Metastatic Non–Small Cell Lung Cancer (NCT00556712); Cappuzzo F et al. *Lancet Oncol* 2010].

The purpose of this study, which was conducted by the Clinical Oncology and Nuclear Medicine Department at Ain Shams University Hospitals in Cairo, Egypt, was to evaluate the efficacy—defined as prolongation of TTP, OS, and safety (grade 3 or 4 toxicity)—of low-dose gemcitabine as maintenance chemotherapy after first-line gemcitabine and cisplatin in advanced and metastatic NSCLC.

A total of 120 patients with advanced NSCLC presented at the Clinical Oncology and Nuclear Medicine Department at Ain Shams University Hospitals between January 2010 and June 2012. Of these, 75.5% were male, 70% were younger than 60 years, 59.2% had performance status (PS) 2, 2.75% had nonsquamous histology, and 79.2% had stage IV disease. All eligible patients received induction chemotherapy with gemcitabine and cisplatin.

Patients who completed 4 cycles and showed complete response, partial response, or stable disease were randomized into two arms: (1) gemcitabine 250 mg/m^2 given throughout 6 hours on days 1 and 8 every 3 weeks, or (2) BSC. Responses were assessed according to Response Evaluation Criteria in Solid Tumors guidelines every 2 cycles.

After each cycle, toxicities were evaluated according to National Cancer Institute criteria for common toxicities. Patients with progressive disease (PD) were excluded from the study, as were those who did not finish 4 cycles and showed doubling time, PD, or toxicity.

Results showed a median TTP of 6.1 months (CI, 5.3 to 6.6; p=0.454) in arm I and 5.8 months (CI, 5.2 to 6.4; p=0.454) in arm II. The median OS was 9 months (CI, 7.9 to 10.0; p=0.994) in arm I and 8 months (CI, 8.5 to 9.4; p=0.994) in arm II. The trial showed that maintenance therapy was well tolerated, with no grade 3 or 4 toxicity. The only significant finding was grade 2 anemia in 8 patients (22.9%) in the maintenance arm (arm I).

The clinical trial failed to show any statistical significance in TTP or OS between the 2 arms. The authors report that this could be due to the smaller sample size or the use of low-dose rather than conventional-dose gemcitabine. Other factors might include the predominance of nonsquamous histology and PS 2.

Evidence-based data indicate that this analysis of study outcomes is accurate. PS is among the most important prognostic factors for survival with NSCLC [Sweeney CJ et al. *Cancer* 2001]. PS, histology, and age versus comorbidity are the principal determinants of first-line treatment with cytotoxic combination chemotherapy, including platinum with gemcitabine. Treatment goals are to prolong survival and control disease-related symptoms. First-line treatment with platinum combinations, such as gemcitabine, yields similar improvements in survival [National Cancer Institute online 2014].

Benefit and Tolerance to Induction Therapy in Elderly Patients With Locally Advanced NSCLC

Written by Jenny Powers

Elderly patients with locally advanced non--small cell lung cancer (NSCLC) could present similar benefit and tolerance as their younger counterparts to induction chemotherapy (CT) or chemoradiotherapy (CRT) followed by either surgical resection or consolidation radiotherapy. Dr. Diego Márquez-Medina, University Hospital Arnau de Vilanova, Lleida, Spain, noted the conundrum that the elderly population is growing and that half of lung cancers are diagnosed in patients older than 60 years [Gridelli C et al. *Crit Rev Oncol Hematol* 2002]. However, elderly patients are seldom included in multimodal programs of induction CT or CRT [Gridelli C et al. *Crit Rev Oncol Hematol* 2002].

The Spanish investigators conducted a retrospective review of data from 108 consecutive patients with Eastern Cooperative Oncology Group status 0 to 2 locally advanced NSCLC who received induction CT or CRT plus surgery or consolidation radiotherapy, analyzing the feasibility, tolerability, and efficacy of these therapies in patients younger (59.2%) and older (40.7%) than 70 years. Elderly patients tended to present worse Eastern Cooperative Oncology Group scores (p=0.088) and stage IIIB NSCLC. The prevalence rates of squamous cell carcinomas, adenocarcinomas, and unspecified NSCLC were similar between the cohorts.

The CT regimens included platinum doublets with vinorelbine, gemcitabine, and taxanes. Carboplatin doublets were more commonly administered to the elderly patients (p=0.025).

Induction CRT and CT were administered to 59.3% and 40.7% of younger and 49.9% and 50.1% of older patients, respectively. Both age groups had similar radiologic responses. Pathologic responses after resection surgery were also similar between age groups, and no differences regarding overall survival and disease-free survival were found. Interestingly, grade 3 or 4 toxicity was more common among younger patients (p=0.053). No grade 3 or 4 pneumonitis was detected in either age group.

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.