Symposium

[S-16] S-16: TDM of 5-FU

Chairs: Edward Chu, USA / Yasutsuna Sasaki, Japan
Wed. Sep 27, 2017 10:30 AM - 12:00 PM Room D (1F)

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[S-16-5] Pharmacokinetically guided 5-fluorouracil dose adjustment versus body-surface-area dosing in advanced pancreatic cancer patients: real world data

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Keywords: 5-fluorouracil, FOLFIRINOX, PANCREAS, TDM

Background

Therapeutic drug monitoring of 5-fluorouracil (5-FU) in patients with gastrointestinal cancer is being incorporated in the clinical practice, but more data is needed to determine the success of this strategy on clinical outcomes. We compared the efficacy and safety of pharmacokinetically (PK) guided 5-FU dose adjustment to body-surface-area (BSA) dosing in a FOLFIRINOX regimen in advanced pancreatic cancer (PC).

Methods

We retrospectively analysed data from a Spanish multicentre cohort study that included PC patients receiving FOLFIRINOX as first-line treatment between January 2010 and September 2015. Patient data were analysed separately depending on whether the 5-FU dose was PK-guided or body-surface-area based. TDM of 5-FU is routinely performed in one of the hospitals. In the PK-adjusted arm, 5-FU was monitored during the patient’s first course of IV infusion, and the dose for the next cycle adjusted to achieve a therapeutic area under the curve range of 25-30 mcg*h/mL. Baseline plasma levels of uracil and 5,6-dihydrouracil, and uracil:5,6-dihydrouracil (UH2:U) ratios were used as markers of dihydropyrimidine dehydrogenase (DPD) activity. One-compartimenal poblacional model were developed and fitted using bayesian approach. Propensity score matching was constructed to adjust for bias selection. Efficacy was determined as overall survival (OS). Tolerability was assessed according to the US National Cancer Institute Common Terminology Criteria for Adverse Events v.3.

Results :

Fifty-two patients with metastatic (mPC; 69.3%) or locally advanced PC (laPC; 40.7%) were analysed. 34 patients received PK-guided 5-FU and 18 patients standard BSA dosing. In mCP patients the OS was 12.67 months for the PK-adjusted group and 9.13 months for the BSA (death hazard ratio,0.635; IC95% 0.303-0.880; p=0.030). In LAPC patients the OS was also higher in the PK-adjusted (31.37 months) than in the BSA group (16.67 months; p=0.985). In the PK-guided group, the grade 3/4 toxicities were 11.76% for diarrhoea, 0.20% for mucositis; and 28.24% for neutropenia, while in the BSA group they were 12.50%, 2.94%, and 46.25%, respectively.

Conclusions

PK-guided 5-FU dose adjustment improves efficacy and tolerability in advanced PC and should be considered as therapeutic strategy for pancreas cancer patients.

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