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Systemic analysis of injection site pain caused by subcutaneous administration of FKB327 and reference product via different delivery methods

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Protocol status: Other
We have performed a systemic analysis in accordance with this protocol.

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Abstract

FKB327 is a biosimilar of the adalimumab reference product (RP). The formulation excipients of the FKB327 differ from those of the citrate-containing formulation of the RP, thus injection-site pain (ISP) at subcutaneous injection were assessed in single-dose studies (FKB327-001 and -004) in healthy subjects and multiple-dose studies (FKB327-002 (NCT02260791) and -003 (NCT02405780) in patients with rheumatoid arthritis. Outline of individual study design can be refered to in appendicies 1 to 4 for FKB327-001, -002, -003, and -004 studies, respectively. In all 4 studies, ISP was assessed using visual analog scale (VAS) with a horizontal scale from 0 to 100 mm (0 to 100 scale in KB327-002 and -003 using ePRO device) with the left end point signifying “no pain” and the right end point signifying “intolerable pain”. In order to evaluate potencial difference in ISP among products, devices of FKB327, or the other subjects’ background factors, this systemic anapysis using pooled data from these studies was planned.

Attachments

FKB327-ISP-Systemati...
35KB

FKB327-001 protocol ...
60KB

FKB327-002_Protocol ...
81KB

FKB327-003_Protocol ...
75KB

FKB327-004_protocol ...
239KB

1 Data to be analyzed in systemic analysis
The VAS data of injection site pain from FKB327-001, -002, -003, and -004 are integrated for the systemic analysis. All cumulative data will be analyzed for the randomized subjects with injection site pain data collected immediately after injection at Day 1. Some subjects had multiple assessments as FKB327-003 was an extension study following FKB327-002.

2 Planned analysis
All summary data will be provided for each treatment group, i.e. FKB327 and Humira®. Unless otherwise specified, categorical data will be summarized using frequencies and percentages. Summary statistics on continuous data will include number of subjects, mean, standard deviation (SD), minimum, median, and maximum.

2.1 Summary of demographic and other baseline characteristics
Demographic and other baseline characteristics data will be summarized by study. The variables to be summarized include study visit (baseline / week 0 / week 30); device (syringe / auto injector / pre-filled syringe); subject type (healthy volunteer / RA patient); country; gender; age; race; ethnicity; and weight. Age and weight will also be summarized categorically.

2.2 Forest plot of injection site pain data
Subgroup analyses will be performed for VAS data. The mean treatment difference and 95%CI will be presented for each subgroup through the forest plot. The subgroups include study, device, subject type, age group, gender, weight group, race, ethnicity, and country.

2.3 Linear mixed model
The least squares mean treatment difference and 95%CI will be calculated by using linear mixed model with fixed effects (subject type, age group, gender, race, ethnicity, weight group, device, and treatment) and random effects (country and subject). P-value will also be calculated with the same model.
The other fixed effects will also be estimated with the same model.

2.4 Device
For the VAS data collected after FKB327 injection in all subjects, the device comparison will be performed by using linear mixed model with fixed effects (subject type, age group, gender, race, ethnicity, weight group, and device) and random effects (country and subject). P-value will also be calculated with the same model.
The same model will also be analyzed only for the subjects who experienced three types of FKB327 device.

2.5 Location of injection
For the VAS data collected after FKB327 injection in all subjects, the location comparison will be performed by using linear mixed model with fixed effects (subject type, age group, gender, race, ethnicity, weight group, device, and location of injection) and

random effects (country and subject). P-value will also be calculated with the same model.

2.6 Injection site reaction

All injection site reaction data will be summarized by study visit for the randomized subjects with injection site reaction data collected immediately after injection at Day 1. The number and percentage of subjects will be presented for each category of reaction by treatment.