**Introduzione**

- Un biosimilare è un prodotto farmaceutico che è "comparabile" (EMA) o "fisicamente similare" (US FDA) a un prodotto originale farmacologico, detto anche "originator drug".

**METHODS**

**Study design**

- The study was a randomised, double-blind, two-way cross-over study with two treatment periods (Figure 1).

In treatment period I, subjects were randomised to receive a single 50 mg subcutaneous (sc) injection of GP2015 or etanercept originator on Day 1. Following a wash-out period of at least 28 days after dosing, in treatment period II, subjects underwent cross-over and received a single s.c. injection of GP2015 or etanercept originator on Day 1.

**Objectives**

- To compare GP2015 and etanercept originator with respect to the following criteria:
  - time to the maximum observed serum concentration (t_max)
  - elimination rate constant (k, el)
  - apparent terminal half-life of elimination phase (t_{1/2})
  - immunogenicity, safety and tolerability

**Assessments**

- PK: Blood samples were drawn at 0, 6, 12, 24, 36, 48, 60, 72, 84, 96, 120, 150, 216, 240, 300, 360 and 432 hours after dosing in each treatment period. GP2015 and etanercept originator were both validated using an enzyme-linked immunosorbent assay (ELISA). The half-life of elimination and the area under the curve (AUC) were within the pre-defined bioequivalence range of 0.80 – 1.25, indicating comparable bioavailability and PK between GP2015 and etanercept originator. Anti-drug antibody (ADA) development was evaluated using a competitive ligand binding assay and no major immunogenicity was detected.

- Immunogenicity: All samples from the pre-dose (Day 1) of each period were ADA negative. There were no clinically relevant differences in safety, tolerability and immunogenicity between GP2015 and etanercept originator.

**RESULTS**

- The mean serum concentration-time profiles were comparable between GP2015 and etanercept originator. The mean serum concentration-time profiles were also comparable using a validated enzyme-linked immunosorbent assay (ELISA) and neutralising capacity was evaluated using a competitive ligand binding neutralising assay.

- The most common TEAEs overall, regardless of relationship to study drug were presented in Table 3.

**CONCLUSIONS**

- This PK study (EudraCT number 2013–004902–25) demonstrated that GP2015 is a proposed etanercept biosimilar comparable to the originator.

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INTRODUCTION

- Local-inflammation diseases such as rheumatoid arthritis, are often associated with required doses.

- The use of an autoinjector [AI] for drug delivery has been shown to increase patient adherence, acceptability and safety, in comparison to conventional pre-filled syringes (PFS).

- GP2015, a proposed etanercept biosimilar, is planned to be presented in a two treatment periods (Figure 1).

- In the second treatment period, subjects received PFS in treatment period 1 followed by AI in treatment period 2 (PFS/AI).

- In-clinic assessments were performed at: 0, 12, 24, 48, 60, 72, 96, 120, 144, 168, 216, 240, 288 and 336 hours after dosing in each treatment period. Pharmacokinetic analysis included all serum concentrations above the lower limit of quantification.

- The primary PK parameter was a ratio of geometric mean AUC0–inf. Phases I and II were conducted in parallel with the aim to provide additional evidence for a similar delivery of GP2015 via the two devices.

- Immunogenicity: Blood samples were collected at –0.5 h pre-dose on Day 1 of each period and at the end of each treatment period. Serum concentrations in the sera were quantified using a validated enzyme-linked immunosorbent assay. AUC0–inf, area under the serum concentration-time curve measured from the time of dosing and an ending time.

- Safety assessments: Treatment emergent adverse events (TEAEs) and serious adverse events (SAEs), with their severity and relationship to study drug were analysed.

- A single dose of 50 mg GP2015 administered by AI or PFS was well tolerated, with no unexpected adverse events.

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