Letter to the Editor from Colle et al

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Letter to the Editor from Colle *et al*

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ABSTRACT

In their article, Fucà *et al* highlight that early tumor shrinkage and depth of response predict the prognosis of patients with metastatic colorectal cancer (mCRC) microsatellite instability (MSI-H)/deficient mismatch repair (dMMR) treated by immune checkpoint inhibitors (ICI). We are surprised that no cases of pseudoprogression (PSPD) were reported in their study. PSPDs were described under ICI in patients treated for MSI/dMMR mCRC. In a cohort of 123 patients treated with anti-PD1±antiCTL-4 for MSI/dMMR mCRC, we reported 12 patients with PSPD, representing 10% of the cohort. Of 12 patients with PSPD, 8 secondary achieved an objective response and were alive and free of progression at the data lock. Conversely, in Fucà's article, no PSDP was observed and the patients with primary radiological progression (21.7%) had a poor overall survival. These differences between the two series could be probably explained by the following points. First, Fucà *et al* use RECIST 1.1 criteria for radiological evaluation. Second, the first imaging was done after 8–9 weeks of treatment in Fucà's article, which may be late to detect PSPD. In conclusion, if the first evaluation is made during the first 3 months of treatment, using iRECIST criteria seems mandatory to avoid stopping treatment prematurely, especially in patients receiving anti-PD1 alone.

Dear Editor,

We read the article written by Fucà *et al*[1] with great interest. In their article, Fucà *et al* highlight that early tumor shrinkage (ETS) and depth of response predict prognosis of patients with metastatic colorectal cancer (mCRC) microsatellite instability (MSI-H)/deficient mismatch repair (dMMR) treated by immune checkpoint inhibitors (ICI). In this population, ETS and depth of response could help to better select patients for intensification/de-intensification and in our opinion, to better define the duration of treatment.

We would like to question the authors on the issue of pseudoprogression (PSPD). The existence and frequency of such a phenomenon is crucial in terms of clinical practice, as it would support the continuation of ICI beyond progression and the systematic use of iRECIST criteria to detect it, especially during the three first months of therapy. The major change from RECIST 1.1 to iRECIST is the concept of "unconfirmed progressive disease' (iUPD). Confirming PD after iUPD requires new imaging with further progression.[2]

We are surprised that no cases were reported in their study.[1] PSPDs were described under ICI in patients treated for MSI/dMMR mCRC, more frequently with anti-PD1 alone compare to anti-PD1+antiCTL-4.[3 4] In a cohort of 123 patients treated with anti-PD1±antiCTL-4 for MSI/dMMR mCRC, we reported 12 patients with PSPD, representing 10% of the cohort. Imaging was retrospectively and centrally reviewed by two radiologists according to RECIST 1.1 and iRECIST. PSPD was defined as an unconfirmed progressive disease according to iRECIST. All PSPDs were observed among patients with primary radiological PD (PD according to RECIST 1.1 criteria occurring within the first 3 months of treatment). Of 12 patients with PSPD, 8 secondary achieved an objective response and were alive and free of progression at the data lock.[2] Conversely, in Fucà's article, no PSDP was observed and the patients with primary radiological progression (21.7%) had a poor overall survival.

These differences between the two series could be probably explained by the following points. First, Fucà *et al* use RECIST 1.1 criteria for radiological evaluation which do not allow the detection of PSPDs. In our cohort, the majority of patients with radiological PD per RECIST 1.1 continued ICIs beyond PD and had a confirmation imaging according to iRECIST criteria.[2] Second, in our cohort, median time to first evaluation was 6 weeks whereas the first imaging was done after 8–9 weeks of treatment in Fucà's article, which may be late to detect PSPD.[1 2]

In conclusion, if the first evaluation is made during the first 3 months of treatment, using iRECIST criteria seems mandatory to avoid stopping treatment prematurely, especially in patients receiving anti-PD1 alone.

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Competing interests TA reports consulting/advisory role and or received honoraria from Amgen, Bristol-Myers Squibb, Chugai, Clovis, Gristone Oncology, HalioDx, MSD Oncology, Pierre Fabre, Roche/Ventana, Sanofi, Servier, and GSK and has received travel, accommodations, and expenses from Roche/Genentech, MSD Oncology, and Bristol-Myers Squibb.

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