A study to assess the tolerability, pharmacokinetics *and* pharmacodynamics of ONS-3010 (Adalimumab, Oncobiologics Inc.) compared to Humira® EU/US, AbbVie) in healthy subjects

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INTRODUCTION

ONS-3010 is being developed as a biosimilar of Humira® (Adalimumab), a full-length recombinant human IgG1 monoclonal antibody specific for TNFα.

AIM

This randomized, double blind study was performed to demonstrate pharmacokinetic (PK) bioequivalence (BE) between two reference products (Humira® EU/US) and ONS-3010 in healthy subjects to compare the tolerability and immunogenicity profiles *and* to assess and compare the intended pharmacological activity (PD) by application of a whole blood challenge.

METHODS

- 198 healthy subjects (*n*=66 per treatment arm, male:female, 1:1);
- Single subcutaneous 40 mg dose (ONS-3010, Humira® EU/US);
- Immunogenicity blood sample collections;
- PK: $AUC_{0\text{-}inf}$, C_{max}, $AUC_{0\text{-}last}$ (limits of BE between 80-125%);
- PD: whole blood LPS/Al(OH)$_3$ challenge (*n*=36; *n*=12 per treatment arm; male:female, 1:1).

RESULTS

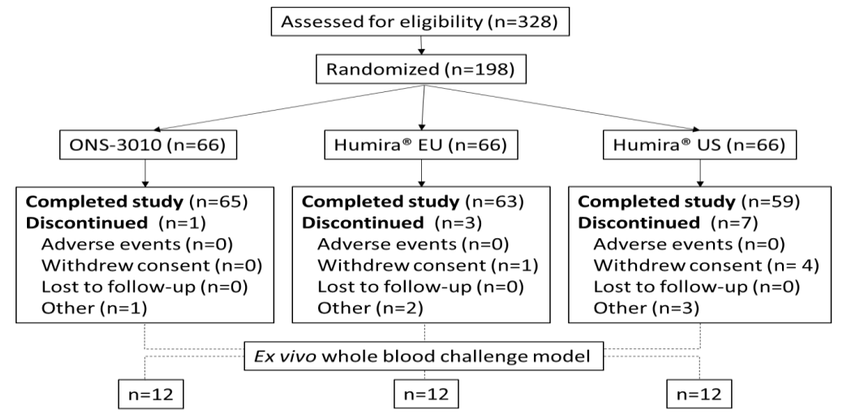

Figure 1: Subject disposition

- Comparable tolerability and immunogenicity profiles;
- PK: comparable concentration-time profiles (*Figure 2, Table 1*);
- PD whole blood LPS/Al(OH)$_3$ challenge:
  - Significantly reduced TNFα levels (> 99%);
  - Reduced IL-8 release (≤ 30%);
  - No effect on IL-1β and IL-6 release.

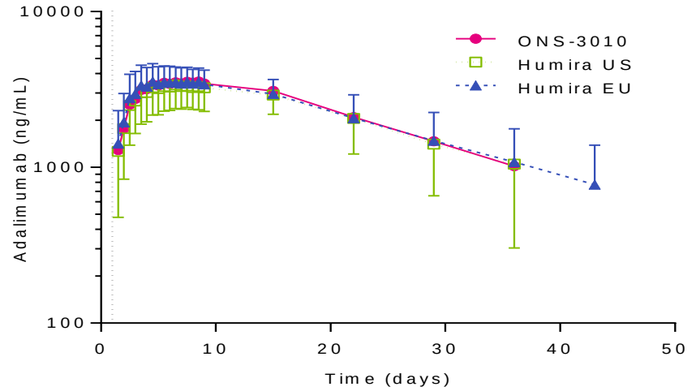

Figure 2: Adalimumab concentration-time profile for ONS-3010, Humira® EU/US (SD as error bars)

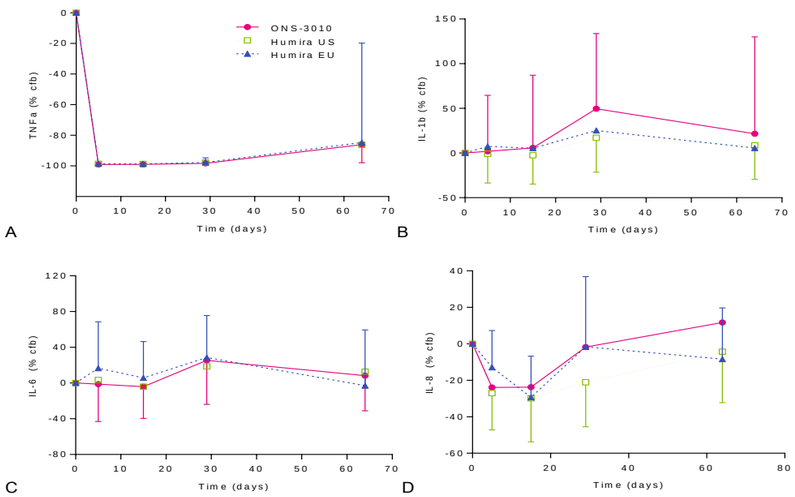

Figure 3: TNFα (A), IL-1β (B), IL-6 (C) and IL-8 (D) release after ex vivo LPS/Al(OH)$_3$ stimulation of blood samples (change from baseline,%, SD as error bars)

CONCLUSIONS

This study demonstrates:

- **Pharmacokinetic BE between ONS-3010 and Humira®;**
- **The value of whole blood LPS/Al(OH)$_3$ challenge to monitor proximal drug effects in healthy subjects to demonstrate PD similarity in early pharmacology trials.**

	Humira® EU *vs* Humira® US		ONS-3010 *vs* Humira® US		ONS-3010 *vs* Humira® EU	
	Contrast	90% CI (p-value)	Contrast	90% CI (p-value)	Contrast	90% CI (p-value)
$AUC_{0\text{-}inf}$ (ng*hr/mL)	1.04	0.92 - 1.17 (0.6365)	1.06	0.94 - 1.20 (0.4061)	1.03	0.91 - 1.16 (0.7141)
$AUC_{0\text{-}last}$ (ng*hr/mL)	1.05	0.92 - 1.20 (0.5118)	1.01	0.89 - 1.15 (0.8705)	0.96	0.85 - 1.09 (0.6160)
C_{max} (ng/mL)	1.07	0.99 - 1.15 (0.1811)	1.06	0.98 - 1.15 (0.1899)	1.00	0.92 - 1.08 (0.9746)

Table 1: Non-compartmental PK analysis - Contrasts of ANOVA

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