Surgical outcomes with neoadjuvant durvalumab + chemotherapy followed by adjuvant durvalumab in resectable NSCLC (AEGEAN)

Background: In the phase 3 AEGEAN study (NCT03800134), perioperative durvalumab + neoadjuvant chemotherapy (CT), versus neoadjuvant CT alone, significantly improved both primary endpoints of event-free survival and pathological complete response, with a manageable safety profile, in patients with resectable (R) NSCLC. We report key surgical outcomes from AEGEAN.

Methods: 802 patients with treatment-naive R-NSCLC (stage II–IIIB[N2]; AJCC 8th edition) and ECOG PS 0/1 were randomised (1:1) to receive four cycles of platinum-based CT plus durvalumab 1500 mg IV or placebo every 3 weeks (Q3W) before surgery, followed by continued durvalumab or placebo (Q4W, 12 cycles). Randomisation was stratified by disease stage (II vs III) and PD-L1 expression (<1% vs ≥1%). Confirmation of EGFR/ALK aberration status was required pre-randomization following a protocol amendment. Patients with known EGFR/ALK aberrations were excluded from the modified intent-to-treat (mITT) population for efficacy analyses. Lobectomy, sleeve resection, or bilobectomy were allowed as planned surgeries (at enrolment); however, the protocol was amended with enrolment ongoing to exclude patients with tumours classified as T4 for any reason other than size (>7 cm) or whose planned surgery was pneumonectomy (originally allowed). Surgical outcomes were summarized for the mITT population using descriptive statistics. Here, safety was assessed in patients from the mITT population with ≥1 study treatment dose.

Results: 737/740 patients randomized to the mITT population received study treatment, 366 and 371 in the durvalumab and placebo arms, respectively. In the mITT population, 80.6% and 80.7% underwent surgery, respectively; 77.6% and 76.7% completed surgery (investigator assessment), with disease progression the most common reason for cancelled (6.8% vs 7.8%) or non-completed surgery (1.4% vs 2.1%); among treated patients who underwent surgery, 17.6% and 21.9% had delayed surgery, most commonly for logistical reasons (e.g. scheduling issues; 9.8% vs 12.0%). Median time from last neoadjuvant treatment dose to surgery was the same in each arm (34.0 days). Among patients who underwent surgery, similar proportions in the durvalumab and placebo arms had open (49.2% vs 50.7%) and minimally invasive procedures (49.2% vs 47.0%); lobectomy was the most common procedure (80.7% vs 73.2%), followed by pneumonectomy (9.2% vs 9.6%). Among patients who completed surgery, a numerically higher proportion had R0 resection in the durvalumab versus placebo arm (94.7% vs 91.3%). Median time from surgery to first adjuvant treatment dose was similar in each arm (50.0 vs 52.0 days). During the post-surgery period, 40.2% and 39.2% of durvalumab- and placebo-treated mITT patients, respectively, who underwent surgery, had any AEs possibly related to surgery; 8.4% and 9.3% had maximum grade 3/4 AEs possibly related to surgery. Surgical complications by Clavien-Dindo classification occurred with similar frequency (59.3% vs 59.9% of mITT patients who had surgery); most were maximum grade 1/2 (53.2% vs 51.7%). Key results by disease stage will be presented.

Conclusions: The addition of perioperative durvalumab to neoadjuvant CT did not adversely impact the feasibility, type, extent, or timing of surgery in patients with R-NSCLC and was associated with a tolerable surgical safety profile. Furthermore, the addition of durvalumab resulted in numerically higher R0 resection rates.

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