Pharmacoeconomic evaluation of genetic profiling to prevent FOLFIRI-induced toxicities in mCRC patient

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BACKGROUND

Improving the efficacy-toxicity balance in oncology remains an unmet need. Most anticancer drugs are characterized by narrow therapeutic indexes, most affected by inter-individual variability, often responsible of severe toxicities after treatment and of a reduced effectiveness. With the constant rise in oncology treatment costs, the use of chemotherapeutic drugs needs to become more conscious as well focused where it has the chance to produce an effective clinical benefit. Several studies report that adjusting dosing regimens on pharmacogenetic-basis in the daily clinical practice bring measurable clinical benefit in terms of reduced toxicity and improved outcome (Cicciolini et al 2010, Fety et al 1998). In order to prevent FOLFIRI-induced toxicities international guidelines recommend the predictive genetic screening for fluoropyrimidines (*DPYD* gene) and Irinotecan (*UGT1A1*).
Several recent studies have been trying to understand whether the therapy (drug choice and dosage) adjustment based on pharmacogenomic profiling, besides its clinical advantage, is cost-effective compared with the treatment of chemotherapy toxicities.

AIM

The objective of this study consists of obtaining detailed information on direct costs of toxicities observed in a group of metastatic colorectal cancer (mCRC) patients homogenously treated with a first line FOLFIRI regimen (fluoruracil, leucovorin, irinotecan). This objective was pursued by assessing the hospital costs of all toxicities arisen in a group of 250 patients enrolled at CRO Aviano. The ultimate aim is to obtain persuasive data about UGT1A1*28 (rs8175347) genotyping as cost-effective tool to limit fluorouracil and irinotecan-related toxicities.

METHODS

A complete database was created of FOLFIRI-related toxicities developed during the entire course of therapy by the group of patients in exam. Each toxic event (hematological, gastrointestinal, dermatological, neurological, cardiac and other) was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events v.3.0 (Ref. CTCAEv3). The database is integrated with detailed information on the patient genotypes (including DPYD rs3918290, rs55886062, DPYD rs6737679 and UGT1A1*28).
A cost analysis was performed matching the expect cost of each toxicity management at the CRO-National Cancer Institute focusing on direct medical cost, which includes hospitalization, laboratory analysis, therapies, physician visits, instrumental examinations, facility fees and other health practitioner fees.
Data are presented as medians and Interquartile Range (IQR). Differences in costs between different SNPs were analyzed with Kruskal-Wallis test.

RESULTS

A total of 250 patients mCRC treated with first line FOLFIRI regimen were included in this analysis whereof 29 did not develop any toxicity.
Toxicity costs for UGT1A1*28 patients fell from the mutate genotype (7/7) with a median of 3256.7 € (IQR 2305.6–4061.5) to the wild type genotype (6/6) with a median of 723.8 € (IQR 534.3-993.5). The 6/7 is not statistically different, in terms of costs, than the 6/6 type.

DISCUSSION

This preliminary analysis suggests that upfront UGT1A1*28 genotyping before FOLFIRI treatment will be useful to reduce its related toxicity handling costs. Indeed, toxicities expenses underwent a 3.5x increase from WT to mutated UGT1A1*28 genotypes.
This study has highlighted that upfront genotyping of validated predictive markers in drug-induced toxicity besides their critical role in therapy optimization could also imply costs reduction derived from FOLFIRI-caused toxicities.