Reviewer's report

Title: Clinical outcome of metastatic colorectal cancer (MCRC) patients treated with intensive triplet chemotherapy plus bevacizumab (Flr-B/FOx) according to KRAS genotype and disease extension

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Reviewer: Paolo Correale

Reviewer's report:

The manuscript by Bruera et al describes the results of an interesting Phase II trial in metastatic colon cancer patients undergone to a newest polychemotherapy triplet plus bevacizumab (Flr-B/Fox) evaluating the response, PFS and OS according to Kras genotype and disease extension.

In the abstract the result section is very confounding as it describe at some timed a large amount of results which include in the same time mix LL /MCRC ,kras, Braf etc and the reader is lost

Introduction

The authors should describe much more clearly from which kind of study they have extrapolated their analysis (It was a Phase II, III, retrospective analysis or what?) and their objectives.

Activity and efficacy ... according to… on a retrospective study is too ambitious for this kind of study

May be that they evaluated the predictive and prognostic value of several parameters in patients undergone to Flr-B/Fox biochemotherapy

Authors should describe what is bevacizumab and cetuximab etc and in a synthetic way they chose to evaluate kras, braf and disease extension as predictive markers or response to their treatment containing bevacizumab.

They should explain why Kras BRAF genotype status was taken in consideration in cancer patients undergone bevacizumab based treatment. It should not be considered as a statement that activating Kras mutation is a negative prognostic/predictive factor in this patient setting.

The sentence increased survival over doublet requires reference

Role of Liver metastasectomy subset and description should be included in the discussion concerning statistical analysis of that subgroup of patients who could receive surgery

Methods
Authors should describe treatment protocol, ethical procedures and clinical study design not just the treatment

Kras and BRAF genotypic analysis should be shortened

Statistical analysis should be described and referenced

Results

These interesting results are presented in inconsistent manner and should be reorganized

All of the patients should be considered in the analysis further subgroup analysis should be performed for liver limited patients undergone surgery after treatment.

I suggest a better use of table and use of COX analysis for subgroups

LL or LO should be included as parameters and not as separate setting of patients

In the survival curves there is a trend to difference this should be commented

Even though PFS and OS are not significant within their patient group the results should be expressed as RISC RATIO and P value showed. In this kind of study a trend may be stimulation for further studies with a greater patient sample

Discussion

Is too long with conclusions which are not clear.

The manuscript should be shortened reorganized. The authors should make a much better effort to clarify the importance of this study.

Declaration of competing interests:

I declare that I have non competing interests correlated to the above entined study