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**REPLY:** We thank Seban et al. for their interest and their insightful comments on our study (*1*). We very much agree with them on the remarkable potential role of the quantitative parameters derived from $^{18}$F-FDG PET/CT in predicting response to immune checkpoint inhibitors (ICIs). Furthermore, as has emerged from the latest publications, the combination of ICIs with circulating biomarkers such as neutrophil-to-lymphocyte ratio, derived neutrophil-to-lymphocyte ratio, circulating tumor cells, and cell-free DNA can provide complementary information and appears promising in predicting clinical outcomes.

However, we believe that some aspects require more thorough clarification. On the basis of the 2 time points (baseline and 8 wk after ICI start) used in our study to define hyperprogressive disease (HPD) (*1*), Seban et al. affirm that patients might already have been progressing rapidly before the initiation of ICI. Indeed, most classifications define HPD by using tumor growth rate (TGR), which considers the tumor growth during ICI treatment in comparison with a reference period immediately before ICI. Nevertheless, this computation of TGR is not free from drawbacks and might underestimate the real number of patients experiencing HPD, primarily because the assessment of new lesions and nonmeasurable disease is not considered in the definition of TGR (whereas we know quite well that progressive disease often is driven by the appearance of new lesions or an increase in nontarget lesions) and secondarily because it can be difficult to reach a TGR doubling in tumors with a higher TGR before treatment. For instance, an increase from 60% before ICI to 80% during ICI treatment will not configure HPD on the basis of the above criteria, despite a significant absolute increase in tumor burden. In other words, using TGR might exclude HPD in tumors with a large tumor burden before ICI. Similarly, nonmeasurable lesions, for example, lymphangitis, bone metastases, and pleural or peritoneal effusions, might not be represented in the whole tumor burden based on pure morphologic criteria (RECIST). In this regard, we must not forget that a high number of metastatic sites can be as valid surrogate of tumor burden, as has emerged in previous studies (*2*). Along with the TGR clinical limits, there is also a logistical limitation: TGR computation requires a prior CT scan, which is sometimes difficult to retrieve; for example, a prior CT scan could not be retrieved in 30% of the cases in the study of Matos et al. (*3*). Therefore, in our criteria we also included time to treatment failure, which can be clinically useful when TGR cannot be evaluated.

Finally, Seban et al. highlight the high prevalence of HPD in our study, that is, 30%, compared with other series. Besides the different criteria used in defining HPD, most other studies include all tumor types, whereas our cohort was limited to non–small cell lung cancer patients. When only this tumor type is considered, our results are quite consistent with those of other studies dealing with a similar patient cohort (*2*).

In the end, what comes out of our study is that we were able to identify a subgroup of patients with a worse outcome during ICI therapy, and this ability alone is relevant evidence independently of whether it resulted from the treatment itself or the intrinsic behavior of the tumor. In our opinion, distinction between fast and accelerated progression is still premature and is a purely semantic license so far, because methods proposed for HPD have their own limitations. Therefore, a universally accepted consensus on how to define and measure HPD is necessary, and that need for a universally accepted consensus is in line with our conclusions and those derived by Seban et al. in their letter to the editor.

## DISCLOSURE

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# $SUV_{max\text{-}V}$ for Assessing Treatment Response in $^{18}$F-FDG PET Imaging of Patient-Derived Tumor Xenografts Involving Triple-Negative Breast Cancer

**TO THE EDITOR:** In the preclinical arm of a coclinical trial, Savaikar et al. recently optimized $^{18}$F-FDG PET imaging biomarkers of response to a combined docetaxel and carboplatin therapy in patient-derived tumor xenografts involving triple-negative breast cancer (*1*). Twenty-one necrotic-core-phenotype tumors and