Strong Correlation Between the Apparent Clearances of Guselkumab and Golimumab Following Co-administration to Healthy Volunteers

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Statement of Purpose

- Guselkumab is a human IgG1λ monoclonal antibody targeting interleukin-23 (IL-23), while golimumab is a human IgG1κ monoclonal antibody directed against tumor necrosis factor alpha (TNFα).
- It was hypothesized that clearance of antibody therapeutics could be strongly correlated when non-specific Fc receptor-mediated catabolism is the predominant elimination pathway.
- The present work intended to examine the correlations between apparent clearance and other PK parameters between these two distinct monoclonal antibodies.

Methods

A randomized, open-label, Phase 1 study in healthy participants (N=162) evaluated the relative bioavailability of guselkumab and golimumab when co-administered as a combination therapy using two different formulations. Co-administration of both monoclonal antibodies within the same participants provided a unique opportunity to examine correlations between PK parameters of these two distinct monoclonal antibodies. The study evaluated the PK of guselkumab and golimumab co-administration following a single-dose subcutaneous (SC) injection of guselkumab and golimumab. Serial serum samples were collected to characterize the PK parameters of both agents. PK parameters were calculated using noncompartmental analysis (NCA) implemented in Phoenix™ WinNonlin® Version 8.4 (Certara L.P., Princeton, USA). All PK calculations used actual sampling times. Pearson correlation was performed on PK parameters. A Shapiro-Wilk test was used to evaluate the normality of the distribution of log-transformed PK parameter values. Since the PK is linear across the studied dose ranges of both mAbs, the PK parameters from the 3 different dose levels could be combined for correlation analysis with dose normalization when necessary.

Table 1. Participant demographics and baseline characteristics

Variables [a]	Group 1: High-dose Gus/Gol	Group 2: Mid-dose Gus/Gol	Group 3: Low-dose Gus/Gol	Total
Number of subjects	53	54	52	159
Sex -Male	35 (66.0%)	38 (70.4%)	29 (55.8%)	102 (64.2%)
Age (years)	29.1 (8.2)	28.5 (8.0)	30.5 (9.8)	29.4 (8.7)
Race - White	40 (75.5%)	40 (74.1%)	45 (86.5%)	125 (78.6%)
Body Weight (kg)	72.8 (8.4)	73.1 (10.7)	71.0 (10.3)	72.3 (9.8)

[a]mean (standard deviation) are shown for age and body weight while frequency is shown for sex and race

Results & discussion

Figure 1. Correlation of PK parameters between guselkumab and golimumab

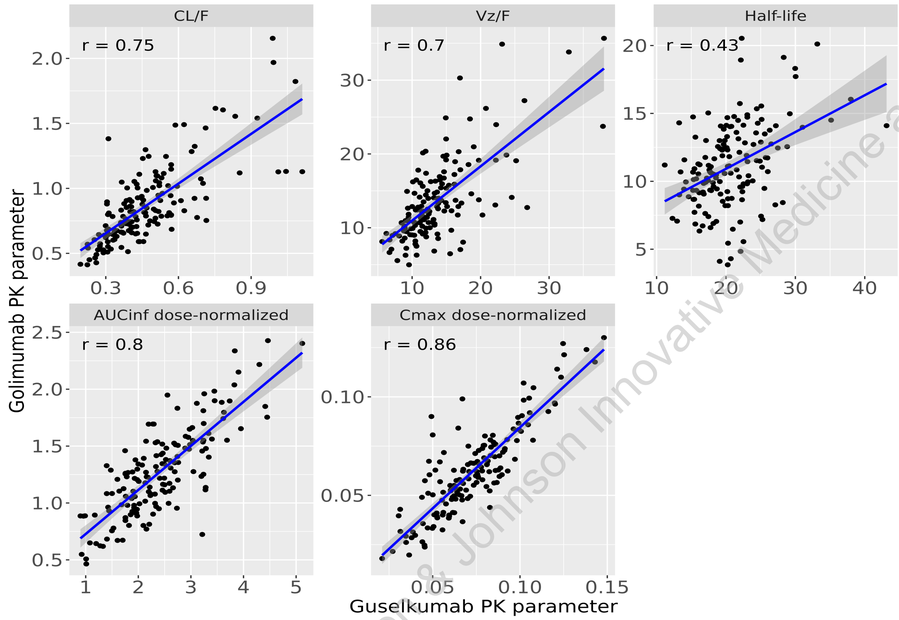


Figure 2. Frequency distribution of CL/F of guselkumab and golimumab

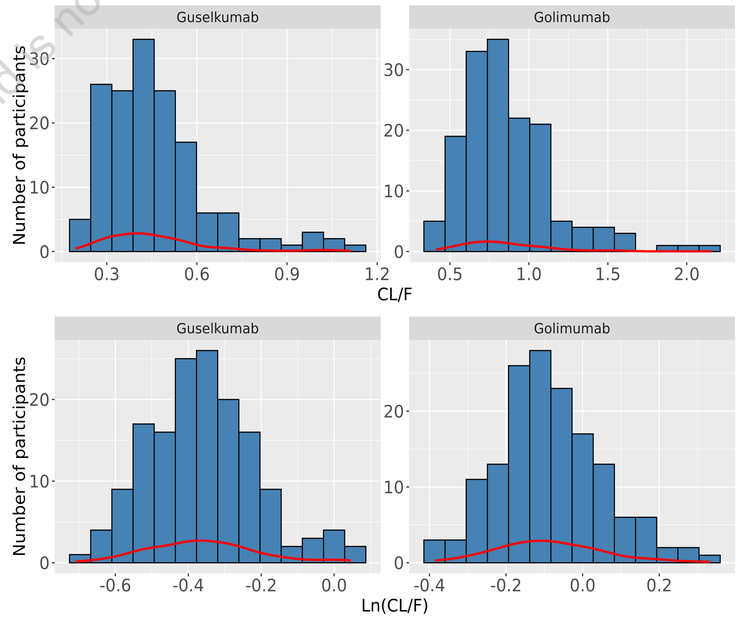
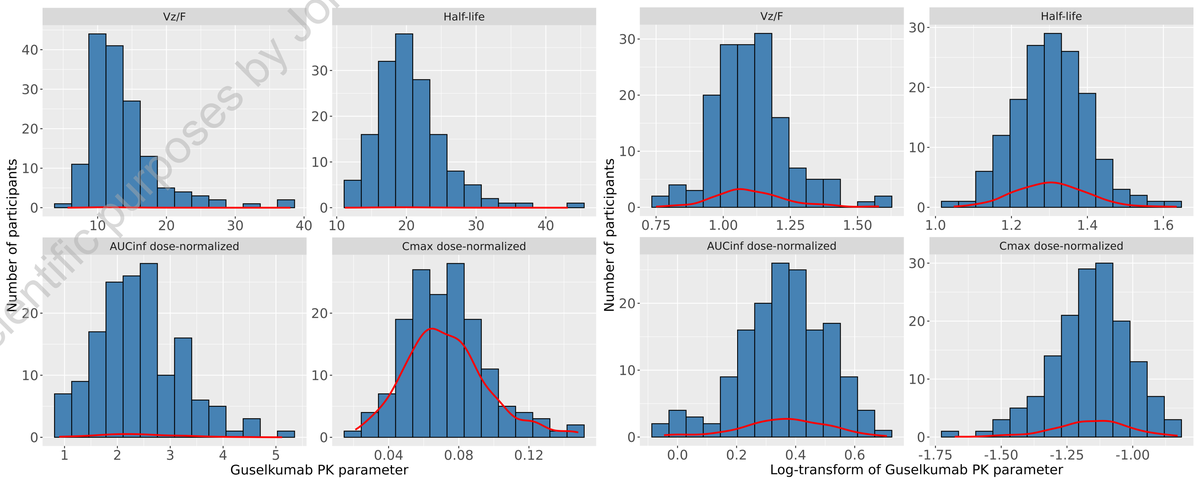


Figure 3 . Frequency distribution of other PK parameters of guselkumab and golimumab



- Figure 1 demonstrates strong correlations between guselkumab and golimumab for dose-normalized C_{max} (r = 0.86), AUC_{inf} (r = 0.80), CL/F (r = 0.75), and V_z/F (r = 0.70). $T_{1/2}$ exhibited a moderate correlation (r = 0.43).
- Figures 2 and 3 show histograms of CL/F and log-transformed CL/F for guselkumab and golimumab. Shapiro-Wilk testing confirmed that the log-transformed CL/F values did not deviate from normality.

Conclusion & Significance

The finding that especially CL/F is strongly correlated between guselkumab and golimumab may represent a step toward developing a universal and convenient approach to “phenotype” an individual’s catabolic capacity of IgG-based therapeutics