**ABSTRACT**

Tocilizumab (TCZ) is a recombinant humanized IL-6 receptor monoclonal antibody that targets IL-6. The purpose of this analysis was to describe the time course of peripheral neutrophil counts (PNCs) after TCZ administration in pediatric patients with systemic juvenile idiopathic arthritis (sJIA).

**METHODS**

Serum TCZ concentrations and PNCs were available from 76 patients who received 12 mg/kg or 8 mg/kg patients ≥30 kg or ≥30 kg of TCZ or placebo every 2 weeks (total of 64 doses). Neutrophil counts were assessed at screening, baseline (week 0), and at 1, 2, 3, 6, 8, 10, and 12 weeks. A previously developed 2-compartment model with parallel linear and Michaelis-Menten elimination was used to characterize the relationship between TCZ exposure and PNCs. Different pharmacokinetic (PK)/pharmacodynamic (PD) models with direct and indirect response models were tested to characterize the TCZ-PNC relationship.

**RESULTS**

The TCZ-PNC relationship was described by a model that included an immediate TCZ effect on PNC decline (possibly, neutrophil margination) and a longer-term effect on PNC decline (near normal levels) due to improvement in patient condition. The magnitude of the immediate effect was 0.166 day–1 and the TCZ concentration corresponding to half-maximal effects was 0.724, EC50 = 6.38 µg/mL). These parameters were very similar to the respective values obtained earlier for adult patients (Emax = 0.788, EC50 = 7.49 µg/mL). The maximum rate of decline of the PNC was 0.25 day–1 (no. of observations in a bin). The TCZ-PNC relationship was described by a model that included an immediate TCZ effect on PNC decline (toward normal levels) due to improvement in patient condition.

**CONCLUSIONS**

Diagnostic plots and predictive check simulations indicated good agreement of model predictions with observed data. Diagnostic plots and predictive check simulations indicated good agreement of model predictions with observed data. The model was used to evaluate the long-term effect on PNCs associated with sJIA patients who received TCZ at various doses.

**REFERENCES**

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