
Oral

[O27-4] O27-4: Oncology (2)

Chairs: Takayasu Kurata, Japan / Etienne Chatelut, France

Wed. Sep 27, 2017 2:30 PM - 3:30 PM Room C1 (1F)

(Wed. Sep 27, 2017 2:30 PM - 3:30 PM Room C1)

[O27-4-3] The effects of advanced age and serum alpha1-acid glycoprotein on Docetaxel unbound exposure and dose-limiting toxicity in cancer patients

Hirotsugu Kenmotsu¹, Chiyo K. Imamura², Akira Ono³, Shota Omori⁴, Kazuhisa Nakashima⁵, Kazushige Wakuda⁶, Tetsuhiko Taira⁷, Tateaki Naito⁸, Murakami Haruyasu⁹, Takahashi Toshiaki¹⁰, Yusuke Tanigawara¹¹ (1.Shizuoka Cancer Center, 2.Keio University School of Medicine, 3.Shizuoka Cancer Center, 4.Shizuoka Cancer Center, 5.Shizuoka Cancer Center, 6.Shizuoka Cancer Center, 7.Shizuoka Cancer Center, 8.Shizuoka Cancer Center, 9.Shizuoka Cancer Center, 10.Shizuoka Cancer Center, 11.Keio University School of Medicine)

Keywords: alpha1-acid glycoprotein, age, docetaxel, neutropenia, unbound exposure

Background

Alpha1-Acid glycoprotein (AAG), which is a major binding protein of docetaxel, is considered to be a determinant for docetaxel pharmacokinetics. However, there are no reports about the impact of serum AAG on pharmacokinetics and pharmacodynamics in elderly patients treated with docetaxel. The aim of this prospective study was to elucidate the effects of advanced age and serum AAG on docetaxel unbound exposure and neutropenia, dose-limiting toxicity, in cancer patients.

Methods

Docetaxel was administered at 60 mg/m² to 51 patients with non-small cell lung cancer, 17 of whom were 75 years of age. Pharmacokinetics, unbound fraction (fu), neutropenia, serum protein levels of AAG and albumin, as well as baseline absolute neutrophil count (ANC) were assessed during the first course. Population pharmacokinetic and pharmacodynamic analyses were performed to evaluate the influence of clinically relevant factors on docetaxel pharmacokinetics and neutropenia.

Results

Clearance of docetaxel and the degree of fu were significantly associated with serum AAG level, but not with age. Area under the concentration-time curve (AUC) of unbound docetaxel (fu·AUC) was significantly higher in patients aged 75 years (0.389 ± 0.114 μg·h/mL) compared with patients aged <75 years (0.310 ± 0.121 μg·h/mL). Percent decrease in ANC at nadir related to fu·AUC, and was dependent on baseline ANC.

Conclusions

Regardless of aging, serum level of AAG determines docetaxel unbound exposure and related dose-limiting toxicity. Serum AAG level and ANC at baseline appear to be predictive of neutropenia for patients of all ages following the administration of docetaxel.