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SUMMARY OF RESEARCH

Summary of Research: Switching Between Adalimumab Reference Product and BI 695501 in Patients with Chronic Plaque Psoriasis (VOLTAIRE-X): A Randomized Controlled Trial

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ABSTRACT

This Summary of Research overviews the results of the VOLTAIRE-X study (NCT03210259), which looked at what happened when people with plaque psoriasis continually took the adalimumab reference product (adalimumab RP; known by the brand name Humira®) or switched three times between taking the adalimumab RP and BI 695501 (adalimumab-adbm, known by the brand name Cyltezo®), an adalimumab biosimilar. The VOLTAIRE-X study showed that the pharmacokinetics of adalimumab were similar in people who stayed continuously on adalimumab RP and people who switched between adalimumab RP and adalimumab-adbm. There were no differences in effectiveness, side effects, or antibodies to adalimumab when comparing people who stayed continuously on adalimumab RP with those who switched between adalimumab RP and the adalimumab biosimilar adalimumab-adbm. On the basis of these results, adalimumab-adbm was approved by the US Food and Drug Administration (FDA) as interchangeable with adalimumab RP, meaning that a pharmacist can substitute the biosimilar adalimumab-adbm for adalimumab RP without requiring permission from the original prescriber (unless required to by state law).

Keywords: Adalimumab; Biosimilar; Interchangeable; Switching; Chronic plaque psoriasis

INTRODUCTION

This is a summary of the original article: 'Switching Between Adalimumab Reference Product and BI 695501 in Patients with Chronic Plaque Psoriasis (VOLTAIRE-X): A Randomized Controlled Trial' [1] (Fig. 1).

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PEER-REVIEWED FEATURE

Summary of Research Article

Summary of Research: Switching Between Adalimumab Reference Product and BI 695501 in Patients with Chronic Plaque Psoriasis (VOLTAIRE-X): A Randomized Controlled Trial

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What is an interchangeable biosimilar?

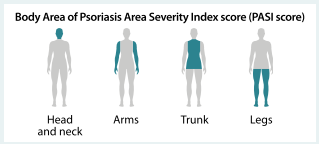
- If a biosimilar is interchangeable it means that a pharmacist can automatically substitute the biosimilar for its reference biologic without first consulting the prescriber, if this is permitted by state law. Laws on interchangeable biosimilars vary from state to state.
- An interchangeability study checks for safety, effectiveness, and blood drug levels when a patient is switched at least 3 times between the reference product and the biosimilar.
- VOLTAIRE-X **was an interchangeability study.**

What did the VOLTAIRE-X study look at?

The VOLTAIRE-X study looked to see if the pharmacokinetics of adalimumab are similar in people who continuously stayed on adalimumab reference product (RP; known by the brand name Humira) or switched between adalimumab RP and Cyltezo® (adalimumab-adbm, BI 695501), an adalimumab biosimilar.

Researchers wanted to find out if continuously staying on adalimumab RP compared to switching between adalimumab RP and adalimumab-adbm resulted in similar effectiveness. The effectiveness of each treatment was assessed by comparing improvements in plaque psoriasis.

- This was measured using the Psoriasis Area and Severity Index score (PASI), in which redness, thickness, and scaling of plaques are evaluated on a scale of 0 (no plaques) to 4 (very severe) on 4 areas of the body (right).
- The higher the PASI score, the greater the severity of psoriasis. The PASI percentage of response is used in clinical studies to measure effectiveness; a PASI75 means that a person's PASI score has decreased 75% from the start of the trial.
- The proportion of participants with a static Physician's Global Assessment Score (sPGA) ≤1 (clear or almost clear) at Week 32 was also reported.



The study also looked at how many people developed antibodies against adalimumab.

- Sometimes a patient may develop antibodies against a biologic drug called anti-drug antibodies.
- Some anti-drug antibodies, called neutralizing antibodies, can bind to a drug and reduce how well the drug works.

Who took part in the VOLTAIRE-X study?

The study involved **238 people** from **49 study sites** across North America and Europe.

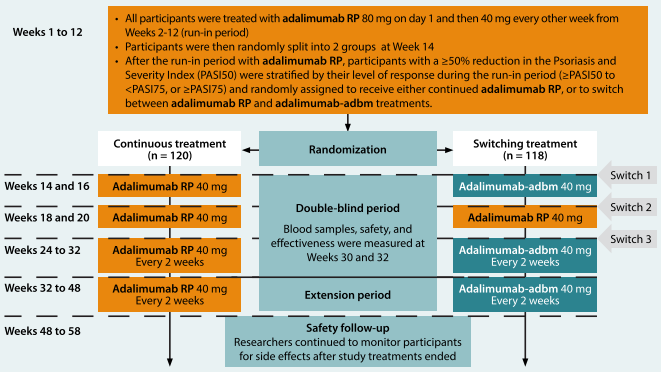
People who took part in the study:

- Were men and women aged 18–80 years old
- Had moderate-to-severe plaque psoriasis based on their PASI score over at least 10% of their body for 6 months or more
- Some also had psoriatic arthritis, a complication related to psoriasis that causes swelling and pain in muscles and joints

People could not take part in the study if they:

- Had any other inflammatory disease, such as rheumatoid arthritis
- Had previously taken biologics for an auto-immune disease (for example, rheumatoid arthritis, psoriasis)
- Had cancer or a history of cancer in the past 5 years (except for some skin cancers)

How was the VOLTAIRE-X study conducted?



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What were the main results of the VOLTAIRE-X study?

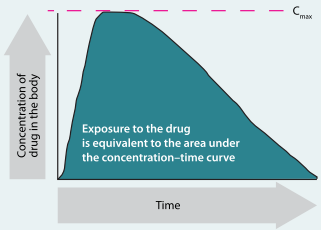
1. What were the characteristics of participants at the start of the study?

The characteristics of participants in the switching group and the continuous group were similar.

	Participants switching between adalimumab-adbm and adalimumab RP	Participants continuously treated with adalimumab RP	All participants
Average age	46 years	44 years	45 years
Sex	31% female	37% female	34% female
Race	96% White	99% White	97% White
No antibodies to adalimumab at baseline	84%	92%	88%

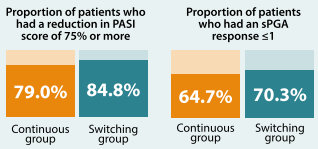
2. Was there a difference in pharmacokinetics in the switching group and the continuous group?

- Total adalimumab exposure was assessed as area under the concentration–time curve (AUC) between Week 30–32, as shown in the graph.
- The study also measured the highest concentration of adalimumab in the blood (C_{max}) in patients who stayed on adalimumab RP compared with those who switched.
- AUC and C_{max} were similar in people who stayed on adalimumab RP or switched between adalimumab RP and adalimumab-adbm, with 90.2% confidence intervals for both pharmacokinetic measures within the bioequivalence range of 80.0–125.0%.



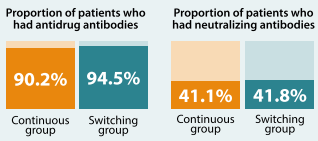
3. Was there a difference in effectiveness?

- At Week 32, a similar proportion of participants in the continuous group and switching groups achieved a 75% reduction in their PASI score.
- At Week 32, a similar proportion of participants in the continuous group and the switching group had sPGA responses ≤1.
- These results suggest that switching between adalimumab RP and adalimumab-adbm worked as well as staying continuously on adalimumab RP to improve symptoms of psoriasis.



4. Was there a difference in participants' immune response?

- A similar proportion of participants developed antidrug antibodies and neutralizing antibodies in the continuous group and switching groups.
- This suggests that staying on adalimumab RP compared with switching between adalimumab RP and adalimumab-adbm does not impact how the immune system responds to the drugs. The response of the immune system triggered by a drug is also called **immunogenicity**.



5. How many participants in the study experienced side effects following randomization to treatment?

In the VOLTAIRE-X study, the continuous treatment and switching treatment groups had similar side effects.

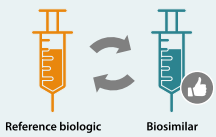
- Any side effect that occured during the study was recorded.
  - **62.5%** of participants in the continuous treatment group reported any treatment-emergent adverse event
  - **56.8%** of participants in the switching treatment group reported any treatment-emergent adverse event
- Researchers then decide if the side effect could be considered related to the study treatment.
  - **18.3%** of participants in the continuous treatment group reported side effects that were considered **related to** the study drug
  - **11.9%** of participants in the switching treatment group reported side effects that were considered **related to** the study drug

A serious side effect is one that might cause death, hospitalization, disability, or permanent damage.

- No one died following randomization to adalimumab-adbm or adalimumab RP in VOLTAIRE-X study.
- Nine patients had at least one serious side effect reported after randomization (5 in the switching and 4 in the continuous group), with one serious side effect considered related to study product in the continuous group.
- Fewer than 5% of patients experienced severe treatment-emergent side effects, side effects of special interest, or treatment-emergent side effects resulting in treatment discontinuation, with no notable difference between treatment groups.

What do the results of this study mean?

- In VOLTAIRE-X, primary and secondary pharmacokinetic endpoints were equivalent and clinical outcomes were highly similar in patients with moderate-to-severe chronic plaque psoriasis who received either adalimumab RP continuously or in those who switched three times between adalimumab-adbm and adalimumab RP.
- Based on the results of the VOLTAIRE-X switching study, adalimumab-adbm has been approved by the FDA as interchangeable with adalimumab RP, allowing a pharmacist to provide adalimumab-adbm when adalimumab RP has been prescribed, without seeking approval from the prescriber unless required to by state law.



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Conflict of Interest Please see original article for full author disclosures.

Ethical Approval This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by the author.

Data Availability Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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REFERENCE

1. Menter A, Cohen S, Kay J, et al. Switching between adalimumab reference product and BI 695501 in patients with chronic plaque psoriasis (VOLTAIRE-X): a randomized controlled trial. Am J Clin Dermatol. 2022;23:719–28. https://doi.org/10.1007/s40257-022-00708-w.