

Enhanced Safety Profile of IMC-002, an Affinity-Optimized Anti-CD47 Antibody: Preclinical and Phase 1a/1b Findings

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BACKGROUND

- IMC-002 is a fully human anti-CD47 IgG4 mAb with enhanced tumor selectivity and reduced hematologic toxicity. Preclinical studies demonstrated absence of *in vitro* hemagglutination and no hematologic toxicity in monkeys at doses up to 100 mg/kg.
- Here, we present updated binding site modeling results, as well as safety and soluble biomarker findings from Phase 1a/1b study (NCT05276310).

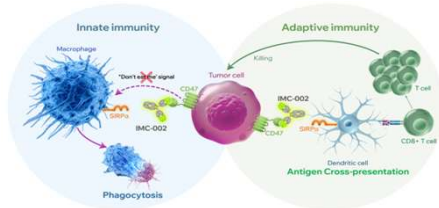


Figure 1. Mechanism of Action of IMC-002

METHODS

In vitro Study

- In vitro* binding selectivity:** CD47⁺ MDA-MB-231 tumor cells co-cultured with human erythrocytes (RBC: tumor cell ratio = 20:1).
- In vitro* hemagglutination:** human RBCs incubated with IMC-002 or Hu5F9-G4 overnight (37°C).
- O-deglycosylation:** RBCs treated with O-glycosidase and three exo-glycosidases to remove O-linked oligosaccharides from glycoproteins.
- Epitope mapping:** Linear and CLIPS-constrained peptide screening
- In silico* docking:** AlphaFold3 and LightDock simulations
- O-glycosylation prediction:** O-GlcNAc Database v2.0 (Choi J et al., AACR 2025; Abstract #4789).

Phase 1a/1b Study

- Primary Objective:** Safety
- Secondary Objectives:** PK, efficacy, and biomarker

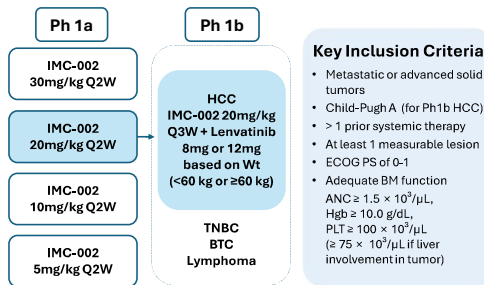


Figure 2. Study Design

- Treatment:** Up to 2 years, until PD or unacceptable toxicity.
- Tumor Assessment:** Every 6 weeks (RECIST 1.1 & iRECIST).
- Safety Assessment:** CTCAE v.5.0.
- Biomarker Assessment:** Serum proteomics using SomaScan.

Key Inclusion Criteria

- Metastatic or advanced solid tumors
- Child-Pugh A (for Ph1b HCC)
- > 1 prior systemic therapy
- At least 1 measurable lesion
- ECOG PS of 0-1
- Adequate BM function ANC ≥ 1.5 × 10⁷/μL, Hgb ≥ 10.0 g/dL, PLT ≥ 100 × 10³/μL (≥ 75 × 10³/μL if liver involvement in tumor)

Next-Generation CD47 Blockade

IMC-002 ± Lenvatinib: favorable safety and durable tolerability

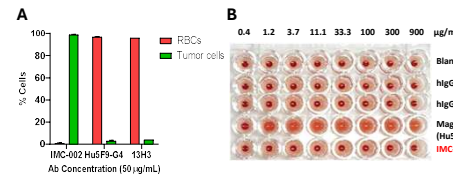
- Noble epitope recognition beyond 1st-generation anti-CD47
- Well tolerated: No neutropenia or thrombocytopenia, transient anemia
- Sustained clinical dosing feasible for up to 22 months
- Proteomic profiling identified candidate biomarkers

RESULTS

Tumor Selectivity and Hemagglutination

- IMC-002 showed high selectivity for CD47⁺ tumor cells with minimal off-target binding to RBCs.
- No hemagglutination observed at concentrations up to 900 μg/mL.

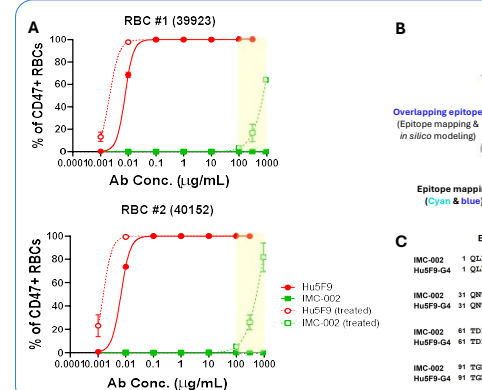
Figure 3. (A) *In vitro* tumor selectivity. (B) Hemagglutination assay.



Epitope Characterization and Structure

- IMC-002 binding to RBCs increased following enzymatic O-deglycosylation.
- Peptide-based epitope mapping and *in silico* modeling provided complementary insights into epitope characterization.
- Unlike Hu5F9-G4, IMC-002 did not induce hemagglutination, likely due to distinct epitope recognition influenced by O-glycosylation.

Figure 4. (A) Effect of O-deglycosylation on RBC binding. (B) Epitope characterization using peptide mapping and *in silico* modeling (O-glycans as sticks). (C) Epitope regions of IMC-002 and Hu5F9-G4. (D) Superimposed Fab structures of IMC-002 and Hu5F9-G4 (PDB 5IWL).



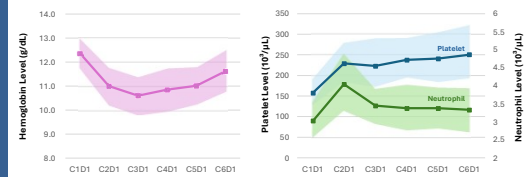
Safety Results in Ph1a and Ph1b

- From May 2022, 3 patients were enrolled in each dose level (1-4) of Ph1a with no DLT observed, and 13 patients were enrolled and treated with IMC-002 plus Lenvatinib in Ph1b.
- Most TRAEs were grade 1-2 (94%), with 92% occurring during cycle 1.
- No thrombocytopenia, neutropenia, or infection.
- Anemia and hemolytic anemia were mostly resolved following cycle 1.

Table 1. Treatment related AEs with IMC-002

Preferred Term	Ph1a				Ph1b		Total (n=25)
	5 mpk (n=3)	10 mpk (n=3)	20 mpk (n=3)	30 mpk (n=3)	20 mpk (n=13)		
Hematologic							
Anemia	-	-	-	1	2	3 (12%)	
Hemolytic anemia	-	-	2	2	-	4 (16%)	
Neutropenia	-	-	-	-	0	0 (0%)	
Thrombocytopenia	-	-	-	-	0	0 (0%)	
Non-hematologic, ≥ 2 patients							
Fatigue	-	-	-	1	1	2 (8%)	
Headache	1	1	-	-	1	3 (12%)	
Myalgia	-	-	2	-	-	2 (8%)	
Nausea	1	-	1	-	-	2 (8%)	
Pyrexia	-	-	-	1	1	2 (8%)	
Rash	2	3	2	2	9	18 (72%)	
Vitreous floaters	3	3	-	2	5	13 (52%)	

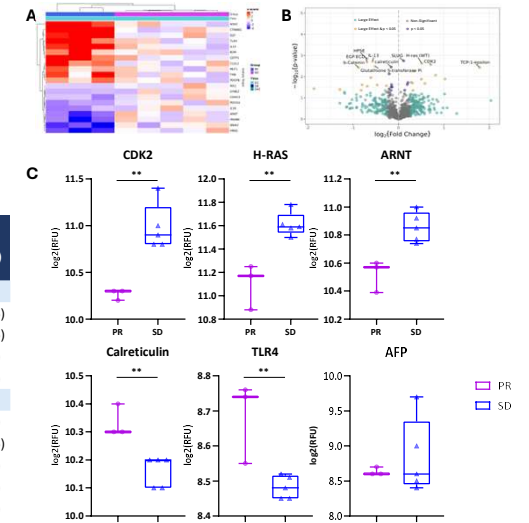
Figure 5. Hematologic Parameters: Mean ± 95% CI Over Time



Biomarker analysis in Ph1b

- Baseline proteomic profiling by SomaScan revealed differential expression of multiple analytes distinguishing PR from SD groups.

Figure 6. (A) Heatmap and (B) volcano plot depicting the top analytes identified by differential expression analysis. (C) Univariate analysis of CDK2, H-RAS, ARNT, Calreticulin, TLR4, and AFP between the two groups. t-test (**p<0.01)



CONCLUSIONS

- The IMC-002 epitope and an adjacent O-linked glycosylation site were identified by peptide mapping and *in silico* modeling, while *in vitro* experiments confirmed increased IMC-002 binding following enzymatic O-glycan removal from RBCs.
- IMC-002 exhibited a highly favorable safety profile, with minimal hematologic toxicity and no infectious complications.
- These preclinical and translational findings provide strong rationale for advancing IMC-002 into clinical development at the recommended 20 mg/kg Q3W dosing regimen.
- Clinical efficacy and biomarker exploration using SomaScan identified candidate biomarkers of IMC-002 plus Lenvatinib responsiveness, highlighting differences between PR and SD groups.

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Conflict of Interest

Jin Seok Ahn, MD, PhD, ajis@skku.edu Consulting for ImmuneOncia Therapeutics.