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Dear Editor,

We thank Dr Barel et al. for their letter concerning our article [1]. In this letter, the authors reported their experience of 1264 RAS tests performed between 2015 and 2017 in a French area of Brittany using a massively parallel sequencing method. Even if the mean duration between receipt of tumour samples by the Molecular Genetics platform and the transmission of the RAS test report was shorter than that we previously reported (11.03 days versus 19.5 in our study), it exceeds anyway the recommended duration between test request and results feedback [2-4]. Indeed, as mentioned by the authors, this delay does not take into account the time between the request of RAS test by physicians and the receipt of tumour samples by the molecular genetics platform, which may take a long time, especially when tumour samples have been archived in other regional institutions than the Hospital where the molecular genetics platform is located. Moreover, it is noteworthy that there was a significant increase in turnaround time of the RAS test performed in their institution between 2015 and 2017, for a reason that would be interesting to know.

In accordance with our data, results of Barel et al. therefore confirm that despite many efforts and a well-organised nationwide network of molecular genetics platforms, the delay to obtain

RAS mutational status in France remains long and has to be reduced to better match with clinical practice and with the therapeutic management of metastatic colorectal cancer patients. In order to reduce the delay of RAS test procedure without altering the quality of mutation detection, Barel et al. propose in their letter an alternative diagnostic strategy based on a first line molecular analysis with the fully automated real-time PCR Idylla™ system, which would be secondarily supplemented by a massively parallel sequencing only in non-mutated cases. Indeed, Idylla™ was shown to be faster than other existing molecular tests for BRAF and EGFR mutations detection in metastatic melanoma and non-small cell lung cancer [5-7]. It also has the advantage of allowing a mutational analysis directly on FFPE tumour tissue with a good or increased sensitivity compared to other standard molecular tests in different types of cancers including colotectal cancer [5-8]. Finally, Idylla™ system is an easy-to use test requiring less than five minutes of hands on time.

Therefore, we agree with the authors that Idylla™ method may be a way to reduce in part the turnaround time of RAS test. However, it is important to underline the higher costs generated by this full-automated system in centres with high volume of activity. Furthermore, Idylla™ is not able to reduce the time between request of the RAS test by physician and the receipt of tumour tissue by the molecular genetics platform that may be long (mean duration of 9.7 days in 2011 and 7.7 days in 2014 in our French experience) [1, 9] as already mentioned.

To conclude, Idylla™ may be currently an interesting alternative to reduce the turnaround time of RAS test but we think that the search and validation of other methods (like liquid biopsy) that could bypass the time-consuming and limiting steps of unarchiving, selecting and dispatching samples to the molecular genetics platform is of greater interest to reach this goal.

Authors' disclosures of potential conflicts of interest:

AL: Merck, Shire, Ipsen (board member), Merck, Amgen, Roche, Lilly, Novartis (lecturer).
JLM: Merck, Amgen (board member and lecturer), Sanofi (lecturer)
JCS: Merck, Amgen, MSD, BMS, Roche, Astra Zeneca, Pfizer, Boehringer Ingelheim (board member)
PA: Roche, Merck (board member) Sanofi, Amgen, Lilly (lecturer)
PLP: Merck, Boehringer-Ingelheim, Pfizer, Astra Zeneca, Biocartis (board member), Lilly, Sanofi, Roche, Astra-Zeneca (lecturer)
MD: Roche, Merck Serono, Amgen, Lilly, Sanofi, Novartis, Servier, Ipsen (board member and lecturer), Sanofi (grant)

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