Immune-Related AEs After Low-Dose, Finite-Duration Budigalimab ± Trosunilimab in People With HIV

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Katharine Bar,[1] Manal Abunimeh,[2] Claudia Martorell,[3] Heide Betman,[2] Ana Gabriela Pires dos Santos,[2] Shawn Hassler,[4] Theo Hodge,[5] Simiso Mandisa Sokhela,[7] Alireza Farabi,[7] Kimmie Pringle,[2] Andrew Topp,[2] John Marcinak,[2] **Sharon R. Lewin[8]**

[1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [2]AbbVie Inc., North Chicago, IL, USA; [3]The Research Institute, Springfield, MA, USA; [4]Optimus Medical Group, San Francisco, USA; [5]Washington Health Institute, Washington DC, USA ; [6]Ezintsha, University of the Witwatersrand, Johannesburg, South Africa; [7]Division of Infectious Diseases (AF), University Medical Center of Southern Nevada, Las Vegas, NV, USA; [8]Department of Infectious Diseases, The University of Melbourne at the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia

BACKGROUND

- Budigalimab, a PD-1 inhibitor and trosunilimab, anti-α4β7 integrin antibody, were studied as a potential strategy for immune-mediated viral control in people with HIV (PWH)
- In oncology indications, anti-PD-1 antibodies such as budigalimab (250-500 mg) are typically associated with immune-related adverse events (irAEs) in ~40% of patients (5% grade ≥ 3)[1]
- However, the safety profile of budigalimab, used in much lower doses (compared to doses in oncology) for a finite duration in PWH, is unknown
- Here we report irAEs in PWH who received 10 mg budigalimab intravenous ± trosunilimab in the global phase 2 trial with an analytical treatment interruption (ATI)

METHODS

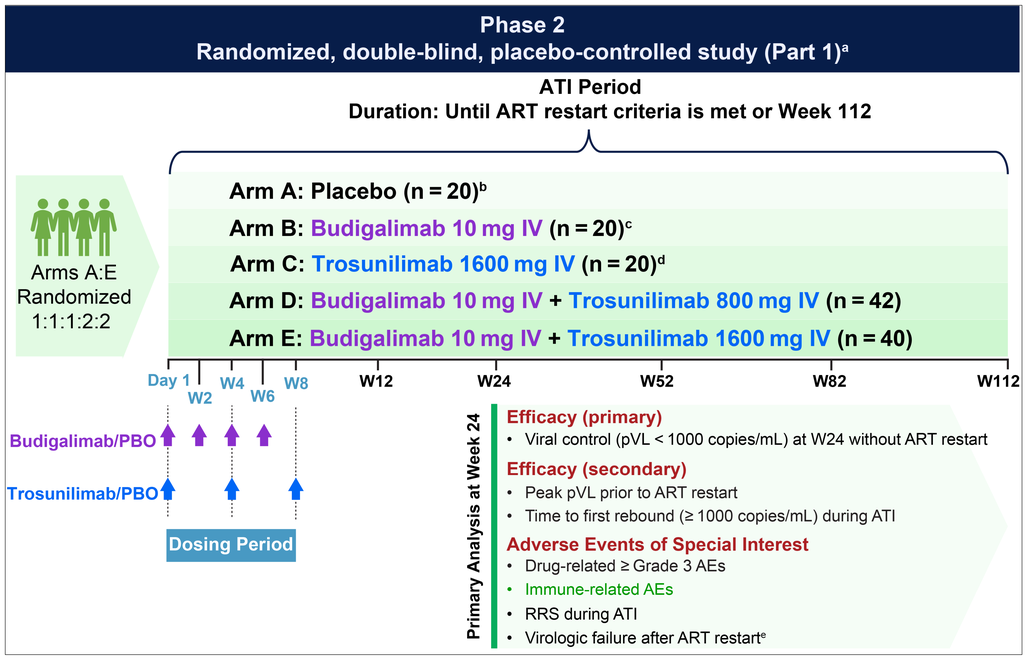
Design (Part 1 of the phase 2 study)

- Included 142 (≥ 18 years old) PWH on stable antiretroviral therapy (ART for ≥ 12 months before screening), randomized to one of 4 active treatment arms or placebo (**Figure 1**)

Adverse Event of Special Interest (24-week analysis)

- All participants in the study were assessed for the development of irAEs (suspected or confirmed)
- Diagnosis of an irAE was based on the investigator's judgment, considering clinical findings, complementary tests, specialist evaluation, as needed, and oncology irAE guidelines

Figure 1. Study Design



[a]This figure represents Part 1 of the study; Part 2 was an open-label arm receiving budigalimab 20 mg subcutaneous and data for this arm are not available for this presentation. [b]Participants received placebo for budigalimab and placebo for trosunilimab. [c]Participants received placebo for trosunilimab. [d]Participants received placebo for budigalimab. [e]Failing to achieve confirmed (2 consecutive) pVL >20 copies/mL within 24 weeks of ART restart or confirmed pVL ≥200 copies/mL after suppression. **Abbreviations**: AE, adverse event; ART, antiretroviral therapy; ATI, analytical treatment interruption; IV, intravenous; PBO, placebo; pVL, plasma viral load; RRS, retroviral rebound syndrome; W, week.

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Rate of irAEs with short-term (up to 6 weeks) budigalimab was 8.8% in PWH, which is lower than rates seen in patients with cancer who receive higher doses and longer duration of budigalimab

RESULTS

- No discernible patterns were observed in the demographics or baseline disease characteristics of PWH who experienced irAEs

Immune-related AEs

- In total, 102 PWH received ≥ 1 dose of budigalimab
- By week 24, 9/102 (8.8%) PWH experienced an irAE (**Table 1**)
- All irAEs occurred in budigalimab-containing arms, and most were grade 1 (55.6%)
  - The events observed in this study have been previously described in patients with cancer and can be attributed to PD-1 inhibition by budigalimab

Serious irAEs

- Two of the grade 3 irAEs were serious, requiring hospitalization
  - One PWH experienced new-onset diabetes mellitus after a rapid onset of diabetic ketoacidosis (DKA) that was deemed related to budigalimab
    - DKA presented as a classic, although rare, anti-PD-1 irAE
    - Other potentially contributing factors were older age and concomitant medication
  - Another PWH experienced a serious event of inflammatory arthritis that was ongoing at the time of analysis
    - The investigator deemed this irAE as related to budigalimab, although there were confounding factors of infectious arthritis and prosthesis use

Table 1. irAEs in PWH Receiving Budigalimab Treatment[a]

MedDRA 27.1 Preferred Term	Severity	Serious Criteria (Y/N)	Day of Onset	Day Ended (length)	Budigalimab Doses Received	Other Actions Taken
Hyperthyroidism	Grade 1	N	15	29 (15 days)	2	Additional lab monitoring
Hyperthyroidism	Grade 1	N	22	36 (15 days)	2	Additional lab monitoring
Hyperthyroidism	Grade 1	N	22	57 (36 days)	3	None
Hyperthyroidism	Grade 1	N	52	113 (62 days)	4	Additional lab monitoring
Eczema	Grade 1	N	23	Ongoing	4	Topical steroid as needed
Thrombocytopenia	Grade 2	N	29	43 (15 days)	3	Additional lab monitoring
Zoster sine herpete	Grade 3	N	20	44 (25 days)	2	Pain medication
Diabetic ketoacidosis	Grade 3	Y	48	54 (7 days)	4	Hospitalized, intravenous insulin administered
Inflammatory arthritis	Grade 3	Y	48	Ongoing	2	Hospitalized, knee surgery/revision (multiple) and anti-inflammatory treatment administered

[a]No irAEs were observed in placebo (n = 20) or trosunilimab 1600 mg monotherapy arm (n = 20). **Abbreviations:** AE, adverse event; irAE, immune-related adverse event; PWH, people with HIV

CONCLUSIONS

- Incidence of budigalimab-associated irAEs was 8.8%, with grade ≥ 3 events observed in 3% of PWH
- All but 2 irAEs resolved within a reasonable span of 2 to 3 weeks
  - The rate of irAEs observed here was substantially lower than rates reported with budigalimab in oncology indications
- A participant with an irAE of diabetic ketoacidosis developed new-onset diabetes mellitus that was ongoing at the time of the analysis

PLAIN LANGUAGE SUMMARY

In this study, people with HIV temporarily stopped their HIV medicine and received two experimental antibodies. With higher doses of one of these antibodies, budigalimab, side effects of the immune system (autoimmune disease) have been well documented in patients with cancer. This study used a lower dose for a limited treatment duration. Although side effects were less frequent, a rare, serious autoimmune complication did occur.

Reference: 1) Italiano A, et al. *Cancer Immunol Immunother*. 2022;71(2):417-431.

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