Aim: LY2510924, an antagonist to the chemokine receptor CXCR4, inhibits tumor growth and metastasis in xenograft models. A Phase I trial with LY2510924 demonstrated an acceptable safety profile with a robust pharmacodynamic profile. This open-label phase II trial evaluated the clinical benefit of carboplatin/etoposide plus LY2510924 versus carboplatin/etoposide, the standard of care (SOC), as a first-line therapy in patients (pts) with extensive-stage SCLC.

Methods: Treatment-naive extensive-stage SCLC pts were randomized 1:1 to receive six 21-day cycles of either LY+SOC (Arm A) or SOC (Arm B). A 20-mg dose of LY2510924 was self-administered by the patient subcutaneously on days 1-7 of each cycle. Efficacy was evaluated using RECIST v. 1.1; adverse events were evaluated using MedDRA v. 14.0. The primary end point, progression-free survival (PFS), was analyzed using a stratified log-rank test. Secondary end points were objective response rate (ORR), duration of overall response (DoR), overall survival (OS), and safety.

Results: Median follow-up time was 8.4 months. Pt characteristics were comparable in Arm A (N=47) and Arm B (N=43). Median PFS for Arm A was 5.88 months (95% confidence interval 4.83, 6.24) and Arm B 5.85 months (4.63, 6.51), p=0.9806. ORRs were 74.5% and 81.0%; median DoR were 4.83 months (3.58, 5.09) and 4.67 months (3.32, 5.78) for Arms A and B, respectively. The median OS was 9.72 months (6.64, 11.70) and 11.14 months (8.25, 13.44), p=0.1120 for Arms A and B, respectively. Grade 3/4 treatment-emergent adverse events>8% in Arm A included neutrophil count decrease (40% vs. 56%), anemia (30% vs. 33%), platelet count decrease (23% vs. 16%), lung infection (11% vs. 0%), white blood cell count decrease (9% vs. 9%), and febrile neutropenia (9% vs. 2%) (Arm A vs. Arm B). No pts died due to adverse events.

Conclusions: No improvements in PFS, ORR, DoR, or OS in treatment-naive extensive-stage SCLC pts were observed when LY2510924 was added to SOC. The addition of LY2510924 to SOC appeared to increase incidence of lung infection and febrile neutropenia; otherwise, the overall toxicity profile was acceptable in this patient population.

Disclosure: O. Hamid: Oday Hamid is employed by Eli Lilly, the sponsor of the study and owns stock in the company; J.R. Stille: Employee of Eli Lilly and Company; J. Polzer: Employee of Eli Lilly and Company. S. Roberson: Employee of Eli Lilly and Company. All other authors have declared no conflicts of interest.