Poster

[P26-9] P26-9: Oncologic drugs (5): Pharmacokinetics, TDM practice

Chair: Kiyoshi Mihara, Japan

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[P26-9-10] A preliminary study for evaluation of docetaxel exposure and the occurrence of drug-induced toxicity in a Brazilian population

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Background

Docetaxel (DTX) is a widely used anticancer drug. Currently, DTX dosing is mostly based on patient’s body-surface area (BSA). However, this approach is associated to an extensive interindividual variation in drug exposure and, consequently, efficacy and toxicity. This variability have been related to polymorphisms on genes encoding proteins involved on DTX metabolism (*CYP3A*) and transport (*ABCB1*, *ABCC2*, *SLCO1B3*). Since DTX has a narrow therapeutic window and over exposure is associated to severe toxicity, particularly the grade 3/4 neutropenia, it can be a potential candidate for therapeutic drug monitoring (TDM). Engels et al. (2011) have proposed a target area under the curve (AUC) for DTX of 2.5 to 3.7 mg.h/L for a 75 mg/m2 dose. The aim of this pilot study was to evaluate the systemic exposure to DTX and the occurrence of drug-induced toxicity in a Brazilian group of patients.

Methods

seven patients participated in the study (n=5 prostate cancer and n=2 breast cancer) during the first DTX chemotherapy cycle. Plasma sampling followed Engels et al. (2011) limited strategy protocol for estimation of DTX area under the curve (AUC), being collected 5± min before and 60±10 min after the end of the infusion. Plasma concentrations of DTX were quantified by LC-MS/MS after liquid-liquid extraction and the AUC estimated after the Bayesian model proposed by Engels et al. (2011). Adverse were classified according to NCI-CTCAE version 4.

Results

Patients mean age was 64 years (51 to 70 years). All patients received a 75 mg/m2 dose, administrated as monotherapy (n=4) or in combination with leuprolide (n=1), cobinacarboplatin and trastuzumab (n=1) and zolendronic acid (n=1). The DTX AUC values ranged from 2.9 to 4.1 mg.h/L (mean 3.19 ±0.43 mg.h/L). One patient had AUC above the target (4.1 mg.h/L) and developed severe toxicity, grade 3 neutropenia and grade 2 mucosytis/diarrhea, endorsing the association between drug exposure and toxicity even in a small group of patients. No other significant adverse event was reported.

Conclusions

This first report on a follow-up in a Brazilian population confirmed the importance of DTX TDM. Currently a

pharmacogenetic study in a larger group is in progress.