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Meeting abstract



# MTHFR (C677T) polymorphism determination in patients with metastatic colon cancer and its effect on the treatment with 5-fluorouracil and folinic acid

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## Background

Fluoropyrimidine-based chemotherapy is the most common treatment for colon cancer, especially the combination of 5-fluorouracil (5FU) and folinic acid (FA). Despite the existence of other treatment choices, more than 50% of the patients in Mexico cannot afford their cost, and the regimen used is still 5FU/FA. However, not every patient responds to this treatment, and it will be useful to have a biological marker that helps to predict the response to 5FU/FA giving the basis for treatment selection. The enzyme called Methylentetrahydrofolate Reductase (MTHFR) plays an important role in the metabolism of folates. The MTHFR substrate is needed for the synthesis of a tertiary complex with 5FU and thymidylate synthase, which inhibits thymine synthesis. A mutation in MTHFR has been identified as one of the most common polymorphisms in the Mexican population (thymine instead of cytosine in gene position 677). This genetic variation has been correlated with a reduction in the enzymatic activity and increases substrate levels, which increases the activity of 5FU. The aim of this study was to evaluate the presence of C667T MTHFR polymorphism and its relation with progression-free survival in patients with metastatic colon cancer treated with 5FU and FA.

## Materials and methods

We studied 29 patients with metastatic colon cancer treated with 5FU/AF at the *Instituto Nacional de Cancerología*, in Mexico City. Healthy mucosa from paraffin blocks were used to obtain DNA and determine C667T polymorphism by PCR and allele specific digestion.

## Results

The following proportions were found: 27% CC homozygous, 52% CT heterozygous and 21% TT homozygous. There was no difference regarding gender, functional status, tumor differentiation, site and number of metastases between the three groups. The median time for progression was: CC 3.43, CT 4.77 and TT 4.80 months, respectively (p = 0.047 log rank). When comparing the non-polymorphic (CC) and polymorphic groups (CT and TT), we observed a greater time to progression (4.80 *vs.* 3.43 months) in the polymorphic group (p = 0.031 log rank).

## Conclusion

Our findings are the first to suggest that the C677T MTHFR polymorphism plays a role as a predictive marker of progression-free survival in patients with metastatic colon cancer treated with 5FU/FA.