Preliminary results of the PERFU study: PERsonalized predication and regulation of 5-FluoroUracil exposure.

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Abstract [max. 350 words]

Introduction

5-fluorouracil (5-FU) is the cornerstone of modern treatment regimens for pancreatic cancer (PC) and colorectal cancer (CRC). The starting dose of 5-FU is currently based on body surface area (BSA) and dihydropyrimidinedehydrogenase (*DPYD*) genotyping. Despite this approach, inter- and intra-individual variability of exposure remains high. The aim of this study is to evaluate whether therapeutic drug monitoring (TDM) using a preset target exposure of 20-30 mg*h/L, as proposed by the IATDMCT consensus guideline, is an effective tool to regulate individual 5-FU exposure.

Objectives

The primary objective of this study was to determine the percentage of patients that achieve optimal 5-FU exposure defined as an AUC between 20-30 mg*h/L or experience dose increase limiting toxicity after two dose cycles.

Methods

In this mono-center intervention study in PC and CRC patients undergoing 5-FU chemotherapy in combination with leucovorin, irinotecan and/or oxaliplatin were eligible for inclusion. Blood samples were taken at 2h and/or 45h after start of a 46-hour continuous infusion, and toxicity was assessed according to the CTCAE v 5.0. The 5-FU dose algorithm by Kaldate et al. (2012) was adapted to accommodate a maximum dose increase of 40% for this study.

Results

27 patients were enrolled from 2020 until 2024. For this interim analysis, 15 patients with 5-FU measurements in the first 2 cycles, were included. In 10 (67%) of these patients, optimal 5-FU exposure was achieved after two dose cycles. In 4 (27%) of the patients dose limiting toxicity prevented dose increases while AUCs remained <20 mg*h/L. Patients who were able to undergo dose adjustments based on their AUC in cycle 1 and lack of toxicity showed significantly higher AUCs in cycle 2 compared to those for whom dose adjustments were not feasible. Mean AUCs (mg*h/L) were 18 (SD=6; n=9) and 11 (SD=4; n=6), respectively (p=0.02). The risk of grade ≥3 toxicity was 21%, 25% and 50% at AUCs of <15, 15-20, and 20-30 mg*h/L, respectively.

Conclusion

Based on our preliminary results, the additional value of 5-FU TDM seems to be limited. Further studies are warranted to validate our findings and reevaluate the current AUC target between 20-30 mg*h/l.