Topic: 29. Enzymopathies, membranopathies and other red blood cell disorders

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GAMGERTAMIG (OM336), A NOVEL B CELL MATURATION ANTIGEN (BCMA) X CD3 T CELL ENGAGER ANTIBODY, AMELIORATES DISEASE IN PATIENTS WITH WARM OR COLD AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA)

Type: Poster Presentation

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Background

Autoimmune hemolytic anemia (AIHA), including warm (wAIHA) and cold subtypes (cold agglutinin disease [CAD]), is an autoantibody driven disease with high unmet need. Current therapies include immunosuppressive and/or cytotoxic drugs, often associated with adverse effects and incomplete or non-durable efficacy. Long-lived plasma cells are critical producers of autoantibodies in AIHA but are not specifically targeted by current therapies. Gamgertamig (OM336) is an investigational, humanized, T cell engager (TCE) antibody targeting B cell maturation antigen (BCMA), leading to potent depletion of plasma and memory B cells, with the goal of “resetting” the immune system. >60 patients with highly active autoimmune diseases have received gagmertamig to date. Prior compassionate use of gamgertamig in patients with wAIHA has demonstrated compelling results [Zhang et al, NEJM, 2025].

Aims

To report the initial experience for gamgertamig in patients with AIHA in a clinical trial setting, including the first report of a patient with CAD treated with a BCMA-targeting TCE.

Methods

NCT07083960 is an open-label, Phase 1b, multiple ascending dose, multinational study to assess the safety and tolerability of gamgertamig in adults with active autoimmune cytopenias (e.g., ITP, wAIHA, CAD or mixed forms). Eligible patients receive gamgertamig as a fractionated dose for a total of up to four subcutaneous injections. Three patients with AIHA have been enrolled, including one patient with CAD and two patients with wAIHA (Table 1).

Table 1. Baseline Demographics

Patient #	Diagnosis	Age, years	Sex	Prior medications for AIHA	Medications for AIHA at enrolment	Baseline Hb (g/dL)	Gamgertamig regimen
1	CAD (PMHx of RA & CLL)	76	F	Zanubrutinib (CLL), Rituximab, Darbepoietin, Adalimumab (RA), Methotrexate (RA)	Zanubrutinib (CLL)	8.6	High dose
2	wAIHA	44	F	Prednisolone, Rituximab, Mycophenolate, Povetacicept	Prednisolone, Folic Acid	6.8	Mid dose
3	wAIHA	71	M	Prednisolone, Rituximab, Mycophenolate	Prednisolone, Mycophenolate	9.9	High dose

Results

Administration of gamgertamig has been completed in two patients. Gamgertamig was well-tolerated, with no cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), infections, or serious adverse events.

At baseline for the patient with CAD, hemoglobin (Hb) was 8.6 g/dL which continued to decline, requiring one unit of packed red cells on Day 12 which resulted in a temporary improvement in Hb (9.2 g/dL on Day 15). After completion of gamgertamig, Hb improved to 10.6 g/dL on Day 81 with associated declines in lactate dehydrogenase (LDH), indirect bilirubin and increase in haptoglobin.

In the patient with AIHA, the Hb at baseline was 6.8 g/dL which increased to 8.5 g/dL by Day 15. LDH and reticulocytes were both significantly reduced by Day 15.

Preliminary PK were consistent with data from other gamgertamig trials. The patients will continue to be followed to Week 52 to assess ongoing clinical response.

Summary/Conclusion

This is the first clinical report of gamgertamig in patients with AIHA in a clinical trial setting. Preliminary

efficacy data suggest improvements in anemia and biomarkers of hemolysis following a short course of gamgertamig; short-term safety and PK were favorable. These data warrant additional clinical investigation, with longer-term follow-up to assess the durability of response.

Keywords: B cell depletion, AIHA (see autoimmune hemolytic anemia), Monoclonal antibody, Clinical trial