CLINICAL IMPORTANCE OF GENETIC VARIANTS IN CAPECITABINE BIOACTIVATION PATHWAY FOR THE PREDICTION OF RESPONSE IN COLORECTAL CANCER PATIENTS

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BACKGROUND AND IMPORTANCE

Colorectal cancer (CRC) is one of the most prevalent neoplasms worldwide. Capecitabine (Xeloda®), an oral prodrug of 5-Fluorouracil, is one of the standard treatments for patients with advanced CRC (Stages III-IV). In clinical practice, capecitabine response shows high interindividual variability. This variability may be due to the presence of polymorphisms in genes related to the bioactivation of capecitabine to fluorouracil (*CES1*, *CES2*, *CDA*, *TYMP*), that may alter drug bioavailability.

AIM AND OBJECTIVES

To assess treatment response and evaluate the influence of genetic polymorphisms in *CES1* (rs71647871, rs71647871), *CES1P1* (rs rs7187684, rs11861118), *CES2* (rs11075646), *CDA* (rs532545, rs602950, rs2072671), *TYMP* (rs11479) as predictive biomarkers in CRC patients treated with capecitabine.

MATERIAL AND METHODS

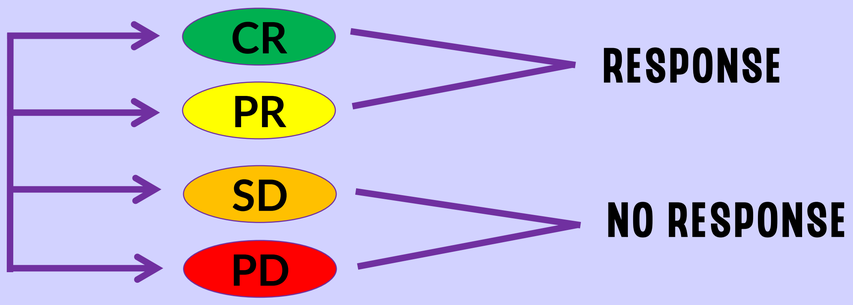
Prospective cohort study in CRC patients under adjuvant capecitabine treatment

DNA extracted from buccal swabs

Genetic variants determined by RT-PCR with TaqMan® probes

RECIST V.1.1

Treatment response was assessed using RECIST criteria v1.1



RESULTS

53 CRC patients were included

43.4% female

63 ±11 Mean age

54.72% had family history of cancer

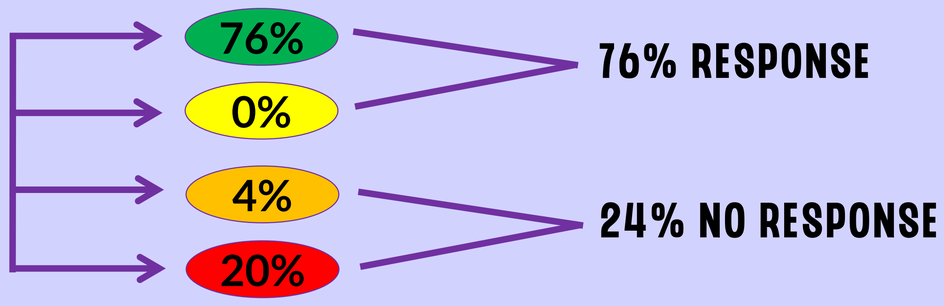
IIIB major cancer stage 57.69%

G2 Main histological grade 54.72%

XELOX Main treatment regimen 58.49%

RECIST V.1.1

Assessed in 50 patients



An association between tumor grade and response was observed (p=0.03), OR = 2,71; CI95% [1.82-189.39] for G1 vs G3 and OR = 2.17; CI95% [1.35-78.39] for G2 vs G3.

No significant association was found between treatment response and the analyzed polymorphisms (p>0.05).

CONCLUSION AND RELEVANCE

CRC patients with lower histological grades are associated with capecitabine positive response. No significant association was found between response and genetic variants in *CES1*, *CES2*, *CDA*, and *TYMP*.

Keywords: *Colon cancer, Capecitabine, Bioactivation, Polymorphisms, Response*

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