

RATIONALE-315: Association of Residual Viable Tumor and Nodal Status With Survival Benefit for Patients With Resectable Non-Small Cell Lung Cancer Treated With Perioperative Tislelizumab

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CONCLUSIONS

- Perioperative tisle plus neoadjuvant CT improved survival in stage II-IIIa NSCLC, including in patients who received surgery and had RVT or LN disease
- More tisle- vs control-treated patients had lower RVT%, which correlated with improved EFS
- The current results show the EFS benefit of perioperative tisle plus neoadjuvant CT also extends to patients with RVT after the neoadjuvant phase
- This comprehensive analysis by RVT% and LN status further supports perioperative tisle as a treatment option for patients with resectable NSCLC regardless of disease stage or nodal status
- These findings may support subsequent treatment decisions, such as adjuvant treatment strategies, by elucidating treatment response in specific patient subgroups

INTRODUCTION

- In RATIONALE-315 (NCT04379635), perioperative tislelizumab (tisle) plus neoadjuvant chemotherapy (CT) showed significant improvement vs placebo plus neoadjuvant CT in event-free survival (EFS) in patients with resectable stage II-IIIa non-small cell lung cancer (NSCLC)²
- The percentage of residual viable tumor (RVT%) and nodal status are strong pathologic, prognostic indicators for survival benefit³
 - Lower RVT% correlates with longer clinical outcomes while increasing lymph node (LN) involvement correlates with lower survival rates³
- RVT% and nodal status assessment after neoadjuvant treatment can inform clinical decision-making on surgical and adjuvant treatment strategies⁴
- This post hoc analysis explored how pathologic regression by RVT% and LN status impacts survival in patients with stage II vs IIIa disease in the RATIONALE-315 study

METHODS

- Patients with untreated stage II-IIIa NSCLC were randomized (1:1) to neoadjuvant tisle plus CT, then surgery and adjuvant tisle (tisle arm), or neoadjuvant placebo plus CT, then surgery and placebo (control arm), as previously reported¹
- This post hoc analysis examined EFS in subgroups of surgery patients by RVT%, LN status, and disease stage (II and IIIa)
 - Some stage IB (n=1) and IIIB (n=2) patients were mistakenly enrolled in RATIONALE-315 and are protocol deviations

RESULTS

Patients

- As of March 7, 2025, 363/453 (80.1%) patients had surgery following neoadjuvant treatment (tisle arm n=190; control arm n=173), of whom 361 (79.7%) had evaluable tumor results after surgery (n=189; n=172, respectively)
- Median (range) study follow-up was 40.1 (2.7-57.0) months

EFS in All Surgery Patients

- Surgery patients in the tisle arm showed an EFS benefit (HR [95% CI]: 0.62 [0.44-0.88]) vs control arm
 - 2-year EFS rate (95% CI) was 72.6% (65.3%-78.6%) in the tisle arm vs 60.1% (51.7%-67.4%) in the control arm
 - 4-year EFS rate (95% CI) was 65.5% (57.4%-72.4%) in the tisle arm vs 47.4% (37.4%-56.8%) in the control arm

RVT%

- In the tisle arm:
 - More patients, including all patients and stage III/IIIA patients, had a pathologic response (0-10% RVT; **Figure 1A**)
 - Pathologic complete response (pCR) correlated with EFS benefit in surgery patients (**Figure 1B**)
 - Lower RVT% correlated with improved 2- and 4-year EFS rates (**Figure 1C**)

Figure 1A. RVT% Distribution in Surgery Patients With Evaluable Tumors*

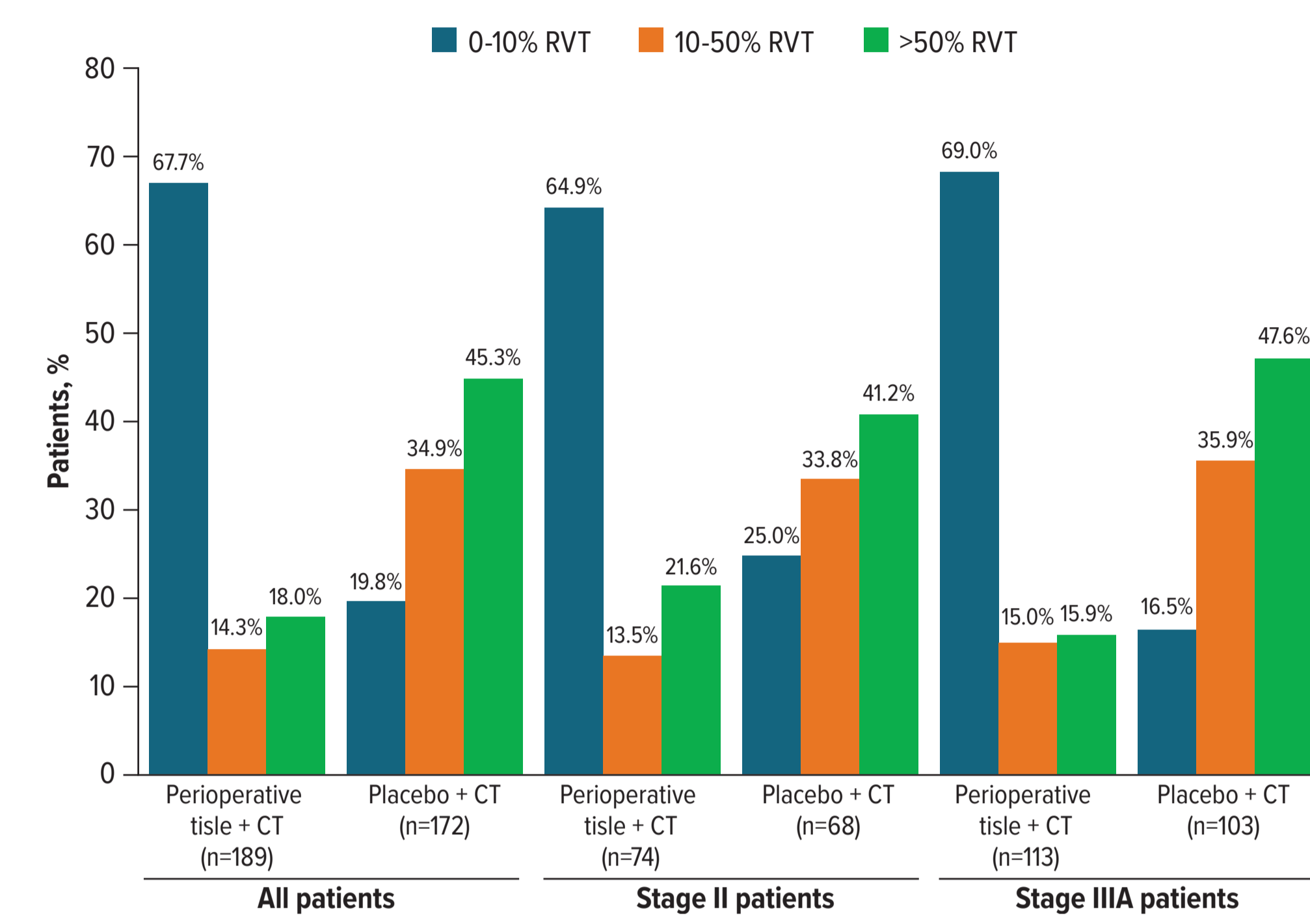


Figure 1B. EFS in Surgery Patients With pCR

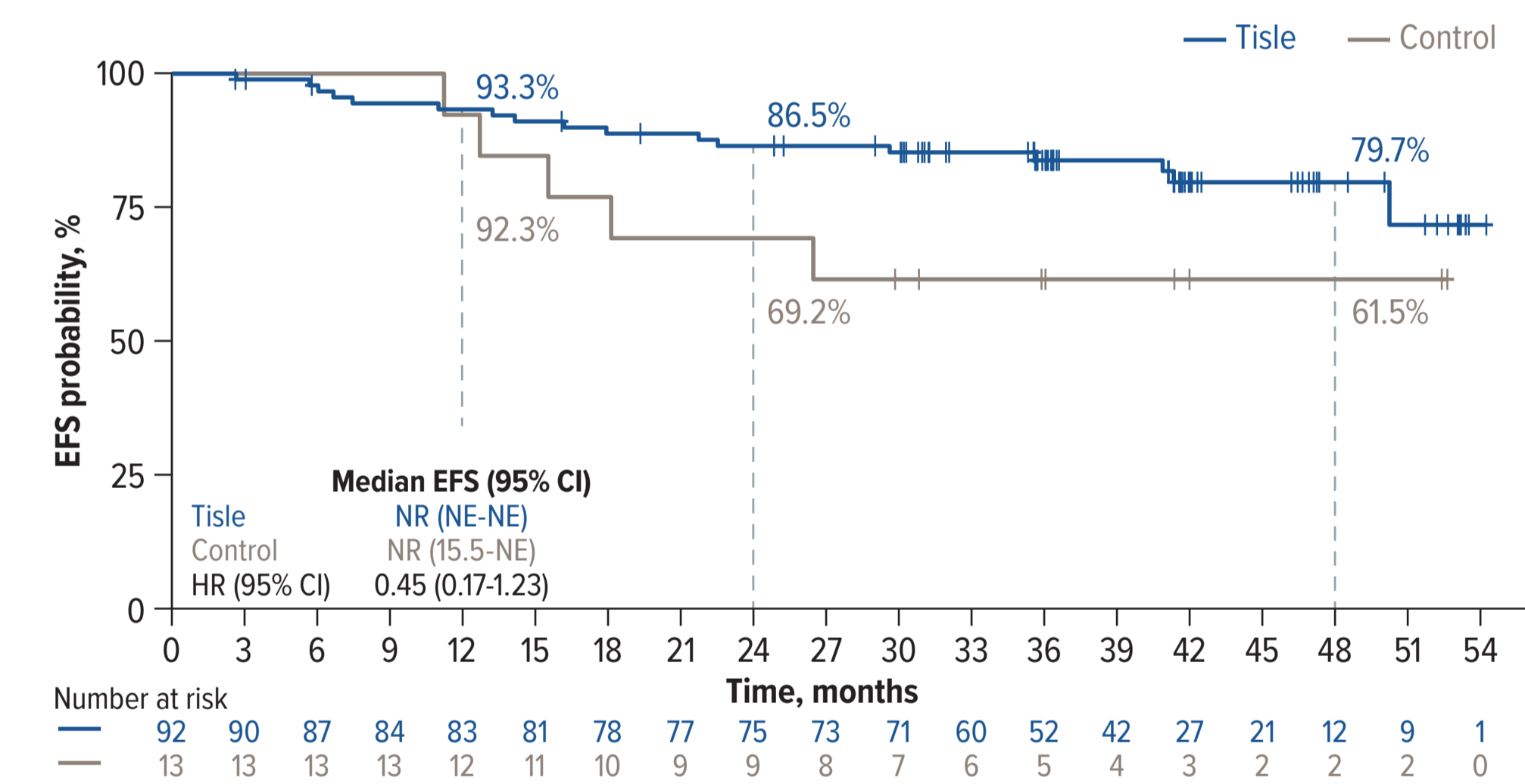
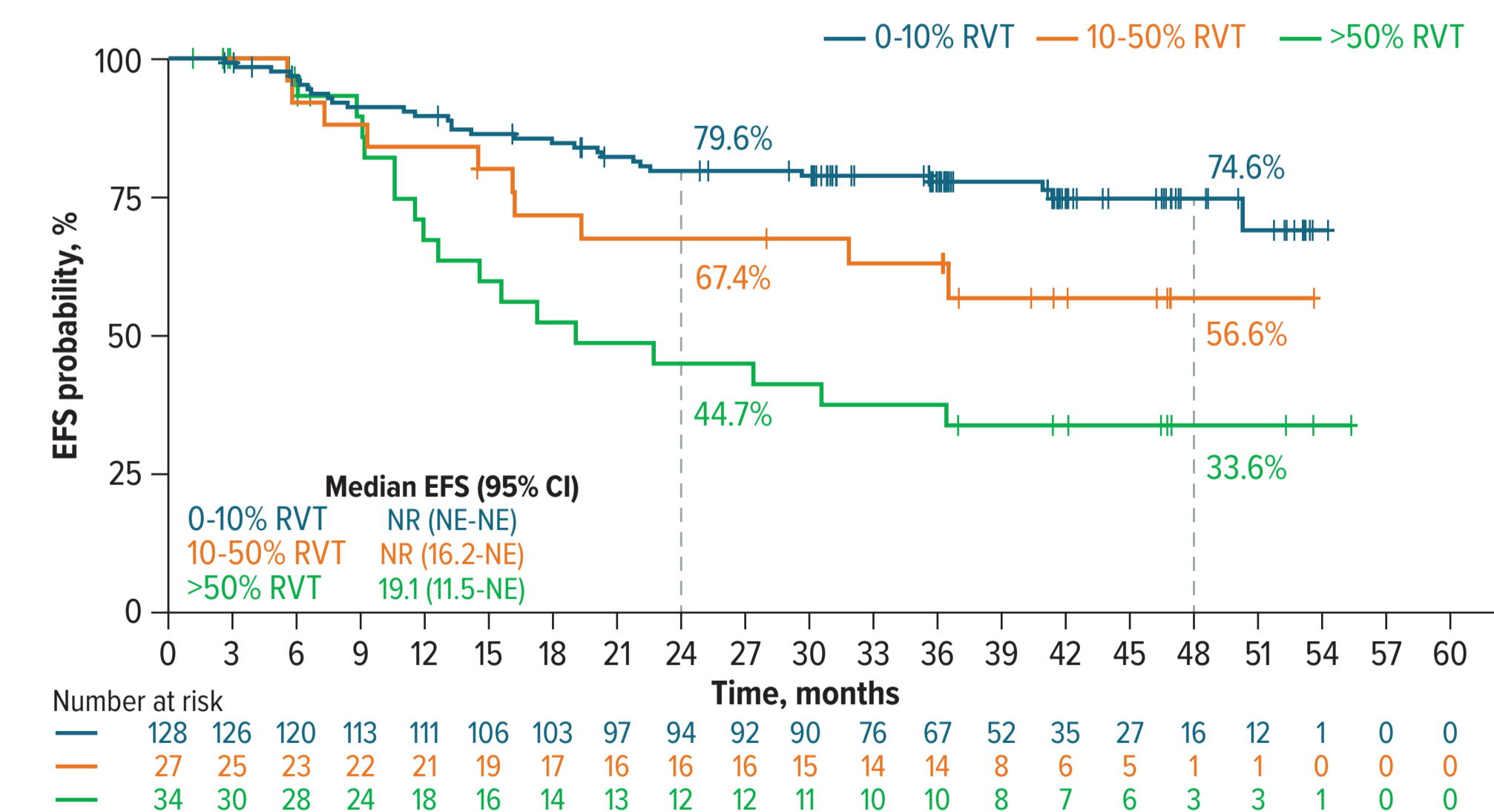


Figure 1C. EFS in Surgery Patients Treated With Tisle + CT by RVT% Distribution



*Two patients had no evaluable tumors.
 Abbreviations: CI, confidence interval; CT, chemotherapy; HR, hazard ratio; NE, not estimable; NR, not reached.

Nodal Downstaging in All Surgery Patients

- In the tisle arm:
 - Downstaging/restaging of surgery patients is diagrammed in **Figure 2A**
 - More patients treated with tisle were downstaged to ypN0
 - Fewer patients had pathologic upstaging with tisle
- In all surgery patients, EFS benefit was observed regardless of LN involvement (**Figure 2B**)
- EFS benefit was greatest in patients without persistent nodal disease (**Figure 2C**)
- Residual disease in the primary tumor led to differences in clinical outcomes, with greatest EFS benefit observed in patients treated with perioperative tisle + CT (**Figure 2D and 2E**)

Figure 2A. Nodal Downstaging in All Patients Downstaged to ypT0N0 Post-Surgery

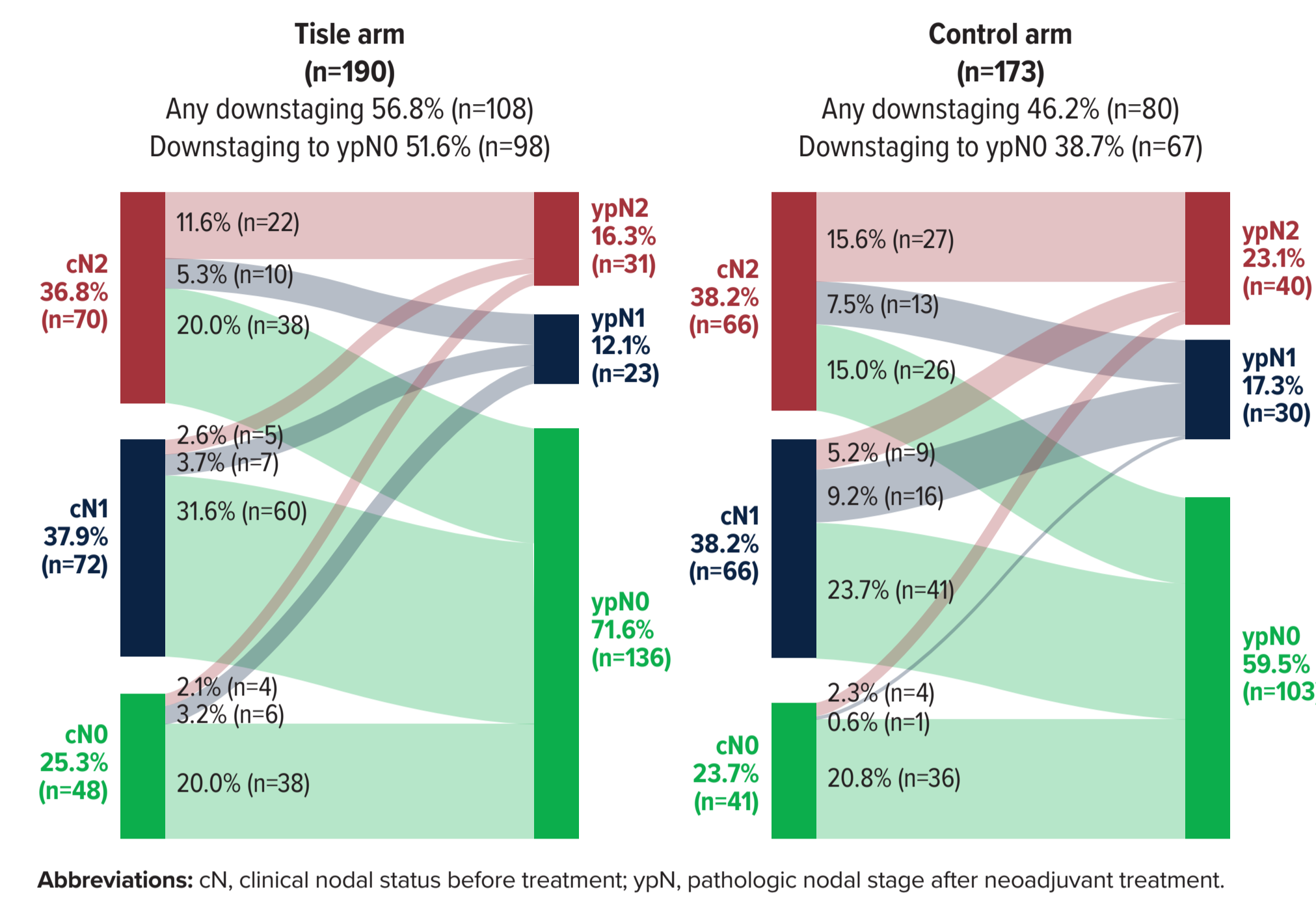


Figure 2B. EFS in All Surgery Patients With and Without LN Involvement

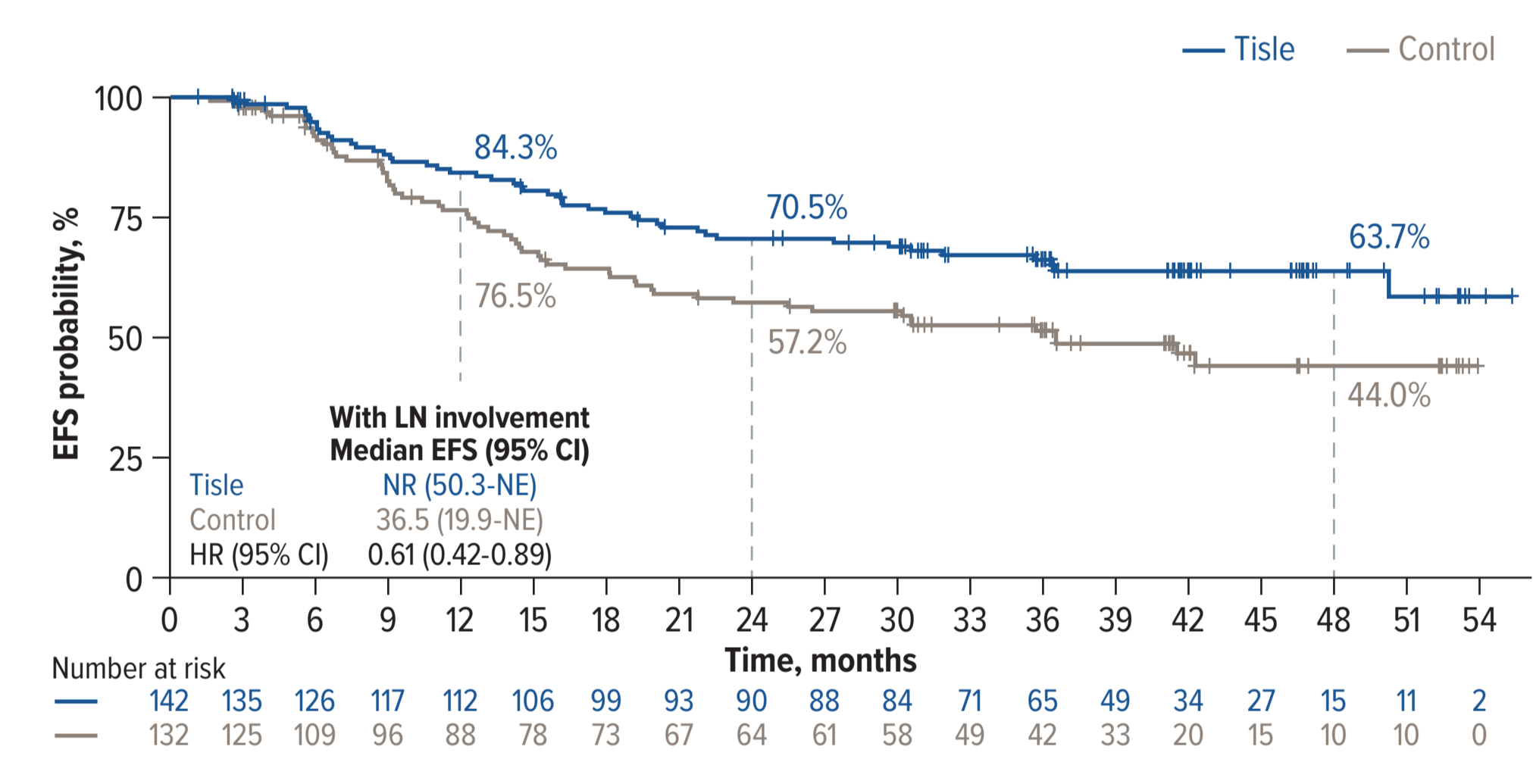


Figure 2C. EFS in Downstaged Patients Treated With Tisle + CT

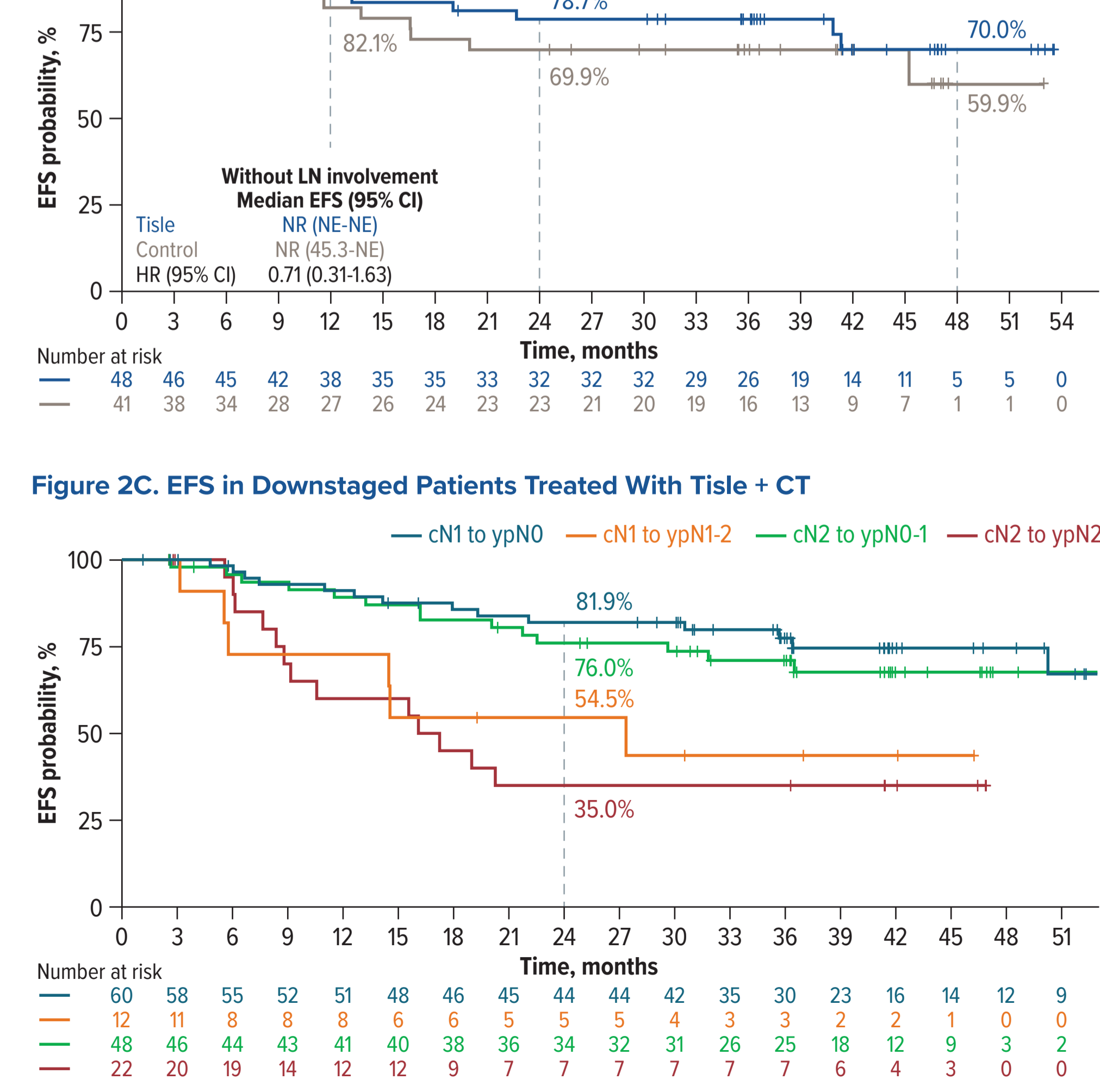


Figure 2D. EFS in All Patients Downstaged to ypT0N0 Post-Surgery

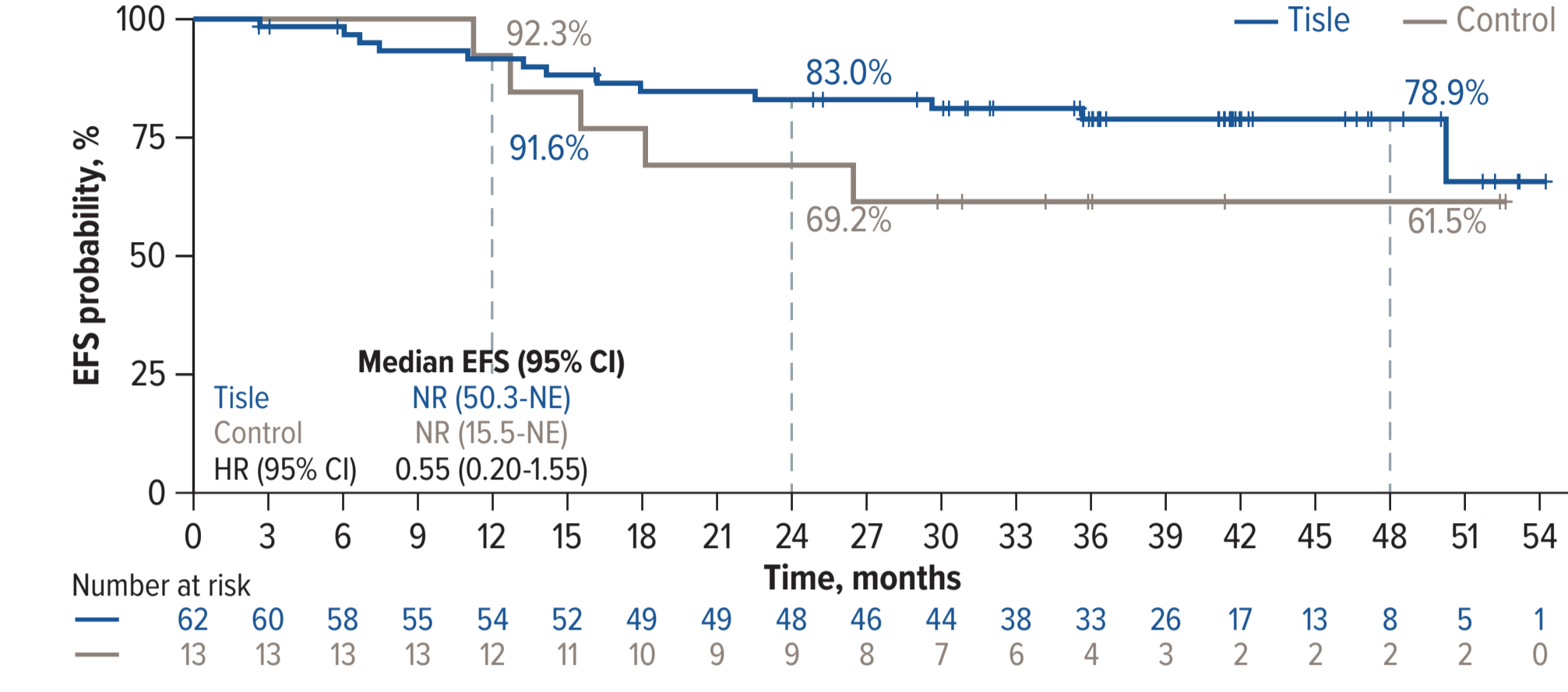
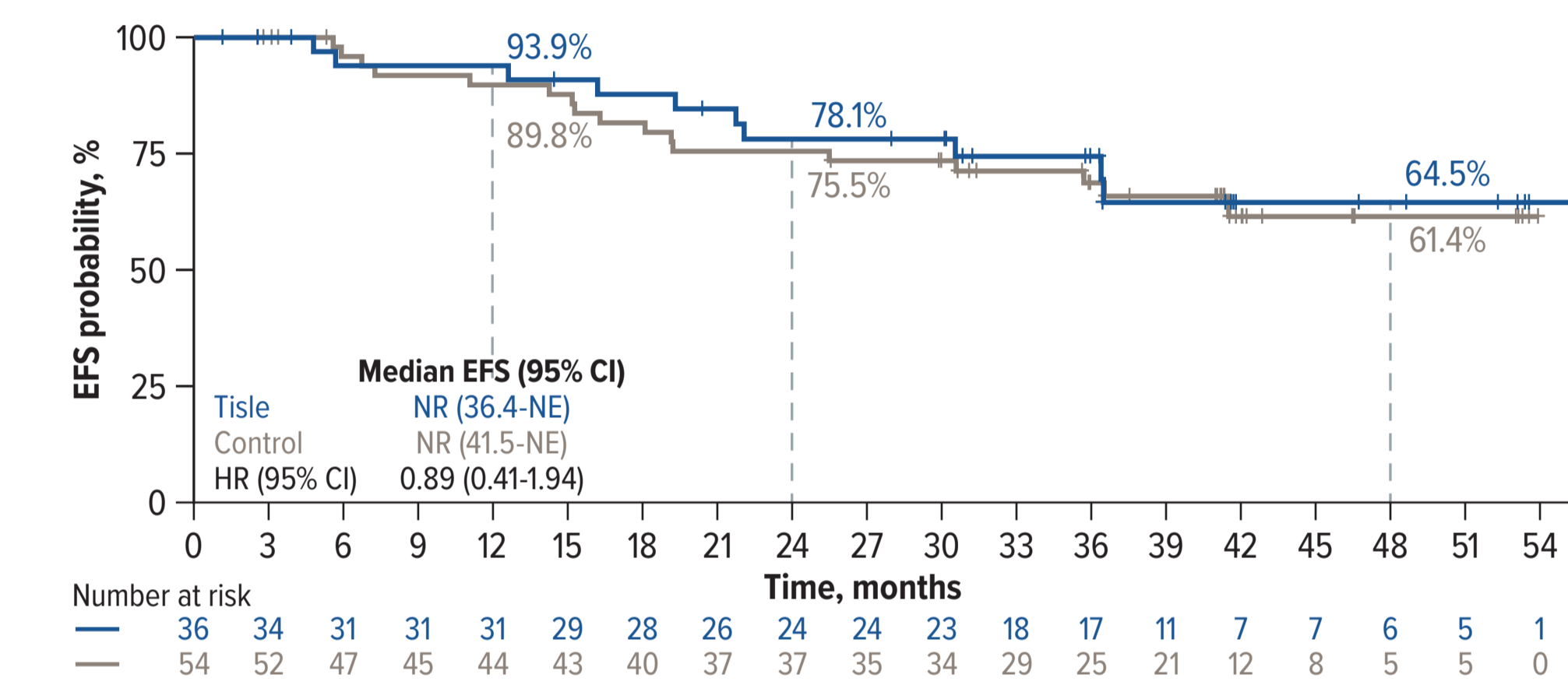


Figure 2E. EFS in All Patients to ypT1+N0 Post-Surgery



Disease Stage

- Disease was stage II in 143/363 (39.4%) patients and stage IIIa in 217/363 (59.8%) patients (**Table 1**)

Table 1. Patient Distribution by Disease Stage With Nodal Involvement and Downstaging

n (%)	Tisle arm	Control arm	Total
Stage II	n=74	n=69	n=143
No LN involvement	33 (44.6)	36 (52.2)	69 (48.3)
LN involvement	41 (55.4)	33 (47.8)	74 (51.7)
Downstaging (cN1 to ypN0)	33 (44.6)	20 (29.0)	53 (37.1)
Stage IIIa	n=114	n=103	n=217
No LN involvement	14 (12.3)	5 (4.9)	19 (8.8)
LN involvement	100 (87.7)	98 (95.1)	198 (91.2)
Downstaging (cN1 to ypN0)	27 (23.7)	21 (20.4)	48 (22.1)
Downstaging (cN2 to ypN0-N1)	47 (41.2)	39 (37.9)	86 (39.6)

- By stage II and IIIa subgroups, more surgery patients were downstaged with tisle vs control (**Table 1**)

In the tisle arm:

- Surgery patients showed an EFS benefit regardless of disease stage. Stage II: EFS HR (95% CI): 0.60 (0.32-1.13); stage IIIa: EFS HR (95% CI): 0.62 (0.41-0.94)
 - Stage II 4-year EFS rate (95% CI) was 73.3% (59.2%-83.2%) vs 61.6% (47.7%-72.9%)
 - Stage IIIa 4-year EFS rate (95% CI) was 59.9% (49.5%-68.8%) vs 40.0% (27.9%-51.9%)
- In stage II and IIIa patients who received surgery, improved EFS benefit was seen, notably in those with pCR and with or without LN involvement (**Figure 3A**)
 - There were insufficient numbers of clinical stage IIIa surgery patients without LN involvement, so they were not included
- EFS benefit was seen in stage II patients with ypT2b-T3N0 and ypT1-T2N1 (**Figure 3B**)
- In stage IIIa patients, EFS benefit was observed in cN1-2, tisle-treated patients downstaged to ypN0-1 (**Figure 3C**)

Figure 3A. Forest Plot of EFS in Stage II and IIIa Surgery Patients With pCR and With or Without LN Involvement

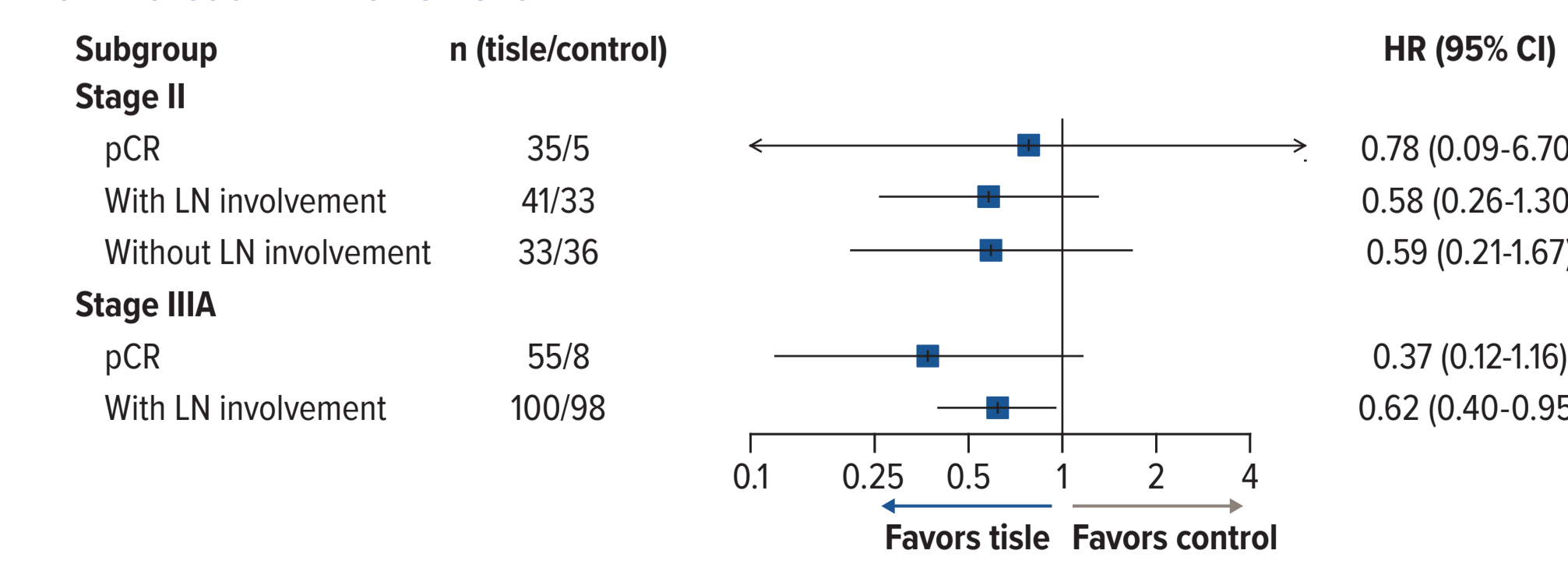


Figure 3B. EFS in Stage II Patients With ypT2b-T3N0 and ypT1-T2N1

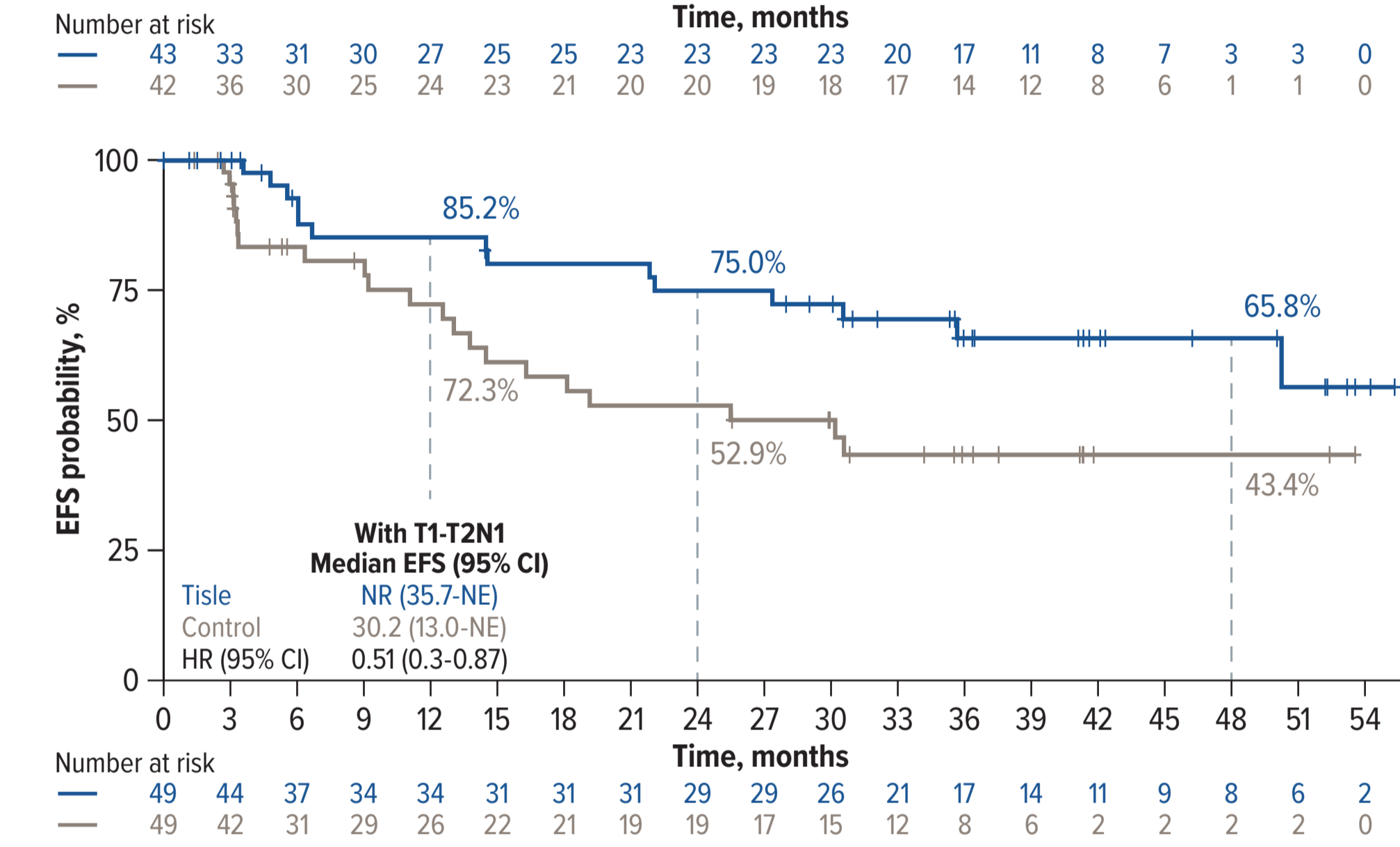
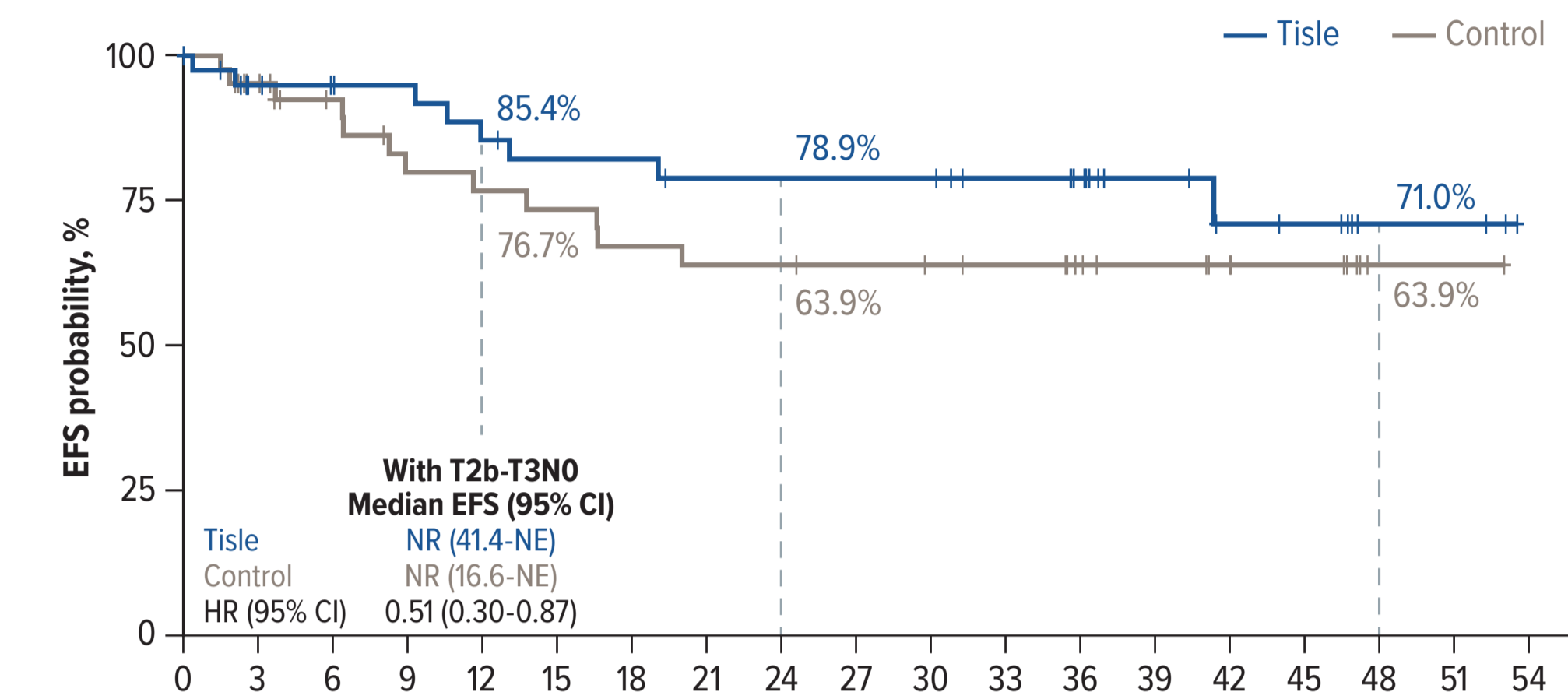
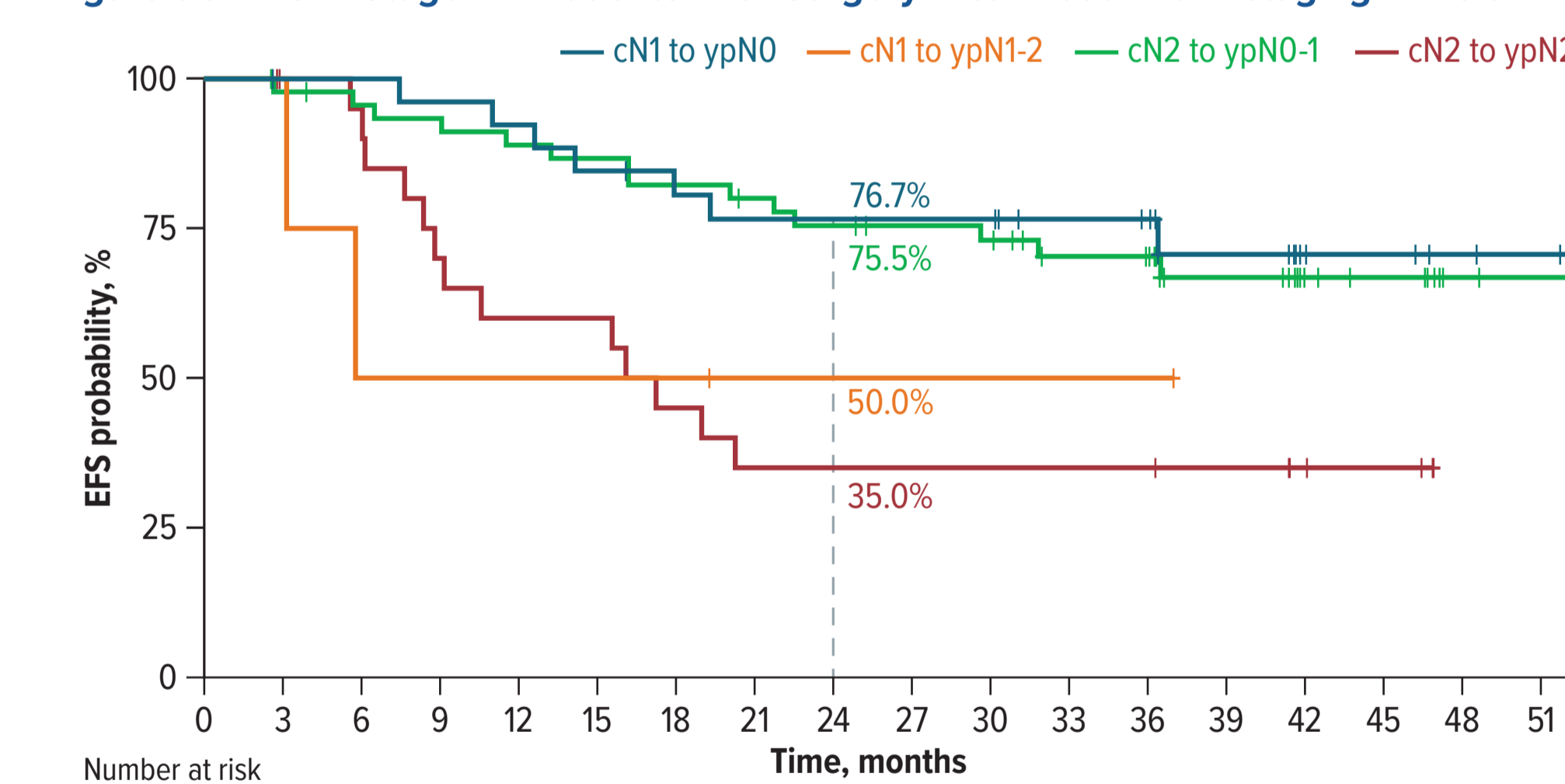


Figure 3C. EFS in Stage IIIa Patients With Surgery After Nodal Downstaging in Tisle Arm



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DISCLOSURES

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