Peer Review File

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Reviewer A

Comment 1:

The manuscript describes in a clear, concise and exhaustive way the state of the art of studies regarding the use of KRAS inhibitors in advanced adenocarcinoma therapy, offering the reader insights for new studies. In my opinion, the commentary can be accepted for publication in the present form.

Reply 1: We thank the reviewer for this positive feedback.

Reviewer B

Comment 1: Good review, just minor points should be discussed.

Reply 1: We thank the reviewer for this positive feedback.

Comment 2:

KRAS G13 mutations should be mentioned that account for 10% and are resistant to G12C inhibitors.

Reply 2: We have added those clarifications page 2 line 49, page 3 line 60 and page 3 line 64.

Comment 3:

The combinations of KRAS inhibitors with immunotherapy may result in severe liver toxicity.

Reply 3: We have added those clarifications page 5 line 154.

Comment 4

For the KRYSTAL-14 study it is not forbidden to mention the BI-1701963 SOS1 inhibitor, the first one of its class in clinical trials.

Overall, it became clear that KRAS G12C inhibitors alone are only partially active for less than one year and cannot prolong survival/or studies could not yield results in respect to OS.

Reply 4: We agree with this comment. We have added those clarifications page 3 line 89 and page 6 line 183.