

# Letter to the Editor

## Comment on “Tegafur gimeracil oter combined with oxaliplatin for advanced colorectal cancer.” Is it cost effectiveness?

Dear Editor,

Colorectal cancer (CRC) is one of the most commonly diagnosed cancers in the world and remains the second leading cause of cancer death in Western countries. Approximately 50% of patients with CRC present, at diagnosis, distant metastases. From the late 1990s the median overall survival (OS) for patients with mCRC has increased from about 12 months, for those treated with a 5-fluorouracil (5-FU)-based chemotherapeutic regimens, to approximately 18 months with the addition of irinotecan and oxaliplatin<sup>1</sup>. The availability of targeted biologics, in fact, next to the results obtained with chemotherapy alone, has increased the median OS of mCRC to more than 24 months. The use of monoclonal antibodies such as cetuximab, panitumumab and bevacizumab has improved the treatment options and the OS, but, on the other hand, has made the planning of treatment strategies increasingly articulated and complex<sup>2</sup>.

We read with great interest the article by Yang et al<sup>3</sup> regarding the use of tegafur/gimeracil/oteracil, combined with oxaliplatin, for the treatment of mCRC.

They reported data on 41 patients affected by mCRC and subdivided in two groups: 21 treated with tegafur/gimeracil/oteracil combined with oxaliplatin versus a control group (20 patients), treated with capecitabine and oxaliplatin. The Authors also reported the relationship between the K-ras gene mutation status and the expression of peripheral blood cell keratin (CK20 mRNA).

The treatment investigated seems to be safe and efficient but some considerations are necessary: (1) Considering the high incidence of CRC and its significantly impact on public health, we think that to treat only 21 patients, with this “new” combinations of drugs is limited and does not allow clear considerations; (2) No data regarding the mutations status of K-ras gene codons are reported; (3) No figures are reported on progression free survival (PFS) and OS; (4) Are the patients that obtained a partial or complete remission evaluated for surgical approach for the metastatic disease? (5) The data on toxicities are scarce. Moreover, in the “era” of targeted therapy, the use of “new” drugs, as bevacizumab, cetuximab, panitumab are suggested/mandatory<sup>4</sup>. Moreover, current models in cancer treatments are based primarily on validated multifaced approach that includes, often, the newer expensive patented drugs (i.e. tegafur/gimeracil/oteracil). In contrast, the global concept of healthcare systems stimulates that the new therapies should be delivered at equal or lower cost with improved patient outcomes. Personalized medicine includes the genomic tests of each patients and his/her illness into clinical treatments, in order to minimize the toxicity and maximize the benefits thanks to specifically tailored treatments<sup>5</sup>. It is well known that pharmacogenomic tests performed before drug treatment for oxaliplatin-based therapy, lower the overall medical costs and provide a higher quality of life and a longer life expectancy, a method for measuring it is the Quality-Adjusted Life-Years (QALYs) that combines heterogenic information on outcomes, analytical, and cost-effectiveness of each treatment<sup>6,7</sup>.

The future implementation of the methods for measuring the QALYs will guide to personalized treatments and eventually will shift the balance from disease relapse toward disease eradication<sup>8</sup>.

Furthermore, it is understood that the natural history of mCRC is not always the same; patients with mCRC may have various long-term prognosis and respond differently to the same treatment. All this justifies the frantic search for biological, prognostic and predictive markers able to implement the knowledge on the biology of the tumour and guide the clinician in an increasingly personalized decision-making process.

We believe that the combination of tegafur/gimeracil/oteracil and oxaliplatin is efficient but in our opinion more patients are needed to confirm these data.

We think that this kind of study should be designed differently.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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