Durvalumab added to standard chemotherapy improved overall survival in mesothelioma

Phase 2 trial PrE0505 selected for oral presentation at ASCO 2020; data signals the combination should advance to a randomized phase 3 study

Philadelphia, May 20, 2020—PrECOG, LLC is reporting clinical efficacy and biomarker analyses from its single-arm phase two study PrE0505 for the initial treatment of patients with malignant pleural mesothelioma. The trial evaluated adding durvalumab, an immune checkpoint antibody targeting PD-L1, to chemotherapy consisting of pemetrexed and cisplatin (Pem-Cis), the only FDA approved regimen, in 55 patients of any histologic subtype. The study met its primary endpoint with a median overall survival (OS) rate of 20.4 months (one-sided P=0.0014) as compared to historical control (Vogelzang et al. J Clin Oncol 2003) of 12.1 months. OS rates at 12 and 24 months were 70.4% and 44.2%, respectively. The combination was well-tolerated with no unexpected toxicities.

The American Society of Clinical Oncology (ASCO) is highlighting these data in an oral session (Abstract 9003) at its virtual Annual Meeting, May 29-31.

“Durvalumab plus standard chemotherapy delivered a promising median overall survival rate for patients with previously untreated, inoperable malignant pleural mesothelioma,” said lead investigator Patrick Forde, MD, of Johns Hopkins University, pictured. “The data signal us to move forward with a phase three study.”

PrE0505 study investigators at 15 US clinical sites rapidly enrolled 55 patients into the study over 13 months, between June 2017 and June 2018.
Eligible patients received the combination of pemetrexed (500 mg/m²) and cisplatin (75 mg/m²) with durvalumab (1120 mg) every three weeks for up to six cycles. Substitution of carboplatin (AUC 5) for cisplatin was permitted if toxicity occurred during the initial treatment. After up to six cycles of concurrent chemotherapy with durvalumab, patients who had a partial response or stable disease could continue on durvalumab until disease progression. The maximum duration of durvalumab treatment was 12 months from the start of therapy.

“This is a remarkable result in mesothelioma, and warrants confirmation in a randomized phase three trial, which is already in the planning,” said Peter J. O’Dwyer, MD, CEO and Chair, PrECOG, LLC, pictured.

The secondary endpoints in the PrE0505 trial are safety and tolerability, PFS, and objective response rate. PFS at six months was 69.1%. Best responses to treatment were measured by the RECIST criteria and included 31 patients (56.4%) with partial response, 22 (40%) with stable disease, and one (1.8%) who progressed during the evaluation period. One patient was not evaluable for response. All patients were evaluated for safety, and there were no unexpected toxicities. Adverse events reported by investigators as associated with durvalumab were generally mild in severity (Grade 1 and 2).

In analyses of exploratory objectives, researchers saw no statistically significant associations between tumor sample expression of PD-L1 or tumor mutational burden and progression or survival. They observed neoantigen-specific T-cell responses in some selected cases. Analytical work for the study is ongoing.

The PrE0505 study was conducted independently by PrECOG, LLC, with funding from AstraZeneca Pharmaceuticals LP.

The clinicaltrials.gov record for PrE0505 is NCT02899195.

About PrECOG

PrECOG, LLC is a cancer research group formed as a not-for-profit limited liability company in 2006 by the ECOG Research and Education Foundation, Inc. It operates outside of the National Cancer Institute’s federal funding structure, known as the National Clinical Trials Network. A central focus of PrECOG is to support the overall scientific research goals of the ECOG-ACRIN Cancer Research Group. PrECOG aims to reduce the burden of cancer by advancing research in all aspects of cancer care and thereby improve survival, patient benefit, and quality of life. The current PrECOG portfolio includes phase one and two multi-center trials, as well as US-based and multi-national phase three trials. For further information, please visit www.precogllc.org and www.ecog-acrin.org, and follow us on Twitter @PrECOGonc and Facebook.