Purpose
The purpose of this work is to obtain data to choose a personalized therapy based on individual gene variations, minimize adverse events (AE) and avoid the discontinuation of therapy resulting in tumor progression.

Material and methods
A retrospective study was conducted on 57 males and females, age ≥ 18, with colorectal cancer, in therapy with 5 protocols using different combinations of 5-fluorouracil, Irinotecan and Oxaliplatin. The study evaluated the number of cases where therapy was temporarily discontinued or suspended due to AE that concerned hematological, neurological and gastrointestinal toxicity according to CTCAE system, which provides a numerical grading scale for AE description.

The prevalence of polymorphisms and association between toxicity and polymorphisms were evaluated calculating ODDS Ratios (OR) with 95% confidence interval. Chi-square statistical significance test was applied.

Results
OR values allowed finding the association between toxicity above 2nd grade and presence of polymorphisms. The association is:

- **Strong positive** for DPYD*2A1.905+1G>A (OR=10.68) and UGT1A1*28 (OR=7.43)
- **Moderate positive** for DPYDc.1129–5923C>G (OR=3.58) and SLC31A1 (OR=2.13)
- **Moderate negative** for ABCC2rs818 (OR=0.33)
- **Absent** for DPYD*13c.1679T>G, DPYDc496A>G, ABCC2rs717 and GSTPi

### GENE | VARIANT | STANDARD GENOTYPE | TOXICITY >G2 | OR (95% CI) | P VALUE
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DPYD | *2A1.905+1G>A | GG | 1,75% | 10,68 (0,41-278,65) | NS
UGT1A1 | *28 | **G** | 22,22% | 7,43 (0,81-67,83) | <5%
DPYD | c.1129–5923C>G | CC | 1,75% | 3,58 (0,21-61,62) | NS
SLC31A1 | rs1098189 4T>G | TT | 7,89% | 2,13 (0,27-16,60) | NS
ABCC2 | rs8187710(4544G>A) | GG | 3,85% | 0,33 (0,03-3,51) | NS
DPYD | *13c.1679T>G | TT | 0% | 1,07 (0,04-27,93) | NS
DPYD | c496A>G | AA | 3,51% | 0,96 (0,17-5,31) | NS
ABCC2 | rs177620(24C>T) | CC | 3,85% | 0,80 (0,07-8,91) | NS
GSTPi | rs1695(313>G) | AA | 11,54% | 1,13 (0,15-8,21) | NS

Conclusion
Often patients express different polymorphisms at the same time, developing a toxicity related to the summed effects of all the polymorphic variants. This problem is particularly important for chemotherapeutics that are administered at very high doses, close to toxic doses, and takes on a clinical and economic relevance. The study of genes, involved in the metabolism and transport of many drugs, allows predicting drugs toxicity and efficacy and, based on individual variations, establishing a personalized and safe therapy before the beginning of the treatment.