

IMPACT OF DRUG INTERACTIONS IN HIGH DOSE METHOTREXATE ELIMINATION

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BACKGROUND AND IMPORTANCE

HIGH DOSE METHOTREXATE, is used to treat several oncological and hematological malignancies. Despite appropriate hydration, urine alkalization and leucovorin rescue, nephrotoxicity remains a **RISK WHICH CAN LEAD TO SIGNIFICANT MORBIDITY AND MORTALITY**. Different drugs have been associated with HDMTX **ALTERED ELIMINATION (AE) DUE TO DELAYED ELIMINATION OR TO NEPHROTOXICITY**.

HDMTX
Dose ≥ 500 mg/m²

AIM AND OBJECTIVES

Describe the incidence of AE and assess the impact of drug interactions in HDMTX induced AE.

MATERIALS AND METHODS

Bibliographic research

Lexicomp®

DRUG INTERACTIONS WITH HDMTX.

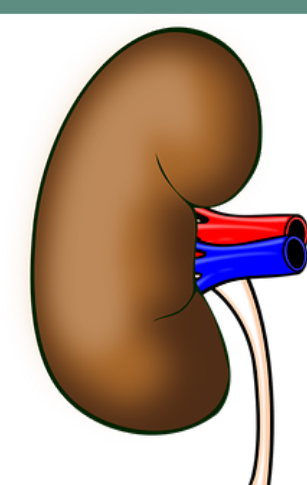
DESIGN

Retrospective study
All patients who received HDMTX 2010 - 2019.

DATA

Age, sex, methotrexate dosage, number of HDMTX cycles, creatinine before and after HDMTX, serum levels of methotrexate and potentially interacting medications (PIM) prescribed 24 hours before of HDMTX infusion and during methotrexate elimination

Association of PIM with AE was determined by odds ratio (OR) and χ^2 test or Fisher's exact probability test



AE = plasma concentration $\geq 1\mu\text{mol/l}$ at 48 hours and/or $0.1\mu\text{mol/l}$ at 72 hours OR nephrotoxicity, according to CTCAEcv4.0.

RESULTS

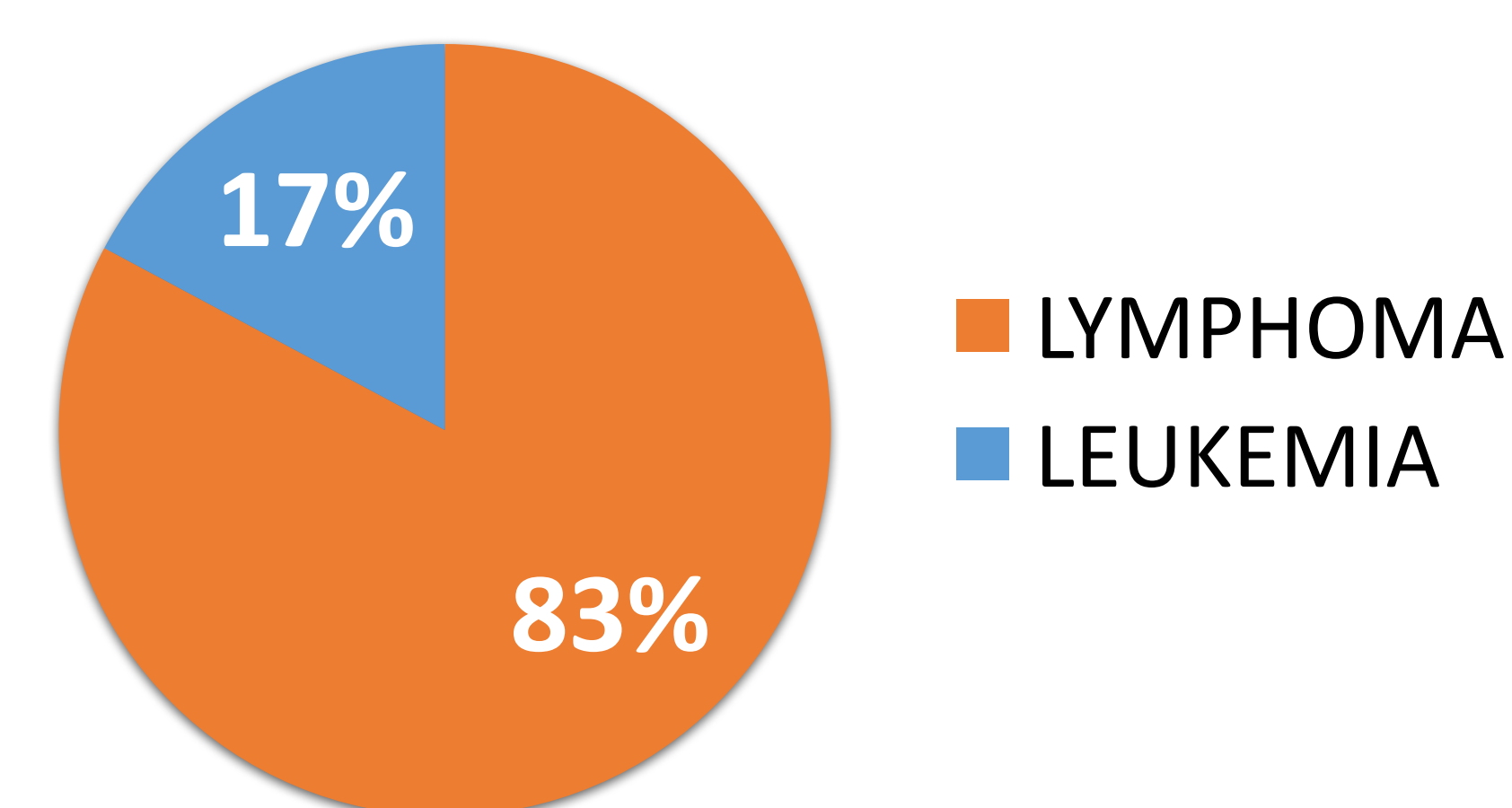
64 patients



42.2% ♀
66.4 years (IQR:55.6-75.3)

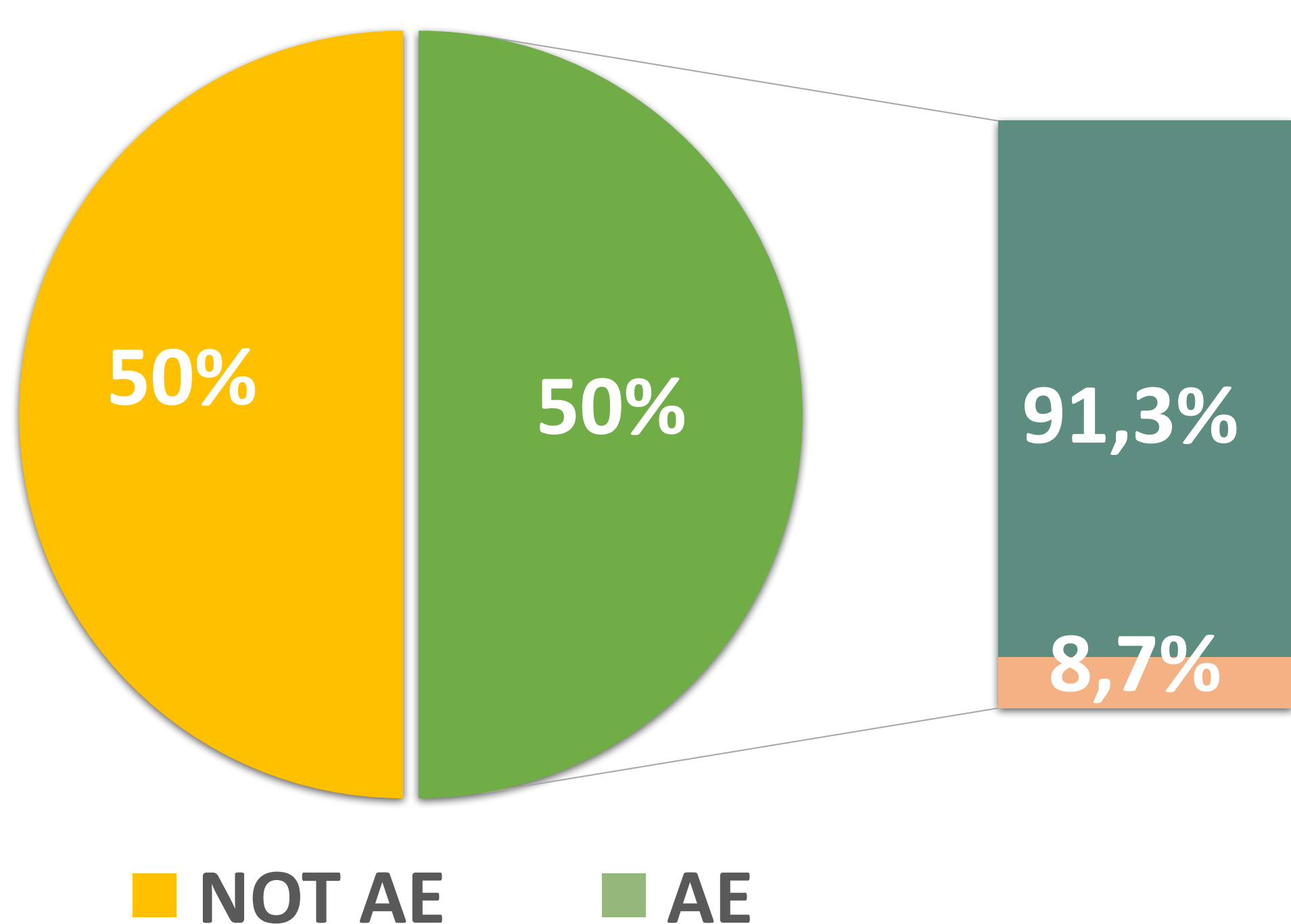
Median baseline creatinine baseline 0.66 (IQR:0.57-0.78) mg/dL

DIAGNOSIS



160 cycles

Median HDMTX dose of 11760 mg (IQR:3370-14207.5mg)



PIM	OR
LEVETIRACETAM	6.9 IC:1.5-32.4 p<0.05
NON-STEROIDAL ANTI-INFLAMMATORY DRUGS	10.9 95%CI:2.4-49.4 p<0.05
DOXYCYCLINE	0.5 95%CI:0.4-0.6 p<0.05
Proton pump inhibitors, loop diuretics, amphotericin B, penicillin and derivate, aminoglycosides, ciprofloxacin nor p-glycoprotein/ABCB1 inhibitors.	Not significant differences

CONCLUSION AND RELEVANCE

- There is a **HIGH PREVALENCE** of patients with AE of HDMTX.
- Potentially interacting medications with HDMTX **ARE FREQUENTLY USED** during treatment.
- Only **LEVETIRACETAM AND NON-STEROIDAL ANTI-INFLAMMATORY** drugs were associated with methotrexate AE in our patients.



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