Author's response to reviews

Title: Antitumor activities of ATP-competitive inhibitors of mTOR in colon cancer cells

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Dear Editor,

We would like to submit the manuscript entitled “Antitumor activities of ATP-competitive inhibitors of mTOR in colon cancer cells” for publication in BMC Cancer as a research article.

Targeting mTOR in colon cancer is a promising approach. Indeed, components of mTOR signaling pathway are often activated in colon cancer and several experimental studies have demonstrated that the inhibition of mTOR using rapamycin reduces the growth of colon cancer.

Recently, mTOR based cancer therapies have entered a new era. A new class of inhibitors that act as ATP-competitive inhibitors has been developed. In contrast to rapamycin they block both mTORC1 and mTORC2 and are therefore theoretically more potent than rapamycin. The anticancer efficacy of ATP-competitive inhibitors of mTOR in colon cancer cells has however only been partially characterized.

In this study, we have evaluated the anticancer activities on colon cancer cells of two ATP-competitive inhibitors of mTOR; PP242 that blocks mTORC1 and mTORC2 and NVP-BEZ235, a dual PI3K/mTOR inhibitor. Overall our results show that ATP-competitive inhibitors of mTOR have a stronger and broader antitumor activity compared to rapamycin. They also show that the anticancer efficacy of these inhibitors is enhanced by the simultaneous inhibition of the MEK/MAPK signaling pathway. Our study therefore provides a rationale for the use of ATP-competitive inhibitors in colon cancer.

Our manuscript is not under consideration for publication in another journal, and has not already been published elsewhere. The manuscript is also original and does not contain any material that infringes existing copyrights.

We trust that this study will be of interest to the readership of BMC Cancer and we hope that you will find it satisfactory following review.

Yours sincerely,

Olivier Dormond, MD-PhD