UGT1A1*28 POLYMORPHISM AND IRINOTECAN EFFECTIVENESS

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OBJECTIVES

UGT1A*28 polymorphisms have been related with an increased in SN-38, active metabolite of irinotecan. Thus some authors also related the presence of this mutated allele with an increased in the effectiveness of irinotecan treatment.
The purpose of the present study **is to assess the influence of UGT1A1*28 polymorphism in the irinotecan effectiveness.**

METHODS

Prospective, observational, four-year unicentre study (november 2012-may 2016). All adult colorectal cancer patients treated with FOLFIRI protocol (Irinotecan 180 mg/m2/Fluorouracil 400mg/m2/ Fluorouracil 2400 mg/m2/Leucovorin 200-400mg/m2) were included. Inclusion criteria were: ECOG 0-1, hemoglobin > 10 g/dL, leucocytes > 3000/mm3 and platelets > 100000/mm3).

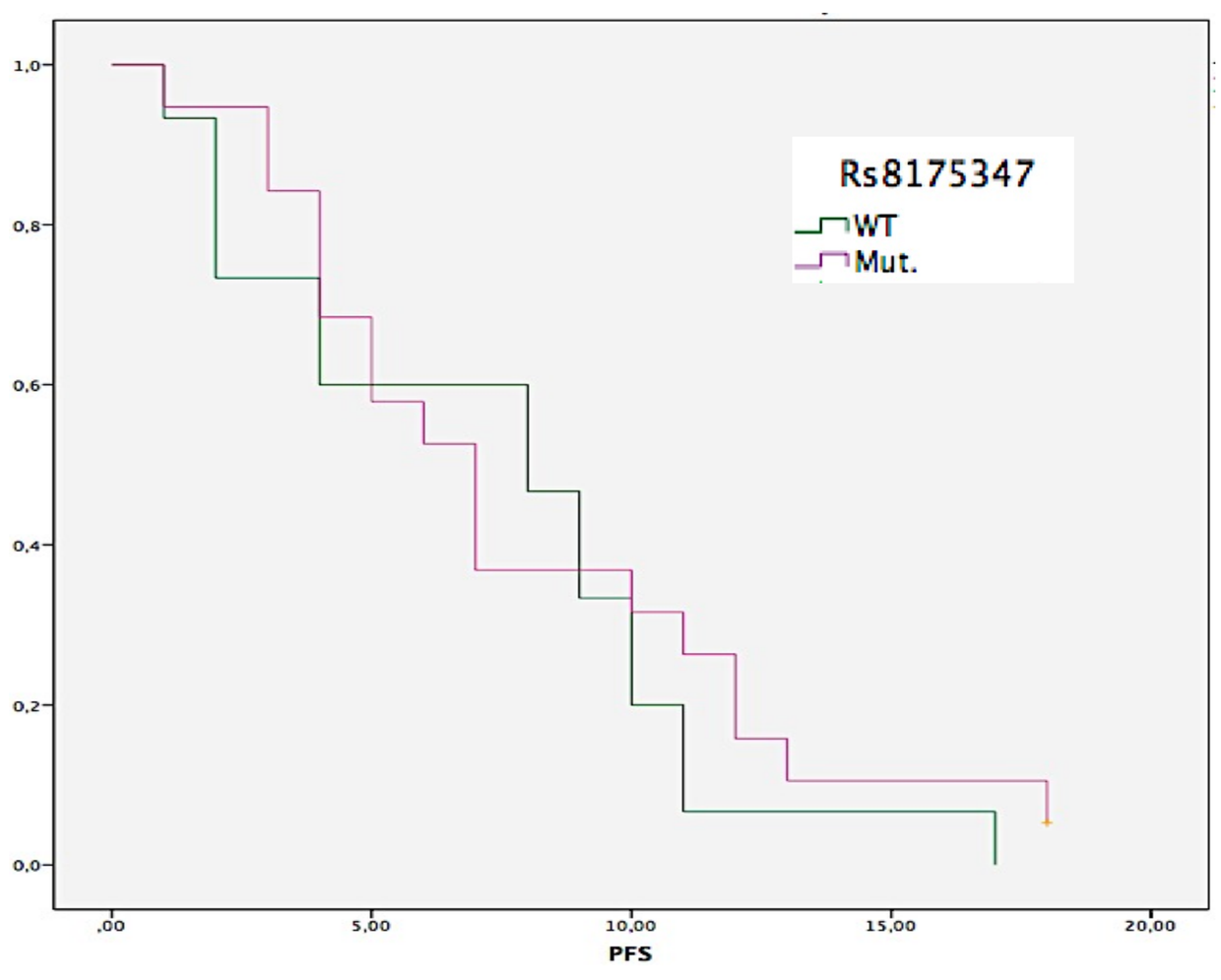
Effectiveness was evaluated as progression free survival (PFS) and overall survival(OS). The rs8175347 UGT1A1 polymorphism were established by analysing the genomic DNA of a peripheral blood sample.
Genetic characterization was carried out using LightClycler® 480 platform and specific allele HybProbe fluorescent probes.

The study had been approved by the hospital's Ethical Committee (CEIC) and classified as EPA-SP by the Spanish Agency for Drugs and Health Products (AEMPS) with GNC-QUI-2013-01 code. Patients were requested to sign an informed consent form prior to the inclusion.

RESULTS

The study included **34 patients**, average age of 60 (27-81), of which 77.7% were male. 90.6% of patients were treated with anti-VEGFR or anti-VEGFA and irinotecan was prescribed as second-line treatment .

The 44.4% of patients showed UGT1A1 wild-type (WT) alleles , while 41.2% and 14.7% had heterozygous and mutated homozygous alleles respectively. After 4 years follow-up median PFS and OS were 7.0 and 23.0 months for patients with any mutated allele in UGT1A1 gene; while for patients with WT genotype were 8.0 *(p= 0.4590)* and 15.0 *(p= 0.6128)* respectly. Moreover median PFS and OS were 4.0 *(p=0.648)* and 44.0 *(p=0.1628)* months for patients with *28/*28 genotype and 7.0 *(p=0.650)* and 23.0 *(p=0.8354)* for heterozygous patients.



CONCLUSIONS

Our results show that **rs8175347 polymorphism in UGT1A1 doesn't influence in irinotecan effectiveness**. Prospective, randomized studies with a large number of patients are required to establish if it exist influence by this polymorphism in the effectiveness of irinotecan therapy.

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