Surgeon preferences for self-treatment in locally advanced non–small cell lung cancer: Would we practice what we preach?

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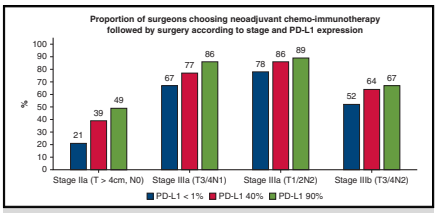
Supplemental material is available online.

Recent trials have shown that the preoperative, postoperative, or perioperative use of immunotherapy agents or targeted therapies with or without chemotherapy improves outcomes for selected groups of patients with locally advanced resectable non–small cell lung cancer (NSCLC). However, the extent to which healthcare providers have adopted these evolving approaches is unknown, particularly as it may pertain to their hypothetical own potential treatment. In particular, the risk perception of surgeons playing the role of patients and undergoing multimodal treatment in different hypothetical scenarios provides thought-provoking perspective that may help identify knowledge and evidence gaps for future investigations and educational activities.



Proportion of surgeons choosing neoadjuvant chemoimmunotherapy.

CENTRAL MESSAGE

We report surgeons' preferences for their own treatment in the event that they were diagnosed with stage II or III resectable lung cancer in the context of multimodal immunotherapy and targeted therapy strategies.

PERSPECTIVE

This survey reflects the current personal understanding of surgeons regarding multimodal treatment of potentially resectable lung cancer in the era of immunotherapy and targeted therapies. Although the work is not meant as a best practice document, it may represent valuable educational material for the multidisciplinary team and an information tool to aid the shared decision making process.

See Commentary on page XXX.

Therefore, the European Society of Thoracic Surgeons (ESTS) and the General Thoracic Surgical Club (GTSC) recently approved a survey aimed at capturing clinicians' current subjective perception of the risk of undergoing multimodality treatment from a personal standpoint. The strategy of this survey was to provide respondents with different scenarios to be interpreted as though the surgeon is the patient, having been diagnosed with stage II-III NSCLC, and is being offered various treatments by the hypothetical responsible clinician.

Through this survey, we aimed to provide a more personalized representation of the acceptance of current

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* See Table E1 for a list of collaborators in the Working Group.

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Abbreviations and Acronyms

ALK = anaplastic lymphoma kinase
EGFR = epidermal growth factor receptor
ESTS = European Society of Thoracic Surgeons
NSCLC = non–small cell lung cancer
PD-L1 = programmed death-ligand 1
TKI = tyrosine kinase inhibitor

pharmacologic and multidisciplinary treatment strategies among members of the thoracic surgical community from a deliberately subjective standpoint. We hypothesized that there may be potential differences between the strategies recommended by surgeons to their patients compared to the strategies that they may choose for themselves in terms of optimal management of NSCLC.

METHODS

No patients were involved in this study, and Institutional Review Board approval was not necessary. A core group of 5 surgeons (A.B., M.B.A., B.S., R.H.P., and D.A.W.) generated the survey questions. The questions were designed to explore the preferred management in the hypothetical scenario in which the respondent was diagnosed with a locally advanced lung cancer and was offered different multimodal treatment strategies (assuming all treatments were available and funded at the local hospital).

The questions represented several scenarios, including different stages of disease, different expression levels of programmed death-ligand 1 (PD-L1), and the presence of actionable targeted mutations. These topics were used to generate 9 demographic questions and 29 procedural questions, which are shown in Table E2. The questions were collated into a survey, which was sent by email to a group of 404 thoracic surgeons using a commercially available platform (www.surveymonkey.com). The selection criterion for survey participation was membership on the board, a committee, or a working group of the European Society of Thoracic Surgeons; membership in the Thoracic Domain of the European Association of Cardiothoracic Surgery; or active membership in the General Thoracic Surgical Club.

The initial survey was sent on November 27, 2023, and responses were closed on December 22, 2023. Three reminders were sent during this period.

Statistical Analysis

Descriptive statistics were used to summarize the results. There were no missing answers because all the answers were mandatory. No confidential information was required for this study. Data were reported as number and percentage. The analysis was performed using Stata 15.1 statistical software (StataCorp).

RESULTS

Respondent Cohort

A total of 143 surgeons from 26 countries completed the survey; the response rate was 35%. All respondents answered all questions, as required. In terms of geographic distribution, 85 (59.4%) of the surgeons worked in Europe, and 46 (32%) practiced in the United States or Canada. Most respondents were men (n = 116; 81%). Approximately one-third (n = 46; 32%) were age <45 years, the majority were age 45 to 54 years, and only 9 were age >65 years. There was no difference in age distribution between the surgeons practicing in Europe and those practicing in North America ($P = .28$). Similar proportions of surgeons in the 2 groups were age <45 years (32% vs 30%) and age >55 years (29% vs 35%). Twenty-two percent were in practice for ≤10 years, and 41% were in practice for >20 years. No statistical trend in differences in experience were detected overall between European and North American surgeons ($P = .21$). However, there was a higher proportion of surgeons with ≤10 years of practice experience in North America (30% vs 19%). Conversely, more surgeons with ≥20 years of experience were seen in Europe (46% vs 33%). Eighty-one percent of all respondents reported working in an academic/university hospital, and all respondents judged themselves to be fit or very fit to undergo multimodal cancer treatment, including surgery.

Scenario Responses

Stage IIA (T>4 cm N0). In the scenario "without EGFR-actionable mutations" (Figure 1, Table E3), upfront surgery alone or with adjuvant chemotherapy was the most frequent choice when PD-L1 expression was <1%. At higher levels of PD-L1 expression, many respondents would still prefer surgery upfront, followed by adjuvant chemoimmunotherapy (43% in the event that PD-L1 was 40% and 40% if PD-L1 was 90%). However, if PD-L1 expression was 90%, the neoadjuvant or perioperative chemoimmunotherapy approach was the favored strategy (49%).

Compared to European surgeons, a larger proportion of North American surgeons favored a neoadjuvant or perioperative approach (41% vs 9% with low PD-L1 expression [$P < .001$] and 70% vs 41% with high PD-L1 expression [$P = .002$]). European surgeons preferred surgery alone or surgery followed by adjuvant systemic treatment (91% vs 59% with low PD-L1 expression and 59% vs 30% with high PD-L1 expression).

In the setting of "EGFR-actionable mutations," the preferred treatment was surgery followed by adjuvant osimertinib regardless of the PD-L1 expression level (Figure 2, Table E4). In the setting of high PD-L1 expression, 34% of respondents would prefer a perioperative approach including neoadjuvant chemoimmunotherapy and adjuvant osimertinib. European and North American surgeons had similar preferences in this situation. The majority would prefer surgery followed by adjuvant osimertinib (72% vs 65% with low PD-L1 expression and 44% vs 43% with high PD-L1 expression). In the scenario with high PD-L1 expression, many surgeons from both continents preferred neoadjuvant chemoimmunotherapy followed by adjuvant osimertinib after surgery (35% vs 37%).

Stage IIIA (T3/4 N1). In the scenario "without EGFR-actionable mutations" (Table 1), the preferred approach was neoadjuvant or perioperative chemoimmunotherapy

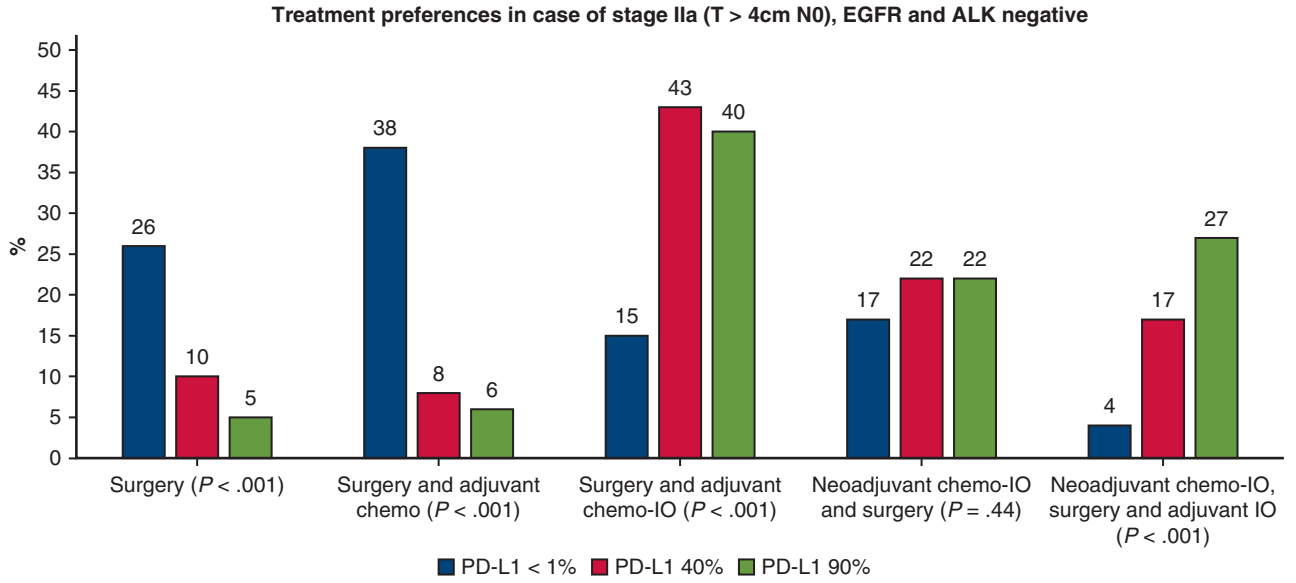

FIGURE 1. Treatment preferences in the scenario of stage IIa (T>4 cm N0), EGFR- and ALK-negative. *EGFR*, Epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase; *PD-L1*, programmed death-ligand 1.

(67% with low PD-L1 expression and 86% with high PD-L1 expression). There were differences between European and American surgeons, as the latter expressed a greater preference for a neoadjuvant/perioperative approach (98% vs 53% with low PD-L1 expression [$P < .001$] and 98% vs 81% with high PD-L1 expression [$P = .006$]). Forty-five percent of European surgeons would prefer surgery followed by adjuvant chemotherapy or chemoimmunotherapy in case of low PD-L1 expression. This percentage drops to 18% when PD-L1 expression is 90%.

In the scenario "with EGFR-actionable mutations," at low PD-L1 expression levels, the preferred strategy was to use osimertinib in the adjuvant setting after upfront surgery (29%) or neoadjuvant chemoimmunotherapy (27%) (Table 2). At higher PD-L1 expression levels, more than one-half of the respondents prefer neoadjuvant chemoimmunotherapy, followed by surgery and adjuvant osimertinib. A similar proportion of surgeons from Europe and North America prefer adjuvant osimertinib following surgery alone or neoadjuvant treatment with chemotherapy

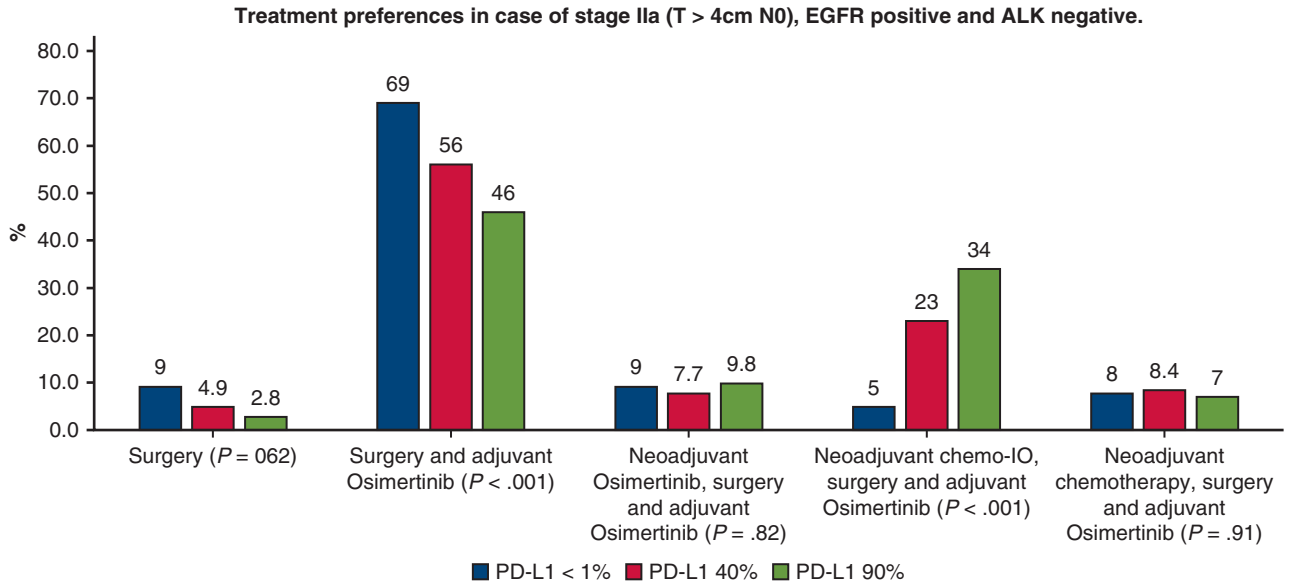

FIGURE 2. Treatment preferences in the scenario of stage IIa (T>4 cm N0), EGFR-positive and ALK-negative. *EGFR*, Epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase; *PD-L1*, programmed death-ligand 1.

TABLE 1. Treatment preferences in the scenario of stage IIIa (T3/4 N1), EGFR- and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Surgery alone	1 (0.7)	0	0	.38
Surgery and adjuvant chemotherapy	31 (22)	9 (6.3)	2 (1.4)	<.001
Surgery and adjuvant chemoimmunotherapy	14 (9.8)	23 (16)	17 (12)	.26
Neoadjuvant chemoimmunotherapy and surgery	51 (36)	33 (23)	29 (20)	.007
Neoadjuvant chemoimmunotherapy, surgery, and adjuvant immunotherapy	44 (31)	77 (54)	94 (66)	<.001
Definitive chemoradiotherapy	1 (0.7)	1 (0.7)	0	.61
Chemoradiotherapy and durvalumab	1 (0.7)	0	1 (0.7)	.61

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

or chemoimmunotherapy (73% vs 80% with low PD-L1 expression and 75% vs 85% with high PD-L1 expression).

Stage IIIA (T1/2N2). In the scenario "without EGFR actionable mutations" (Table 3), the most preferred treatment by far was the neoadjuvant or perioperative approach with chemoimmunotherapy (78% of respondents with low PD-L1 expression and 89% with high PD-L1 expression), with the perioperative approach the favorite at all levels of PD-L1 expression. Compared to European surgeons, North American surgeons were more frequently in favor of the neoadjuvant or perioperative approach at lower levels of PD-L1 expression, but preferences were similar at higher PD-L1 levels (73% vs 89% with low PD-L1 expression [$P = .043$] and 86% vs 96% with high PD-L1 expression [$P = .14$]).

In the scenario "with EGFR actionable mutations," the preferred strategy was neoadjuvant chemoimmunotherapy, followed by surgery and adjuvant osimertinib (34% of respondents with low PD-L1 expression and 58% with high PD-L1 expression). At low PD-L1 expression, many surgeons would prefer either neoadjuvant chemotherapy (27%) or neoadjuvant osimertinib (20%) followed by surgery and adjuvant osimertinib (Table 4). The preferences of European and North American surgeons appeared consistent with this scenario, with most favoring neoadjuvant chemoimmunotherapy, surgery, and adjuvant osimertinib (31% vs 46% with low PD-L1 expression [$P = .13$] and 55% vs 70% with high PD-L1 expression [$P = .14$]). Slightly more surgeons in Europe would prefer a perioperative osimertinib monotherapy approach, especially at higher level of PD-L1 expression (21% vs 15% with low PD-L1 expression [$P = .48$] and 15% vs 4.3% with high PD-L1 expression [$P = .084$]).

Stage IIIB (T3/4N2). In the scenario "without EGFR actionable mutations" (Figure 3, Table E5), the perioperative strategy with neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy was the preferred treatment at all levels of PD-L1 expression (36% with low PD-L1 expression and 57% with high PD-L1 expression). A considerable proportion of surgeons

TABLE 2. Treatment preferences in the scenario of stage IIIa (T3/4 N1), EGFR-positive and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Best supportive care	1 (0.7)	0	0	.37
Surgery and adjuvant osimertinib	42 (29)	31 (22)	21 (15)	.011
Neoadjuvant osimertinib, surgery, and adjuvant osimertinib	26 (18)	15 (11)	18 (13)	.15
Neoadjuvant chemoimmunotherapy, surgery, and adjuvant osimertinib	38 (27)	73 (51)	79 (55)	<.001
Neoadjuvant chemotherapy, surgery, and adjuvant osimertinib	29 (20)	15 (11)	15 (11)	.021
Definitive chemoradiation	1 (0.7)	0	0	.37
Neoadjuvant chemoimmunotherapy, surgery, osimertinib only for recurrences after surgery	6 (4.2)	7 (4.9)	9 (6.3)	.72
Chemoradiotherapy and duvalumab	0	2 (1.4)	1 (0.7)	.37

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

TABLE 3. Treatment preferences in the scenario of stage IIIa (T1/2 N2), EGFR- and ALK–negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Best supportive care	1 (0.7)	0	0	.37
Surgery and adjuvant chemotherapy	15 (10)	3 (2.1)	0	<.001
Surgery and adjuvant chemoimmunotherapy	4 (2.8)	11 (7.7)	9 (6.3)	.18
Neoadjuvant chemoimmunotherapy and surgery	49 (34)	31 (22)	23 (16)	.001
Neoadjuvant chemoimmunotherapy, surgery and adjuvant immunotherapy	63 (44)	92 (64)	104 (73)	<.001
Definitive chemoradiation	3 (2.1)	1 (0.7)	0	.17
Chemoradiotherapy and durvalumab	8 (5.6)	5 (2.1)	7 (4.9)	.69

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

would prefer a nonsurgical approach including definitive chemoradiation and durvalumab (27% at low PD-L1 expression and 29% at high PD-L1 expression) or definitive chemoradiation alone if PD-L1 expression is low (15%). A large proportion of both European and North American surgeons would prefer a nonsurgical approach if PD-L1 expression is low (42% vs 41%). These proportions dropped to 32% and 24%, respectively, at high levels of PD-L1 expression. The preferred strategy for surgeons from both continents was the neoadjuvant chemoimmunotherapy or perioperative treatment including adjuvant immunotherapy (49% vs 54% at low PD-L1 expression and 66% vs 76% at high PD-L1 expression), with a slightly higher preference for perioperative treatment expressed by North American surgeons (46% vs 31% at lower levels of PD-L1 expression [$P = .086$]; 70% vs 53% at higher PD-L1 expression [$P = .065$]).

In the scenario "with EGFR-actionable mutations," the preferred strategy was neoadjuvant chemoimmunotherapy followed by surgery and adjuvant osimertinib (Figure 4, Table E6). Approximately 28% of surgeons would prefer a nonsurgical modality in the event of low PD-L1 expression, with the PACIFIC regimen preferred by approximately 20% of respondents at all PD-L1 expression levels.

Approximately the same proportion of European and North American surgeons would prefer a nonsurgical treatment (28% vs 26% at low PD-L1 expression and 27% vs 22% at high PD-L1 expression). Adjuvant osimertinib after neoadjuvant chemotherapy and surgery (22% vs 20% at low PD-L1 expression and 11% vs 13% at high PD-L1 expression) or after neoadjuvant chemoimmunotherapy and surgery (22% vs 37% at low PD-L1 expression and 42% vs 57% at high PD-L1 expression) was the preferred approach for both European and North American surgeons.

Special Clinical Scenarios

cT3N2 stage IIIB NSCLC, PD-L1 50%, and no actionable mutations; cancer only appears resectable by pneumonectomy. The majority of all respondents (52%) preferred reassessment after several cycles of chemoimmunotherapy to determine further treatment (chemoradiation or surgery). Nearly one-quarter (23%) chose to receive

TABLE 4. Treatment preferences in the scenario of stage IIIa (T1/2 N2), EGFR-positive and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Best supportive care	1 (0.7)	1 (0.7)	0	.61
Surgery and adjuvant osimertinib	16 (11)	9 (6.3)	7 (4.9)	.104
Neoadjuvant osimertinib, surgery, and adjuvant osimertinib	29 (20)	23 (16)	18 (13)	.21
Neoadjuvant chemoimmunotherapy, surgery, and adjuvant osimertinib	48 (34)	77 (54)	83 (58)	<.001
Neoadjuvant chemotherapy, surgery, and adjuvant osimertinib	38 (27)	24 (17)	19 (13)	.012
Definitive chemoradiation	4 (2.8)	1 (0.7)	0	.072
Neoadjuvant chemoimmunotherapy, surgery, osimertinib only for recurrence after surgery	6 (4.2)	4 (2.8)	11 (7.7)	.14
Chemoradiotherapy and duvalumab	1 (0.7)	4 (2.8)	5 (3.5)	.26

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

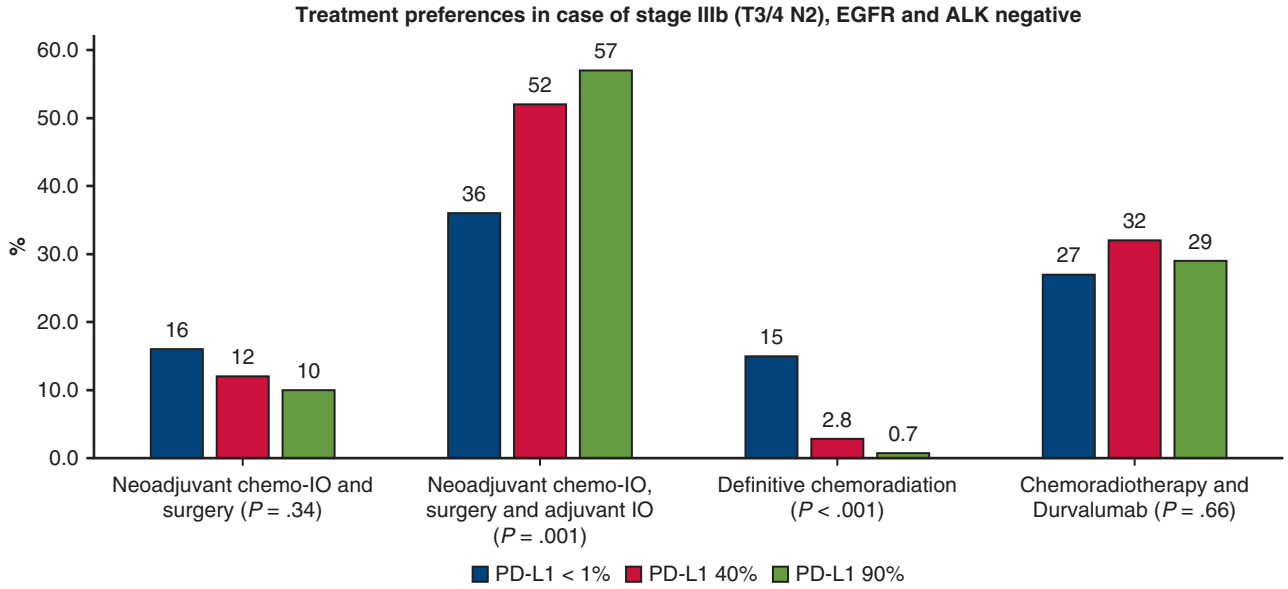

FIGURE 3. Treatment preferences in the scenario of stage IIIb (T3/4 N2), EGFR- and ALK-negative. *EGFR*, Epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase; *PD-L1*, programmed death-ligand 1.

neoadjuvant chemoimmunotherapy and then pneumonectomy, 22% chose the PACIFIC regimen (chemoradiotherapy followed by durvalumab), and a much smaller minority (3.5%) chose best supportive care.

cT3N2 NSCLC, PD-L1 expression 80%; the restaging CT scan following neoadjuvant chemoimmunotherapy shows a nearly complete radiologic response. The majority (48%) chose to undergo resection at a lesser extent than that planned before neoadjuvant treatment. Another 36% preferred to receive the same extent of surgery as planned before neoadjuvant treatment.

cT3N2 NSCLC, PD-L1 90%; the definitive pathology after neoadjuvant chemoimmunotherapy and lobectomy shows a complete pathologic response. The majority of respondents (62%) preferred to continue immunotherapy, 28% chose to undergo cancer surveillance only, and 10% preferred to continue chemoimmunotherapy.

cT3N2 NSCLC, PD-L1 70%, and EGFR-positive; definitive pathology after neoadjuvant chemoimmunotherapy shows a complete pathologic response. Nearly one-half of the respondents (46%) would prefer to continue osimertinib and reserve immunotherapy for systemic

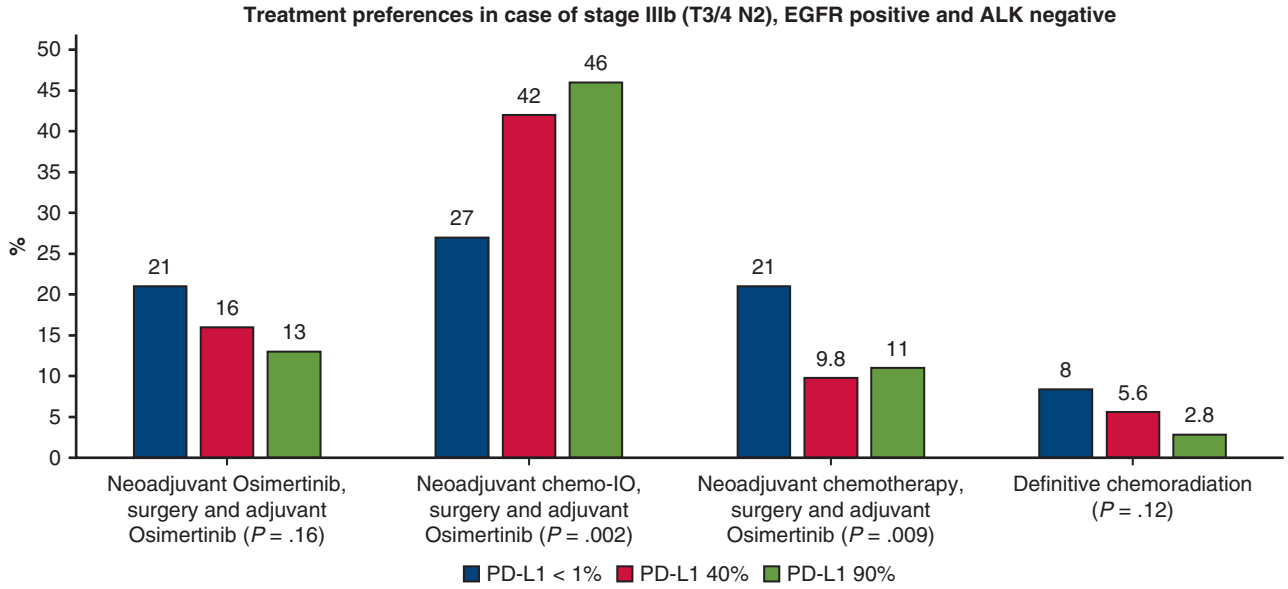

FIGURE 4. Treatment preferences in scenario of stage IIIb (T3/4 N2), EGFR-positive and ALK-negative. *EGFR*, Epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase; *PD-L1*, programmed death-ligand 1.

recurrence. Another 29% would continue immunotherapy and reserve osimertinib for recurrence, and 17% would choose cancer surveillance and no further treatment. Only 8% would continue chemoimmunotherapy and reserve osimertinib for recurrence.

Stage IV NSCLC with systemic metastases to bones and adrenals and an actionable EGFR mutation; follow-up during treatment with osimertinib shows a nearly complete radiologic response with only residual disease seen in the right upper lobe. Most of the respondents (64%) would choose consolidation surgery to the lung after osimertinib. Another 21% would choose radiation to the lung as consolidation treatment, and 14% would continue systemic treatment with osimertinib.

DISCUSSION

One of the most frequently asked questions from the patients during a surgical consultation is: "doctor, what would you choose in my place?" Previous studies have shown that physicians may choose different treatments for themselves than they would recommend to their patients.[1] In fact, when we make recommendations for others, we tend to focus on a single dimension of the alternatives,[2] typically on specific outcomes, such as risk of death or complications. In contrast, when we choose for ourselves, our decisions are influenced by multiple factors.[2] In addition, because we do not have to justify our choice to others, we may be more susceptible to cognitive biases.

The increasing complexity of multimodality treatments for locally advanced NSCLC, with multiple valuable options available to patients and providers, may make the shared decision making process more challenging. In this context, knowing what surgeons would choose for themselves if they were the patient might provide a useful information aid tool during patient consultation.

Stage IIA (EGFR-Negative and EGFR-Positive)

Stage II disease (T>4 cm, N0) historically has been treated with surgical resection in surgical candidates followed by adjuvant platinum-based chemotherapy, with the best evidence for this being in patients with N1 disease.[3-6] Despite existing evidence, adjuvant therapy in N0 patients with larger tumors (T>4 cm) remains controversial in mainstream clinical practice and is used less frequently. Recent data for the benefit of adjuvant chemoimmunotherapy, particularly in patients with PD-L1 expression levels >50%, has provided further options for the stage II EGFR-negative subgroup of patients.[7,8] These options are reflected in the surgeon preferences shown in Table 1, with the majority opting for surgery followed by adjuvant chemotherapy only for PD-L1 expression <1% but adjuvant chemoimmunotherapy for PD-L1 expression ≥50%. Other less popular preferences for this stage II EGFR-negative subgroup included either neoadjuvant only or "sandwich" therapy of neoadjuvant immunotherapy/surgery/adjuvant immunotherapy independent of PD-L1 expression status. We now have results from 3 different trials providing evidence of benefit for this approach, including KEYNOTE-671 (pembrolizumab), AEGEAN (durvalumab), and CheckMate77T (nivolumab).[9-11]

For EGFR-positive stage II patients, evidence from the ADAURA trial[12-14] demonstrates benefit of the use of adjuvant osimertinib for 3 years following surgical resection. This is reflected in the surgeon preferences shown in Figure 2, where the majority opted for surgery followed by adjuvant osimertinib. Other choices included sandwich therapy involving neoadjuvant osimertinib in addition to a smaller number opting for neoadjuvant chemotherapy or chemoimmunotherapy. Advocates for the use of immunotherapy were strongest for the 40% and 90% PD-L1 expression level subgroups.

Stage IIIA N1 (EGFR-Negative and EGFR-Positive)

In this survey, surgeons showed a preference for upfront surgery if diagnosed with cN0 NSCLC and for neoadjuvant therapy if diagnosed with cN2 NSCLC. However, a much wider variation in personal preferences was noted if diagnosed with cN1 cancer in scenarios with tumors with or without an EGFR mutation. This finding is not unexpected, given that decisions regarding multimodality treatment of patients with clinical N1 NSCLC are arguably among the most challenging for surgeons. Excellent neoadjuvant and adjuvant immunotherapy choices are available, as is adjuvant targeted therapy for patients with EGFR mutations. Although most surgeons historically have performed upfront surgery on patients with cN1 NSCLC, that practice has undergone rapid transformation because of recent clinical trials. In the present survey, the preference toward neaodjuvant therapy perhaps was driven by the higher T classification (T3/4) in the scenarios presented, with patients consequently staged as cIIIA, a clinical stage in which surgeons are already comfortable with neoadjuvant therapy. Still, for tumors with PD-L1 expression level <1%, 40%, or 90% and in the absence of EGFR/ALK molecular drivers, 31.8%, 22.3%, and 13.4% of surgeons preferred upfront surgery, respectively. Surgeons showed a greater preference for the addition of immunotherapy with higher tumor PD-L1 expression levels, with 67%, 77%, and 86% offering either neoadjuvant or perioperative chemoimmunotherapy for tumors with PD-L1 expression levels <1%, 40%, and 90%, respectively. Surgeons favored the addition of adjuvant immunotherapy to neoadjuvant chemoimmunotherapy except at a PD-L1 expression level <1%.

Perhaps more interesting is the approach that surgeons would take if their tumor was cT3/4N1, stage IIIA and

had an EGFR mutation. In the metastatic setting, treatment of EGFR-mutated tumors with immunotherapy has been unsuccessful.[15] Concerns also exist regarding the additive toxicity of tyrosine kinase inhibitors such as osimertinib and immunotherapy, particularly regarding the potential for pneumonitis.[16] As such, immunotherapy generally is avoided for stage IV patients with EGFR mutations. However, data exist suggesting that some patients with EGFR-mutated locally advanced cancer may respond to chemoimmunotherapy. In an early prospective trial by Shu and colleagues utilizing neoadjuvant atezolizumab and doublet chemotherapy, 2 of 4 patients with EGFR mutation had a pathologic complete response.[17] In the recently reported KEYNOTE-671 trial, among 33 patients with EGFR mutations, the hazard ratio (HR) for event-free survival was 0.09 (95% confidence interval [CI], 0.01-0.74) favoring the addition of pembrolizumab to neoadjuvant chemotherapy.[9] In contrast, in the AEGEAN trial, no significant difference in event-free survival was noted with the addition of neoadjuvant durvalumab to doublet chemotherapy (HR, 0.86; 95% CI, 0.35-2.19), although a trend in improvement was seen for median event-free survival (30.8 vs 19.6 months) and major pathologic response/complete pathologic response (11.5% vs 4.0%).[10] For their own treatment, 31.2%, 55.9%, and 61.3% of surgeons would prefer the addition of neoadjuvant chemoimmunotherapy if their EGFR-mutated tumors had PD-L1 expression levels of <1%, 40%, and 90% respectively. Interestingly, this is despite clinical trial protocols and practice guidelines that suggest excluding patients with known EGFR mutations or ALK rearrangements from neoadjuvant chemoimmunotherapy.

Clearly surgeons seem to believe in the potential of immunotherapy to potentiate cures in locally advanced lung cancer, which perhaps is not the case with targeted therapy. As data accumulate from real world practice and as trials continue to explore the role of neoadjuvant TKIs and chemotherapy for patients with EGFR-mutated lung cancer, the most beneficial treatment paradigm hopefully will become clearer.[18] Regardless, it seems that surgeons are embracing the concept of neoadjuvant and perioperative systemic therapy, even for patients with cN1 NSCLC.

Stage IIIA N2 (EGFR-Negative and EGFR-Positive)

For stage IIIA N2, most surgeons favored a neoadjuvant or perioperative approach with chemoimmunotherapy. The favorable results of CheckMate 816 particularly in this stage and for patients with PD-L1 expression>1% may justify this preference.[19] The greater clinical experience with neoadjuvant nivolumab in United States due to earlier regulatory approval may explain the slight differences between European and North American surgeons. With increasing PD-L1 status, most surgeons (73% at PD-L1 >90%) favored perioperative treatment with neoadjuvant chemoimmunotherapy and surgery followed by adjuvant immunotherapy. Despite the encouraging results of recent trials, the evidence for adding adjuvant immunotherapy is still considered immature, weighting the greater risk of adverse events of adding 1 year of immunotherapy to the potential survival benefit.[9-11]

In the event of an additional EGFR mutation, neoadjuvant chemoimmunotherapy and surgery followed by osimertinib was the surgeons' preferred approach in this survey with increasing PD-L1 expression level (34%, 54% and 58%). The choice of osimertinib as adjuvant treatment in EGFR-mutated stage IIIA tumors is in line with current evidence.[12-14] As discussed above, although the use of immunotherapy in this context remains a topic of debate, surgeons appeared to believe in this strategy for their own treatment.

Stage IIIB N2 (EGFR-Negative and EGFR-Positive)

When asked about stage IIIB N2 disease, the respondents favored multimodal therapy, consisting most frequently of neoadjuvant chemoimmunotherapy, followed by resection and adjuvant therapy that was appropriately dependent on the presence of driver mutations and PD-L1 status. It is interesting to note that more than one-quarter opted for a nonoperative, PACIFIC-type regimen in this setting. We noted a greater preference for perioperative systemic therapy among North American surgeons compared to their European counterparts. Reasons for these differences may include cultural, financial, and health system variations across regions.

It is notable that when faced with the setting of IIIB N2 disease and actionable EGFR mutations, surgeons preferred neoadjuvant chemoimmunotherapy followed by adjuvant osimertinib. Although we recognize that this preference is based on existing published data[12-14] and currently approved drugs, it is unclear whether this will remain the preferred approach after completion of additional ongoing trials, specifically the LAURA trial evaluating adjuvant osimertinib after chemoradiation, which has been reported as positive.[18]

Special Situations

When asked about their preferences for treating tumors that would anatomically require pneumonectomy, the respondents tended to prefer reassessment after systemic therapy, perhaps hoping that the extent of resection might be reduced with neoadjuvant treatment. Less than a one-quarter of respondents would commit to pneumonectomy without reassessment. Interestingly, more than 1 in 5 preferred a PACIFIC-type regimen upfront, with an intent for definitive chemoradiation and immunotherapy in the absence of surgical resection. Whether these preferences relate to a perceived lack of benefit of surgery in such locally extensive disease, concerns about the morbidity of

pneumonectomy, or a combination thereof is unclear. Given that respondents often chose to reduce the extent of resection following radiographic response to therapy in high-PDL1 stage III disease, it follows that perception of response also would influence the decision regarding pneumonectomy.

It is interesting to note that when pathology reports identified a complete response to chemoimmunotherapy in high PD-L1 disease, most respondents opted to continue with adjuvant immunotherapy. Although an argument could be made that the risk of recurrence is substantially lower in such circumstances, it is also true that the tumor is clearly responsive to the therapy and the potential benefit may be great. However, if a targetable EGFR mutation were identified, respondents would shift their treatment preference to adjuvant osimertinib, most certainly based on their familiarity with the ADAURA trial results.[12-14]

In the setting of stage IV disease, with multiorgan metastases having responded to targeted therapy, most surgeons would choose local consolidative surgery. This is particularly interesting in the setting of an increasing body of evidence to support this approach,[20-24] with surgical guidelines in preparation, but a preponderance of multidisciplinary trials focusing on radiation for local consolidation.[25] More than 3 times as many surgeon respondents would choose resection rather than radiation in this setting. This is particularly notable given the surgeons' familiarity with the nuances of these types of operative procedures.[26] The finding that many surgeons would choose resection for themselves in this setting serves as impetus for discussions regarding the infrequent offering of surgery to so many patients with stage IV lung cancer. This certainly is an area for improved patient-centered discussions of treatment choices and transparency in sharing all available options.

Limitations

This study is not without some inherent limitations, and the survey results represent the personal opinions of a sizeable number of surgeons but should not be interpreted as standard of care. Surgeons were selected for this survey based on predefined criteria (membership to leadership groups of ESTS and the European Association of Cardiothoracic Surgery and active members of the GTSC). This approach was chosen to make the selection more objective; however, it may introduce other biases. For instance, only 22% of respondents were in practice for <10 years, and the majority worked in academic centers. The generalizability of our findings to a junior group of surgeons or working in community hospitals needs to be verified.

In addition, most of the respondents were practicing in either Europe or North America, owing to the members' affiliation with the sponsoring organizations (ESTS and GTSC). This may prevent the global generalizability of our findings to surgeons working in other continents.

We acknowledge a possibility of nonresponse bias, because surgeons more interested in lung cancer treatment or working in environments in which novel systemic treatments are already approved and funded were more likely to participate. It is also important to recognize that the findings of this survey reflect the personal preferences of surgeons asked to ponder which treatment they would prefer for themselves rather than what they would recommend to their patients, and as such might not reflect the best of clinical care. For instance, one aspect warranting consideration is the fact most of the surgeons deemed themselves very fit for treatment, which is not always the case with lung cancer patients.

Personal preferences also may reflect first-hand experience with cancer treatment, on a personal basis or for a close family member. Unfortunately, we have not collected this information in the questionnaire.

The order of the survey questions was not varied. There is a risk of potential survey fatigue considering the length of the questionnaire, which may have been more relevant for the last questions of the survey. However, we did not notice a reduced completion rate of the last questions, which may indicate that this was not a relevant problem.

As with all surveys, the wording of the questions may have influenced the responses. The scenarios and the questions were developed by the steering group of 5 surgeons with experience in this field; however, no qualified qualitative researcher was consulted to this purpose. The fact that the survey was addressed to peers rather than patients and used jargon commonly used during tumor board discussions likely minimized this limitation.

The results of the comparisons between surgeons practicing in different continents should be interpreted taking into consideration that these novel strategies for treating stage II and III NSCLC might not have been approved in many European countries at the time of the survey. This might have caused a lack of direct clinical experience among European surgeons compared to their North American counterparts. The current study was launched prior to the availability of a proven targeted therapy for patients with resectable ALK-rearranged NSCLC and as such did not include this scenario in the survey.

Finally, the responses to this survey certainly were affected by the currently available evidence and understanding of the published literature. It is anticipated that the publication and diffusion of new high-level evidence on this topic and the ongoing educational efforts from scientific organizations will influence future surgeons' perspectives on multimodal treatment of locally advanced, potentially resectable lung cancer.

CONCLUSIONS

This survey reflects the current perception and understanding of surgeons on multimodal treatment of potentially resectable lung cancer in the era of immunotherapy and targeted therapies from a very personal standpoint. We believe that this study offers an interesting perspective with a specific focus on the relative preferences of surgeons working in Europe and North America, which perhaps reflect differing experiences with the application of these novel strategies to their patients. The work is not meant as a best practice document, but it provides some valuable material for reflection and discussion with patients and the wider tumor board about the more controversial aspects of multimodal lung cancer treatment.

Conflict of Interest Statement

Dr Brunelli receives consulting fees from Astra Zeneca, MSD, BMS, Ethicon, Medtronic, and Roche. Dr Petersen receives consulting fees from Medtronic, AstraZeneca, AMBU, Medela. Advisory Board AstraZeneca, BMS, Roche, and MSD. Dr Wigle receives consulting fees from Intuitive Surgical and Genentech. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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TABLE E2. Questions included in the survey (multiple-choice answers in bold type)

	Question
1	What is your age? **(18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75 or older)**
2	What is your gender?
3	In what country do you work?
4	Years of practice **(0-5, 6-10, 11-20, >20)**
5	Type of practice? **(public hospital, academic/university hospital, private hospital, community hospital, others)**
6	What is your specialty? **(thoracic surgeon, radiation oncologist, medical oncologist, respiratory physician, other)***
7	How would you judge your ECOG Performance Status **(0, 1, 2, 3, 4)**
8	How would you judge your pulmonary reserve for a lobectomy **(normal, satisfactory, borderline, prohibitive)**
9	Taking into account your co-morbidities, how would you judge your overall fitness to undergo multimodal treatment? **(very fit, fit, borderline fit, unfit)**
10	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 1a: stage IIa (T>4 cm, N0) NSCLC, PD-L1 <1%, EGFR-negative, ALK-negative **(surgery alone, surgery and adjuvant chemotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation)**
11	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 1b: Stage IIa (T>4 cm, N0) NSCLC, PD-L1 40%, EGFR-negative, ALK-negative **(surgery alone, surgery and adjuvant chemotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation)**
12	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 1c: Stage IIa (T>4 cm, N0) NSCLC, PD-L1 90%, EGFR-negative, ALK-negative **(surgery alone, surgery and adjuvant chemotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation)**
13	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 2a: Stage IIIa (T3/4, N1) NSCLC, PD-L1 <1%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
14	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 2b: stage IIIa (T3/4, N1) NSCLC, PD-L1 40%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
15	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 2c: stage IIIa (T3/4, N1) NSCLC, PD-L1 90%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
16	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 3a: Stage IIIa (T1/2, N2) NSCLC, PD-L1 <1%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
17	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 3b: Stage IIIa (T1/2, N2) NSCLC, PD-L1 40%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
18	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 3c: Stage IIIa (T1/2, N2) NSCLC, PD-L1 90%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**

(Continued)

TABLE E2. Continued

	Question
19	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 4a: Stage IIIb (T3/4, N2) NSCLC, PD-L1 <1%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
20	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 4b: Stage IIIb (T3/4, N2) NSCLC, PD-L1 40%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
21	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 4c: Stage IIIb (T3/4, N2) NSCLC, PD-L1 90%, EGFR-negative, ALK-negative **(surgery alone, surgery upfront and then adjuvant chemotherapy, surgery followed by adjuvant chemoimmunotherapy, neoadjuvant chemoimmunotherapy followed by surgery, neoadjuvant chemoimmunotherapy followed by surgery and adjuvant immunotherapy, definitive chemoradiation, definitive chemoradiation followed by durvalumab, BSC)**
22	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 5a: Stage IIa (T>4 cm, N0) NSCLC, PD-L1 <1%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, definitive chemoradiation and osimertinib)**
23	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 5b: Stage IIa (T>4 cm, N0) NSCLC, PD-L1 40%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, definitive chemoradiation and osimertinib)**
24	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 5c: Stage IIa (T>4 cm, N0) NSCLC, PD-L1 90%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, definitive chemoradiation and osimertinib)**
25	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 6a: Stage IIIa (T3/4, N1) NSCLC, PD-L1 <1%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
26	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 6b: Stage IIIa (T3/4, N1) NSCLC, PD-L1 40%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
27	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 6c: Stage IIIa (T3/4, N1) NSCLC, PD-L1 90%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
28	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 7a: Stage IIIa (T1/2, N2) NSCLC, PD-L1 <1%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
29	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 7b: Stage IIIa (T1/2, N2) NSCLC, PD-L1 40%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**

(Continued)

TABLE E2. Continued

	Question
30	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 7c: Stage IIIa (T1/2, N2) NSCLC, PD-L1 90%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
31	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 8a: Stage IIIb (T3/4, N2) NSCLC, PD-L1 <1%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
32	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 8b: Stage IIIb (T3/4, N2) NSCLC, PD-L1 40%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
33	You are diagnosed with the following clinical scenario. Which treatment would you prefer? Scenario 8c: Stage IIIb (T3/4, N2) NSCLC, PD-L1 90%, EGFR-positive, ALK-negative **(surgery alone, surgery upfront and then adjuvant osimertinib, neoadjuvant chemotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and then adjuvant osimertinib, neoadjuvant osimertinib followed by surgery and then adjuvant osimertinib, neoadjuvant chemoimmunotherapy followed by surgery and osimertinib in case of systemic recurrence, definitive chemoradiation, definitive chemoradiation and osimertinib, BSC)**
34	Scenario 9: You are diagnosed with cT3N2 stage IIIB NSCLC (PD-L1 50% and no actionable mutations). Your cancer only appears resectable by pneumonectomy at this point due to broad effacement of the pulmonary artery by the primary tumor and lymph nodes. Which would you prefer? **(chemoradiation followed by durvalumab, neoadjuvant chemoimmunotherapy followed by pneumonectomy if no progression after neoadjuvant therapy, reassessment of resectability after several cycles of chemotherapy and immunotherapy with determination of chemoradiation or surgery made after neoadjuvant therapy, BSC)**
35	Scenario 10: You were diagnosed with a cT3N2 NSCLC, PD-L1 expression 80%, and underwent neoadjuvant chemoimmunotherapy. The restaging CT scan shows a nearly complete radiologic response. You discuss several options with your surgeons. Which one you would prefer? **(perform a resection lesser than the one planned before neoadjuvant treatment (ie, lobectomy instead of bilobectomy or segmentectomy instead of lobectomy), perform the same extent of resection which was planned before the neoadjuvant treatment regardless the radiologic response, decline surgery and follow up the evolution of the tumour, decline surgery and perform additional systemic treatment, decline surgery and ask for radiotherapy to the residual radiologic lesion, request ctDNA liquid biopsy and decline surgery if this result is negative)**
36	Scenario 11: You underwent a lobectomy for a cT3N2 NSCLC after neoadjuvant chemoimmunotherapy (PD-L1 90%). The definitive pathology shows a complete pathologic response with no viable tumor cells identified in the specimen. The responsible clinician proposes to you the following options. Which would you prefer? **(no further adjuvant systemic treatment, cancer surveillance only, continue with adjuvant immunotherapy only, continue with adjuvant chemotherapy and immunotherapy)**
37	Scenario 12: You underwent a lobectomy for a cT3N2 NSCLC after neoadjuvant chemotherapy (PD-L1 70% and EGFR-positive). The definitive pathology shows a complete pathologic response with no viable tumour cells identified in the specimen. The responsible clinician proposes to you the following options. Which would you prefer? **(no further adjuvant systemic treatment, cancer surveillance only; continue with adjuvant immunotherapy only and reserve osimertinib for relapse; continue with adjuvant chemo and immunotherapy and reserve osimertinib for possible relapse; continue with adjuvant osimertinib (reserve immunotherapy for possible relapse))**
38	Scenario 13: Unfortunately, you were diagnosed with a stage IV NSCLC with systemic metastases to bones and adrenals and an actionable EGFR mutation. Follow-up during treatment with osimertinib shows a nearly complete radiologic response with only residual disease seen in right upper lobe. The responsible clinician discusses with you the following treatments. Which would you prefer? **(surgery to the lung for local consolidation treatment after systemic osimertinib, radiation to the lung for local consolidation treatment after systemic osimertinib, continue with osimertinib alone, No further treatment/best supportive care)**
39	For authorship purposes only, please write your full name, email, and affiliation as you would like to appear in the manuscript (these details will be dealt with confidentiality). Those who opt not to write their name would not be listed among the collaborators.

NSCLC, Non–small cell lung cancer; *PD-L1*, programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase; *BSC*, best supportive care. *For the purposes of this study, only the responses from thoracic surgeons were included.

TABLE E3. Treatment preferences in the scenario of stage IIa (T>4 cm N0), EGFR- and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Surgery alone	37 (26)	14 (10)	7 (5)	<.001
Surgery and adjuvant chemotherapy	54 (38)	12 (8)	9 (6)	<.001
Surgery and adjuvant chemoimmunotherapy	22 (15)	61 (43)	57 (40)	<.001
Neoadjuvant chemoimmunotherapy and surgery	24 (17)	31 (22)	32 (22)	.44
Neoadjuvant chemoimmunotherapy, surgery and adjuvant immunotherapy	6 (4)	25 (17)	38 (27)	<.001

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

TABLE E4. Treatment preferences in the scenario of stage IIa (T>4 cm N0), EGFR-positive and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Surgery alone	13 (9.1)	7 (4.9)	4 (2.8)	.062
Surgery and adjuvant osimertinib	99 (69)	80 (56)	66 (46)	<.001
Neoadjuvant osimertinib, surgery, and adjuvant osimertinib	13 (9.1)	11 (7.7)	14 (9.8)	.82
Neoadjuvant chemoimmunotherapy, surgery, and adjuvant osimertinib	7 (4.9)	33 (23)	49 (34)	<.001
Neoadjuvant chemotherapy, surgery, and adjuvant osimertinib	11 (7.7)	12 (8.4)	10 (7.0)	.91

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

TABLE E5. Treatment preferences in the scenario of stage IIIb (T3/4 N2), EGFR- and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Best supportive care	3 (2.1)	0	0	.049
Surgery and adjuvant chemotherapy	6 (4.2)	0	0	.002
Surgery and adjuvant chemoimmunotherapy	0	3 (2.1)	3 (2.1)	.22
Neoadjuvant chemoimmunotherapy and surgery	23 (16)	17 (12)	15 (10)	.34
Neoadjuvant chemoimmunotherapy, surgery, and adjuvant immunotherapy	51 (36)	74 (52)	82 (57)	.001
Definitive chemoradiation	22 (15)	4 (2.8)	1 (0.7)	<.001
Chemoradiotherapy and durvalumab	38 (27)	45 (32)	42 (29)	.66

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.

TABLE E6. Treatment preferences in the scenario of stage IIIb (T3/4 N2), EGFR-positive and ALK-negative

Treatment	PD-L1 expression <1%, n (%)	PD-L1 expression 40%, n (%)	PD-L1 expression 90%, n (%)	*P* value
Best supportive care	1 (0.7)	1 (0.7)	1 (0.7)	1
Surgery and adjuvant osimertinib	2 (1.4)	1 (0.7)	1 (0.7)	.77
Neoadjuvant osimertinib, surgery, and adjuvant osimertinib	30 (21)	23 (16)	18 (13)	.16
Neoadjuvant chemoimmunotherapy, surgery, and adjuvant osimertinib	38 (27)	60 (42)	66 (46)	.002
Neoadjuvant chemotherapy, surgery, and adjuvant osimertinib	30 (21)	14 (9.8)	15 (11)	.009
Definitive chemoradiation	12 (8.4)	8 (5.6)	4 (2.8)	.12
Neoadjuvant chemoimmunotherapy, surgery, osimertinib only for recurrence after surgery	2 (1.4)	5 (3.5)	6 (4.2)	.36
Chemoradiotherapy and durvalumab	28 (20)	31 (22)	32 (22)	.83

PD-L1, Programmed death-ligand 1; *EGFR*, epidermal growth factor receptor; *ALK*, anaplastic lymphoma kinase.