**Expected spesolimab plasma exposure following intravenous and subcutaneous dosing in patients with generalized pustular psoriasis**

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**Aim**

To simulate the PK of IV vs SC doses of spesolimab to compare drug exposure profiles and support dosing recommendations in patients with GPP

**Introduction**

GPP is a rare, chronic, and potentially life-threatening inflammatory skin disease characterized by episodic flares of widespread pustular eruptions and erythema. Spesolimab is a fully human anti-interleukin-36 receptor monoclonal antibody approved to treat GPP flares in adults via IV infusion in the US and many other countries. A population PK model was developed using clinical PK data collected in patients treated with spesolimab to simulate the plasma drug exposure levels over time in patients following administration of IV spesolimab vs SC spesolimab.

**Methods**

A population PK model was developed using individual-level PK, ADA, and covariate data from 18 studies in which patients were treated with IV or SC spesolimab. The mathematical model quantified the PK of spesolimab following IV and SC administration, including the effect of patient-specific factors on PK (e.g. body weight, disease state, ADA titers). The resulting population PK model was used to simulate concentration–time profiles over 12 weeks (84 days) of various IV and SC doses: IV spesolimab 300 mg and 900 mg administered over 90 minutes, as 1 dose or 900 mg as 3 doses (1 week apart), and SC spesolimab 300 mg, 600 mg, 900 mg, and 2350 mg injections, as 1 dose or as 2 doses (1 week apart).

For each dose, Cmax, Tmax, and AUC over 14 and 84 days were summarized in patients with GPP.

**Results**

PK data from this simulation suggest that treatment with IV and SC spesolimab can result in differences in drug exposure in clinical practice. Specifically, higher Cmax and more rapid Tmax were observed for the IV vs SC doses of spesolimab. To match the Cmax of the 900 mg IV dose, a SC dose 2.5× greater (2250 mg, equivalent to 10 injections of the 235 mg SC pre-filled syringe) would be required.

The immediate and high bioavailability of IV spesolimab compared with SC spesolimab are characterized by episodic flares of widespread pustular eruptions and erythema. A population PK model was developed using individual-level PK, ADA, and covariate data from 18 studies in which patients were treated with IV or SC spesolimab. The resulting population PK model was used to simulate concentration–time profiles over 12 weeks (84 days) of various IV and SC doses:

**Conclusions**

To simulate the PK of IV vs SC doses of spesolimab to compare drug exposure profiles and support dosing recommendations in patients with GPP.