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

P. Montejano-Hervás, I. Reyes-Torres, M. Aumente, F. Franco-García, I. Viguera-Guerra.
Hospital Universitario Reina Sofía, Farmacia Hospitalaria, Córdoba, Spain.
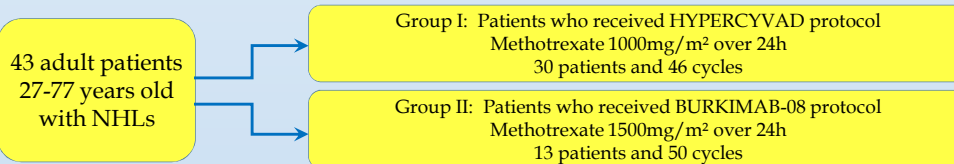
Background

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 ($>1000mg/m^2$) to justify the need to individualize the dose and optimize the treatment

Material and methods

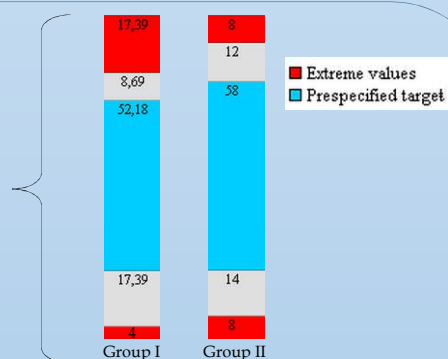- Retrospective observational study, between October 2007 and June 2014.

43 adult patients 27-77 years old with NHLs

Group I: Patients who received HYPERCYVAD protocol
Methotrexate $1000mg/m^2$ over 24h
30 patients and 46 cycles

Group II: Patients who received BURKIMAB-08 protocol
Methotrexate $1500mg/m^2$ over 24h
13 patients and 50 cycles

- **The <u>target range of exposure</u> was defined as ±20% of the AUC average value, considering the <u>extreme values</u> 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

	Group I	Group II
AUC	$471,05 \pm 188,59$ µM.h [235,29 - 1231,34]	$560,77 \pm 194,63$ µM.h [308,53 – 1414,62]
Prespecified target: (AUC±20%)	[376,84 – 565,26] **52,18 %**	[448,62 – 672,93] **58 %**
Extreme values: (AUC±40%)	(>659,47 or <282,63) **21,74 %**	(>785,08 or <336,46) **16 %**

Legend: ■ Extreme values ■ Prespecified target
Group I: 17,39 / 8,69 / 52,18 / 17,39 / 4
Group II: 8 / 12 / 58 / 14 / 8

- 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.