Population Pharmacokinetics and Exposure–Response Analyses for Abatacept in Juvenile Idiopathic Arthritis

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Introduction

- Polycythaemic juvenile idiopathic arthritis (pJIA) is the most common chronic rheumatic disease in children and one of the leading causes of childhood-acquired disability.
- Treatment with biologics (TNF-α and IL-1) is now well established, leading to improved clinical outcomes for patients with pJIA.
- Abatacept has a mechanism of action that is fundamentally different from that of other TNFαRDs, with a proven efficacy and safety profile in pJIA.

Methods

- Combined data from studies with IV or SC abatacept were analyzed to assess clinically relevant exposure outcomes applicable to both formulations.
- The PPK model was developed from data from 13 Phase III studies in RA (11 studies; n=2213) and pJIA (patients aged 2–17 years; 2 studies; n=389). A similar PPK analysis was conducted for the cohort of 2–5-year-old patients with pJIA (data not shown).
- The E–R model for the American College of Rheumatology pediatric scores (pJIA-ACR100) was developed to determine whether the proposed weight-tiered SC regimen provided near-maximal efficacy by achieving the target exposure and was therapeutically comparable to the 10 mg/kg/month regimen in patients with pJIA.

PPK analysis

- Continuous covariates at baseline: age, body weight, albumin, calculated glomerular filtration rate, serum creatinine, total bilirubin, tender joint count (TJC) and swollen joint count (SJC).
- Categorical covariates: sex (male vs female), race (white vs non-white), disease activity (ACR scoring criteria), and other subtypes (polychromatic red blood cell disorder and polycythemia vera).

E–R analysis

- A total of 357 (91.8%) patients aged 6–17 years were included in the E–R analysis.
- Cminss was the best measure for predicting the JIA-ACR response using a proportional odds model.

Conclusions

- The final PPK model adequately described abatacept concentration–time profiles for patients with RA and those with pJIA (excluding patients aged 2–5 years).
- A proportional odds model with a log linear function of Cminss adequately described the E–R relationship for abatacept in patients with pJIA administered IV or SC abatacept.
- The PPK and E–R analyses demonstrated that the proposed weight-tiered SC abatacept dosing regimen provides near-maximal efficacy (JIA-ACR100) by achieving the target exposure of Cminss = 10 µg/mL and is therapeutically comparable to the IV abatacept regimen in pJIA.