PKP-014. VARIABILITY OF EXPOSURE PARAMETERS OF ADULTS TREATED WITH HIGH DOSES METHOTREXATE


**Background**

In the current treatment of Non-Hodgkin lymphoma (NHLs) with high-dose methotrexate, the dosage is performed according to different protocols, regardless of patients pharmacokinetic variability.

**Purpose**

To evaluate the variability of exposure to methotrexate in adult patients with NHLs who received high-dose methotrexate (>1000mg/m²) to justify the need to individualize the dose and optimize the treatment.

**Material and methods**

- Retrospective observational study, between October 2007 and June 2014.
- The target range of exposure was defined as ±20% of the AUC average value, considering the extreme values positioned outside ±40%.
- Methotrexate was measured by a fluorescence polarization immunoassay (TDx/FLx System, Abbot) in plasma samples obtained at 2, 12, 23, 36, 42 and 60 hours after the start of infusion.
- Methotrexate pharmacokinetics parameters were estimated by Nonlinear Least Squares Regression (software abbott PKs).

**Results**

<table>
<thead>
<tr>
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<th>Group I</th>
<th>Group II</th>
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<tbody>
<tr>
<td>AUC</td>
<td>43.00 ± 13.86 μM.L/h</td>
<td>36.00 ± 19.68 μM.L/h</td>
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<tr>
<td>Prespecified target: AUC±20%</td>
<td>[35.29 - 51.34] μM.L/h</td>
<td>[30.81 - 141.02] μM.L/h</td>
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<tr>
<td>Extreme values: AUC±10%</td>
<td>(&gt;187.04 or &lt;142.56) μM.L/h</td>
<td>(&gt;116.62 - 29.29) μM.L/h</td>
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- 17.39% and 8% of patients showed high extreme values of exposure versus the 4% and 8% who showed low extreme values, respectively.
- 44.79% of patients showed exposure outside of the prespecified target.
- The variability of exposure to methotrexate was CV=37.99%.
- The variability of the clearance in these patients (90.04 ± 30.59 ml/min/m²) would explain these results.

**Conclusion**

The variability of exposure to methotrexate would justify the need to individualize dosage to optimize therapy. This could prevent an extreme risk of inefficacy or toxicity in the 18.75% of the patients that are outside the prespecified target.