Research Square

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Neoadjuvant EGFR-TKI with or without Platinum-Based Chemotherapy for Stage II–III EGFR-Mutant Non–Small-Cell Lung Cancer: A Multicenter Retrospective Cohort Study

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Abstract

Background

The surgical outcomes and toxicity of neoadjuvant EGFR tyrosine kinase inhibitor (TKI) monotherapy versus TKI plus platinum-based chemotherapy remain uncertain in routine care for EGFR-mutant non–small-cell lung cancer (NSCLC).

Methods

This multicenter retrospective cohort study included 158 patients with stage II–III NSCLC harboring a sensitizing EGFR mutation who initiated neoadjuvant therapy and planned curative-intent surgery (EGFR-TKI, n = 94; EGFR-TKI+platinum-based chemotherapy, n = 64). The primary endpoint was R0-ITT (R0 resection among all treatment initiators), with patients not undergoing surgery counted as failures. Overlap weighting was used to balance pretreatment covariates.

Results

Stage III disease accounted for 63.8% and 93.8% of the monotherapy and combination groups, respectively. After weighting, R0-ITT rates were 70.3% and 87.2%, respectively (risk difference [RD] 16.9 percentage points; 95% confidence interval [CI], 2.9 to 31.1). Surgery completion was higher with combination therapy (RD 17.9; 95% CI, 5.1 to 32.3), and disease-related failure to undergo surgery was lower (RD − 16.1; 95% CI, − 28.4 to − 4.5). For major pathologic response among all treatment initiators (ITT-MPR), the weighted RD was 6.5 percentage points (95% CI, − 7.1 to 20.1). Among patients with evaluable surgical specimens, MPR rates were similar (15.3% vs. 16.1%). Grade ≥ 3 adverse events (AEs) were more frequent with combination therapy (RD 14.2; 95% CI, 2.5 to 26.4).

Conclusions

Combination therapy was associated with higher R0-ITT and surgery completion rates and more grade ≥ 3 AEs. Pathologic response rates among patients with evaluable surgical specimens were similar. Treatment-selection bias may persist after weighting; prospective studies are needed.

Background

The role of EGFR-TKIs has expanded from advanced disease to perioperative treatment. The ADAURA trial established the role of adjuvant osimertinib after complete resection but did not address whether an EGFR-TKI should be combined with chemotherapy in the neoadjuvant setting [1–3]. Studies of neoadjuvant EGFR-TKIs have reported radiographic tumor shrinkage and high R0 resection rates, yet

major pathologic response (MPR) and pathologic complete response (pCR) remain uncommon and vary considerably across studies [4–6].

In NeoADAURA, osimertinib with or without chemotherapy improved MPR compared with chemotherapy alone; the two osimertinib groups had similar observed MPR rates, with more grade ≥ 3 adverse events (AEs) in the combination group [7]. Although pathologic assessment requires a surgical specimen, an intention-to-treat MPR analysis can retain patients who do not undergo surgery as nonresponders. R0 resection among all treatment initiators measures how often patients reach surgery and undergo margin-negative resection.

Direct comparisons in routine practice remain limited [8–22], particularly for patients considered potentially resectable. This three-center cohort compared EGFR-TKI monotherapy with TKI plus platinum-based chemotherapy in patients for whom curative-intent surgery was planned. We assessed R0 resection among all treatment initiators (R0-ITT) as the primary endpoint, along with surgery completion, reasons for not undergoing surgery, pathologic response, and toxicity. We also used overlap weighting to account for measured differences between treatment groups and estimate adjusted associations with these outcomes.

Methods

Study Design and Population

This multicenter retrospective cohort study is reported in accordance with the STROBE statement [23]. Figure 1 summarizes treatment, surgery, and outcome evaluability in the included cohort. Consecutive adult patients who initiated neoadjuvant systemic therapy at three centers between October 14, 2020, and November 12, 2024, were included. Inclusion criteria were pathologically or cytologically confirmed lung adenocarcinoma or non-squamous NSCLC; sensitizing EGFR mutation (exon 19 deletion, L858R, or compound mutations containing these alterations); clinical stage II–III disease (AJCC 8th edition); assessed as resectable or potentially resectable by a multidisciplinary team; planned to undergo curative-intent surgery after neoadjuvant therapy; and initiation of either EGFR-TKI monotherapy or EGFR-TKI plus platinum-based chemotherapy. Exclusion criteria were de novo stage IV disease, no surgical intent, disease considered definitively unresectable, predominantly non-sensitizing EGFR alterations, receipt of other preoperative regimens, or inability to determine treatment group or primary endpoint.

Treatment groups were defined by the regimen initiated: EGFR-TKI monotherapy or EGFR-TKI plus platinum-based chemotherapy. TKI generation, treatment duration, and number of chemotherapy cycles were summarized as treatment characteristics and were not included in the propensity score model.

Endpoint Definitions

The primary endpoint was R0-ITT, defined as surgery with microscopically negative margins (R0) among all treatment initiators. Patients who did not undergo surgery were counted as not achieving R0. Here, ITT refers to the inclusion of all treatment initiators in this observational cohort. Secondary efficacy endpoints included surgery completion, disease-related failure to undergo surgery, and ITT-MPR. Disease-related failure comprised recorded disease progression or new metastases and insufficient response to permit R0 resection. Other recorded reasons for not undergoing surgery were reported separately. For ITT-MPR, patients without surgery or evaluable MPR were classified as nonresponders.

Safety was assessed by the incidence of grade ≥ 3 AEs recorded during neoadjuvant therapy. Outcomes assessed among patients who underwent surgery included R0 resection, MPR, pCR, percentage of residual viable tumor, and perioperative measures. MPR was defined as ≤ 10% residual viable tumor and pCR as no residual viable tumor, and pathologic assessment followed IASLC recommendations [24]. Postoperative disease-free survival (DFS) was measured from surgery using the recorded recurrence/censoring status and follow-up duration. This analysis included only patients who underwent surgery.

Statistical Analysis

Categorical variables were summarized as n/N (%) and continuous variables as median (interquartile range). Baseline differences were evaluated using standardized mean differences (SMDs) without covariate selection based on P values. A logistic regression model estimated the propensity score, with covariates including center, age, sex, smoking history, ECOG performance status, overall clinical stage, cT, cN, pretreatment multidisciplinary assessment of resectability, tumor size, EGFR L858R status, and co-mutation status. Smoking history was complete; patients with missing co-mutation status were classified as having no co-mutation.

Overlap weights were defined as 1 minus the propensity score for the combination group and as the propensity score for the monotherapy group. This approach estimates outcomes in patients for whom either treatment could plausibly have been selected [25]. An absolute SMD < 0.10 was considered to indicate adequate balance. The primary effect measure was the weighted absolute risk difference, with risk ratios and odds ratios reported as supplementary effect measures. We estimated 95% confidence intervals (CIs) using 2,000 patient-level bootstrap iterations and refitted the propensity score model in each iteration. No multiplicity adjustment was applied to secondary endpoints.

DFS was estimated using the Kaplan–Meier method; groups were compared using the log-rank test and a univariable Cox model. Sensitivity analyses included restriction to third-generation TKIs, truncated stabilized inverse probability weighting, a parsimonious outcome model, and leave-one-center-out analyses. All analyses were performed using Python 3.12.13, primarily with NumPy 2.3.5 and pandas 3.0.1.

An exploratory analysis compared postoperative DFS between patients with and without MPR who had both pathology and follow-up data, using Kaplan–Meier estimates, a log-rank test, and an unadjusted

Cox model. An R0-restricted analysis assessed sensitivity to margin status. These analyses used lifelines 0.30.3 and were descriptive, without multiplicity adjustment.

Results

Study Population and Covariate Balance

A total of 158 patients who initiated treatment were included: 94 in the EGFR-TKI monotherapy group and 64 in the combination group. Treatment assignment, surgery, and margin status were ascertainable for all patients. Before weighting, the combination group had greater disease burden: stage III, classification as potentially resectable, cT3–4, and cN2b were more frequent, and tumors were larger (Table 1). The maximum absolute SMD was 0.786. Among patients with evaluable TKI generation, 81 of 92 (88.0%) in the monotherapy group and 53 of 63 (84.1%) in the combination group received a third-generation TKI. Median TKI treatment durations were 68 d (interquartile range [IQR] 57–80) and 58 d (IQR 52–70), respectively. All 64 patients in the combination group had chemotherapy cycle records, with a median of three cycles (IQR 3–4). The propensity score distributions overlapped between 0.028 and 0.894. After overlap weighting, all covariates had absolute SMDs < 0.001, and the overall effective sample size was 109.2 (Fig. 2).

Table 1
Baseline characteristics and treatment exposure

Characteristic	EGFR-TKI monotherapy (n = 94)	EGFR-TKI plus chemotherapy (n = 64)	Absolute SMD before weighting
Age, years	60.0 (53.0–69.0)	61.5 (55.0–70.2)	0.153
Female	54/94 (57.4%)	34/64 (53.1%)	0.087
ECOG PS ≥ 2	9/94 (9.6%)	6/64 (9.4%)	0.007
Clinical stage III	60/94 (63.8%)	60/64 (93.8%)	0.786
Potentially resectable	41/94 (43.6%)	41/64 (64.1%)	0.419
cT3–4	43/94 (45.7%)	46/64 (71.9%)	0.551
cN2b	15/94 (16.0%)	29/64 (45.3%)	0.672
Tumor size, mm	40.0 (35.0–51.8)	51.7 (42.5–60.0)	0.669
EGFR exon 19 deletion	59/94 (62.8%)	31/64 (48.4%)	0.291
EGFR L858R	32/94 (34.0%)	32/64 (50.0%)	0.328
Third-generation EGFR-TKI	81/92 (88.0%)	53/63 (84.1%)	N/A
TKI treatment duration, days	68 (57–80)	58 (52–70)	N/A
Chemotherapy cycles	N/A	3 (3–4), n = 64	N/A

Note: Data are median (IQR) or n/N (%). The SMD column applies only to pretreatment variables; third-generation TKI use, TKI treatment duration, and chemotherapy cycles are postbaseline treatment characteristics and are not used to evaluate baseline balance. Complete covariate balance is shown in Fig. 2.

Efficacy and Safety

R0-ITT was achieved in 71 of 94 patients (75.5%) in the monotherapy group and 53 of 64 (82.8%) in the combination group, yielding an unadjusted risk difference of 7.3 percentage points (95% CI, − 6.1 to 19.3). After overlap weighting, R0-ITT rates were 70.3% and 87.2%, respectively; the risk difference was 16.9 percentage points (95% CI, 2.9 to 31.1), with a risk ratio of 1.24 (95% CI, 1.04 to 1.53) and an odds ratio of 2.88 (95% CI, 1.22 to 8.33; bootstrap P = 0.024).

Surgery was completed in 74 of 94 patients (78.7%) in the monotherapy group and 57 of 64 (89.1%) in the combination group; disease-related failure to undergo surgery occurred in 14 of 94 (14.9%) and four of 64 (6.2%), respectively. After weighting, surgery completion was higher with combination therapy (RD 17.9 percentage points; 95% CI, 5.1 to 32.3), and disease-related failure to undergo surgery was lower (RD − 16.1; 95% CI, − 28.4 to − 4.5). Of 34 patients who did not achieve R0-ITT, 27 did not undergo surgery

and seven underwent non-R0 resection. Therefore, most R0-ITT failures occurred before surgery; non-R0 resection accounted for a smaller proportion.

ITT-MPR occurred in 11 of 94 patients (11.7%) and nine of 64 (14.1%), with weighted rates of 8.8% and 15.4%, respectively, yielding a between-group difference of 6.5 percentage points (95% CI, − 7.1 to 20.1). The interval included both lower and higher ITT-MPR rates with combination therapy (Table 2, Fig. 3).

Table 2
Outcomes among all treatment initiators

Outcome	EGFR-TKI monotherapy: raw n/N (%); weighted rate	EGFR-TKI plus chemotherapy: raw n/N (%); weighted rate	Unadjusted RD (95% CI), percentage points	Overlap-weighted RD (95% CI), percentage points	Overlap-weighted RR (95% CI)
R0-ITT	71/94 (75.5%) Weighted: 70.3%	53/64 (82.8%) Weighted: 87.2%	7.3 (− 6.1 to 19.3)	16.9 (2.9 to 31.1)	1.24 (1.04 to 1.53)
Surgery completion	74/94 (78.7%) Weighted: 73.9%	57/64 (89.1%) Weighted: 91.8%	10.3 (− 1.9 to 21.2)	17.9 (5.1 to 32.3)	1.24 (1.06 to 1.52)
Disease-related failure to undergo surgery	14/94 (14.9%) Weighted: 19.7%	4/64 (6.2%) Weighted: 3.6%	−8.6 (− 18.0 to 1.9)	−16.1 (− 28.4 to − 4.5)	0.18 (0.01 to 0.57)
ITT-MPR	11/94 (11.7%) Weighted: 8.8%	9/64 (14.1%) Weighted: 15.4%	2.4 (− 8.0 to 14.1)	6.5 (− 7.1 to 20.1)	1.74 (0.52 to 7.32)
Grade ≥ 3 AEs	7/94 (7.4%) Weighted: 6.6%	18/64 (28.1%) Weighted: 20.7%	20.7 (8.8 to 33.3)	14.2 (2.5 to 26.4)	3.16 (1.21 to 20.49)

Note: In each treatment-group cell, the first line shows the raw n/N (%) and the second line shows the overlap-weighted rate. Weighted rates are model estimates and do not correspond to integer numerators/denominators. Risk differences were calculated as combination minus monotherapy. Overlap-weighted 95% CIs were estimated from 2,000 bootstrap iterations. No multiplicity adjustment was applied to secondary endpoint.

Grade ≥ 3 AEs were recorded in seven of 94 patients (7.4%) in the monotherapy group and 18 of 64 (28.1%) in the combination group, with weighted rates of 6.6% and 20.7%, respectively (RD 14.2 percentage points; 95% CI, 2.5 to 26.4). Additional file 1 (Supplementary Table S2) summarizes grade ≥ 3 AE occurrence and the recorded types among affected patients.

Pathologic and Perioperative Outcomes, DFS, and Sensitivity Analyses

Among the 131 patients who underwent surgery (74 monotherapy, 57 combination), R0 resection rates were 95.9% and 93.0%, respectively. Pathologic response was evaluable in 128 patients (72 monotherapy, 56 combination); MPR rates were 11 of 72 (15.3%) and nine of 56 (16.1%), and pCR rates were three of 72 (4.2%) and two of 56 (3.6%). Among 126 patients with quantitative residual viable tumor data (71 monotherapy and 55 combination), the median percentages were 45.0% and 42.0%, respectively. Operative time, length of stay, and postoperative complication rates were similar in the unadjusted summaries (Table 3).

Table 3
Pathologic and perioperative outcomes among patients who underwent surgery

Outcome	EGFR-TKI monotherapy	EGFR-TKI plus chemotherapy
R0 resection	71/74 (95.9%)	53/57 (93.0%)
MPR	11/72 (15.3%)	9/56 (16.1%)
pCR	3/72 (4.2%)	2/56 (3.6%)
Residual viable tumor, %	45.0 (26.5–60.5), n = 71	42.0 (21.5–55.0), n = 55
Operative time, min	120 (100–150)	110 (84–140)
Postoperative length of stay, days	5 (4–6)	5 (4–6)
Postoperative complications	5/74 (6.8%)	5/57 (8.8%)

Note: Data are n/N (%) or median (IQR). Denominators correspond to the number of patients who underwent surgery or had evaluable specimens for each outcome. These are unadjusted, surgery-conditional descriptions and do not represent treatment effects for all treatment initiators.

Among the 131 patients who underwent surgery, 129 were evaluable for DFS (73/74 monotherapy, 56/57 combination). After a median follow-up of 29.7 months, 27 DFS events had occurred. The 24-month DFS rates were 76.3% and 77.7%, respectively (log-rank P = 0.660; hazard ratio [HR] 0.84; 95% CI, 0.38 to 1.83; Fig. 4). These postoperative estimates exclude patients who did not undergo surgery; they do not describe survival outcomes for the full treatment cohort.

MPR and DFS were jointly evaluable in 127 patients: 20 with MPR (four recorded recurrences) and 107 without MPR (23 recurrences). The unadjusted HR for MPR versus non-MPR was 0.87 (95% CI, 0.30 to 2.53; log-rank P = 0.804). The R0-restricted analysis was similarly inconclusive (Additional file 1; Supplementary Table S3 and Fig. S1).

The R0-ITT point estimates favored combination therapy in all sensitivity analyses, but several confidence intervals included no difference. Residual imbalance remained after truncated stabilized

inverse probability weighting, and the parsimonious outcome model may have been overfitted (Additional file 1; Supplementary Table S1).

Discussion

After overlap weighting, surgery completion and R0-ITT rates were higher in the combination group, and disease-related preoperative failures were less frequent. The combination group had more advanced disease at baseline (stage III, 93.8% vs. 63.8%). This imbalance may have attenuated the unadjusted association, which increased after weighting; however, residual treatment-selection bias remains possible. Of the 131 patients who underwent surgery, 124 (94.7%) achieved R0 resection. Therefore, difference in R0-ITT arose mainly before surgery, with little difference in margin status among those who underwent resection.

MPR rates among patients with evaluable surgical specimens were similar (15.3% and 16.1%), but this comparison excludes patients who did not reach surgery and cannot establish equivalent treatment effects. In the ITT-MPR analysis, the weighted rate was higher in the combination group (15.4% vs. 8.8%), but the CI was compatible with either lower or higher MPR rates with combination therapy. One possible explanation is that combination therapy improves disease control enough to allow surgery without reducing residual viable tumor below 10%. Differences in surgical timing, resectability judgments, or tumor biology could also contribute; these explanations remain hypotheses. The observed association was clearer for reaching surgery than for pathologic response.

NeoADAURA provides the most directly relevant randomized evidence. MPR rates in the full analysis set were 26% with osimertinib plus chemotherapy and 25% with osimertinib alone; grade ≥ 3 AE rates were 36% and 13%, respectively [7]. The similar observed MPR rates do not establish equivalence. Its R0 rates of 91% and 95% were calculated among patients who underwent surgery and thus differ in denominator from our R0-ITT endpoint. Disease progression prevented surgery in 1% of each osimertinib group. Our cohort included potentially resectable disease and had more preoperative failures. Eligibility criteria and treatment selection differed between studies, so these rates cannot be used to compare treatment efficacy.

Only one prior direct real-world comparison (60 patients with stage III-N2 disease, predominantly treated with first-generation EGFR-TKIs) showed no statistically significant differences in MPR, objective response, or DFS between combination chemotherapy and TKI monotherapy [12]. Our cohort was larger and predominantly included patients treated with third-generation TKIs, although both studies were non-randomized. Other single-arm trials and real-world studies have similarly shown that neoadjuvant EGFR-TKIs are generally feasible, but radiographic control or R0 resection does not necessarily translate into deep pathologic response [8–11, 14–21]. A 2024 meta-analysis reported pooled MPR, pCR, and R0 resection rates of approximately 11%, 3%, and 91% [6]. Therefore, high R0 rates can coexist with limited pathologic response.

The primary evidence for EGFR-TKI plus chemotherapy remains in advanced NSCLC. FLAURA2 demonstrated that osimertinib plus platinum–pemetrexed prolonged progression-free survival but increased grade ≥ 3 AEs [13]; these findings cannot be directly extrapolated to the resectable setting. Our weighted risk differences corresponded to approximately 17 more R0 resections and 14 more grade ≥ 3 AEs per 100 patients with combination therapy than with monotherapy, with wide CIs for both estimates. These associations should be considered alongside disease burden, the likelihood of surgery, and treatment tolerance.

R0-ITT records whether patients reach margin-negative resection after starting treatment. It captures both failure to reach surgery and non-R0 resection, whereas the R0 rate among operated patients describes the selected surgical population. ITT-MPR also retains preoperative failures as nonresponders, while adding a requirement for deep pathologic response. Neither endpoint establishes a survival benefit. Our exploratory postoperative analysis also had too few events to clarify the prognostic value of MPR. Future studies should report surgical completion, reasons for failure, pathologic response, toxicity, and event-free survival (EFS) from treatment initiation.

The primary analysis retained all treatment initiators across three centers and achieved close balance on measured covariates; however, treatment was not randomly assigned. Weighting cannot account for unmeasured differences in tumor biology, mediastinal nodal burden, physician preference, surgical candidacy, or center experience. The effective sample size after weighting was 109.2, and the wide CIs, including an unadjusted primary-outcome interval that crossed zero, limit the precision of the estimates. Restricting DFS to patients who underwent surgery may also introduce selection or collider bias; it cannot establish the survival effect of the initial treatment strategy.

Conclusions

EGFR-TKI plus platinum-based chemotherapy was associated with more patients reaching R0 resection and more grade ≥ 3 AEs. A benefit in pathologic response was not established. These findings do not support routine addition of chemotherapy; prospective studies must determine which patients, if any, gain enough surgical benefit to offset the added toxicity.

Abbreviations

NSCLC: non–small-cell lung cancer

Declarations

Ethical approval and consent to participate: This study was approved by the Ethics Committee of Xinqiao Hospital (approval number 202536501), the Ethics Committee of Daping Hospital (approval number 2025388), and the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (approval number 2026-0195-01). The study was conducted in accordance with the

Declaration of Helsinki and relevant guidelines and regulations. The requirement for informed consent to participate was waived by all three ethics committees.

Consent for publication: Not Applicable

Availability of data and materials: The datasets analyzed during the current study are not publicly available due to patient confidentiality. De-identified data may be provided by the corresponding author on reasonable request, subject to the necessary institutional and ethics approvals at the three participating hospitals.

Competing interests: The authors declare that they have no competing interests.

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Author contributions: (I) Conception and design: Ming-Jian Ge, Dong Zhou, and Qing-Shu Li; (II) Collection and assembly of data: Liang Chen, Guang Fu, and Tao Bao; (III) Data analysis and interpretation: Liang Chen, Guang Fu, and Tao Bao; (□) Drafting of the manuscript: Liang Chen; (□) Critical revision of the manuscript for important intellectual content: Ming-Jian Ge, Dong Zhou, and Qing-Shu Li; (□) Administrative, technical, or material support: Liang Chen; (□) Supervision: Ming-Jian Ge. All authors have read and approve the final version of the manuscript for publication.

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Figures

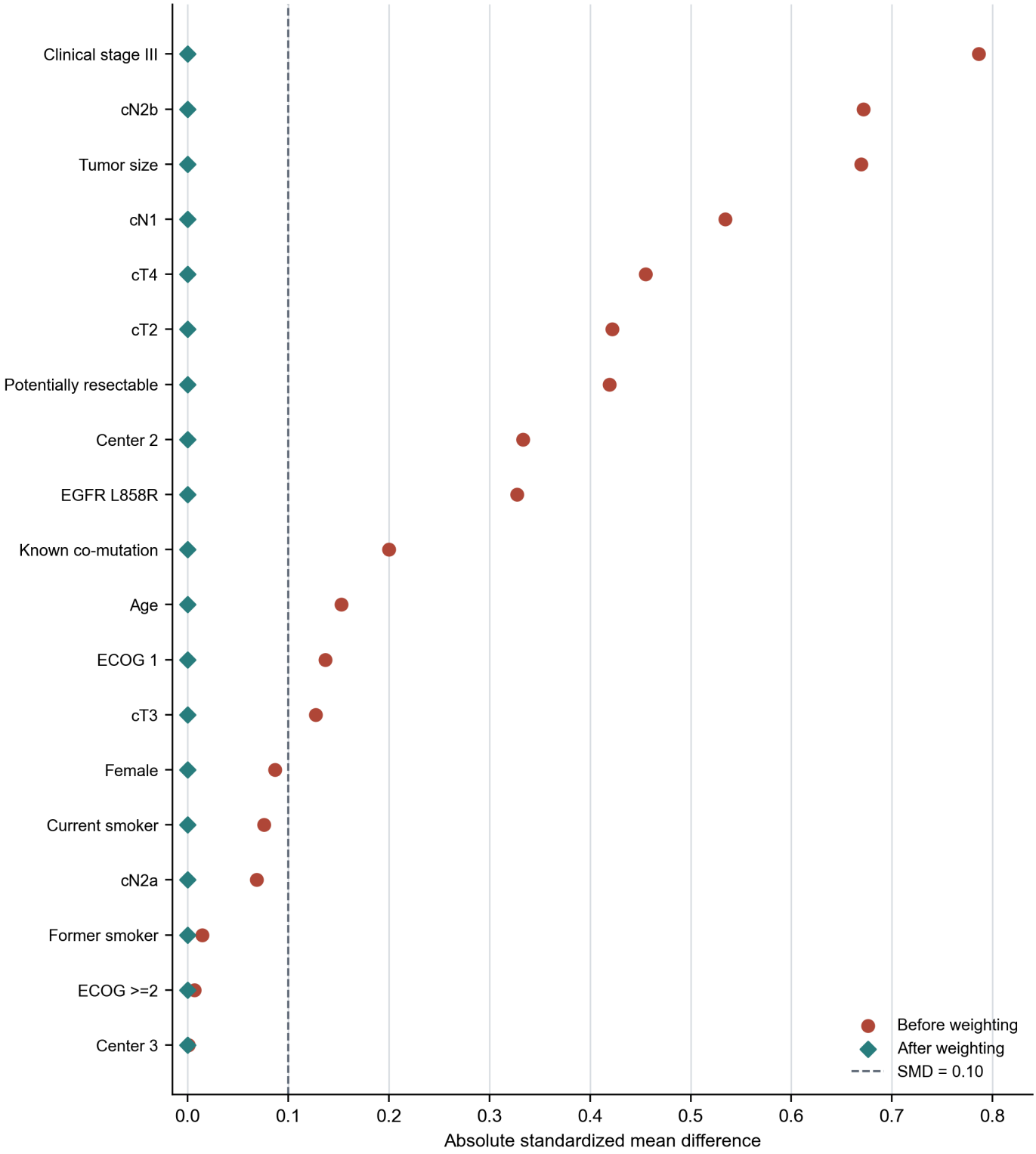
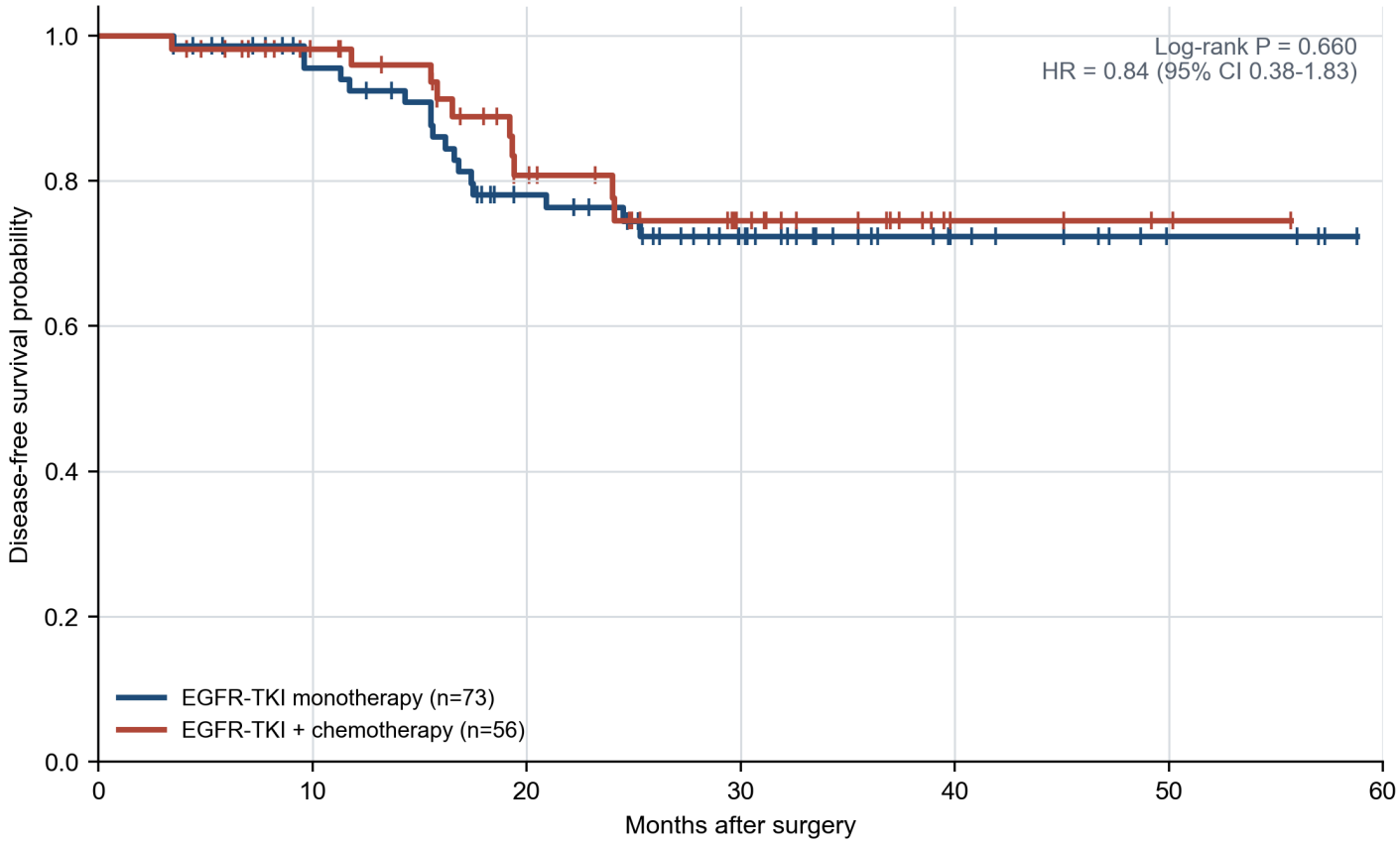


Figure 1

Covariate balance before and after overlap weighting. Points show absolute SMDs for the covariates and non-reference category indicators in the propensity score model. The dashed line marks 0.10; all absolute SMDs were < 0.001 after weighting. This balance applies to measured covariates and does not exclude unmeasured confounding. Abbreviations: SMD, standardized mean difference; ECOG, Eastern Cooperative Oncology Group; cT, clinical T category; cN, clinical N category

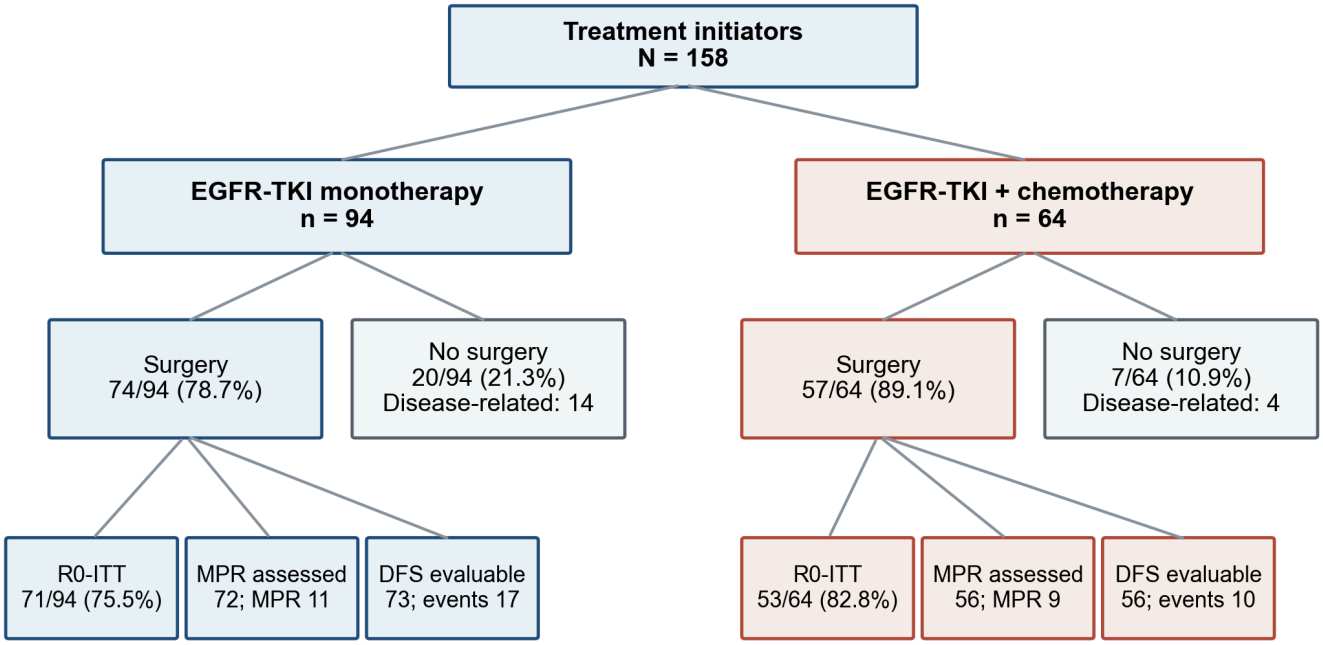


No. at risk

Mono	73	60	40	17	6
Combo	56	43	26	11	3

Figure 2

Unadjusted Kaplan–Meier curves for recorded postoperative DFS in 129 patients with evaluable follow-up after surgery (73 monotherapy, 56 combination). Tick marks indicate censoring; numbers at risk are shown at 0, 12, 24, 36, and 48 months. The HR compares combination therapy with monotherapy. The analysis uses recorded recurrence/censoring status, which does not separately identify deaths, and excludes patients who did not undergo surgery. Abbreviations: DFS, disease-free survival; HR, hazard ratio; CI, confidence interval



R0-ITT and ITT-MPR retain all treatment initiators in the denominator.

Figure 3

Treatment and outcome flow for the 158 patients who initiated neoadjuvant therapy. R0-ITT uses all treatment initiators as the denominator (94 monotherapy, 64 combination); MPR and DFS evaluability refer to overlapping subsets of patients who underwent surgery, not mutually exclusive branches. Disease-related failure includes progression or new metastases and insufficient response to permit R0 resection; all reasons for not undergoing surgery are listed in Table 4. Abbreviations: R0, microscopically margin-negative resection; ITT, intention-to-treat; MPR, major pathologic response; DFS, disease-free survival

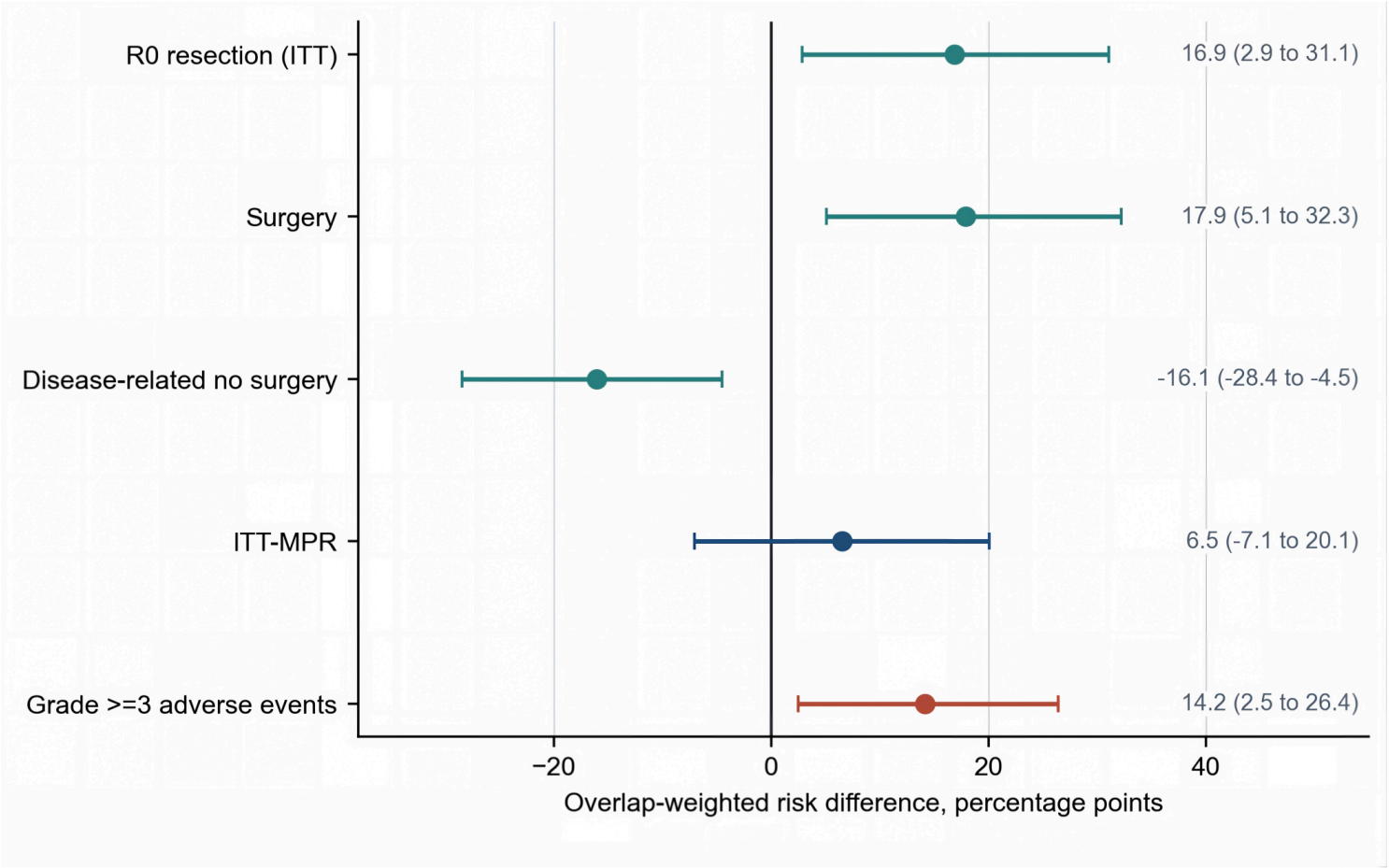


Figure 4

Overlap-weighted absolute risk differences (combination minus monotherapy) for R0-ITT, surgery completion, disease-related failure to undergo surgery, ITT-MPR, and grade ≥3 AEs. Dots show point estimates and error bars show 95% CIs from 2,000 patient-level bootstrap iterations. Positive values indicate higher rates with combination therapy; higher adverse-event rates represent greater toxicity. Negative values for disease-related failure indicate fewer such events with combination therapy. The vertical line at zero marks no difference. Abbreviations: R0, microscopically margin-negative resection; ITT, intention-to-treat; MPR, major pathologic response; CI, confidence interval; AE, adverse event

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- UDUVW24Supplementarymaterials.docx