A Response to the Letter to the Editor

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A Response to the Letter to the Editor: Comment on "Clinical Utility of Circulating Tumor DNA in Patients With Advanced KRAS(G12C)-Mutated NSCLC Treated With Sotorasib"

To the Editor:

We thank Jiang and Zhang for their interest in our study and appreciate their suggestions for future research. We acknowledge that our study has certain limitations, including the limited sample size. We agree that the limited sample size may restrict the generalizability of our findings to a broader patient population. However, our cohort's baseline characteristics and clinical outcomes were comparable to those reported in other U.S. and European real-world cohorts evaluating sotorasib.[1–4] Owing to the limited sample size, we did not conduct multivariate analyses. Therefore, we agree that future studies with larger sample sizes are necessary to evaluate the impact of potential confounders on our findings.

However, we disagree with the statement that our study lacked sufficient long-term follow-up data. The median overall survival of the sotorasib arm in the CodeBreaK 200 trial was 10.6 months,[5] and by the data cutoff, 75% of patients in our cohort had already progressed, and 66% had died. Nine patients were still on sotorasib at data cutoff, with a median follow-up duration of 17.7 months. Therefore, we believe that our median follow-up duration of 15.1 months was adequate to address our primary study questions. Jiang and Zhang also suggested that the lack of long-term follow-up data hindered the assessment of safety of our study results. However, assessing the safety of sotorasib was outside the scope of this study. We have previously reported on the occurrence of severe hepatotoxicity during sotorasib treatment in this population.[6]

Lastly, we acknowledge the suggestion to evaluate the actionability and cost-effectiveness of our findings in clinical settings. Although we agree that these are important considerations, our observational study is not suitable for assessing cost-effectiveness. The first step would be to determine whether pretreatment circulating tumor DNA and molecular response can effectively guide interventions, such as adjusting the frequency of radiological response assessments or treatment escalation/de-escalation in clinical trials. If that is indeed the case, subsequent studies would be necessary to evaluate the cost-effectiveness of circulating tumor DNA-guided adaptive treatment strategies.

CRediT Authorship Contribution Statement

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