Phase II trial shows addition of durvalumab to radiation does not improve outcomes over cetuximab for HNSCC patients

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The Phase II results of the NRG Oncology HN004 trial indicate that radiotherapy (RT) with the PD-L1 inhibitor durvalumab did not improve progression-free survival (PFS) and led to significantly higher rates of locoregional failure (LRF) when compared to RT + cetuximab in patients with locoregionally advanced head and neck squamous cell carcinoma (HNSCC) that have a contraindication to cisplatin. These findings were presented during the plenary session at American Society for Radiation Oncology (ASTRO) annual meeting held in San Antonio, Texas. This was one of four NRG Oncology papers presented during the 2022 ASTRO plenary session.

NRG-HN004 accrued 186 eligible patients who were 18 or older with previously untreated stage III-IVB squamous cell carcinoma of the larynx, hypopharynx, oral cavity, p16-oropharynx/unknown primary, or selected stage I-II p16-positive oropharynx/unknown primary with a contraindication to cisplatin. The primary phase II endpoint was PFS with a planned sample size of 234 patients and 69 PFS events (hazard ratio of 0.65, 80% power, and 1-sided alpha 0.20).

"While this trial did not meet its primary aim, the results are crucial in establishing the feasibility of accrual of a trial of this size, for this unique population using the specific eligibility criteria that were established for the first time," stated Loren K. Mell, MD, Vice Chair of Clinical and Translational Research at the University of California San Diego School of Medicine and the lead author of this NRG-HN004 abstract.

Patients who were eligible for NRG-HN004 were randomly assigned 2:1 to receive RT at 70 Gy in 35 fractions for 7 weeks with either durvalumab or cetuximab. The durvalumab arm included 123 patients versus 63 patients on the cetuximab arm.

The trial closed to accrual in July 2021 with 186 randomized patients, following an interim futility analysis. In June 2022 the study reached the required number of PFS events, which initiated the protocol-specified phase II primary endpoint analysis. At this time, 87% of patients in the durvalumab arm completed RT versus 89% of patients in the cetuximab arm. In the durvalumab arm, 89% of patients completed concurrent durvalumab and 63% completed adjuvant durvalumab. 81% of patients on the cetuximab arm completed 7 or greater cycles of cetuximab. The median follow-up was 1.2 years.

Results indicated 2-year PFS rates were 51% for patients treated with durvalumab versus 66% for patients treated with cetuximab. Two-year LRF rates were 32% with durvalumab versus 15% with cetuximab. Two-year overall survival and distant metastasis rates were 70% and 9% with durvalumab and 78% and 11% with cetuximab, respectively. However, grade 3 or higher adverse events, including dysphagia, mucositis, and dermatitis, were experienced by 69% of patients in the durvalumab arm versus 79% in the cetuximab arm.

Based on these findings, NRG-HN004 has been permanently closed to accrual and will not move to the phase III portion of the study.

"As there is currently no well-defined standard of care for cisplatin-ineligible HNSCC patients, it is important that we continue to support randomized national trials seeking to improve outcomes in this population," Dr. Mell added.

Provided by NRG Oncology