

Tislelizumab Plus Chemotherapy Versus Concurrent Chemoradiotherapy in Stage IIIA Non-Small Cell Lung Cancer

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CONCLUSIONS

- Perioperative tislelizumab plus chemotherapy demonstrated improved pathological response and survival outcomes compared with neoadjuvant CCRT in resectable stage IIIA NSCLC
- This study represents one of the first comparisons between immunotherapy-based strategies and CCRT in resectable stage IIIA NSCLC
- These findings support the use of perioperative immunotherapy in this treatment setting
- Further validation in additional real-world datasets and prospective comparative studies is warranted

INTRODUCTION

- Stage IIIA non-small cell lung cancer (NSCLC) is a heterogeneous population with variable resectability, leading to variability in treatment strategies^{1,2}
- In South Korea, neoadjuvant concurrent chemoradiotherapy (CCRT) is widely used in clinical practice³
- The RATIONALE-315 trial (NCT04379635) demonstrated improved pathological and survival outcomes with perioperative tislelizumab plus platinum-based chemotherapy, consisting of neoadjuvant tislelizumab plus chemotherapy followed by adjuvant tislelizumab therapy (hereafter referred to as TISLE)⁴
- However, direct comparisons between immunotherapy-based approaches and CCRT are lacking⁵
- This study compared efficacy outcomes between the TISLE cohort from RATIONALE-315 and a real-world neoadjuvant concurrent CCRT cohort in patients with resectable stage IIIA NSCLC under a target trial emulation framework

METHODS

- This study compared the Samsung Medical Center (SMC) neoadjuvant CCRT cohort (patients treated from January 2018 to February 2024, with follow-up through February 2025) with the TISLE cohort from the RATIONALE-315 trial (enrolled from June 2020 to August 2022; data cut-off March 7, 2025)
- Eligible patients were aged ≥18 years, had resectable stage IIIA NSCLC, Eastern Cooperative Oncology Group (ECOG) performance status 0-1, and no known EGFR or ALK alterations
- The index date was defined as the date of treatment initiation in both cohorts
- Cohort balance was achieved using stabilized inverse probability of treatment weighting (IPTW) based on age, sex, smoking status, and histology
- All analyses were based on the full eligible cohorts, with a prespecified time-aligned sensitivity analysis to align calendar time by restricting the SMC cohort to patients treated during the RATIONALE-315 enrollment period
- Efficacy outcomes included pathological complete response (pCR), event-free survival (EFS), and overall survival (OS)

RESULTS

- A total of 335 stage IIIA patients were included (132 TISLE vs 203 CCRT), and after IPTW, 97 vs 184 patients were retained (**Table 1**)
- In the time-aligned analysis, 220 stage IIIA patients were included (132 TISLE vs 88 CCRT), and after IPTW, 117 vs 75 patients were retained
- After weighting, the selected baseline factors were well balanced, with all standard mean differences ≤0.03. Although PD-L1 expression was imbalanced at baseline, it was not included in the IPTW adjustment because PD-L1 status is not considered a strong predictor of response to immunotherapy

Table 1. Baseline Characteristics

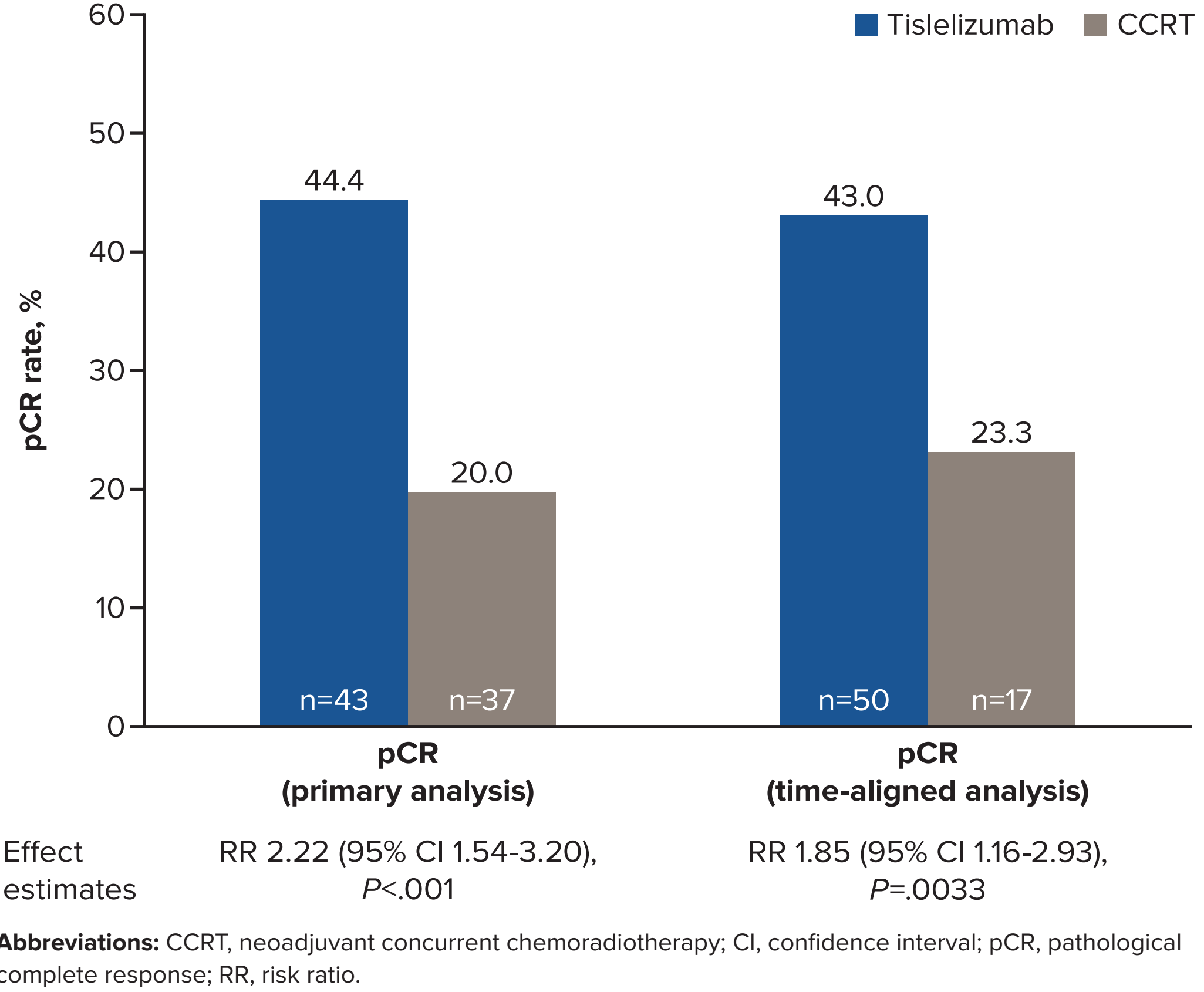
Characteristic	RATIONALE-315 TISLE (n=132)	SMC CCRT (n=203)	Total (N=335)
Age, n (%)			
<65 years	83 (62.9)	113 (55.7)	196 (58.5)
≥65 years	49 (37.1)	90 (44.3)	139 (41.5)
Sex, n (%)			
Male	120 (90.9)	173 (85.2)	293 (87.5)
Female	12 (9.1)	30 (14.8)	42 (12.5)
ECOG performance status, n (%)			
0	90 (68.2)	83 (40.9)	173 (51.6)
1	41 (31.1)	120 (59.1)	161 (48.1)
Missing	1 (0.8)	0	1 (0.3)
Smoking status, n (%)			
Former or current	115 (87.1)	165 (81.3)	280 (83.6)
Never	17 (12.9)	38 (18.7)	55 (16.4)
Histology from CRF, n (%)			
Squamous	103 (78.0)	79 (38.9)	182 (54.3)
Non-squamous	28 (21.2)	118 (58.1)	146 (43.6)
Other ^a	1 (0.8)	6 (3.0)	7 (2.1)
PD-L1 expression from central lab, n (%)			
Not evaluable/indeterminate	3 (2.3)	65 (32.0)	68 (20.3)
<1%	52 (39.4)	69 (34.0)	121 (36.1)
≥1%	77 (58.3)	69 (34.0)	146 (43.6)

^aOther category of histology was grouped into 'squamous' if patients used paclitaxel in neoadjuvant treatment and into 'non-squamous' if patients used pemetrexed in neo-adjuvant treatment for baseline balancing.

Abbreviations: CCRT, neoadjuvant concurrent chemoradiotherapy; ECOG, Eastern Cooperative Oncology Group; IRT, interactive response technology; PD-L1, programmed death-ligand 1; SMC, Samsung Medical Center; TISLE, perioperative tislelizumab plus platinum-based chemotherapy (including adjuvant tislelizumab therapy).

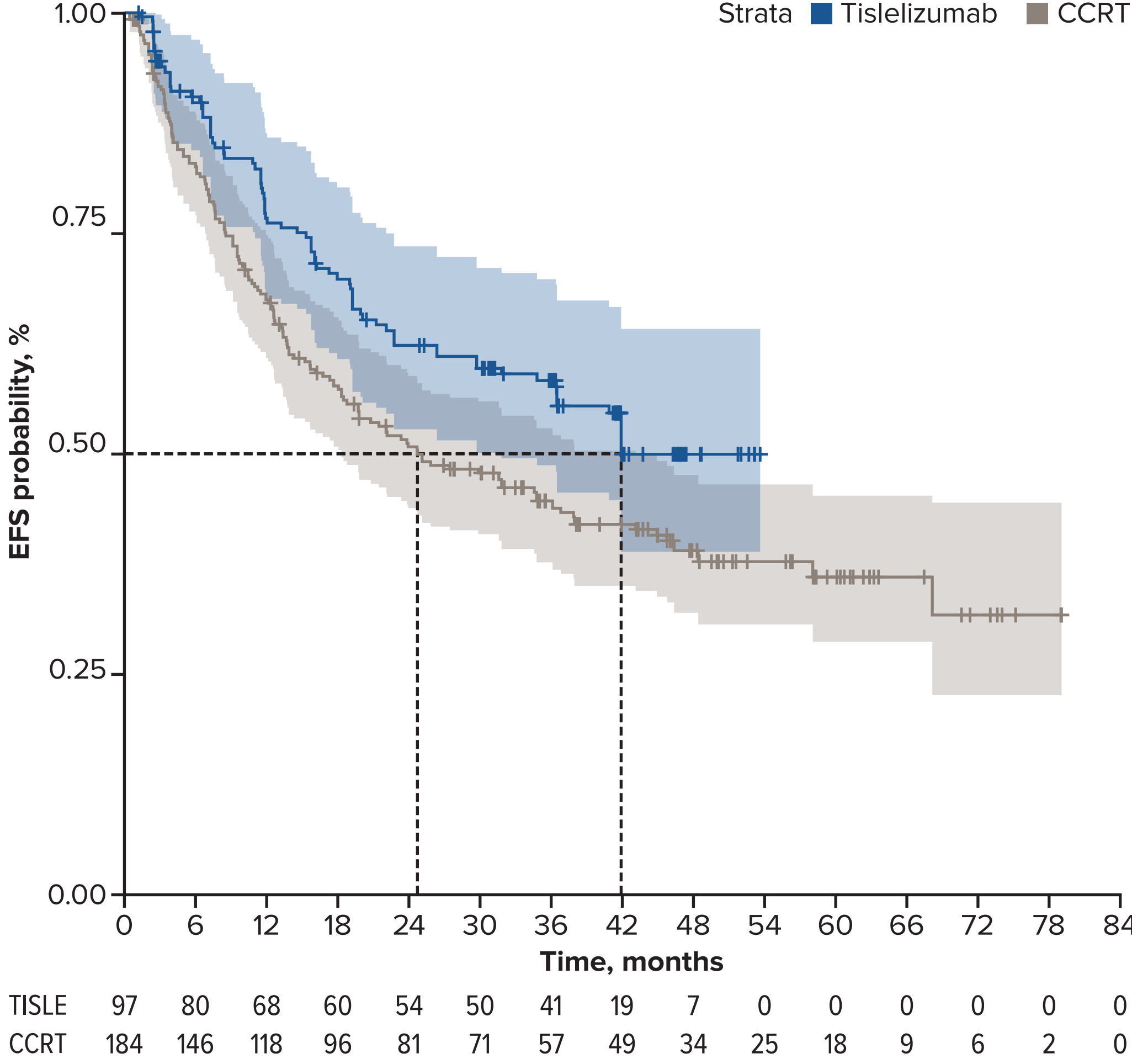
- The pCR rate was significantly higher in the TISLE cohort than in the CCRT cohort (44.4% vs 20.0%; risk ratio (RR) 2.22, 95% confidence interval (CI) 1.54-3.20; *P*<.001; **Figure 1**)
- Similar results were observed in the time-aligned analysis (43.0% vs 23.3%; RR 1.85, 95% CI 1.16-2.93; *P*=.003)

Figure 1. Pathological Complete Response



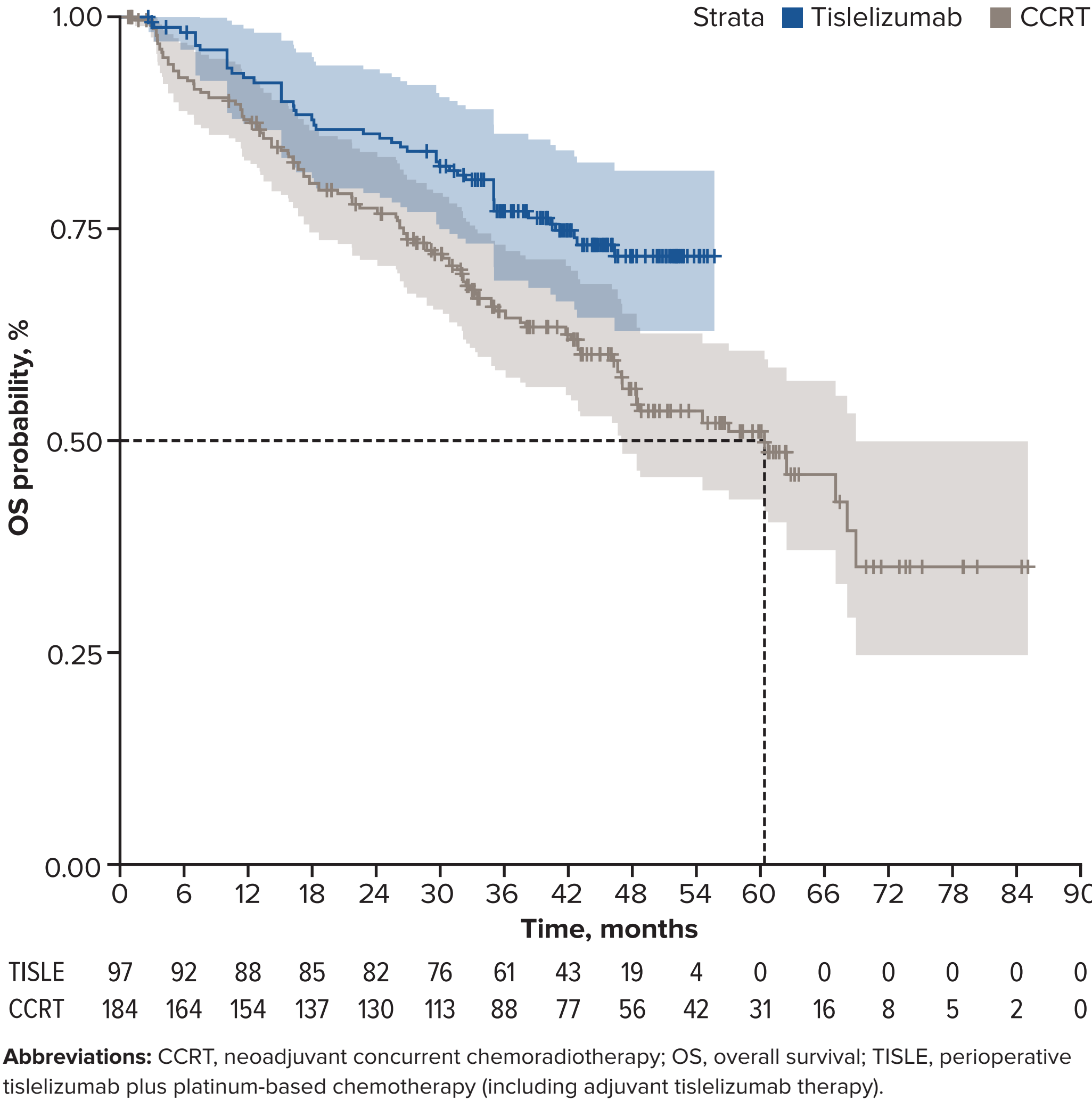
- With a median OS follow-up of 44.5 vs 48.5 months, TISLE was associated with improved EFS (median 41.9 vs 24.7 months; hazard ratio (HR) 0.69, 95% CI 0.50-0.95; **Figure 2**)

Figure 2. Event-Free Survival in the Weighted Population



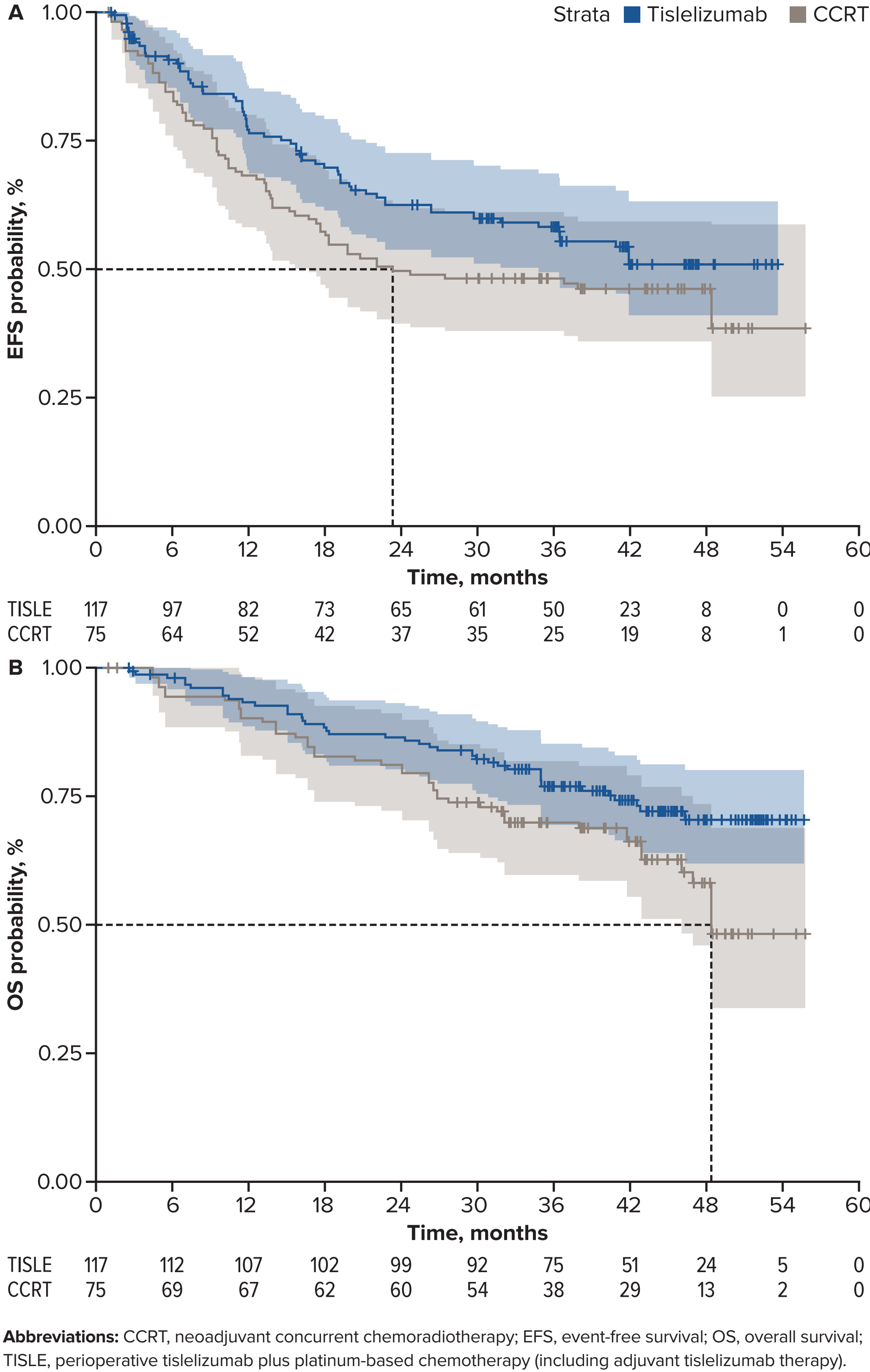
- TISLE was also associated with improved OS (median not reached vs 60.4 months; HR 0.57, 95% CI 0.38-0.86; **Figure 3**)

Figure 3. Overall Survival in the Weighted Population



- Results were consistent in the time-aligned analysis (median EFS not reached [NR] vs 23.3 months: HR 0.74, 95% CI 0.50-1.09; median OS NR vs 48.4 months: HR 0.63, 95% CI 0.39-1.02) (**Figure 4**)

Figure 4. Sensitivity Analysis for A) EFS and B) OS in the Time-Aligned Population



LIMITATIONS

- Residual confounding may remain despite IPTW adjustment due to the non-randomized comparison of clinical trial and real-world cohorts
- Imbalances in selected baseline characteristics, particularly PD-L1 expression, ECOG performance status, and histology, should be considered when interpreting the results

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