Oral

[O26-3] O26-3: Pharmacogenomics (1)

Chairs: Ichiro Ieiri, Japan / Vincent Haufroid, Belgium
Tue. Sep 26, 2017 3:00 PM - 4:00 PM Room C1 (1F)

(Tue. Sep 26, 2017 3:00 PM - 4:00 PM Room C1)

[O26-3-4] Dihydropyrimidine dehydrogenase deficiency in patients treated with 5FU or capecitabine based regimens: a tertiary care centre experience

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Keywords: Dihydropyrimidine dehydrogenase deficiency 5FU, Capecitabine, Toxicity,

Background

Dihydropyrimidine dehydrogenase (DPD) is the rate-limiting enzyme in the degradation of 5 fluorouracil (5FU) and capecitabine and its deficiency leads to severe toxicities, including death. Several studies have shown that genetic variations in the DPYD gene lead to partial or complete deficiency of DPD activity resulting in adverse drug reactions.

Methods

The study involved male and female patients receiving 5FU or capecitabine based combination chemotherapy for stomach, oesophagus and colon cancer. The sampling was done after obtaining written informed consent from the patients. DPD testing was done by GOMED (Genomics and other omics technologies for Enabling Medical Decision) clinical decision support service for four high confidence pharmacogenetically relevant variants in DPYD gene using Sanger sequencing.

Results

Among 95 patients who were screened, 15 (12.6%) had deleterious mutations in DPYD for the rs2297595 (c.496A>G) variant. 14 of the patients with the altered genotype had side effects of grade II-IV. Amongst which 3 patients had febrile neutropenia, one had myocardial infraction, 9 patients had hand foot syndrome G II –III, peripheral neuropathy in 5 cases and diarrhoea in 3 cases. In subsequent cycles chemotherapy was continued with dose modifications without any serious adverse events

Conclusions

Mutated DPYD is frequently observed in Indian patients who experience toxicities while receiving 5-FU/capecitabine. Screening of patients for DPYD mutations prior to administration of 5-FU/capecitabine using new pharmacogenetic testing methods may help identify those patients who are at greatest risk for adverse effects, allowing a more individualized approach to their chemotherapy management.

Acknowledgement:
GOMED (http://gomed.igib.in) for doing the tests free of charge