OBJECTIVES
To identify covariate factors that may influence the PK-neutrophil count relationship

METHODS
A population PK-PD model was developed in NONMEM 7.2.0. The population PK model (poster W-026) was used to predict individual TCZ neutrophil counts after TCZ IV doses were developed earlier.1 The current analysis builds on those models to incorporate both IV and SC dosing of TCZ in a mixed-effects approach using model-based simulation.

RESULTS
The relationship between neutrophil counts and TCZ concentration is independent of the route of administration. The indirect-response model with stimulation of elimination driven by TCZ serum concentrations adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. Additionally, SC and IV treatments, regardless of treatment arm or treatment duration, were adequately described using a stimulation of elimination mechanism. The parameter estimates, standard errors, and confidence intervals are presented in Table 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>kout</td>
<td>0.20</td>
<td>0.05</td>
<td>(0.10, 0.30)</td>
</tr>
<tr>
<td>tPDL</td>
<td>100</td>
<td>20</td>
<td>(60, 120)</td>
</tr>
<tr>
<td>Emax</td>
<td>0.83</td>
<td>0.22</td>
<td>(0.40, 1.26)</td>
</tr>
</tbody>
</table>

No covariate, including the presence of neutralizing anti-TCZ antibodies, was found to have a clinical impact on the effect of TCZ on circulating neutrophil counts.

SUMMARY/CONCLUSIONS
The current analysis, with simulation of stimulation-driven by TCZ serum concentrations accurately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The indirect-response model with stimulation of elimination adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The relationship between neutrophil counts and TCZ concentration is independent of the route of administration. The current analysis, with simulation of stimulation-driven by TCZ serum concentrations accurately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The indirect-response model with stimulation of elimination adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo.

REFERENCES
1. Kivitz A et al.
2. Koizumi et al.
4. Koizumi et al.

To receive a PDF of this poster on your mobile device:
1. Go to getscanlife.com from your mobile browser to download the free barcode reader
2. Scan the QR code on the image above to download the PDF
4. Koizumi et al.
5. Kivitz A et al.

The relationship between neutrophil counts and TCZ concentration is independent of the route of administration. The current analysis, with simulation of stimulation-driven by TCZ serum concentrations accurately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The indirect-response model with stimulation of elimination adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo.

The relationship between neutrophil counts and TCZ concentration is independent of the route of administration. The current analysis, with simulation of stimulation-driven by TCZ serum concentrations accurately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The indirect-response model with stimulation of elimination adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo.

The relationship between neutrophil counts and TCZ concentration is independent of the route of administration. The current analysis, with simulation of stimulation-driven by TCZ serum concentrations accurately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The indirect-response model with stimulation of elimination adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo.

The relationship between neutrophil counts and TCZ concentration is independent of the route of administration. The current analysis, with simulation of stimulation-driven by TCZ serum concentrations accurately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo. The indirect-response model with stimulation of elimination adequately described the time course of neutrophil counts in patients treated with TCZ 8 mg/kg IV Q4W, TCZ 162 mg SC Q2W, TCZ 162 mg SC QW, and placebo.