Elevated soluble immune biomarkers in subjects with HBsAg loss after treatment with imdusiran and immunotherapeutic agents in the IM-PROVE I and IM-PROVE II studies

Sharie C. Ganchua[1*], Christine L Espiritu[1*], Kevin Gray[1], Deana Antoniello[1], Man-Fung Yuen[2], Grace Lai-Hung Wong[3], Kosh Agarwal[4], Leon Hooftman[5], Bethan Jones[5], Vicky Wheeler[5], Tilly Varughese[1], Karen D Sims[1], Emily P Thi[1]

[1]Arbutus Biopharma, Warminster, PA, USA, [2]The University of Hong Kong, Queen Mary Hospital, Hong Kong, China, [3]The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China, [4]King's College Hospital, London, UK, [5]Barinthus Biotherapeutics, Harwell, UK
*Contributed equally

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Arbutus BIOPHARMA Curing Chronic Hepatitis B

BACKGROUND

Functional cure of chronic hepatitis B (CHB) requires suppression of HBV replication, antigens and induction of anti-HBV immune responses. Imdusiran is an *N*-Acetylgalactosamine–conjugated, pan-genotypic small interfering RNA that blocks all HBV RNA, resulting in suppression of viral replication and all antigens.

IM-PROVE I and IM-PROVE II are Phase 2a studies assessing combination treatment of imdusiran with an immunotherapeutic in nucleos(t)ide analog (NA) treated CHB subjects.

IM-PROVE I assessed 24 weeks (W) of imdusiran lead-in followed by 12W or 24W of pegylated interferon alfa-2a (IFN) with or without additional imdusiran doses.

IM-PROVE II assessed 24W of imdusiran lead-in followed by the Barinthus Biotherapeutics immunotherapeutic VTP-300, VTP-300 + low dose anti-PD-1 antibody nivolumab, or placebo.

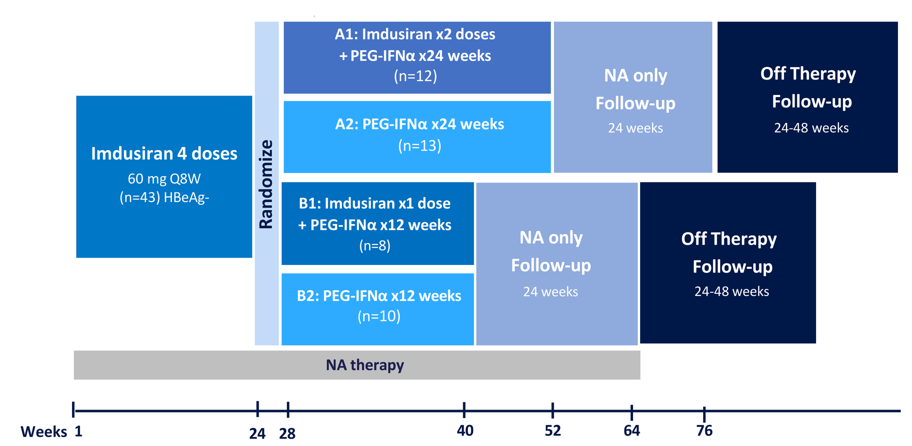
On-treatment comparison of soluble immune biomarker profiles of subjects from the IM-PROVE I and II studies and association with clinical outcomes is presented.

OBJECTIVES

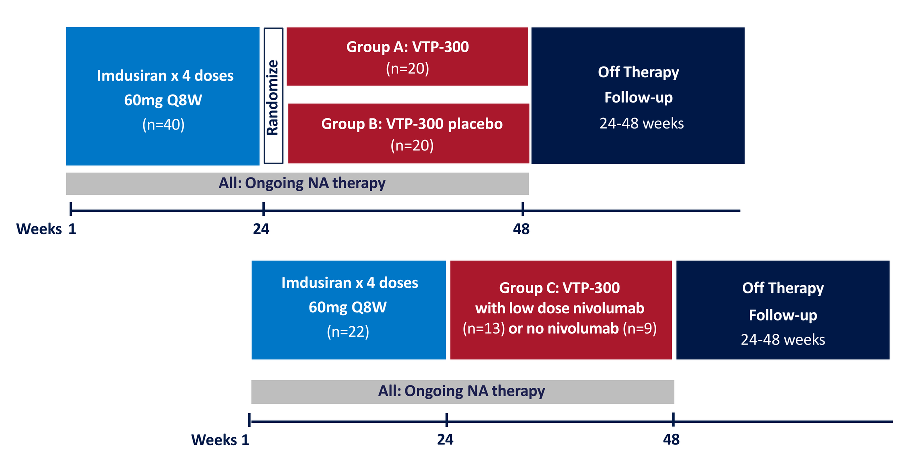
- Compare soluble immune biomarker profiles of subjects from IM-PROVE I and IM-PROVE II studies
- Assess association of immune biomarker elevations with clinical outcomes of meeting NA d/c criteria and functional cure

MATERIALS AND METHODS

IM-PROVE I (AB-729-201) Study Design



IM-PROVE II (AB-729-202) Study Design



- IM-PROVE I enrolled non-cirrhotic, HBeAg-negative, virally suppressed CHB subjects on stable NA therapy for at least 12 months
- IM-PROVE II enrolled non-cirrhotic, HBeAg-negative or positive, virally suppressed CHB subjects on stable NA therapy for at least 12 months
- Baseline characteristics for both studies were presented previously[1-4]
- Longitudinal plasma samples were collected from 43 subjects in IM-PROVE I and 62 subjects in IM-PROVE II during the 24-week imdusiran lead-in and immunomodulator treatment periods
- Soluble immune biomarkers were assessed using Luminex multiplex panels (58 analytes)

RESULTS

1. HBsAg Loss and Clinical Outcomes in IM-PROVE I and II

Table 1: IM-PROVE I

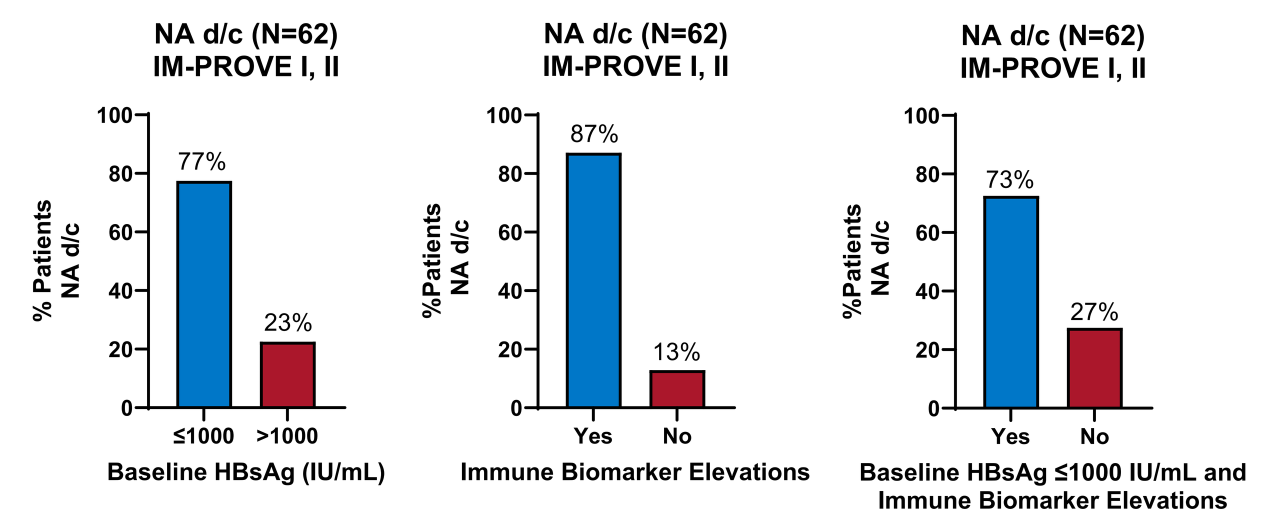
Clinical Outcomes	Cohort A1: Imdusiran x 6 doses + NA + IFN x 24W (N = 12)	Cohort A2: Imdusiran x 4 doses + NA + IFN x 24W (N = 13)	Cohort B1: Imdusiran x 5 doses + NA + IFN x 12W (N = 8)	Cohort B2: Imdusiran x 4 doses + NA + IFN x 12W (N = 10)
HBsAg Loss Baseline HBsAg ≤1000 IU/mL	7/12 (58%) 4/6 (67%)	3/13 (23%) 2/7 (29%)	2/8 (25%) 1/6 (17%)	1/10 (10%) 0/4
Met NA d/c Criteria Baseline HBsAg ≤1000 IU/mL	9/12 (75%) 6/6 (100%)	3/13 (23%) 3/7 (43%)	4/8 (50%) 4/6 (67%)	5/10 (50%) 3/4 (75%)
Functional Cure (FC) Baseline HBsAg ≤1000 IU/mL	3/12 (25%) 3/6 (50%)	2/13 (15%) 2/7 (29%)	0/8 0/6	1/10 (10%) 0/4

Table 2: IM-PROVE II

Clinical Outcomes	Group A: Imdusiran x 4 doses + NA + VTP-300 (N = 20)	Group B: Imdusiran x 4 doses + NA + Placebo (N = 20)	Group C: Imdusiran x 4 doses + NA + VTP-300 (N = 9)	Group C: Imdusiran x 4 doses + NA + VTP-300 + Nivolumab (N = 13)
HBsAg Loss Baseline HBsAg ≤1000 IU/mL	1/20 (5%) 0/12	1/20 (5%) 0/10	0/9 0/6	3/13 (23%) 3/8 (38%)
Met NA d/c Criteria Baseline HBsAg ≤1000 IU/mL	16/20 (80%) 11/12 (92%)	10/20 (50%) 7/10 (70%)	6/9 (67%) 6/6 (100%)	9/13 (69%) 8/8 (100%)
Functional Cure (FC) Baseline HBsAg ≤1000 IU/mL	0/20 0/12	0/20 0/10	0/9 0/6	2/13 (15%) 2/8 (25%)

HBsAg loss defined as HBsAg ≤LLOQ (lower limit of quantitation) at any point in study. Functional cure defined as sustained HBsAg loss and HBV DNA less than LLOQ 24 weeks off-treatment, with or without hepatitis B surface antibodies.[5]
NA discontinuation (d/c) criteria: ALT <2x ULN, HBV DNA <LLOQ, HBeAg negative, and HBsAg <100 IU/mL

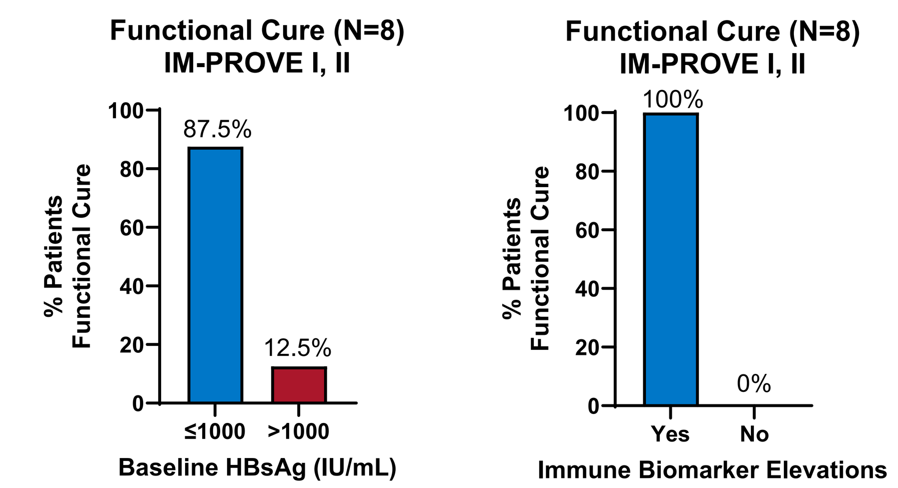
2. Majority of Patients Who Met Criteria to Discontinue NA Therapy Had Baseline HBsAg ≤1000 IU/mL and Increases in Immune Biomarkers On-Treatment



- 77% (48/62) of patients who met NA d/c criteria had HBsAg ≤1000 IU/mL at baseline and 87% (54/62) had immune biomarker elevations ≥3-fold during treatment
- 73% (45/62) of patients who met NA d/c criteria had both immune biomarker elevations ≥3-fold during treatment and HBsAg ≤1000 IU/mL at baseline
- Patients who had both immune biomarker elevations during treatment and baseline HBsAg ≤1000 IU/mL made up the majority of patients who met NA discontinuation criteria across both IM-PROVE I and IM-PROVE II studies

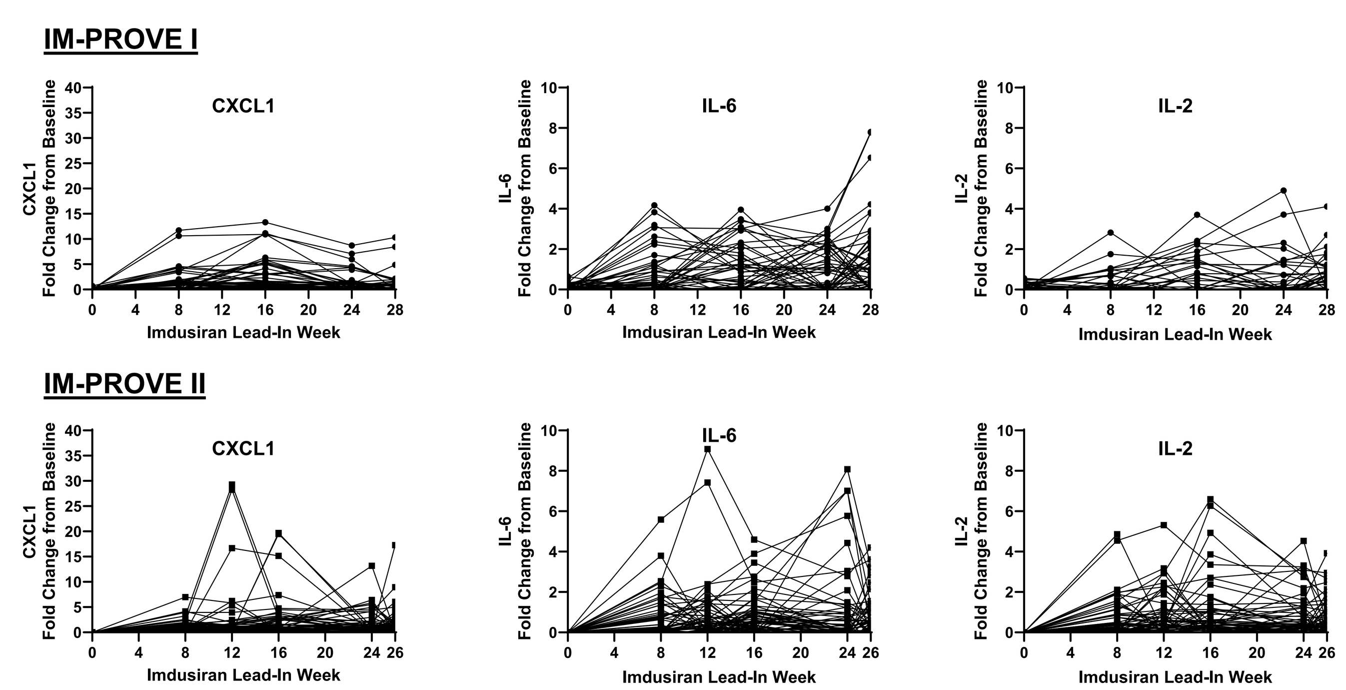
3. All Patients Who Achieved Functional Cure in IM-PROVE I and IM-PROVE II Had Increases in Immune Biomarkers On-Treatment

- All patients who achieved functional cure in IM-PROVE I and IM-PROVE II studies had immune biomarker elevations ≥3-fold during treatment



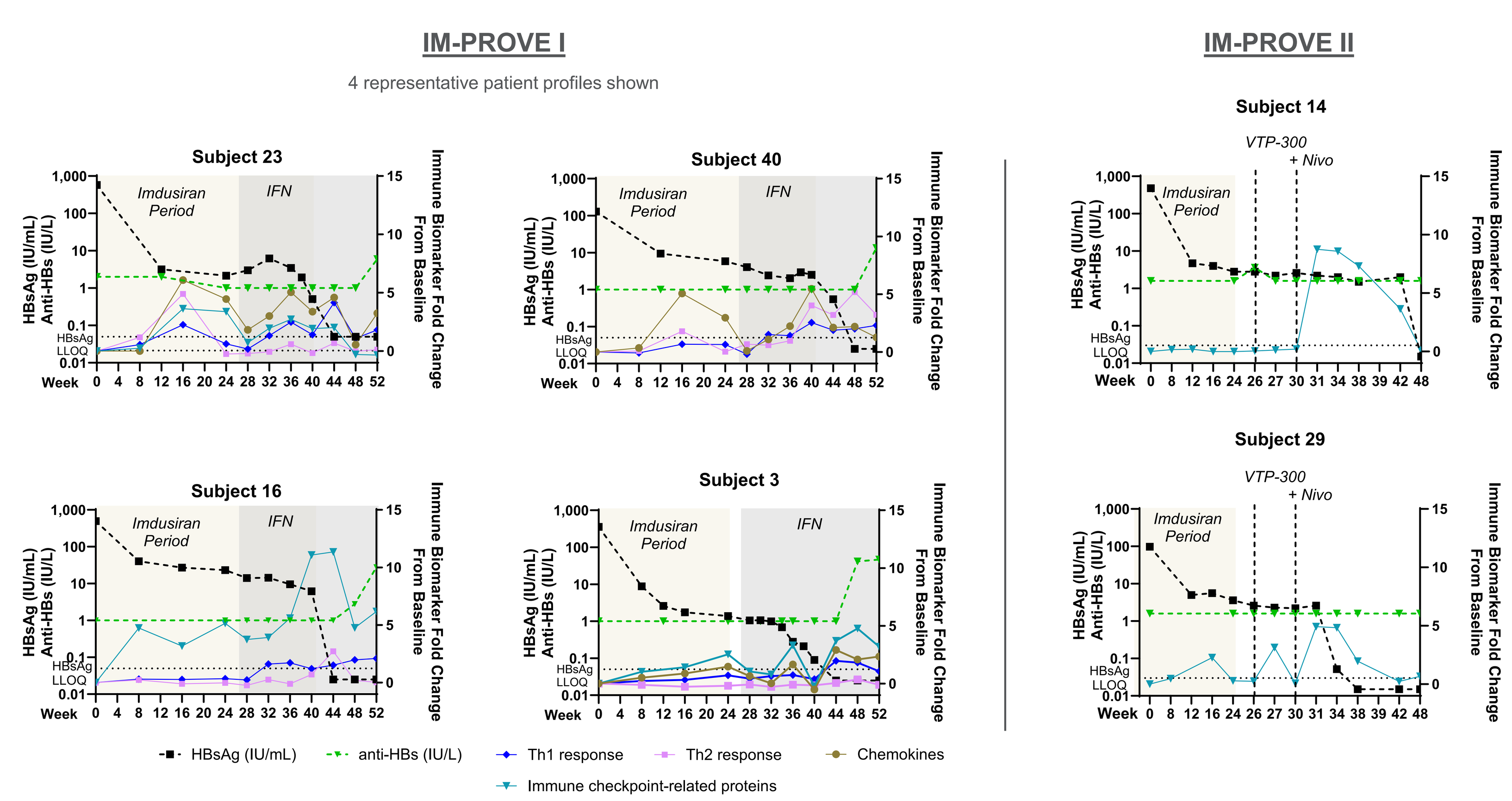
NA d/c = Nucleos(t)ide analog therapy discontinuation

4. Immune Biomarker Elevations During Imdusiran Lead-in Observed in Both IM-PROVE I and IM-PROVE II Studies



- Transient increases in soluble immune biomarkers associated with immune activation, Th1 cell-mediated response, inflammation regulation and immune checkpoint proteins were observed during imdusiran lead-in in both IM-PROVE I and IM-PROVE II studies
- Elevations in sCD80, sCD86, sGITR, sGITRL, sPD-L1, PDGF-AA, VEGF, sBTLA, sCD28, and sICOS also observed (data not shown)

5. Greater Breadth of Immune Biomarkers Elevated in Functional Cure Patients from IM-PROVE I Compared to IM-PROVE II



- Functional cure patients from IM-PROVE I had elevations in more types of immune biomarkers compared to functional cure patients from IM-PROVE II
- Peaks in immune biomarker increases occurred during imdusiran lead-in and during immunotherapy with IFN or VTP-300

CONCLUSIONS

- Majority of patients who met NA discontinuation criteria or achieved functional cure in IM-PROVE I and IM-PROVE II studies had elevations in soluble immune biomarkers during treatment
- Transient increases in soluble immune biomarkers were observed during imdusiran lead-in in both studies
- Greater breadth in the types of immune biomarkers were elevated in functional cure patients from IM-PROVE I vs. IM-PROVE II, suggesting a more profound effect of imdusiran + IFN combination treatment in modulating immune responses

REFERENCES / ACKNOWLEDGEMENTS

1. K Agarwal, *et al.* EASL Congress, Oral presentation 505, 2024
2. MF Yuen, *et al.*, EASL Congress, *Journal of Hepatology*, 2024. 80, S809-S810
3. MF Yuen, *et al.*, Poster 5036. The Liver Meeting, November 15-19, 2024
4. G LH Wong, *et al.*, Poster 5025. The Liver Meeting, November 15-19, 2024
5. MG Ghany, et al., Hepatology, 2023. 78(5), 1654-1673

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CONTACT

Emily Thi, ethi@arbutusbio.com
Sr. Director
Immunology and Biomarkers Research

Authors affiliated with Arbutus Biopharma are current or former employees and may own company stock