# Neoadjuvant Nivolumab (NIVO) + Chemotherapy (Chemo) versus Chemo for Resectable Non–Small Cell Lung Cancer (NSCLC): Event-free Survival (EFS) by Surgical Outcomes from CheckMate 816

Objective: Neoadjuvant NIVO in combination with platinum-doublet chemo previously demonstrated statistically significant and clinically meaningful improvement in pathologic complete response (pCR) and EFS vs chemo alone, without an increase in post-surgical complications, in patients with resectable NSCLC in the phase 3 CheckMate 816 study (NCT02998528). Surgical outcomes, including safety, have been reported previously. Here, we report additional surgical outcomes analyses from CheckMate 816.

Methods: Patients with newly diagnosed, resectable, stage IB (? 4 cm) to IIIA NSCLC (AJCC 7th edition), an Eastern Cooperative Oncology Group performance status of 0-1, and no known sensitizing EGFR mutations or ALK alterations were included. Patients were randomized 1:1 to receive neoadjuvant NIVO 360 mg every 3 weeks (Q3W) plus platinum-doublet chemo Q3W (3 cycles) or chemo Q3W (3 cycles); patients then had surgery ? 6 weeks post-treatment. Primary endpoints were EFS (time from randomization to any disease progression precluding surgery; disease progression or recurrence after surgery; or death) and pCR (0% residual viable tumor in the primary tumor and lymph nodes based on immune-related pathological response criteria), both assessed by blinded independent review. In these post-hoc exploratory analyses, EFS was evaluated in patient subgroups by surgical approach (minimally invasive, thoracotomy, or conversion from minimally invasive to open surgery), by type of surgery (lobectomy or pneumonectomy), and by completeness of resection (R0 or R1).

Results: At database lock (October 20, 2021), median follow-up was 29.5 months. Of the 358 patients randomized to NIVO + chemo (n = 179) or chemo (n = 179), 149/179 (83%) and 135/179 (75%), respectively, received definitive surgery. Overall, EFS improvement was seen with NIVO + chemo vs chemo alone (Table), regardless of surgical approach (hazard ratio [HR]: 0.46 and 0.67 for minimally invasive surgery and thoracotomy, respectively), type of surgery (HR: 0.58 for lobectomy; not calculated for pneumonectomy), or completeness of resection (HR: 0.59 with R0 resection; not calculated with R1 resection); sample size and number of EFS events were limited in some subgroups. Notably, in the NIVO + chemo arm, median EFS was not reached in most patient subgroups by surgical approach, type of surgery, or completeness of resection. In the NIVO + chemo arm, 2-year EFS rates (95% CI) were: 81% (66-90) and 69% (58-78) in patients who underwent minimally invasive surgery or thoracotomy, respectively; 70% (60-78) and 76% (52-90) in those who had lobectomy or pneumonectomy, respectively; and 72% (62-79) in patients who had R0 resection.

Conclusions: In CheckMate 816, the addition of NIVO to neoadjuvant chemo did not impede surgical feasibility. EFS benefit was observed in patients treated with NIVO + chemo vs chemo, regardless of surgical approach, type of surgery, or completeness of resection. These results further support neoadjuvant NIVO + chemo as a treatment option for patients with resectable NSCLC.

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**Table. EFS with neoadjuvant NIVO + chemo vs chemo by surgical approach, type of surgery, and completeness of resection**

| Patients with definitive surgery | NIVO + chemo n = 149 | | Chemo n = 135 | | NIVO + chemo vs chemo |
|---|---|---|---|---|---|
| **Parameter** | **Pts, n (%)** | **Median EFS (95% CI), mo** | **Pts, n (%)** | **Median EFS (95% CI), mo** | **HR (95% CI)** |
| Surgical approach | | | | | |
| Minimally invasive surgery | 44 (30) | NR (27.79-NR) | 29 (22) | NR (9.46-NR) | 0.46 (0.20-1.07) |
| Thoracotomy | 88 (59) | NR (30.49-NR) | 85 (63) | 31.8 (16.79-NR) | 0.67 (0.41-1.08) |
| Minimally invasive → open surgery | 17 (11) | 30.6 (13.57-NR) | 21 (16) | 22.7 (10.41-NR) | ---[a] |
| Type of surgery | | | | | |
| Lobectomy | 115 (77) | NR (30.49-NR) | 82 (61) | 26.2 (16.62-NR) | 0.58 (0.37-0.91) |
| Pneumonectomy | 25 (17) | NR (---) | 34 (25) | 21.1 (13.93-NR) | ---[a] |
| Completeness of resection[b] | | | | | |
| R0 | 124 (83) | NR (30.65-NR) | 105 (78) | 26.2 (18.17-NR) | 0.59 (0.39-0.90) |
| R1 | 16 (11) | NR (12.58-NR) | 21 (16) | NR (10.41-NR) | ---[a] |

[a]HR not calculated due to < 10 events per treatment arm.

[b]EFS medians and HRs were not calculated for patients with R2 or Rx resections due to small patient numbers in the NIVO + chemo (5 and 4) and chemo (4 and 5) arms, respectively.

Chemo, chemotherapy; EFS, event-free survival; HR, hazard ratio; mo, months; NIVO, nivolumab; NR, not reached; Pts, patients.