Platinum-Plus Regimens Equally Effective First Therapies for EGFR Wild-Type NSCLC

Written by Francesca Coltrera

This single-site, retrospective study compared the efficacy of platinum doublet regimens used as first-line chemotherapy for patients with EGFR wild-type, nonsquamous non–small cell lung cancer (NSCLC). Investigators found no difference in survival, response rate, and prognostic factors. Eun Joo Kang, MD, Korea University Guro Hospital, Seoul, Korea, reported study results in a poster presentation [Kang EJ et al. *Ann Oncol*. 2015].

Molecular research and targeted agents like gefitinib and erlotinib have improved outcomes for a subset of NSCLC patients with EGFR mutations. Yet, platinum doublet regimens remain first-line therapy for patients with EGFR wild-type NSCLC, which accounts for more than half of all NSCLC cases. In a randomized phase 3 study, overall survival (OS) was significantly better with pemetrexed + cisplatin than a nonpemetrexed therapy (gemcitabine + cisplatin) in a Western population composed of chemotherapy-naïve patients with adenocarcinoma (12.6 vs 10.9 months; $P < .03$) [Scagliotti GV et al. *J Clin Oncol*. 2008].

Dr Kang and colleagues conducted a retrospective analysis on 165 patients with EGFR wild-type nonsquamous NSCLC who had received first-line treatment with pemetrexed + platinum (PP) or nonpemetrexed + platinum (NPP) chemotherapy at Korea University Guro Hospital between 2007 and 2013, analyzing progression-free survival (PFS), OS, response rate, and prognostic factors.

Almost all patients (91.5%) had adenocarcinoma. Average age was 66 years and 71.5% were men. At diagnosis, 80.6% had stage IV disease. During treatment, 43% had received PP and 57% had received NPP. In the NPP group, patients had mainly received gemcitabine + carboplatin (37.2% of all NPP patients), paclitaxel + carboplatin (19.1%), gemcitabine + cisplatin (18.1%), docetaxel + cisplatin (11.8%), or paclitaxel + cisplatin (7.4%). Patient characteristics were similar in the PP and NPP groups.

No difference between the 2 groups was reported in median PFS ($P = .12$) or OS ($P = .42$), nor did OS differ depending on which specific regimen was used ($P = .82$). For patients who had received PP, median PFS and OS were 4.6 months (95% CI, 3.8 to 5.4) and 18.7 months (95% CI, 11.7 to 25.8), respectively. For patients who had received NPP, median PFS and OS were 6.2 months (95% CI, 3.4 to 5.0) and 12.2 months (95% CI, 10.3 to 14.1), respectively. There were no significant differences in response rate, which was 26.8% in the PP group and 28.7% in the NPP group ($P = .78$).

During multivariate analysis looking at prognostic factors, prolonged OS was associated with a few subgroups:

- In PP patients:
  - Stages I–III at diagnosis
  - Metastasis restricted to lung, pleura, or both
  - Treatment ≥ 2nd-line chemotherapy vs 1st-line only
- In NPP patients:
  - Metastasis restricted to lung, pleura, or both
  - Treatment ≥ 2nd-line chemotherapy vs 1st-line only

The data suggest no clear advantage in PFS, OS, or response rate for patients with wild-type EGFR, nonsquamous NSCLC given PP or NPP as first-line therapy. Although pemetrexed plus platinum has been regarded as superior in nonsquamous NSCLC, this study did not support that belief. Because the study was retrospective, relatively small-scale, and conducted only on patients from 1 hospital, further confirmation is needed.

SBRT as Effective Treatment Option for Medically Operable Stage I NSCLC

Written by Anita Misra-Press, PhD

A surgical lobectomy, or segmental, wedge, or sleeve resection, is the primary treatment option for patients with stage I (T1-2aN0M0) non–small cell lung cancer (NSCLC) [*National Cancer Institute*. http://www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/healthprofessional/page7. Accessed April 22, 2014]. However, in patients with medically inoperable tumors, stereotactic body radiation therapy (SBRT) is a safe and effective treatment option conferring local control in > 90% of patients [Timmerman R et al. *JAMA*. 2010]. An international study of SBRT that reported high rates of local control, low toxicities, and favorable overall survival (OS) in this patient population has led to a recent increase in the number of patients with medically operable early stage NSCLC who prefer this treatment over surgery [Grills IS et al. *J Thorac Oncol*. 2012].

Although no randomized trial comparing SBRT with surgery has been reported to date, in an attempt to indirectly address this question, Maddalena Rossi, PhD, The Netherlands Cancer Institute, Amsterdam, The Netherlands, and colleagues compared OS within a large cohort of patients with medically operable stage

I NSCLC who refused surgery and opted for SBRT with those patients who were surgically treated [Rossi M et al. *Ann Oncol.* 2015].

This nonrandomized retrospective analysis included all patients from 2006 to 2012 who presented with peripheral stage I (T1-T2a) NSCLC to the Netherlands Cancer Institute. Patients with synchronous lung tumors or prior SBRT were excluded. Volumetric image guided radiation therapy was used for verifying tumor position and setup with SBRT (18Gy 3 times within 8-11 days). Patients were excluded from the surgical cohort if they had received chemotherapy prior to or after surgery. The log-rank test for significance was used to compare OS in the SBRT vs surgery groups.

After excluding ineligible patients for this retrospective study, of 517 patients receiving SBRT, 42 patients with medically operable NSCLC had refused surgery. The median follow-up for this SBRT group was 24.2 months (range, 3-85 months). The average age of this 50% male SBRT cohort was 74.2 years with 83% of patients identified as stage T1 and 17% as stage T2a. The 66 patients identified in the surgical cohort (who did not receive SBRT) had a median follow-up of 29.5 months (range, 1-88 months). The average age of this 45% male surgical group was 63.9 years with 78% of patients identified as stage T1 and 22% as stage T2a.

The OS of the SBRT cohort at 1 year (97.0%; 95% CI, 92.0 to 100), 3 years (79.0%; 95% CI, 66.0 to 96.0), and 5 years (72.2%; 95% CI, 55.3 to 94.3) was not significantly different (log-rank $P = .31$) from the surgical cohort at 1 year (93.6%; 95% CI, 88.0 to 100), 3 years (80.6%; 95% CI, 70.0 to 92.0), and 5 years (46.2%; 95% CI, 30.5 to 69.6), respectively.

Based on the results of this retrospective analysis, Rossi and colleagues concluded that despite the higher age of the SBRT 'surgery refusal' cohort compared with the surgical cohort (74.2 years vs 63.9 years), OS after SBRT in patients with peripherally located stage I NSCLC was not significantly different.

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