Effects of gamgertamig (OM336), a B cell maturation antigen (BCMA) x CD3 T cell engager, in a patient with active antiphospholipid antibody syndrome and concurrent autoimmune thrombocytopenia

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Background

- Antiphospholipid syndrome (APS) is a rare autoimmune disease with high unmet need. Standard of care is chronic anticoagulation; there are no approved disease-modifying therapies.
- APS may occur with concurrent autoimmune cytopenias (AICs) such as immune thrombocytopenia (ITP), complicating medical management: thrombocytopenia limits the safe use of anticoagulation, while thrombopoietin receptor agonists may exacerbate thrombotic risks.
- Gamgertamig (OM336) is an investigational, humanized, bispecific, T cell engager (TCE) antibody targeting B cell maturation antigen (BCMA) and CD3, being developed for various autoantibody-driven diseases (***Figure 1***).
- Gamgertamig is designed to mediate potent depletion of both autoantibody-secreting plasma cells and the memory B cells which replenish them, with the goal of "resetting" the immune system.
- Globally, over 170 patients have received gamgertamig in clinical trials, including >70 with highly active autoimmune diseases.

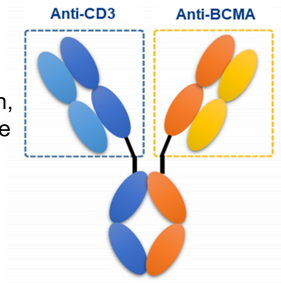

Figure 1. OM336 schematic.
Bispecific 1+1 TCE with IgG4 backbone.

Methods

- NCT07083960 is an open-label, multinational, Ph1b study to assess the use of gamgertamig in AICs: ITP, autoimmune hemolytic anemia, mixed forms, or APS with concurrent AIC (***Figure 2***).
- Eligible patients with AICs receive gamgertamig as a fractionated dose, via a maximum of 4 once-weekly subcutaneous injections.
- No additional gamgertamig is administered after Week 3.

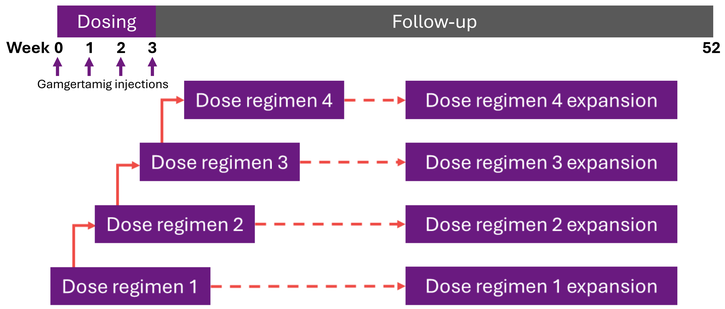

Figure 2. Study design for Ph1b trial NCT07083960.
Participants receive gamgertamig via subcutaneous injections (purple arrows) at the start of the study and are followed up through Week 52.

- A 62-year-old male with APS and concurrent ITP was enrolled into the study; he was receiving prednisolone 7.5 mg QD for ITP, but no chronic anticoagulation given his thrombocytopenia. At study Baseline, platelets were 35x10^9/L.

Methods (continued)

- He was diagnosed with APS in 2017 and fulfilled 2023 ACR/EULAR criteria with history of acute superior mesenteric vein thrombosis and repeat positivity for both anticardiolipin antibody and anti–β2-glycoprotein I IgG.
- Prior therapies for ITP included IVIg, steroids, TPO-RA and rituximab; the patient had previously received warfarin for their APS until 2019 when it was discontinued due to worsening thrombocytopenia.
- The patient received 4 subcutaneous injections of gamgertamig (Days 1, 8, 15 and 22).

Results

- After the first injection, his platelet count rose to 134x10^9/L by Day 8 (***Figure 3***). Platelet counts were in normal range Day 29.
- All background therapies for ITP were discontinued after platelet response, and no rescue therapies were given. Platelet count normalization was durable and ongoing as of latest follow-up at Week 24.
- Anticoagulation for APS was initiated after platelet counts had normalized.

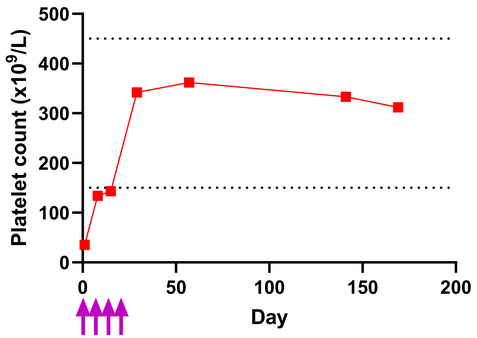

Figure 3. Efficacy over time.
Platelet counts were measured prior to gamgertamig injections (purple arrows). Dotted lines denote normal range for platelets (150-450x10^9/L).

- Consistent with gamgertamig's mechanism of action design, circulating CD19+ B cells declined rapidly to below detectable levels by Day 29 (***Figure 4***). Peripheral CD19+ B cells re-emerged at Week 24 without relapse of disease.

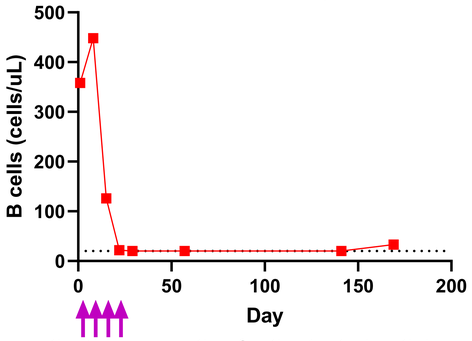

Figure 4. B cell counts over time.
Peripheral CD19+ B cell counts were measured prior to administration of gamgertamig (purple arrows). Dotted line denotes lower level of quantification (20 cells/uL).

- The patient was negative for the tested antiphospholipid antibodies (aPL) at enrollment. He had detectable levels of ANA and anti-Smith/RNP autoantibodies, which decreased significantly after treatment (***Figure 5***).
- The patient will be followed to Week 52 to assess durability of response.

Results (continued)

- Preliminary PK (not shown) was consistent with that of other gamgertamig trials. The patient did not have any cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), infections, thrombosis, or serious adverse events.

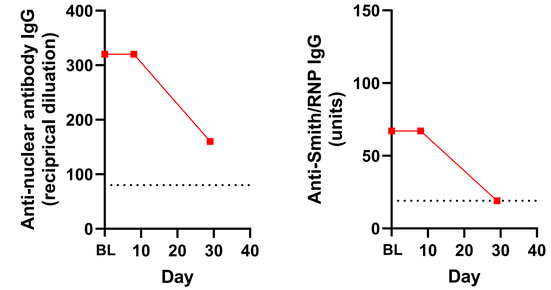

Figure 5. Autoantibody levels over time.
Dotted line denotes threshold for autoantibody positivity; BL, study baseline assessment.

- Other patients (n=4) in the trial who were positive for aPL at enrollment demonstrated reductions in titers following treatment with gamgertamig (***Figure 6***).

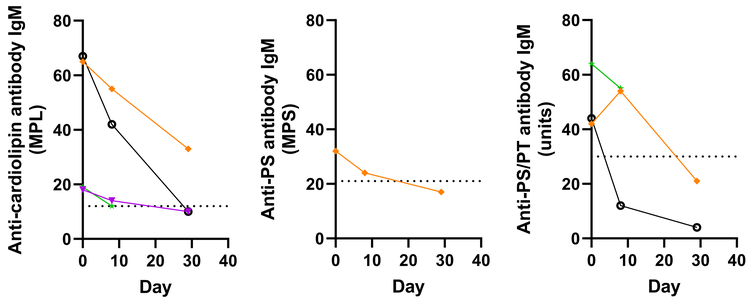

Figure 6. aPL titers over time in other patients who were aPL-positive at Baseline.
Dotted lines denote threshold for autoantibody positivity; aPL antibodies tested were: anti-β2 glycoprotein 1 IgG & IgM, anti-cardiolipin IgG & IgM, lupus anticoagulant, anti-PT IgG & IgM, anti-PS IgG & IgM, anti-PS/PT IgG & IgM (negative if not shown). PS, phosphatidylserine; PS/PT, phosphatidylserine/prothrombin complex.

Conclusions

- This is the first report of a patient with concurrent APS and ITP treated with a BCMA-targeted TCE.
- The results demonstrate platelet normalization and discontinuation of ITP therapies after a short course of gamgertamig.
- Ongoing durability of response off therapies, even after the re-emergence of circulating CD19+ B cells, supports "immune reset".
- NCT07083960 is ongoing and actively enrolling patients.
- The rapid clinical response, favorable short-term safety data, and consistent PK warrant additional clinical investigation.

Acknowledgements

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Disclosures

Charlie Zhou and Neelufar Mozaffarian are employees of Ouro Medicines.

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