The investigators concluded that induction CT or CRT plus surgery or consolidation RT can be used in an elderly population. Elderly patients demonstrated treatment response and outcomes equivalent to those of younger patients.

Brain Metastases Safely Treated With WBRT After Bevacizumab and Chemotherapy in NSCLC

Written by Jenny Powers

Patients who had brain metastases following bevacizumab and chemotherapy (CT) for non-squamous, non–small cell lung cancer (non-Sq NSCLC) were safely treated with whole-brain radiotherapy (WBRT), with a good response and symptom improvement, according to Jennifer Arrondeau, MD, Institut Gustave Roussy, Villejuif, France.

Dr. Arrondeau and her colleagues conducted a multicenter retrospective study to evaluate whether bevacizumab toxicity would increase, because of its long half-life, after whole-brain radiotherapy (WBRT) for treatment of brain metastases in patients with non-Sq NSCLC.

The analysis included 40 patients treated between 2009 and 2013 with bevacizumab and CT followed by WBRT within 6 months.

About half (45.5%) of the patients were women, and the median age was 56 years. The smoking history revealed that 11 (27.5%) patients were never smokers, 28 (70.0%) were current or former smokers, and the smoking history of 1 (2.5%) patient was unknown. Adenocarcinoma was diagnosed in all patients. Mutations in the epidermal growth factor receptor (EGFR) and Kirsten rat sarcoma oncogene 2 (KRAS) were detected in 7 and 6 patients, respectively, and anaplastic lymphoma kinase (ALK) rearrangement was identified in 3 patients.

The patient cohort had a poor prognosis. The median time to development of brain metastasis was 7.5 months (range, 0 to 65) from the diagnosis of non-Sq NSCLC. The median Graded Prognostic Assessment was 1.5 (range, 0 to 5.3).

Bevacizumab was administered after a median of 1 treatment (range, 0 to 7) at a median dose of 15 mg/kg. Patients received bevacizumab for a median 5.1 months (range, 0.7 to 35 months). The median delay was 6 months (range, 0.1 to 61.1) between the diagnosis of brain metastases and the delivery of WBRT, while the median delay between the last dose of bevacizumab and WBRT was 38 days (range, 0 to 167).

Dr. Arrondeau said that this study suggested that the efficacy of WBRT is unaffected by prior bevacizumab.

Following WBTR, 2 patients achieved complete response, 12 patients showed partial response, 15 showed stable disease, and 7 patients experienced disease progression. One patient died during WBRT because of disease progression.

Disease progression in the brain was observed in 12 (30%) patients at a median of 2.5 months (range, 0.3 to 22.6). Leptomeningeal progression was observed in 9 (22.5%) patients at a median of 1.7 months following WBRT (range, 0.03 to 10). Median survival following WBRT was 4 months (range, 0.1 to 36.8 months).

Neurological symptoms were reported in 29 (72.5%) patients prior to WBRT. Following WBRT, 10 patients were asymptomatic, 12 patients experienced improvement, 7 patients had the same symptoms, 9 patients experienced worsening symptoms, and 2 patients were lost to follow-up or had died.

The most common side effects were intracranial hypertension symptoms, reported by 6 patients (1 grade 2, and 5 grade 3), 2 patients experienced grade 2 seizures, 1 patient reported grade 3 vertigo, 1 had grade 3 dizziness, and 2 patients reported grade 2 intracranial bleeding.

A recent Phase 3 study conducted by the European Organisation for Research and Treatment of Cancer comparing patients with 1 to 3 brain metastases of NSCLC who were assigned randomly to receive either WBRT or observation following complete surgery or radiosurgery showed that overall survival was similar in the two arms (median, 10.9 vs 10.7 months, respectively; p=.89). However, the 2-year relapse rate with WBRT was decreased compared to observation, both at initial sites (surgery: 59% to 27%, p<0.001; radiosurgery: 31% to 19%, p=0.040) and at new sites (surgery: 42% to 23%, p=0.008; radiosurgery: 48% to 33%, p=0.023). WBRT also decreased the rates of death from intracranial progression, which occurred in 78 (44%) of 179 patients in the observation arm and in 50 (28%) of 180 patients in the WBRT arm [Kocher M et al. *J Clin Oncol* 2009]. However, the quality-of-life scores reported by patients in the observation group of the same trial were significantly higher on several subscales over 3 time points ending at 1 year [Soffietti R et al. *J Clin Oncol* 2013].

According to Dr. Arrondeau, WBRT could be safely administered to patients with brain metastases within 6 months of having received bevacizumab for NSCLC, but she cautioned that these findings were compromised by the small sample size of the study and should be confirmed in a larger prospective study.