Further clinical outcomes in patients with moderate-to-severe chronic plaque psoriasis receiving adalimumab reference product (RP) continuously or switching between BI 695501 and adalimumab RP in the Phase III, randomized, interchangeability VOLTAIRE-X trial

Alan Menter,[1*] Dorothy McCabe,[2] Benjamin Lang,[3] Jennifer Schaible[3]

[1]Baylor Scott & White, Dallas, TX, USA; [2]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [3]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany

([*]Corresponding author email: amderm@gmail.com)

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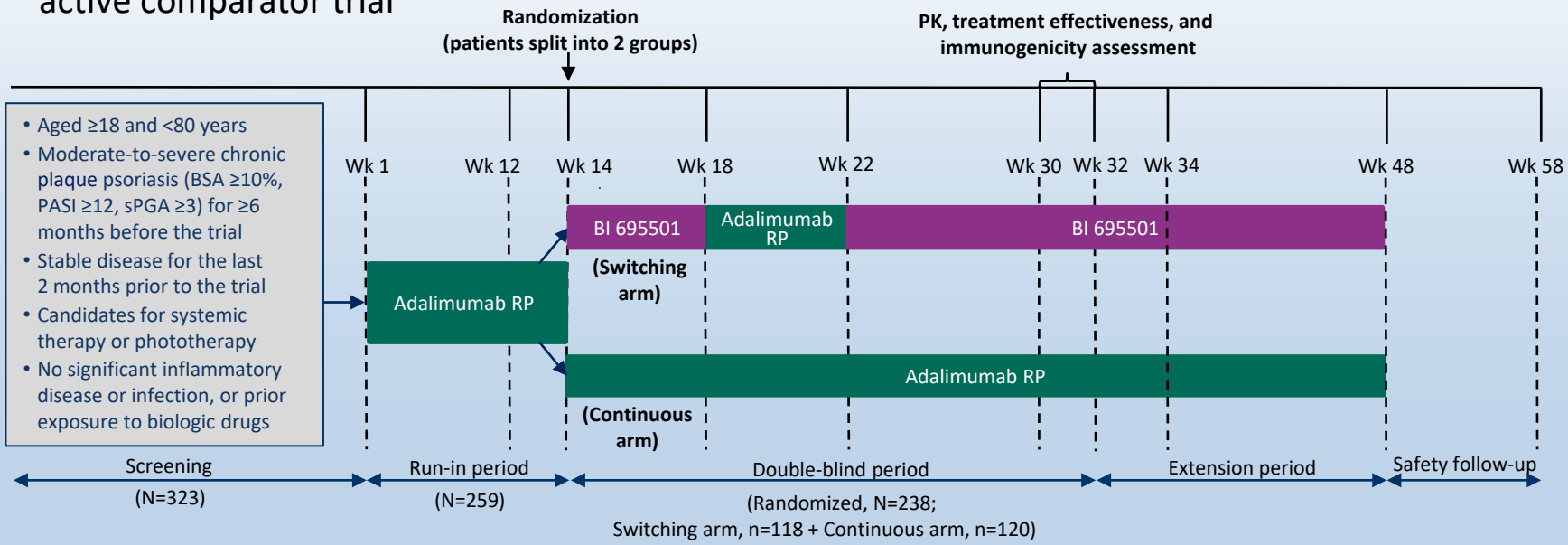
Introduction, Objectives, and Methods

- BI 695501 is similar to adalimumab RP in terms of PK in healthy subjects,[1] and demonstrated equivalent efficacy and highly similar safety and immunogenicity to adalimumab RP in patients with chronic plaque psoriasis in the VOLTAIRE-PSO study[2]
- Here, we present additional secondary and further endpoints from the VOLTAIRE-X study (NCT03210259), a trial designed to demonstrate that BI 695501 is an interchangeable biologic to adalimumab RP. Primary and secondary endpoints were presented previously[3]
- VOLTAIRE-X was a phase III, randomized, double-blind, parallel-arm, multiple-dose, active comparator trial



Objectives

- To assess PK similarity, efficacy, immunogenicity, and safety in patients with moderate-to-severe chronic plaque psoriasis receiving adalimumab RP continuously versus those who switched between BI 695501 and adalimumab RP

Primary endpoints

- **$AUC_{\tau, 30\text{-}32}$** Area under the adalimumab plasma concentration-time curve over the dosing interval Week 30 to 32
- **$C_{max, 30\text{-}32}$** Maximum observed adalimumab plasma concentration during the dosing interval Week 30 to 32

Results: Pharmacokinetics and Safety Endpoints

- Pharmacokinetic parameters were comparable across treatment arms, as shown

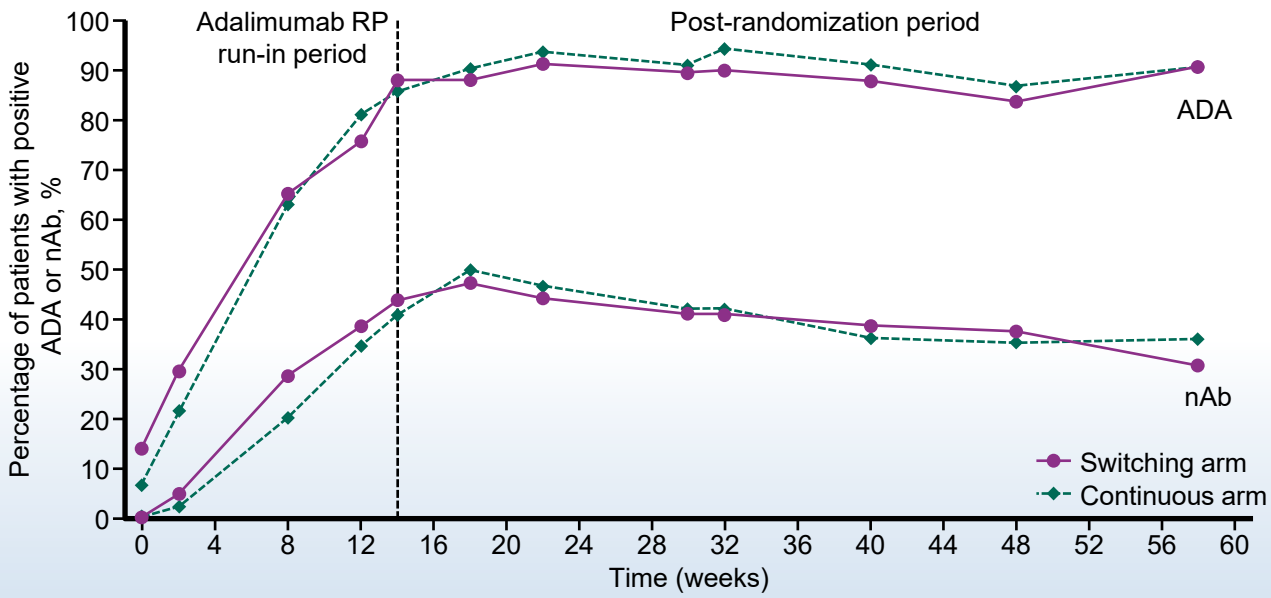
Parameter [unit]	Switching arm			Continuous arm		
	N	Mean	CV (%)	N	Mean	CV (%)
$AUC_{\tau, 12\text{-}14}$ [µg·h/mL]	99	1880	63.9	93	1880	66.0
$C_{max, 12\text{-}14}$ [µg/mL]	101	6.86	59.8	96	6.87	62.6
$C_{min, 12\text{-}14}$ [µg/mL]	100	4.58	71.3	95	4.40	72.0
$t_{max, 12\text{-}14}$[a] [h]	101	73.8	67.7, 336	96	73.4	25.6, 335
$t_{min, 12\text{-}14}$[a] [h]	100	335	67.7, 362	95	335	70.3, 383
$C_{min, 30\text{-}32}$ [µg/mL]	104	5.04	77.2	98	4.66	90.0
$t_{max, 30\text{-}32}$[a] [h]	104	72.7	66.0, 336	99	72.3	46.8, 240
$t_{min, 30\text{-}32}$[a] [h]	104	335	69.4, 359	98	335	48.3, 343

[a] t presented as median (minimum, maximum)

- Overall safety analyses were comparable across treatment arms:
  - Treatment-emergent AEs of special interest were infrequent: In the Switching arm, 1 (0.8%) patient had an event reported as an AE of special interest by the Investigator (gastroenteritis), versus no patient in the Continuous arm (post-randomization period)
  - The incidence of other safety endpoints was low and similar across treatment arms:
    - In the Switching arm, 3 (2.5%) patients experienced ≥1 injection-site reaction, 2 patients (1.7%) experienced ≥1 serious infection, and 4 patients (3.4%) experienced ≥1 hypersensitivity reaction (post-randomization period)
    - In the Continuous arm, 5 patients (4.2%) experienced ≥1 injection-site reaction, 1 patient (0.8%) experienced ≥1 serious infection, and 2 patients (1.7%) experienced ≥1 hypersensitivity reaction (post-randomization period)
    - No drug-induced liver injury was reported (post-randomization, run-in, or overall trial period)

Results (continued): Immunogenicity and Efficacy Endpoints

- Proportions of patients with positive ADAs and nABs were similar in both treatment arms throughout the run-in and post-randomization periods
- At Week 32:
  - ADA: Switching arm 90.2% vs Continuous arm 94.5%
  - nAB: Switching arm 41.1% vs Continuous arm 41.8%
- Distribution of ADA and nAB titers were similar across treatment arms
- At Week 32:
  - Median titer ADA: Switching arm 1:64 vs Continuous arm 1:128
  - Median titer nAB: Switching arm 1:2 vs Continuous arm 1:2



- The proportion of patients achieving PASI50, PASI75, PASI90, and PASI100 response increased from baseline run-in and plateaued mid-trial in both treatment arms
- A similar trend was observed for DLQI response (category 0 or 1) over time in both treatment arms
- Demonstration of sPGA response (≤1 [clear or almost clear]) increased steadily over time from baseline to Week 28 in both treatment arms, after which it plateaued

Conclusions

- To our knowledge, VOLTAIRE-X is the first trial to report outcomes that meet the US FDA's criteria for interchangeable biologic designation[4]
- The results presented support previous data designating BI695501 as an interchangeable biologic to adalimumab RP, based on similar outcomes between the Switching and Continuous treatment arms in terms of PK, immunogenicity, efficacy, and safety

References

1. Wynne C, et al. *Exp Opin Invest Drugs* 2016;25:1361–70; 2. Menter A, et al. *Expert Opin Biol Ther* 2021;21:87–96; 3. Menter A, et al. *AAD VMX* 2021;
4. https://www.fda.gov/media/124907/download

Abbreviations

ADA = Antidrug antibody; AE = Adverse event; $AUC_{\tau, 12\text{-}14}$ = Area under the adalimumab plasma concentration-time curve over the dosing interval Week 12-14; BSA = Body surface area; $C_{max, 12\text{-}14}$ = Maximum observed adalimumab plasma concentration during the dosing interval Week 12-14; $C_{min, 12\text{-}14}$ = Minimum observed adalimumab plasma concentration during the dosing interval Week 12-14; $C_{min, 30\text{-}32}$ = Minimum observed adalimumab plasma concentration during the dosing interval Week 30-32; CV = coefficient of variation; DLQI = Dermatology Life Quality Index; nAB = neutralizing antidrug antibody; PASI = Psoriasis Area and Severity Index; PASI50 = ≥50% reduction in PASI; PASI75 = ≥75% reduction in PASI; PASI90 = ≥90% reduction in PASI; PASI100 = ≥100% reduction in PASI; PK = Pharmacokinetics; RP = Reference product; sPGA = static Physician's Global Assessment; $t_{max, 12\text{-}14}$ = Time to maximum observed adalimumab plasma concentration during the dosing interval Week 12-14; $t_{max, 30\text{-}32}$ = Time to maximum observed adalimumab plasma concentration during the dosing interval Week 30-32; $t_{min, 12\text{-}14}$ = Time to minimum observed adalimumab plasma concentration during the dosing interval Week 12-14; $t_{min, 30\text{-}32}$ = Time to minimum observed adalimumab plasma concentration during the dosing interval Week 30-32

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