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Surgical Results after Neoadjuvant Nivolumab and Platinum-based Chemotherapy for Resectable Lung Cancer. A Multicentre European Real Clinical Practice Analysis

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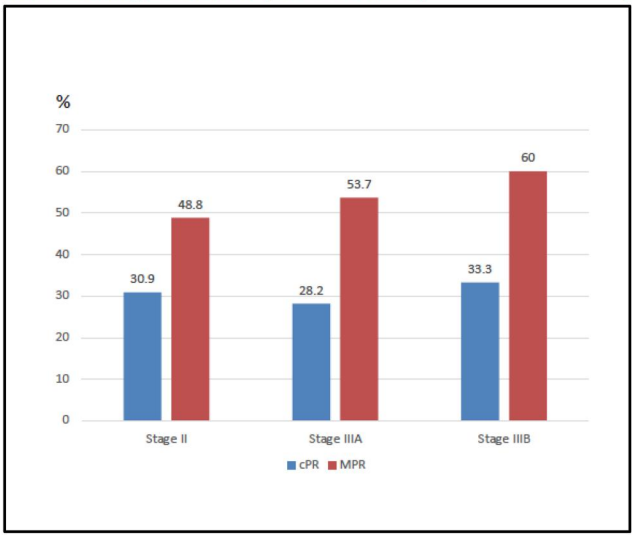
Graphical abstract

Surgical results following neoadjuvant nivolumab and platinum-based chemotherapy for locally advanced resectable NSCLC. A real clinical practice analysis from the European Cooperative Study Group on Resectable Lung Cancer (ECSG-RLC)

Summary

Multicentre study on 340 patients with resectable stages II to IIIB NSCLC undergoing neoadjuvant platin-based chemotherapy and nivolumab.

Attrition to surgery: 6.8%. 90-days postoperative mortality was 2.5%. pCR was 30%, MPR was 52.7%. cPR was higher in patients with PD-L1>50% compared to those with PD-L1<50% (37.5% vs. 27.2%, p=0.082) and in squamous vs. non-squamous histology tumours (39% vs. 23%, p=0.004).



Legend: pCR: complete pathologic response; MPR: major pathologic response

Abstract

Objectives: To evaluate the real clinical practice surgical outcomes following neoadjuvant nivolumab in combination with chemotherapy in a multicentre European cohort of patients.

Methods: Retrospective analysis on consecutive patients treated in 6 tertiary referral hospitals in Europe with neoadjuvant chemotherapy and immunotherapy (nivolumab) for stage II-IIIB non-small cell lung cancer (March 2023-December 2024). Surgical and pathological outcomes were assessed.

Results: A total of 340 patients started neoadjuvant treatment. Three hundred seventeen patients (93.2%) were able to proceed to surgery. Forty-seven percent of patients had surgery more than 6 weeks after completion of the last neoadjuvant cycle. Two hundred eight operations (66%) were started using a minimally invasive approach with a conversion rate of 18%. The most frequent resection was lobectomy in 86% of patients. Ninety-day postoperative mortality rate was 2.5%. The pathologic complete response occurred in 95 patients (30% of the surgical patients), major pathologic response in 167 patients (52.7% of the surgical patients). The incidence of pathologic complete response ($P = .78$) and major pathologic response ($P = .26$) were similar in patients with clinical stage II and III. Pathologic complete response rate was higher in patients with programmed death-ligand 1 (PD-L1) $\geq$ 50% compared to those with PD-L1 $<$ 50% (37.5% vs 27.2%, $P = .082$). A higher pathologic complete response (39% vs 23%, $P = .004$) and major pathologic response (66% vs 45%, $P = .001$) were observed in squamous vs non-squamous histology tumours.

Conclusions: The use of neoadjuvant nivolumab in association with platinum-based chemotherapy in the real clinical practice is safe and effective. Our real clinical practice data represent valuable information to be used during multidisciplinary treatment selection for clinical stage II and III resectable non-small cell lung cancer and shared decision-making.

Keywords: lung cancer; surgery; neoadjuvant; immunotherapy; targeted therapy; chemotherapy.

INTRODUCTION

Recent phase III randomized trials have demonstrated that the neoadjuvant or perioperative treatment with immune-checkpoint-inhibitors in combination with platinum-based chemotherapy is associated with improved pathological response, longer event-free survival,[1-6] and overall survival compared to chemotherapy alone.[1,3,5,6]

The use of nivolumab has been recently approved by the regulatory agencies in Europe for the neoadjuvant treatment of resectable non-small-cell lung cancer (NSCLC) in combination with platinum-based chemotherapy.

There are however only few studies based on the real clinical practice, most of them from Asia.

A recent multicentre national study from England reported favourable surgical outcomes.[7] Real clinical practice data from a

broader Continental perspective appear useful to corroborate the results from the trials on a cohort of patients with similar characteristics and case-mix who are routinely discussed in units across the Europe.

The aim of this study was therefore to evaluate the surgical outcomes following neoadjuvant nivolumab in combination with chemotherapy in a multicentre European cohort of patients operated during the initial phase of its implementation in the clinical practice.

METHODS

The project was reviewed and approved by the Information Governance and Research and Innovation Departments at Leeds Teaching Hospitals (IRAS no. 345443, Ref. LTH24040, approval date 1 July 2024), by the Clinical Effectiveness Team and audit committee at the Clatterbridge Cancer Centre NHS Foundation Trust, and by the Ethic Committee of the Medical University of Vienna, Vienna, Austria (EK Nr. 2037/2024), Hospital Universitario Puerta de Hierro-Majadahonda, Madrid (PI 107/25), and Institut Mutualiste Montsouris, Paris. The need for Clinical Research Ethics Committee approval for this project was waived according to the Salamanca University Hospital and regulations. Local Caldicott approval and data sharing agreements were gained for information sharing between organizations. Patients consent was waived due to the retrospective nature of the study and publication of aggregate and anonymized data only.

Data sharing statement

The data underlying this article will be shared on reasonable request to the corresponding author.

All consecutive patients with stage IIA to IIIB NSCLC (according to the AJCC *Cancer Staging Manual*, eighth edition) and receiving neoadjuvant platinum-based chemotherapy in combination with nivolumab from 6 European centres (European Cooperative Study Group on Resectable Lung Cancer (ECSG-RLC)) were retrospectively analysed. The study period started from March 2023, the time when nivolumab was approved and funded in England (the first country in Europe to have this regimen funded), until December 2024. The time of start of this treatment in the different countries varied according to the national regulatory approval in each country.

Characteristics of the participating units are reported in the **Appendix**.

As a rule, patients considered eligible for the neoadjuvant checkpoint inhibitors (immune checkpoint inhibitor [ICI]) pathway, had a resectable tumour with a clinical stage from IIA to IIIB (N2 only), good performance status (0 or 1), and a molecular test showing the absence of epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) alterations.

Mediastinal staging and treatment pathway are reported in the **Appendix**.

If possible, surgery had to occur within 6 weeks from completion of the third cycle.

Surgery was performed by qualified thoracic surgeons. A systematic mediastinal lymph node dissection was performed in all centres during operation.

Pathological examination was performed in each centre by specialized thoracic pathologists according to the pan-tumour immune-related pathological response criteria.[8,9] Pathological complete response (pCR) was defined as the absence of residual viable tumour cells in the primary tumour and sampled lymph nodes, whereas major pathological response (MPR) was defined as the presence of 10% of less residual viable tumour cells in the primary tumour and sampled lymph nodes. MPR included those cases with pCR.

Statistical analysis

The variables that were collected and used for the analysis are reported in the **Appendix**. There were no missing data in this series.

Descriptive statistics were reported on the incidence of postoperative outcomes and pathological response. Subgroup analyses were performed to assess the incidence of outcomes by stage of disease, extent of surgery, surgical access, and programmed death-ligand 1 (PD-L1) expression level. PD-L1 levels were expressed as categoric variables according to commonly accepted and reported stratification (<1%, 1%-49%, and ≥50%).[1,2] The Cochran-Armitage trend test was used to compare cPR and MPR across PD-L1 categories and clinical nodal stages.

Chi-square or Fisher's exact tests were used to analyse the other categorical variables.

Multilevel mixed effects logistic regression analysis adjusting for clustering effect within the hospitals was performed to assess the factors associated with MPR. The variables entered in the model are reported in the **Appendix**.

All tests were performed using the Stata 15.0 statistical software (Stata Corp, College Station, TX, USA).

RESULTS

A total of 340 patients started neoadjuvant chemotherapy and nivolumab in the study period and were included in this analysis (142 from Liverpool, 72 from Leeds, 58 from Paris, 30 from Vienna, 25 from Madrid, and 13 from Salamanca).

The baseline characteristics of these patients are shown in **Table 1**.

One hundred forty-eight patients (43.5%%) were females and 135 (39.7%) were older than 70 years of age.

One hundred seventy-five (51.5%) patients had adenocarcinoma.

Sixty-eight patients (20%) had PD-L1 expression <1%, 112 (32.9%) had values between 1% and 49%, and 103 (30.3%) had values between 50% and 100%. PD-L1 was unknown in 57 (16.8%) patients.

Twenty-nine patients were in clinical stage IIA, 101 in stage IIB, 162 in clinical stage IIIA, and 48 in clinical stage IIIB.

Most patients received carboplatin-based doublets. Only 15 patients (4.4%) received cisplatin. Three hundred seven patients (90%) completed all 3 cycles of neoadjuvant treatment (89%), whereas 33 received less than 3 cycles due to toxicity, complications, or cancer progression (in 3 patients).

Twenty-three patients of 310 with known data about attrition (7.4%) were not able to proceed to surgery as planned. The reasons for not having surgery were cancer progression (9 patients), toxicity-poor performance status, including 2 deaths (13

Table 1. Baseline Characteristics of the 340 Patients included in the Analysis

Variables	
Age at start of treatment	67.0 (8.6)
Sex female (*n*, %)	148 (43.5%)
FEV1%	82.7 (18.6)
DLCO%	76.1 (18.1)
Histology (*n*, %)	
Non-squamous	175 (53.0%)
Squamous	118 (37.8%)
Other	47 (9.2%)
Clinical stage (*n*, %)	
IIA	29 (8.5%)
IIB	101 (29.7%)
IIIA	162 (47.6%)
IIIB	48 (14.2%)
Clinical nodal stage	
cN0	122 (35.9%)
cN1	107 (31.5%)
cN2 (All)	111 (32.6%)
cN2 single	76 (22.3%)
cN2 multiple	35 (10.3%)
PD-L1 expression (*n*, %)	
<1%	68 (20%)
1%-49%	112 (33.9%)
≥50%	103 (30.3%)
Unknown	57 (16.8%)

Results are expressed as mean and standard deviations for numeric variables and count and percentages for categorical variables. Abbreviations: DLCO: carbon monoxide lung diffusion capacity; FEV1: forced expiratory volume in 1 second; PD-L1: programmed death-ligand 1.

patients), and patient choice (1 patient). We could not identify any patient-related factor associated with surgical drop-off.

We identified 10 cases of grade 2 thyroid toxicity. The true rate of low-grade, subclinical thyroid toxicity was probably higher than the patients we have identified as, unlike the trials, we would not routinely be monitoring their thyroid function after they completed neo-adjuvant chemotherapy.

The median interval from last cycle completion to surgery was 43 days (IQR 33-56).

One hundred sixty patients (47%) had surgery more than 6 weeks after completion of the last neoadjuvant cycle. In 61 patients (19%), the delay to surgery was longer than 9 weeks. The 2 main reasons for surgical delay were logistic/organizational and the patient needing more time to recover from the neoadjuvant systemic treatment.

A total of 317 patients (93.2%) had surgery following neoadjuvant treatment.

One hundred eighty-six procedures were started in VATS and 22 robotically; 109 were approached with open thoracotomy. In total, 66% were started with a minimally invasive approach. Thirty-eight were converted to open (18%). Five were converted for bleeding, the others for difficult dissection due to adhesions or fibrotic hilar tissue.

Overall, 52% of patients had their procedures completed minimally invasive. Conversion rate was similar during VATS or robotic operations (17% vs 27%, $P = .25$).

We were not able to find any association between clinical characteristics and conversion. Similar proportion of cT4 stages (16% vs 20.6%, $P = .50$) or clinical N1 (47% vs 31%, $P = .35$) disease were found in the converted cases and in those completed by a minimally invasive procedure.

Table 2. Surgical and Pathological Results in Patients Who Had Surgery (no. 317 Patients)

Variables	
Time from last cycle to surgery (days, median, IQR)	43 (33-56)
Surgical access	
VATS	186 (58.7%)
Robotic	22 (6.9%)
Open	109 (34.4%)
Lobectomy	275 (86.7%)
Bilobectomy	26 (8.2%)
Pneumonectomy	14 (4.4%)
Wedge	2 (0.7%)
Downstaged to pN0 (among 201 surgical patients with cN+)	136 (67.7%)
Clinical stage downstaged	208 (65.6%)
pCR	95 (30%)
MPR	167 (52.7%)

Results are expressed as mean and standard deviations for numeric variables and count and percentages for categorical variables. Abbreviations: MPR: major pathologic response; pCR: pathologic complete response; VATS: video-assisted thoracoscopic surgery.

The most frequent procedure was lobectomy in 273 patients (86%) (including 14 sleeve resections), followed by bilobectomy in 26 patients (8.2%), pneumonectomy in 14 (4.4%), and sublobar resections in 2 patients (due to declined pulmonary function after neoadjuvant treatment).

Median postoperative hospital stay was 5 days (IQR 3-8). The most frequent postoperative complications were the following (**Table S1**): atrial fibrillation (14 patients), pneumonia (34 patients), and prolonged air leak (35 patients). Thirteen patients required unplanned ICU admission. Seven of them died. Postoperative severe adverse events (grade 3 or higher) occurred in 36 patients (11.4%). Ninety-day postoperative mortality occurred in 8 patients (2.5%). Four patients died of pneumonia and respiratory failure; 1 patient died of immune-related pneumonitis and respiratory failure; 1 patient died of sepsis; 1 died following an immune-related ischaemic colitis; in 1 patient, the cause of death was unknown. To the best of our knowledge, 2 of the deaths were related to immunotherapy.

Two hundred and eight patients (65.6%) were pathologically downstaged at the postoperative definitive pathological report. Ninety-eight percent of resections were staged as R0.

Of the 99 patients with clinical stage N1 who proceeded to surgery, 78 were postoperatively downstaged to ypN0 (78.8%).

Of the 102 patients with clinical stage N2 who proceeded to surgery, 58 were postoperatively downstaged to ypN0 (56.9%) and 16 to ypN1 (15.7%).

Surgical and pathological results are summarized in **Table 2**.

pCR occurred in 95 patients (30% of the surgical patients, 28.1% in the evaluable intention to treat population), and MPR occurred in 167 patients (52.7% of the surgical patients, 48.1% in the evaluable intention to treat population).

Table 3 shows the pCR and MPR by patient- and tumour-related characteristics.

The most notable difference was a larger pCR (39% vs 23%, $P = .004$) and MPR (66% vs 45%, $P = .001$) in squamous cell carcinomas compared to non-squamous histology tumours.

Table 3. Complete Pathological Response (pCR) and Major Pathological Response (MPR) by Patient- and Tumour-related Characteristics in 317 Resected Patients

	pCR (*n*, %)	*P*-values	MPR (*n*, %)	*P*-values
Age ≥ 65 (*n* = 201)	54 (26.9%)	0.112	103 (51.2%)	0.50
Age < 65 (*n* = 116)	41 (35.3%)		64 (55.2%)	
Males (*n* = 179)	56 (31.3%)	0.56	92 (51.4%)	0.60
Females (*n* = 138)	39 (28.3%)		75 (54.3%)	
PD-L1 < 1% (*n* = 62)	21 (33.9%)	0.080	28 (45.2%)	0.004
PD-L1 1%-49% (*n* = 107)	25 (23.4%)		53 (49.5%)	
PD-L1 ≥ 50% (*n* = 96)	36 (37.5%)		66 (68.8%)	
Clinical stage II (*n* = 123)	38 (30.9%)	0.77	60 (48.8%)	0.41
Clinical stage IIIA (*n* = 149)	42 (28.2%)		80 (53.7%)	
Clinical stage IIIB (*n* = 45)	15 (33.3%)		27 (60%)	
Clinical nodal stage		0.148		0.058
cN0 (*n* = 116)	28 (24.1%)		51 (44%)	
cN1 (*n* = 99)	36 (36.4%)		56 (56.6%)	
cN2 (*n* = 102)	31 (30.4%)		60 (58.8%)	
Squamous (*n* = 109)	42 (38.5%)	0.004	71 (65.1%)	0.001
Adenocarcinoma (*n* = 168)	38 (22.6%)		75 (44.6%)	

Results are expressed as count and percentages for categorical variables. Abbreviation: PD-L1: programmed death-ligand 1.

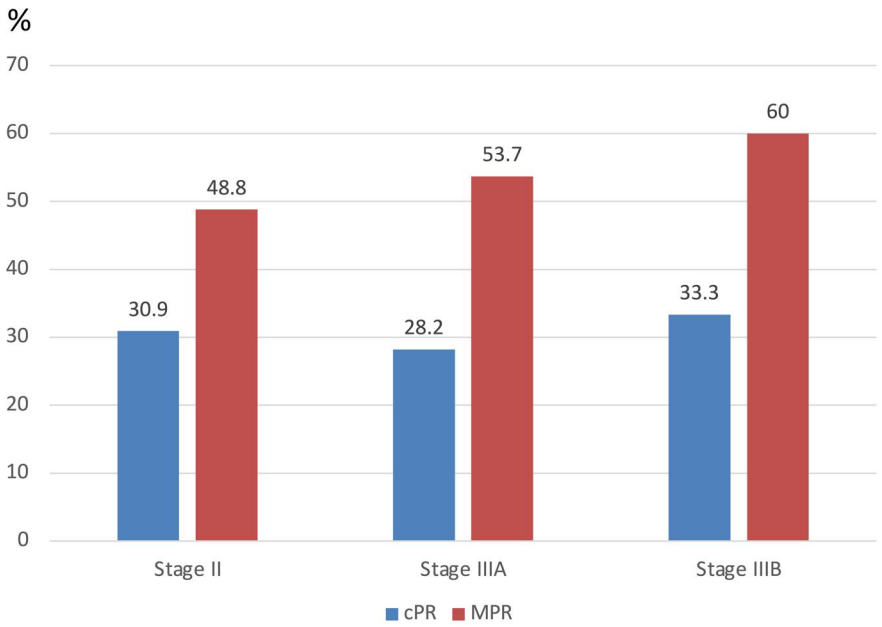


Figure 1. Pathological Response by Clinical Stage in the Resected Patients. Abbreviations: MPR: major pathological response; pCR: complete pathological response

Table S2 shows our main surgical and pathologic results compared to those reported from trials using platinum-based chemotherapy and nivolumab as neoadjuvant treatment.

The incidence of pCR ($P = .78$) and MPR ($P = .26$) were similar in patients with clinical stage II and III (**Figure 1**). pCR was 31% in stage II and 29.7% in stage III. MPR was 49% in stage II and 56% in stage III. pCR was 28.1% in operated patients with clinical stage IIIA and 34.1% in operated patients with clinical stage IIIB.

PDL1 expression showed a trend to higher incidence of pCR or MPR when grouped in 3 categories (<1%, 1%-49%, and ≥50%) ($P = .98$ and $P = .002$, respectively). pCR rate was higher in patients with PD-L1 ≥ 50% compared to those with PD-L1 < 50% (37.5% vs 27.2%, $P = .082$). However, mere PD-L1 positivity was not associated with different complete pathological response (PD-L1 < 1%, 33.9% vs PD-L1 ≥ 1%, 30.0%, $P = .57$), whereas MPR tended to be higher in those with PD-L1 > 1% (58.6% vs 45.2%, $P = .062$).

Notably, 33.9% and 45.2% of patients with PD-L1 < 1% still had pCR and MPR, respectively (**Table 3** and **Figure 2**).

No differences in pCR ($P = .32$) and MPR ($P = .23$) were observed between patients operated within 6 weeks and those operated after 6 weeks from completion of the last treatment cycle (**Figure 3**). pCR in patients operated more than 6 weeks after completion of their neoadjuvant treatment was 32.5% (52 of 160 patients). pCR was 36% also in those patients operated more than 9 weeks after their last chemo-ICI cycle (22 out of 61 patients). Among the patients operated more than 6 weeks from the last neoadjuvant cycle, we were not able to find any difference in cPR ($P = .59$) or MPR ($P = .16$) between different PD-L1 expression levels (**Table S3**).

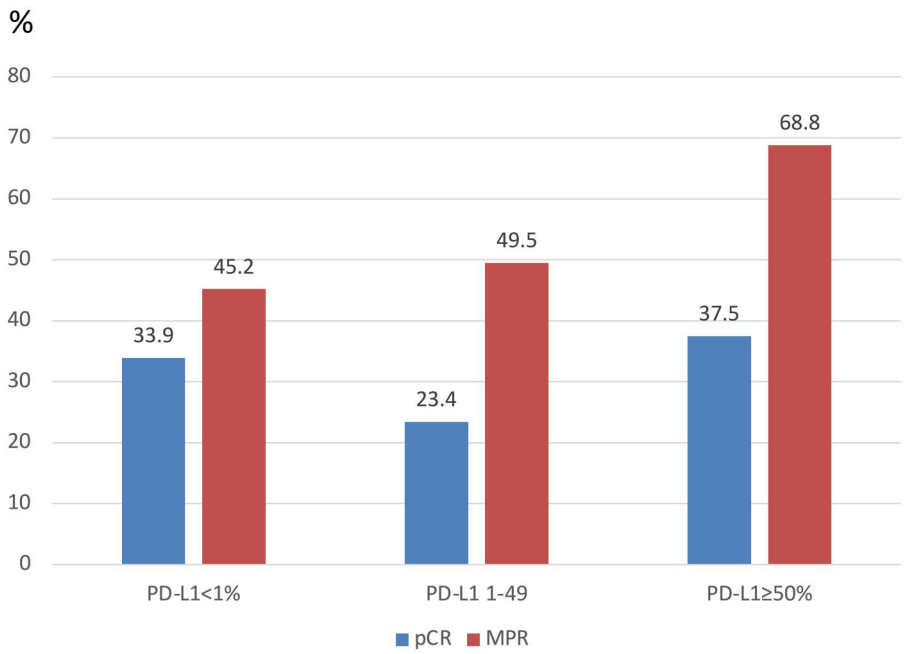


Figure 2. Pathological Response by PD-L1 Expression Level in the Resected Patients. Abbreviations: MPR: major pathological response; pCR: complete pathological response

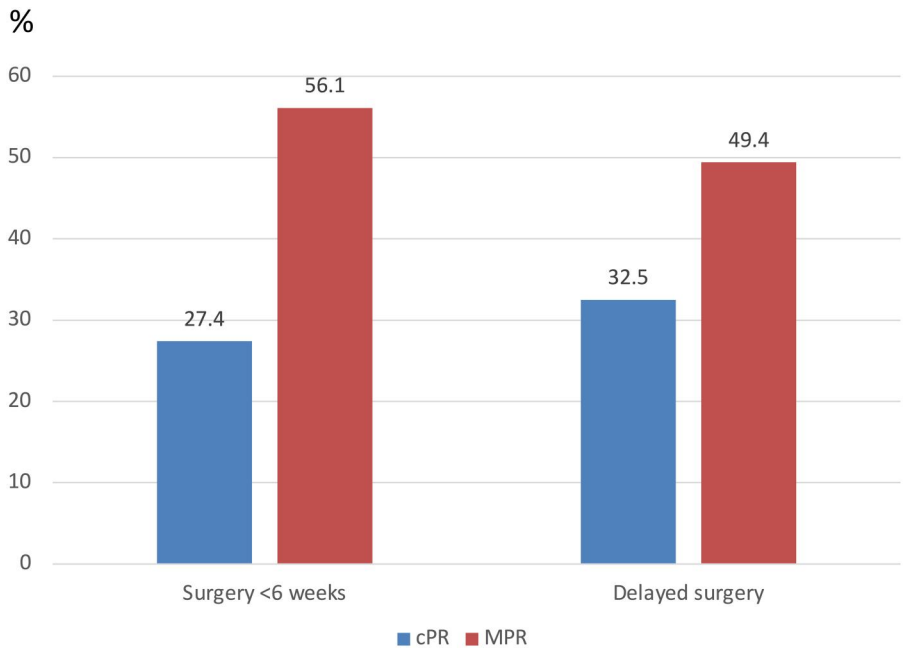


Figure 3. Pathological Response according to Delay to Surgery. Abbreviations: MPR: major pathological response; pCR: complete pathological response

pCR was similar between clinical nodal stages ($P = .39$). pCR was 24.1% in cN0 stage, 36.4% in cN1, and 30.4% in cN2. MPR was also not different between nodal stages (cN0 44%, 56.6% in cN1, and 58.8% in cN2, $P = .068$). Among the 102 patients with cN2 stage who proceeded to surgery, 35 had a multistation cN2 disease (34.3%). These patients had a similar pCR and MPR compared to those with single-station N2: pCR: 31.4% vs 29.9%, $P = .87$; and MPR: 65.7% vs 55.2%, $P = .31$. All resections were staged as pR0 in this subgroup of patients.

After adjustment for patient- and tumour-related confounders and for clustering effect within the hospitals, logistic regression showed that squamous histology (OR 3.1, 95% CI 1.6-6.0, $P = .001$) and PD-L1 $\geq$ 50% level (OR 3.0, 95% CI 1.4-6.4, $P = .004$) were the only factors associated with higher

probability of MPR. The probability of a MPR in a hypothetical patient with squamous cell carcinoma and PD-L1 expression value ≥ 50% is 83%.

DISCUSSION

We found that the pCR and MPR rates in our patients were similar to those reported in clinical trials.[1,2,10-12] This was the case even in the presence of a different case-mix population. Our patients were older, included more females, more adenocarcinomas, and more tumours with higher PD-L1 expression levels than in the Checkmate trials. Importantly, the MPR and pCR rates found in the present study appear consistent with those recently published in a multicentre study from England (including about 30% of the patients in this study[7]) and with those reported by other routine clinical practice studies from Asia and using a variety of ICIs as neoadjuvant agents in combination with platinum-based chemotherapy.[13-16]

Interestingly, we found a higher pCR in squamous tumour compared to non-squamous histology as reported also in the AEGEAN trial.[4] As expected, we found higher pCR and MPR in tumours with PD-L1 ≥ 50%. Nevertheless, even tumours with PD-L1 expression < 1% showed a pCR which was nearly the double of what reported in the Checkmate trial (33.9% vs 16.7%).

We were not able to find any difference of pathologic response between different nodal stages. Even patients with clinical stage N0 had a pCR of about 32% and MPR of 44%. Similarly, patients with multistation clinical N2 disease did not appear to have an inferior pathologic response to their single station counterparts. This is in line with a recent pooled analysis of the Aegean, Checkmate 77 T, and NADIM trials, showing similar HR for EFS between multistation N2 and single station N2 disease (HR 0.50 for multistation vs HR 0.58 for single station).[17]

Noticeably, 66% of patients with a positive nodal disease prior to start treatment were pathologically downstaged to N0. This finding is in line with what reported by Liu et al.[12] Overall, 67% of patients had a pathological downstage compared to pretreatment clinical stage. This is slightly lower rate compared to 90% observed in NADIM trial which, however, included only stage III patients.[11]

Ninety eight percent of the patients in our series had a complete resection, which is higher than the one reported in trials using chemo-nivolumab.[1,2]

We found an attrition to surgery rate of only 7%. This was much lower than what was reported in the Checkmate trials[1,2] and more similar to the rate found in the NADIM and CTONG1804 trials.[9,12] Differences in the attrition rate may be due to different population characteristics and improved selection. In addition, the longer time to surgery with 47% of patients having surgery more than 6 weeks after completion of the neoadjuvant phase (vs 16%-21% of patients in the trials) may have contributed to increase the number of patients fit for surgery. Delaying surgery was not associated with different pCR in our study. The 6 weeks' timeframe was chosen as this value is the one commonly used in trials to define delayed treatment and recommended by regulatory agencies. Most of our delayed surgeries (63%) occurred between 6 and 9 weeks from last neoadjuvant cycle. The small attrition rate is reflected in the high cPR and MPR in the intention to treat population. Unfortunately, the retrospective nature of this study prevented us to perform a more in-depth analysis on the causes of the surgical delay and their association with outcome.

Importantly, we observed a small rate of progressive disease during the neoadjuvant treatment which led to surgery cancellation. This occurrence was rarer than in the trials (2.9% vs 6%-7%). Most of the surgery cancellations occurred due to poor fitness or adverse events, which were however rarer than in trials (4.2% vs 9%-15%).

In our study, two-thirds of the operations started using video-assisted thoracoscopic or robotic approach compared to only 29.5% in the Checkmate 816 series.[1] Our conversion rate to open surgery, however, was 18% compared to 11.4% and 7% reported in the Checkmate trials.[1,2] This higher rate of minimally invasive surgery has also been reported by others.[7,12-15] The higher conversion rate found in our series is likely explained by a larger sample size initially started with a minimally invasive approach and a low threshold for conversion in case of increased surgical complexity. Overall, the proportion of our patients who had their surgery completed by a minimally invasive approach was higher than in most of the trials.

Like other real clinical practice reports,[7,13,14] our rate of pneumonectomies was only 4.4%. This proportion is much lower than those reported in previous trials (1-6,15). This difference may be partly explained by a better patient selection during discussion at the tumour board. Another explanation may be the increased use of non-surgical curative intent approaches for stage III patients with borderline resectability outside clinical trials.

Postoperative mortality and the incidence of grade 3 or higher adverse events was only 11% and not higher than the one reported in trials. Eleven patients required unplanned admission to ICU. No association with advanced stage could be find (8 patients were in stage II and 3 in stage III). This underscores the safety of this treatment in well-selected patients, despite the lower attrition rate compared to previous reports. One of the strengths of the present study is providing real-world data on perioperative outcomes, offering a transparent and clinically relevant picture for the thoracic surgical community, which sometimes is less clear in the trials.

Limitations

This study may have potential limitations.

The 6 participating centres are all large tertiary referral academic thoracic institutions. The reproducibility of these findings in smaller-volume and non-academic units needs to be verified.

We only reported surgical results. Follow-up was not mature enough to report survival figures which will be the object of future analyses.

All patients received nivolumab as immunotherapeutic agent prior to surgery. This was the only immunotherapy agent approved for clinical use as neoadjuvant treatment in Europe at the time of the study. Extrapolating our findings to neoadjuvant treatments, including other types of ICIs, needs to be verified.

The retrospective and multicentre nature of the study may introduce some inherent bias in the recording and definition of variables.

Despite we tried to be as accurate as possible in recording all patients who started the neoadjuvant treatment and were not able to proceed to surgery, we cannot completely rule that we have missed out some occasional patient. We excluded from this specific attrition rate analysis a centre that was unable to track patients who could not proceed to surgery.

Unfortunately, we were not able to precisely analyse the resectability rate among stage IIIA and IIIB as we don't have information about stage-equivalent patients deemed unresectable at the time of MDT discussion and never starting the neoadjuvant treatment.

Finally, given the absence of a central pathological review, the possibility of inter-institutional variability in pathologic response evaluation should be considered when interpreting our results.

CONCLUSIONS

We found that the use of neoadjuvant nivolumab in association with platinum-based chemotherapy in the real clinical practice is associated with outcomes as safe and effective as those reported in the trials. Our real clinical practice data from public academic healthcare systems represent valuable information to be used during multidisciplinary treatment selection for clinical stage II and III resectable NSCLC. In addition, this information may represent a useful information aid tool with patients during shared decision-making.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

FUNDING

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CONFLICTS OF INTEREST

Alessandro Brunelli received consultancy fees for speaker honoraria and advisory Board roles with Astra Zeneca, BMS, Ethicon, MSD, Medela, Medtronic and Roche. Clemens Aigner received consultancy fees for speaker honoraria and advisory Board roles with AstraZeneca, BMS, MSD, Roche and Ewimed, and received institutional grants from BMS, Ewimed, PharmaCept, Medtronic and D-A-CH medical group. Marcelo Jimenez received consultancy fees as Advisor and proctor for Medtronic, Proctor for Intuitive and speaker for BMS. Pooja Bhatnagar received consultancy fees for speaker honoraria and advisory Board roles with Astra Zeneca, MSD, Roche, Pfizer and Takeda. Katy Clarke received consultancy fees for speaker honoraria with Astra Zeneca, MSD, and Takeda. Carles Escriu received consultancy fees for speaker honoraria with BMS. Kevin Franks received consultancy fees for speaker honoraria and advisory Board roles with AstraZeneca, Amgen, Biontech, Boehringer-Ingelheim, Bristol-Meyers-Squibb, ELEKTA, Genesis Cancer Care UK, Lilly, Novartis, Pierre Fabre, Roche, and Takeda. Nicolas Girard received Research grants/support from Abbvie, Amgen, AstraZeneca, Beigene, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi-Sankyo, Gilead, Hoffmann-La Roche, Janssen, LeoPharma, Lilly, Merk Serono, Merck Sharp & Dohme, Novartis, Sanofi, Sivan, and received consultancy fees from Abbvie, Amgen, AstraZeneca, Beigene, Bristol Myers Squibb, Daiichi-Sankyo, Gilead, Ipsen Hoffmann-La Roche, Janssen, LeoPharma, Lilly, Merck Sharp & Dohme, Mirati, Novartis, Pfizer, Pierre Fabre, Sanofi, Sivan Takeda. Mariano Provencio received consulting fees from BMS, AstraZeneca, MSD, Roche, Takeda. Virginia Calvo received consulting fees and honoraria from Roche, AstraZeneca, MSD, BMS, Takeda, Sanofi, Amgen, Pfizer, Janssen. David Gómez de Antonio received fees for speaker honoraria from Astra Zeneca and Bristol-Meyers-Squibb. Michael Shackcloth received consultancy fees for speaker honoraria and advisory Board roles with AstraZeneca and Roche. No disclosures were reported by the other authors.

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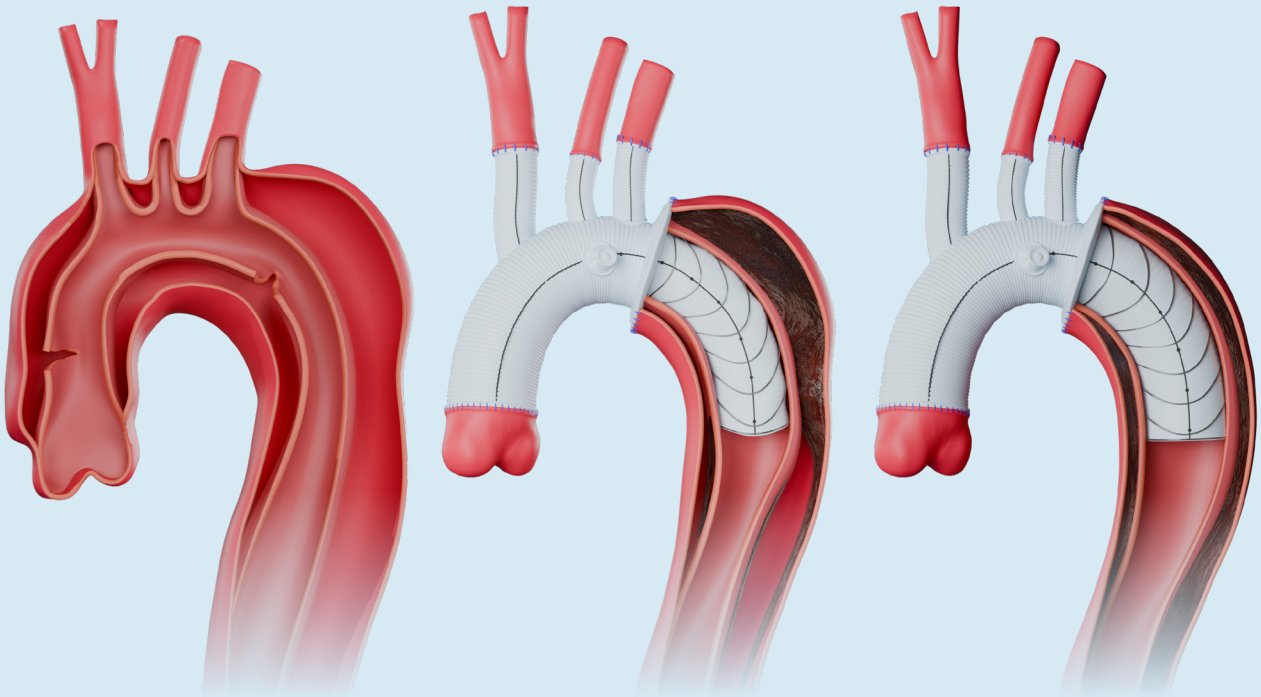

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