Aim: One standard option in the treatment of stage IIIA/N2 NSCLC is neoadjuvant chemotherapy followed by surgery. We investigated in a randomized trial whether the addition of neoadjuvant radiotherapy would improve the outcome. Here we present the final results of this study.

Methods: Patients (pts.) with pathologically proven, resectable stage IIIA/N2 NSCLC, performance status 0-1, and adequate organ function were randomized 1:1 to chemoradiation (CRT) with 3 cycles of neoadjuvant chemotherapy (cisplatin 100 mg/m² and docetaxel 85 mg/m² d1, q3weeks) followed by accelerated concomitant boost radiotherapy (RT) with 44 Gy in 22 fractions in 3 weeks, or neoadjuvant chemotherapy alone (CT), with subsequent surgery for all pts. The primary endpoint was event-free survival (EFS).

Results: 232 pts. were randomized in 23 centers, the median follow-up was 53 months. Two thirds were men, median age was 60 years (range 37-76). Histology was squamous cell in 33%, adenocarcinoma in 43%. Response rate to CRT was 61% vs. 44% with CT. 85% of all pts. underwent surgery, 30-day postoperative mortality was 1%. The rate of complete resection was 91% (CRT) vs. 81% (CT) and the pathological complete remission (pCR) rate was 16% vs. 12%. The median EFS was 13.1 months (95% CI 9.9 – 23.5) for the CRT group vs. 11.8 months (95% CI 8.4 – 15.2) in the CT arm (p 0.665). The median overall survival (OS) with CRT was 37.1 months (95% CI 22.6 – 50), with CT 26.1 months (95% CI 26.1 – 52.1, p 0.938). The local failure rate was 23% in both arms. In the CT arm 12 pts. were given postoperative radiotherapy (PORT) for R1 resection, 6 pts. received PORT in violation of the protocol. Pts. with a pCR, mediastinal downstaging to ypN0/1 and complete resection had a better outcome. Toxicity of chemotherapy was substantial, especially febrile neutropenia was common, whereas RT was well tolerated.

Conclusions: This is the first completed phase III trial to evaluate the role of induction chemoradiotherapy and surgery, in comparison to neoadjuvant CT alone followed by surgery. RT was active, it increased response, complete resection and pCR rates. However, this failed to translate into an improvement of local control, EFS or OS. Notably, surgery after induction treatment was safe, including pneumonectomy. The overall survival rates of our neoadjuvant regimen are very encouraging, especially for a multicenter setting.

Disclosure: M. Pless: Advisory Board for Sanofi; R. Cathomas: Advisory Board Sanofi. All other authors have declared no conflicts of interest.