TPS8615 **Poster Session**

Dares: A phase II trial of durvalumab and ablative radiation in extensive stage small cell lung cancer.

Aditya Juloori, Gregory Gan, Jun Zhang, Mohamed E. Abazeed, Jared H Hara, Andrew Baschnagel, Anne M. Traynor, Michael F. Bassetti, Marina Chiara Garassino, Jyoti D. Patel, Steven J. Chmura, Christine M. Bestvina; University of Chicago Medical Center, Chicago, IL; University of Kansas Medical Center, Kansas City, KS; University of Kansas Medical Center (KUMC), Westwood, KS; Northwestern University, Chicago, IL; University of Chicago, Chicago, IL; Department of Human Oncology, Madison, WI; University of Wisconsin-Madison Carbone Cancer Center, Madison, WI; University of Wisconsin Carbone Cancer Center, Madison, WI; Department of Medicine, Section of Hematology/Oncology, Knapp Center for Biomedical Discovery, The University of Chicago, Chicago, IL; Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL

Background: Most patients diagnosed with small cell lung cancer have extensive stage disease (ES-SCLC) at presentation, portending a poor prognosis with median survival rate of 9 - 11 months and a 2-year overall survival (OS) of less than 5%. Checkpoint inhibitors have recently transformed the landscape for first-line treatment for ES-SCLC patients with the CASPIAN and IMpower133 trials demonstrating an OS benefit with the addition of Durvalumab and Atezolizumab to chemotherapy, respectively. Hypofractionated ablative radiation therapy (RT) provides effective local metastasis control. Increasing evidence suggests that apart from its direct effects, ablative RT can trigger the innate and adaptive immune system. Beyond synergistic mechanisms of modulating the immune response, direct tumor debulking by radiation may also be particularly well suited as an adjunct to immunotherapy. Such upfront cytoreduction can relieve tumor-related immunosuppression and prevent early treatment failure at sites of initial involvement. Prior studies have demonstrated OS and PFS benefits to the addition of local therapy in metastatic non-small cell lung cancer. Multi-site ablative RT has also been shown to be safe in the setting of immunotherapy in multiple published prospective trials. We hypothesize that the addition of RT to chemotherapy and Durvalumab for newly diagnosed ES-SCLC patients will improve PFS. **Methods:** 49 patients will be enrolled across four institutions in this phase II clinical trial. Treatment naive ES-SCLC patients with PS 0-2 who have at least one RECIST measurable lesion meeting criteria for ablative radiation will be eligible for enrollment. Patients with symptomatic brain metastasis will undergo cranial radiotherapy prior to starting on trial. Patients will be treated with four cycles of platinum/etoposide and Durvalumab. During cycle 2, patients will undergo ablative radiation therapy to 1 – 4 sites of extracranial disease. Radiation dose and organ at risk (OAR) constraints are consistent with NRG BR001. During planning, OAR constraints will be prioritized over tumor coverage. Following four cycles of chemotherapy and Durvalumab, patients will continue with maintenance Durvalumab 1500 mg q28 days until progression, toxicity, or study withdrawal. The primary endpoint is PFS. Using a historic control of 5 month median PFS with chemo/immunotherapy from CASPIAN and IMpower133, we hypothesized that the addition of ablative RT would improve the PFS from 5 months to 8 months. sample size of 49 patients was calculated for 80% power with alpha of 0.1. Secondary endpoints include overall survival, time to second line therapy, response rate, and rate of grade 3+ adverse events. Peripheral blood, stool, nasal, and buccal samples will be obtained at baseline, after RT, and at the time of progression and/or immune-related toxicity and will be used for exploratory analysis. NCT05068232. Clinical trial information: NCT05068232. Research Sponsor: AstraZeneca.