow cytometry analysis for CD47 expression and SF9 binding was conducted with anti-IgG4 and anti-CD45, and Sytox green® blue viability dye. Red blood cells (RBCs) were defined as CD45 negative and Sytox® blue negative events and white blood cells (WBCs) as CD45 positive Sytox® blue negative events.
- Mouse strains for non-clinical studies: C57BL/6J, FVB, B6.129-Foxp3 tm1Flv (Flt3 ligand-defective mutant, Taconic), FVB.tg(CD45.1)F1 (FOG, B6.129-Foxp3 tm1Flv*2, Taconic), FVB.tg(CD45.2)F1 (FOX, B6.129-Foxp3 tm1Flv*2, Taconic).

Results

- Anti-CD47 antibody-mediated pruning is independent of neutrophils, macrophages, T, B, NK, and C cells complement.
- CD47 expression and SF9 binding by flow cytometry.
- CD47 pruning (loss) was only observed on RBCs and combination therapy.
- Bone marrow from patients in the Phase I trial for hematologic malignancies (NCT02678338) was assayed for CD47 expression and SF9 binding by flow cytometry.
- AML blasts are defined as CD45 versus SSC profile and RBCs as CD45-

References


Conclusions

- SF9 pruning dose is sufficient to induce CD47 pruning on RBCs and is maintained over the course of treatment.
- CD47 mediated pruning is specific to RBCs and is not detected on WBCs or acute myeloid leukemia blasts.
- Anti-CD47 antibody-induced RBC-specific CD47 pruning is protective for RBCs over the course of treatment.
- To our knowledge, anti-CD47 antibody-mediated pruning represents a novel RBC antigen depletion phenomenon that is independent of known RBC regulatory compartments, including the spleen, liver (organ resection data in mice not shown), major cellular effector cells, complement, and is FC-independent.
- Concerns for potential anti-CD47 antibody mediated effects, i.e. hemolysis/hemoglobinization, decrease significantly given these new findings.