In Reply We appreciate the comments from Mo et al regarding the overall survival (OS) of patients with stable brain metastases (BMs) at baseline in the exploratory subgroup analysis of HER2CLIMB. The HER2CLIMB randomized clinical trial was not designed to conduct a formal comparison between treatment groups or statistically powered for this subgroup. The estimated hazard ratio (HR) across all patients (n = 291) with BMs at baseline showed a 40% reduction in the risk of death in the tucatinib-combination group (HR, 0.60 [95% CI, 0.44-0.81]; P < .001). While the relatively small number of patients in the subset with stable BMs (n = 117) limits the power to draw definitive conclusions, results were consistent with the overall BM population, including a similar magnitude of benefit (30% reduction in the risk of death in the tucatinib-combination group; HR, 0.70 [95% CI, 0.42-1.16]; P = .16). Additionally, the median OS was 5.2 months longer, and the 1-year and 2-year OS rates were numerically higher in the tucatinib-combination group in patients with stable BMs.

Although the EMILIA trial demonstrated that trastuzumab emtansine (T-DM1) was associated with improved OS compared with lapatinib plus capecitabine in patients with treated BMs, the survival benefit of EMILIA cannot be directly compared with that of HER2CLIMB because the patient populations for the 2 trials were different, as were the treatment regimens. The exploratory analysis for the EMILIA trial included 95 patients who had stable BMs and required prior therapy with trastuzumab and a taxane only. Patients with active BMs were excluded from EMILIA. The HER2CLIMB trial subgroup analysis included 291 patients with both stable and active BMs. In addition, all patients enrolled in HER2CLIMB were previously treated with T-DM1. The HER2CLIMB regimen included dual ERBB2 (HER2) blockade with an ERBB2-targeted tyrosine kinase inhibitor and trastuzumab, in addition to capcitabine, further differentiating it from the lapatinib-capecitabine regimen studied in EMILIA. We believe that the OS results accurately reflect the patient population studied.

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CORRECTION

Error in Supplement: In the Original Investigation titled “Avelumab Plus Talazoparib in Patients With BRCA1/2- or ATM-Altered Advanced Solid Tumors: Results From JAVELIN BRCA/ATM, an Open-Label, Multicenter, Phase 2b, Tumor-agnostic Trial,” published online November 17, 2022, there were errors in Supplement 2. eTable 4 was incorrect and has been replaced. This article has been corrected.1


Errors in Figure 3: The Original Investigation titled “Association of MGMT Promoter Methylation With Survival in Low-grade and Anaplastic Gliomas After Alkylating Chemotherapy,” published online May 18, 2023, included errors on the x-axis of each panel in Figure 3; the unit of measure should be time in years, not months. eFigures 1, 2, 5, and 8 in Supplement 1 were also updated. This article has been corrected online.