Interim data on neoadjuvant nivolumab plus platinum-based chemotherapy (neoadjuvant nivolumab plus chemotherapy) in patients with non-metastatic resectable non-small cell lung cancer from the non-interventional study NENI

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Introduction

- Lung cancer is the leading cause of cancer-related mortality worldwide,[1] with non-small cell lung cancer (NSCLC) representing about 80%–85% of all cases[2]
- In Germany, lung cancer is the most frequent cancer-related cause of death in men (22.8%) and the second most frequent in women (15.8%). Five-year survival rates are low: 17% in men and 22% in women[3]
- Although curative surgery remains the standard of care for patients with early-stage resectable NSCLC, disease recurrence occurs in about 25%–70% of patients despite complete resection[2,4]
- The estimated 5-year survival rates range from 73% for stage IB disease to 41% for stage IIIA disease per the pathological staging criteria of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 8th edition[5]
- In the phase 3 CheckMate 816 study, neoadjuvant nivolumab (NIVO) + platinum-doublet chemotherapy (chemo) showed statistically significant and clinically meaningful improvements in event-free survival (EFS) and pathological complete response (pCR) vs chemo alone in patients with resectable NSCLC; the addition of neoadjuvant NIVO to chemo did not impede the feasibility of surgery[6]
  - At 5-year follow-up, NIVO + chemo demonstrated significantly improved overall survival vs chemo[7]
  - This regimen is approved in the United States as a neoadjuvant therapy for adult patients with resectable NSCLC (tumors ≥ 4 cm or node-positive) and in the European Union as a neoadjuvant therapy for resectable NSCLC at high risk of recurrence (tumors ≥ 5 cm or node-positive) in adult patients with tumor programmed death ligand 1 (PD-L1) expression ≥ 1%[8,9]
- However, real-world data on neoadjuvant NIVO + chemo ± adjuvant NIVO in patients with resectable NSCLC are limited
  - In a previous interim analysis of the non-interventional study (NIS) NENI (NCT06169956), the pCR rate was 52.8% and major pathological response (MPR) rate was 66.7% among the 36 patients who had undergone surgery[10]

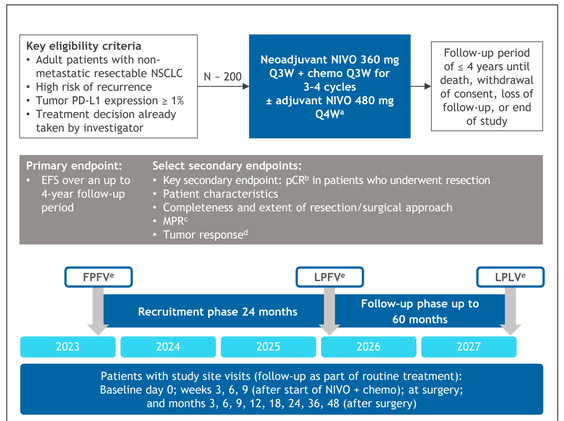
Objective

- NENI, an open-label, prospective, single-cohort, multicenter NIS aims to evaluate neoadjuvant NIVO + platinum-based chemo ± adjuvant NIVO in clinical practice in Germany up to 4 years of follow-up in the post-market authorization approval period
- In this interim analysis (data cut-off: September 30, 2025), we report baseline characteristics, surgery-related outcomes, pathological response, and tumor response after neoadjuvant treatment

Methods

- The study design for NIS NENI is shown in **Figure 1**
- Enrollment for this prospective observational study has been completed, with 200 patients from 40 sites in Germany
- Assessments are conducted per routine local clinical practice
- All data analyses are of a descriptive nature and no formal hypotheses will be tested

Figure 1. Study design



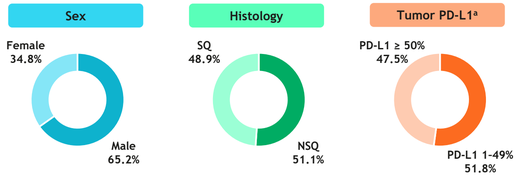
[a]Per the approved label in the European Union for neoadjuvant or perioperative treatment.[b]≤0% residual viable tumor cells in the primary tumor and sampled lymph nodes per investigator assessment. [c]≤ 10% residual viable tumor cells in both primary tumor and sampled lymph nodes per investigator assessment. [d]Investigator-assessed per local clinical routine (not mandatory to use RECIST v1.1). [e]Phase starts in December of the indicated year.
FPFV, first patient first visit; LPFV, last patient first visit; LPLV, last patient last visit; RECIST, Response Evaluation Criteria in Solid Tumors.

Results

Patient characteristics and comorbidities

- At interim analysis, 141 patients were enrolled into the study
  - Of those, 123 (87.2%) patients are still in the study
  - 97 (68.8%) patients completed 3 cycles of neoadjuvant NIVO + chemo; 29 (20.6%) are still receiving neoadjuvant therapy
- Key baseline demographic and clinical characteristics of study patients are shown in **Figure 2** and **Table 1**
  - Median age was 68.1 (range, 42.1–86.5) years
  - Most frequently received type of platinum-based chemo was carboplatin (96.5%)
- About one-fourth of patients (25.5%) had a Charlson comorbidity index ≥ 2 and 48% had stage IIIa at diagnosis (**Table 1**)
- The most frequently reported comorbidity was hypertension (51.1%)

Figure 2. Key baseline characteristics (N = 141)



Data are shown as percentages of the overall study population (N = 141). Percentages may not sum to 100 due to rounding. [a]No patients with tumor PD-L1 < 1%; tumor PD-L1 status was missing for 1 patient due to incomplete documentation owing to withdrawal of consent. NSQ, non-squamous; SQ, squamous.

Table 1. Summary of baseline characteristics

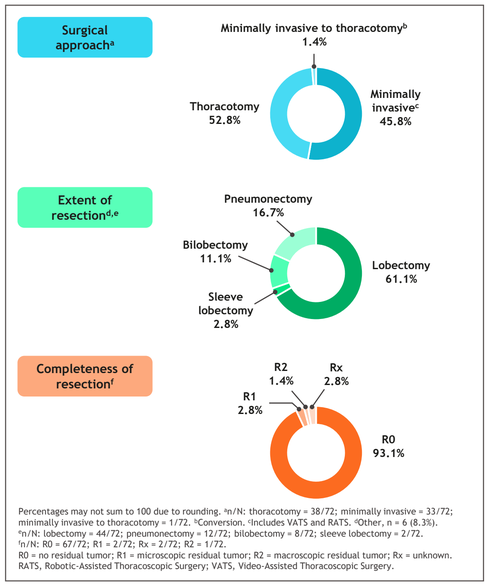
Characteristics	Patients (N = 141)
Age, median (range), y	68.1 (42.1-86.5)
Age group, n (%)	
< 65 y	41 (29.1)
≥ 65 y	100 (70.9)
Smoking status, n (%)	
Current	55 (39.0)
Former	80 (56.7)
Never	6 (4.3)
ECOG PS, n (%)	
0	80 (56.7)
≥ 1	61 (43.3)
UICC stage at diagnosis,[a] n (%)	
IIA	10 (7.1)
IIB	30 (21.3)
IIIA	68 (48.2)
IIIB	29 (20.6)
IIIC	2 (1.4)
Tumor size at diagnosis, n (%)	
T1b	6 (4.3)
T1c	4 (2.8)
T2a	21 (14.9)
T2b	18 (12.8)
T3	39 (27.7)
T4	52 (36.9)
Tx	1 (0.7)
Nodal status, n (%)	
N0	42 (29.8)
N1	43 (30.5)
N2	52 (36.9)
N3	2 (1.4)
Nx	2 (1.4)
Charlson comorbidity index, n (%)	
0	69 (48.9)
1	36 (25.5)
≥ 2	36 (25.5)
Comorbidities (reported in ≥ 10% of patients), n (%)	
Hypertension	72 (51.1)
Chronic obstructive pulmonary disease	43 (30.5)
Hypercholesterolemia	20 (14.2)
Hyperlipidemia	15 (10.6)

Percentages may not sum to 100 due to rounding. [a]Missing, n = 2.
ECOG, Eastern Cooperative Oncology Group; PS, performance status; UICC, Union for International Cancer Control; y, years.

Surgical outcomes

- At the time of this interim analysis, 72 patients underwent surgery, 24 patients did not receive surgery, and 45 patients were still under neoadjuvant treatment or had not yet received surgery
- Of the 72 patients who underwent surgery, 69 (95.8%) underwent resection of lymph nodes
  - Median number of resected lymph nodes was 15.5 (range, 1.0–51.0)
- Subsequent adjuvant immunotherapy was received by 30 of 112 patients (26.8%)
- Surgical approaches and the extent and completeness of resection are shown in **Figure 3**

Figure 3. Surgical outcomes (n = 72)



Percentages may not sum to 100 due to rounding. [a]n/N: thoracotomy = 38/72; minimally invasive = 33/72; minimally invasive to thoracotomy = 1/72. [b]Conversion. [c]Includes VATS and RATS. [d]Other, n = 6 (8.3%). [e]n/N: lobectomy = 44/72; pneumonectomy = 12/72; bilobectomy = 8/72; sleeve lobectomy = 2/72. [f]n/N: R0 = 67/72; R1 = 2/72; Rx = 2/72; R2 = 1/72.
R0 = no residual tumor; R1 = microscopic residual tumor; R2 = macroscopic residual tumor; Rx = unknown.
RATS, Robotic-Assisted Thoracoscopic Surgery; VATS, Video-Assisted Thoracoscopic Surgery.

Tumor response

- At the end of neoadjuvant treatment, 3.8% of all evaluated patients (3/80) achieved complete response and 73.8% (59/80) achieved partial response (**Table 2**)

Table 2. Tumor response[a] (clinical or radiological assessment)

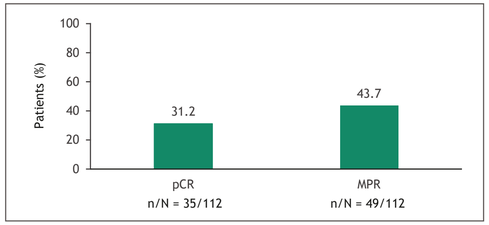
	End of neoadjuvant treatment (n = 112)
Response evaluated, n (%)	
Yes	80 (71.4)
No	23 (20.5)
Missing	9 (8.0)
	Evaluated patients (n = 80)
Response evaluated per RECIST v1.1, n (%)	
Yes	9 (11.2)
No	66 (82.5)
Missing	5 (6.2)
Best overall response, n (%)	
Complete response	3 (3.8)
Partial response	59 (73.8)
Stable disease	8 (10.0)
Progressive disease	6 (7.5)
Missing/not evaluable	4 (5.0)

Percentages may not sum to 100 due to rounding. [a]Tumor response was assessed at the end of neoadjuvant treatment. N = 112 includes all patients who reached end of neoadjuvant treatment, including those who had not yet undergone surgery

Pathological response

- The pathological response in patients who underwent surgery is shown in **Figure 4**

Figure 4. Pathological response in patients who underwent surgery



Conclusions

- At interim analysis, the ongoing NENI study provides real-world evidence reflecting routine clinical practice, with patient characteristics and observed outcomes comparable with those reported in neoadjuvant settings such as CheckMate 816
- Among patients who underwent surgery, the pCR rate was 31.2% and MPR rate was 43.7%
- Overall, 72 patients treated with neoadjuvant NIVO + chemo underwent surgery
  - About one-half (45.8%) of patients received minimally invasive surgery
  - Most patients (93.1%) had no residual tumors after resection (R0)
  - Nearly two-thirds (61.1%) of patients had a lobectomy
- By providing real-world insights into perioperative treatment with neoadjuvant NIVO + chemo and adjuvant NIVO, the NIS NENI supports the clinical understanding of treatment approaches in resectable NSCLC

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Declaration of interests

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