Impact of Clinical Remission on Physical Function in Patients with Rheumatoid Arthritis Treated with ALX-0061: Post-hoc Analysis of Phase I/II Data

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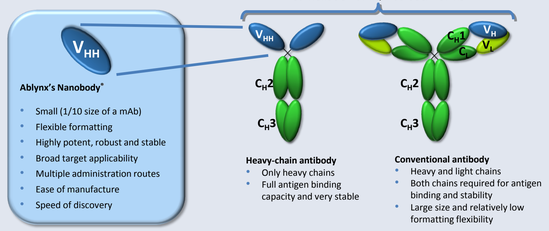
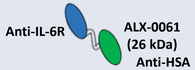
Background: ALX-0061: IL-6R targeting Nanobody

- **Ablynx's Nanobodies®**

Camelidae family has both forms



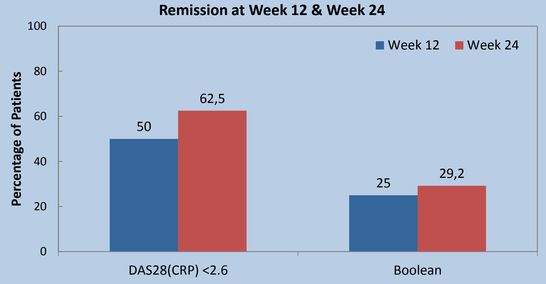
- **ALX-0061 product description**
  - **monovalent interaction** eliminates IL-6R cross-linking
  - no induction of Antibody-dependent cell-mediated cytotoxicity or complement-dependent cytotoxicity due to **lack of Fc**
  - **half-life extension** by binding to Human Serum Albumin (HSA)



Methods (cont'd)

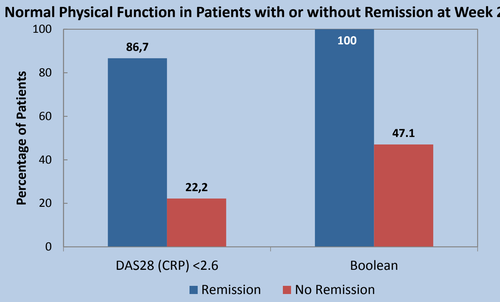
- Data were obtained from the multi-center, randomised, double-blind, placebo (PBO) controlled, dose escalation, Phase I/II study (1).
  - During the first 12 weeks of the **multiple ascending dose** period, **37 patients** received **PBO (n=6)** or **ALX-0061 IV (n=31)** at 1 or 3 mg/kg Q4W, or 6 mg/kg Q8W. Patients received stable doses of MTX ranging from 10-25 mg/week.
  - In the second 12 weeks period, patients with insufficient EULAR response had the ALX-0061 dose increased or switched from PBO to ALX-0061. **24 patients continued on their originally-assigned ALX-0061 IV dose** (8 patients in 1 mg/kg arm, 8 patients in 3 mg/kg arm, and 8 patients in 6 mg/kg arm), 4 patients changed their dosing regimen, and 3 patients switched from PBO to ALX-0061.
- This **post-hoc analysis** utilised data from **patients whose originally assigned ALX-0061 dose remained unmodified**.
- The safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of ALX-0061 was assessed in a Phase I/II study in patients with active RA on stable MTX therapy (1).

ALX-0061 Induces Remission in Patients with RA



- At week 12 and 24, 50% (12/24) and 62.5% (15/24) of patients treated with ALX-0061 achieved DAS28(CRP)<2.6 remission, respectively.
- Remission using the more stringent Boolean criteria was observed in 25% (6/24) and in 29.2% (7/24) of the patients at weeks 12 and 24, respectively.

Normal Physical Function is Regained after Controlling Disease Activity



- More patients in DAS28(CRP) remission at week 24 achieved normal physical function (86.7% vs. 22.2%) compared to patients not in remission.
- Moreover, normal physical function was observed in 100% (7/7) of patients in Boolean remission at week 24.

Objectives and Methods

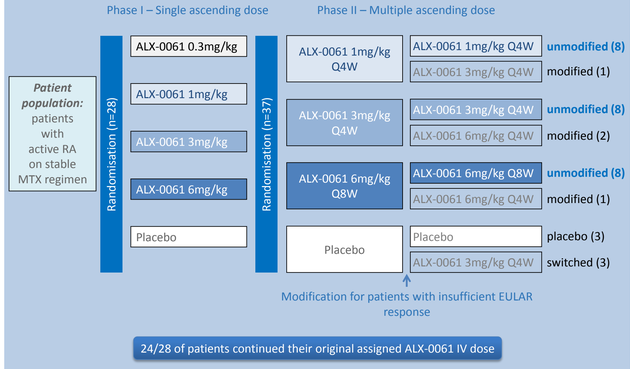
Objectives

- Since **remission** is the **recommended treatment target** in the management of RA, the purpose of this post-hoc analysis was to assess the **induction and maintenance of remission** during **ALX-0061** treatment.
- In addition, the **impact of disease remission on physical function** following 24-week treatment with ALX-0061 was also assessed.

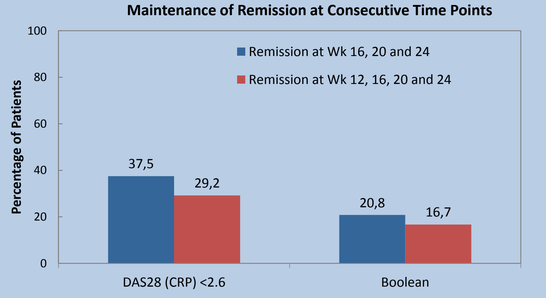
Methods

- Clinical remission was defined by both **DAS28 (CRP) <2.6** and the **ACR/EULAR Boolean-based** definitions.
- Maintenance of remission was defined as being in **remission** at **consecutive time points** (i.e. at weeks 16, 20, and 24 , or at weeks 12, 16, 20, and 24).
- Patient functional status was assessed using the Health Assessment Questionnaire (HAQ) with **HAQ ≤ 0.5** defining **normal physical function**. An **improvement in HAQ score ≥ 0.25** was considered to be **clinically meaningful**.

Study Design of the Phase I/II Clinical Trial



ALX-0061 IV Induces Sustained Remission in Patients with RA



- Looking at maintenance of remission, approximately one third, i.e. 37.5% and 29.2%, of patients treated with ALX-0061 remained in DAS28 remission during the last 3 (at weeks 16, 20, and 24) and last 4 (at weeks 12, 16, 20, and 24) consecutive time points, resp.
- Maintenance of remission based on the Boolean criteria was also observed, being 20.8% and 16.7% of the patients for the last 3 or 4 successive time points.

Conclusions

- This post-hoc analysis showed that in patients with established RA who remained on their originally assigned ALX-0061 dose, **ALX-0061 induced and maintained remission** as assessed by both **DAS28(CRP)** and the more stringent **Boolean** remission definition.
- **Maintenance of remission** during the **last 3 (at weeks 16, 20, and 24)** and even the **last 4 (at weeks 12, 16, 20, and 24) consecutive time points** is possible.
- Control of disease activity, as determined by remission, is also important in **regaining normal physical function.**
- These results suggest that **ALX-0061 has the potential to be a disease modifying treatment** supporting treat-to-target management of RA as reflected in the EULAR recommendations.

(1) J.-B. Holz et al., Ann Rheum Dis 2013;72(Suppl3):64