C-15

Phase II study of frontline maintenance rucaparib in combination with nivolumab in extensive stage small cell lung cancer

Aman Chauhan[1], Jill Kolesar[2], Donglin Yan[2], Zhonglin Hao[2], Ronald McGarry[2], John Villano[2], Ralph Zinner[2], Ashish Maskey[2], Jordan Miller[2], Timothy Mullett[2], Aman Khurana[2], Xitong Zhou[2], Garima Gupta[2], Daniel Flora[3], Colleen Darnell[3], Richard O'Neil[4], Charles Kunos[2], Lowell Anthony[2], Susanne Arnold[2].

[1]Sylvester Comprehensive Cancer Center, University of Miami; [2]Markey Cancer Center, University of Kentucky; [3]St Elizabeth Healthcare, Edgewood, KY; [4]Prisma Health Cancer Institute, Greenville, SC.

BACKGROUND

Immune checkpoint inhibitor (ICI) maintenance therapy is the standard of care for frontline management of extensive-stage small cell lung cancer (ES SCLC). However, the overall survival benefit of the addition of ICI maintenance to frontline ES SCLC treatment is modest and further improvement is needed. We hypothesized that the addition of poly (ADP-ribose) polymerase inhibition to ICI maintenance therapy for patients with platinum-sensitive ES SCLC could improve the antitumor efficacy of ICI.

METHODS

A single-arm, investigator-initiated phase II trial (NCT03958045) enrolled patients with platinum-sensitive ES SCLC who received frontline maintenance nivolumab 480 mg IV every 4 weeks, and rucaparib, 600 mg PO twice a day after the completion of 4-6 cycles of the platinum doublet. The primary outcome was median progression-free survival. Secondary endpoints included assessment of objective response and adverse effects (AEs) per CTCAE 5.0. Correlative studies included pretreatment and during-treatment immune assays and circulating tumor DNA TP53 mutation status.

RESULTS

42 patients consented, and 33 met eligibility criteria and were treated. All patients received 4-6 cycles of frontline platinum doublet and had at least a partial response by RECIST at enrollment. In the 33 participants, the most common grade 3 and 4 AEs (at least possibly related) were hypokalemia (3%), hyponatremia (3%), elevated alanine aminotransferase (3%), neutropenia (3%) and leukocytopenia (3%). No grade 5 AE was noted. The median PFS (mPFS) was 3 months from the time of enrollment on frontline maintenance (post platinum doublet). The mPFS was 11 months from cycle 1 of the platinum doublet. Overall, 89.8% of patients were alive at 12 months, and 54.4 % of patients were alive at 24 months from the start of the platinum doublet. Currently, 2 patients are on active treatment, and the other two have completed study treatment and are on observation with stable disease.

CONCLUSIONS

Maintenance rucaparib combined with immune checkpoint inhibition was tolerable and showed promising activity after completion of frontline chemotherapy in platinum-sensitive extensive-stage small cell lung cancer patients.