

RATIONALE-315: Clinical Outcomes by Adjuvant Treatment Cycles in Perioperative Tislelizumab Plus Chemotherapy in Resectable NSCLC

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CONCLUSIONS

- The RATIONALE-315 trial demonstrated that perioperative tislelizumab plus neoadjuvant chemotherapy significantly improved EFS in patients with resectable NSCLC completing 8 adjuvant cycles of tislelizumab versus adjuvant placebo, with manageable safety across key subgroups
- These exploratory findings should be interpreted with caution given the lack of randomization to address this question. A landmark analysis was performed to reduce the potential for immortal time bias

INTRODUCTION

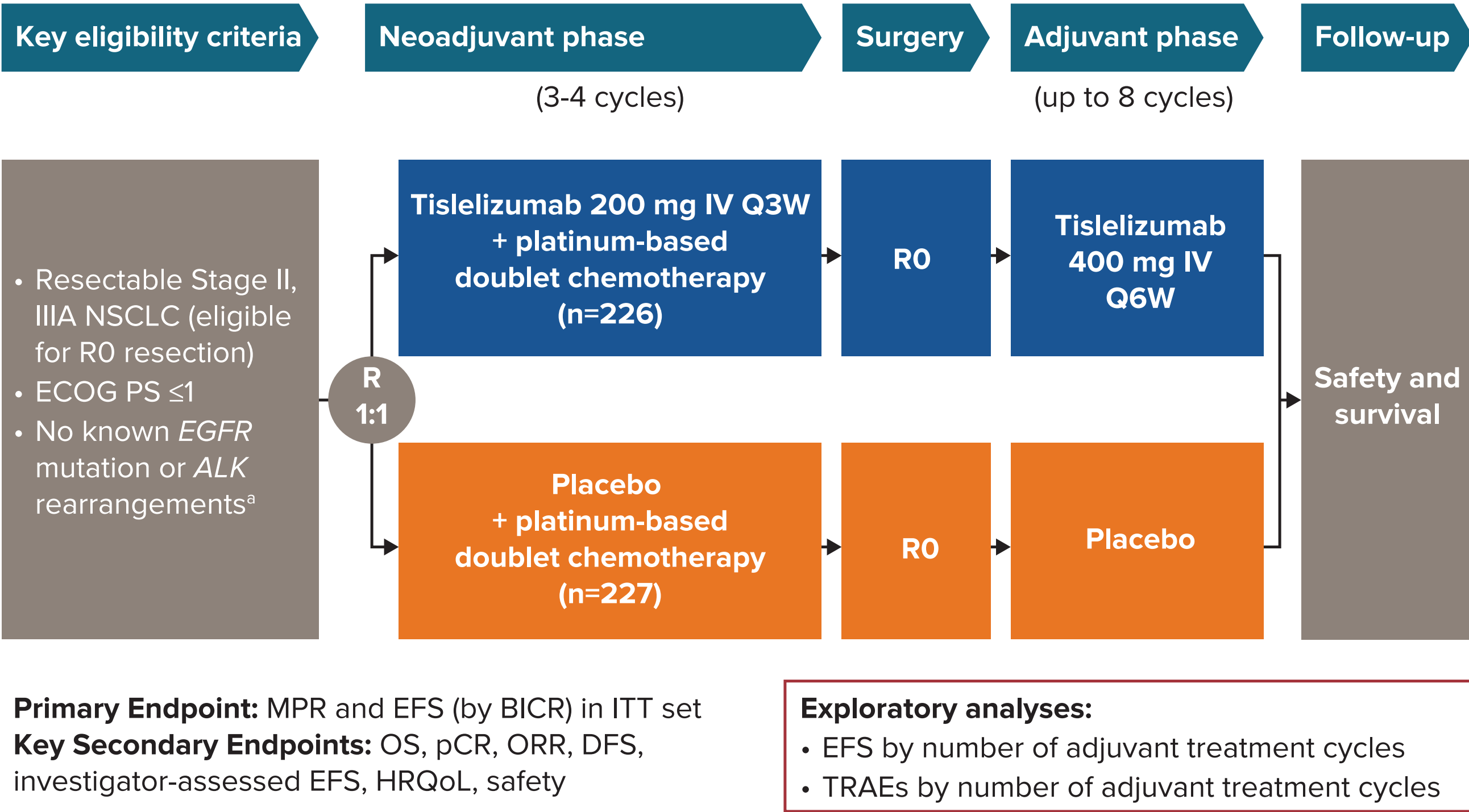
- In RATIONALE-315 (NCT04379635), perioperative tislelizumab plus neoadjuvant chemotherapy significantly improved overall survival (OS) and event-free survival (EFS) versus placebo plus neoadjuvant chemotherapy in patients with resectable non-small cell lung cancer (NSCLC)²
- More adjuvant immunotherapy cycles after neoadjuvant tislelizumab plus chemotherapy may improve outcomes in resectable NSCLC³
 - However, the optimal number of cycles remains unclear, especially for patients with stage II versus III disease or those who do not achieve pathological complete response (pCR)⁴
- This exploratory analysis evaluated the efficacy and safety of 0, 1-7, or 8 cycles of adjuvant tislelizumab versus adjuvant placebo in patients with resectable NSCLC from RATIONALE-315

METHODS

Trial Design

- Patients with untreated stage II-IIIa NSCLC were randomized (1:1) to neoadjuvant tislelizumab plus chemotherapy or placebo plus neoadjuvant chemotherapy, then surgery and adjuvant tislelizumab or placebo (**Figure 1**)

Figure 1. Study Design



Abbreviations: ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; CT, chemotherapy; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; EGFR, epidermal growth factor receptor; HRQoL, health-related quality of life; IRC, independent review committee; ITT, intent-to-treat; IV, intravenous; MPR, major pathological response; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, placebo; pCR, pathological complete response; Q3W, every 3 weeks; Q6W, every 6 weeks; R, randomized; R0, resection with curative intent; TRAE, treatment-related treatment-emergent adverse event.

Exploratory Analyses

- Patients who received surgery were included and analyzed by subgroups who received 0, 1-7, or 8 cycles of adjuvant treatment, up to approximately 1 year of treatment
- EFS was analyzed according to completion of 0, 1-7, or 8 adjuvant cycles in the intent-to-treat (ITT) population and by pCR status or disease stage (II and IIIa) populations
- A landmark EFS analysis was performed from the end of adjuvant treatment (for 0 cycles, analysis is from the date of surgery) to mitigate immortal time bias

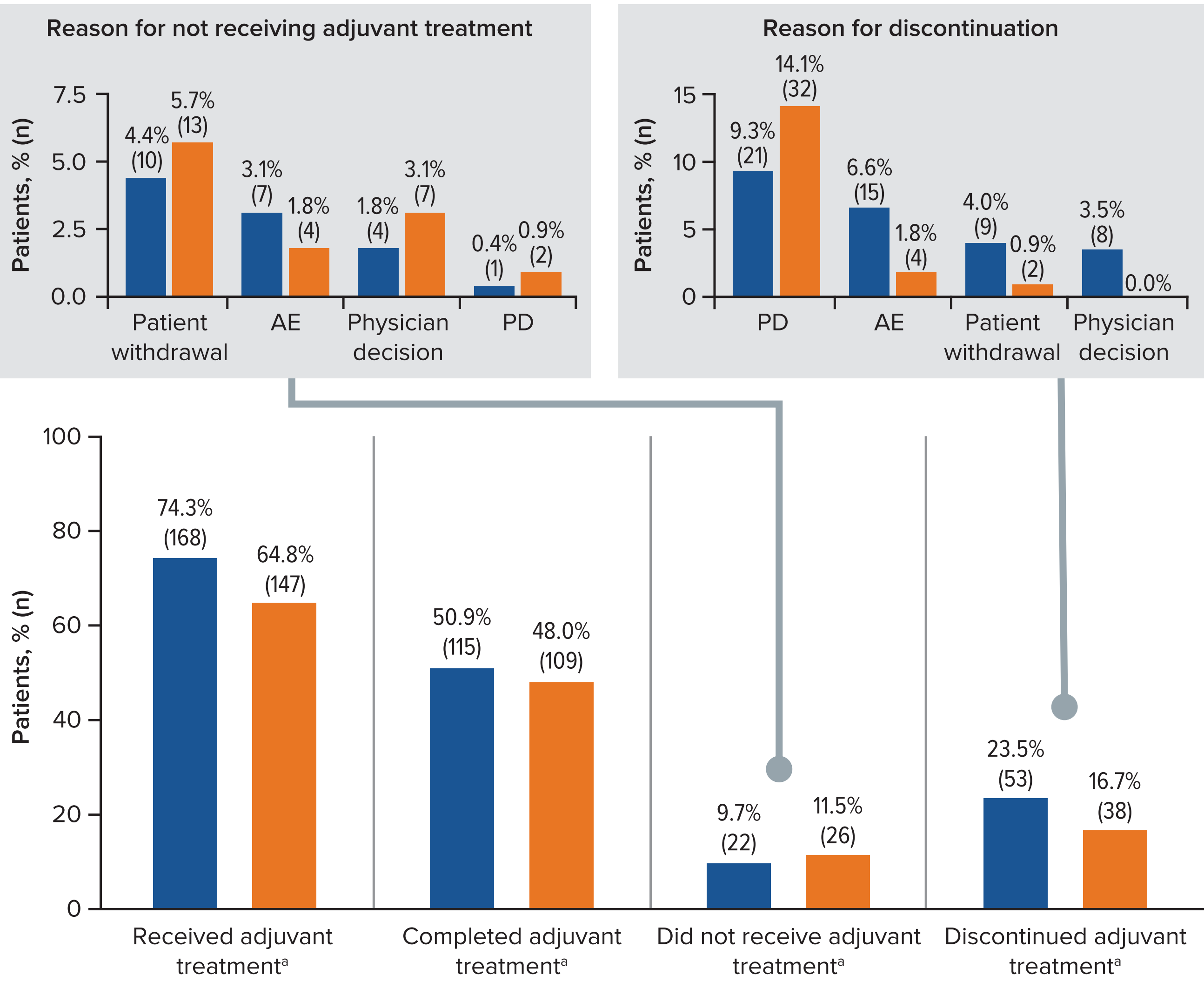
RESULTS

Patients

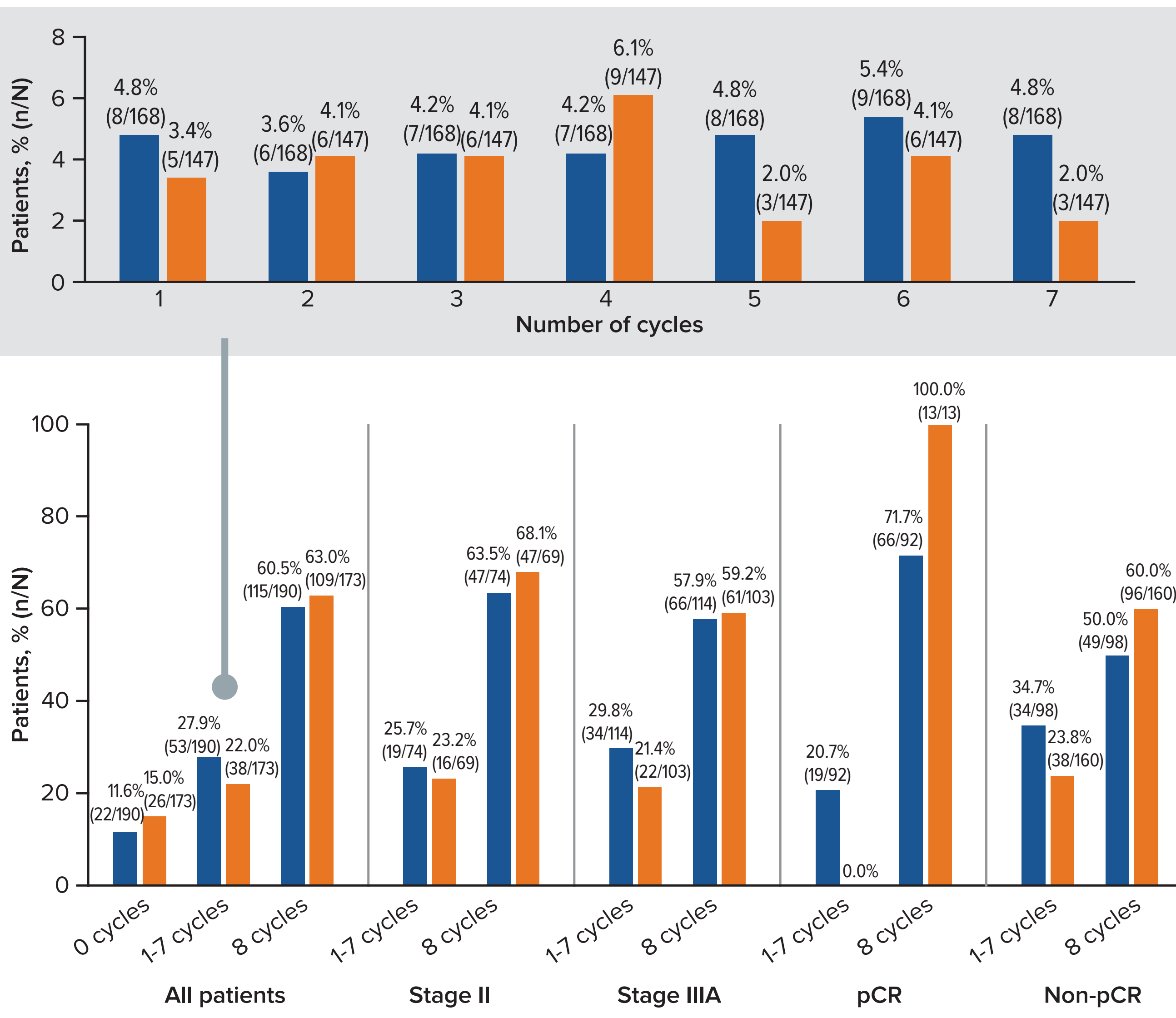
- As of March 7, 2025, 168 patients received ≥ 1 cycle of adjuvant tislelizumab and 147 patients received ≥ 1 cycle of adjuvant placebo; 22 and 26 patients, respectively, did not receive adjuvant treatment (**Figure 2**)

Figure 2.

A. Patient Disposition



B. Adjuvant Treatment Population



The ITT analysis set included all randomized patients.
*Denominator based on randomized patients.

- Baseline characteristics were generally similar among adjuvant cycle subgroups in the tislelizumab arm, except for numerical differences in the proportions of female patients, Eastern Cooperative Oncology Group performance status (ECOG PS) of 1, and programmed cell-death ligand 1 (PD-L1) expression, and in the placebo arm, except for disease stage and PD-L1 expression (**Table 1**)

Table 1. Baseline Demographics and Disease Characteristics by Adjuvant Cycle

	0 cycles		1-7 cycles		8 cycles	
n (%)	Tislelizumab n=22	Placebo n=26	Tislelizumab n=53	Placebo n=38	Tislelizumab n=115	Placebo n=109
Sex						
Female	1 (4.5)	2 (7.7)	2 (3.8)	2 (5.3)	13 (11.3)	10 (9.2)
Male	21 (95.5)	24 (92.3)	51 (96.2)	36 (94.7)	102 (88.7)	99 (90.8)
Age						
<65 years	15 (68.2)	17 (65.4)	36 (67.9)	28 (73.7)	71 (61.7)	62 (56.9)
≥65 years	7 (31.8)	9 (34.6)	17 (32.1)	10 (26.3)	44 (38.3)	47 (43.1)
ECOG PS*						
0	17 (77.3)	19 (73.1)	30 (56.6)	28 (73.7)	77 (67.0)	72 (66.1)
1	5 (22.7)	7 (26.9)	23 (43.4)	10 (26.3)	37 (32.2)	37 (33.9)
Smoking status						
Current/former	20 (90.9)	22 (84.6)	46 (86.8)	31 (81.6)	98 (85.2)	93 (85.3)
Never	2 (9.1)	4 (15.4)	7 (13.2)	7 (18.4)	17 (14.8)	16 (14.7)
Disease stage*						
II	8 (36.4)	6 (23.1)	19 (35.8)	16 (42.1)	47 (40.9)	47 (43.1)
IIIa	14 (63.6)	20 (76.9)	34 (64.2)	22 (57.9)	66 (57.4)	61 (56.0)
PD-L1 expression*						
<1%/NE	8 (36.4)	15 (57.7)	28 (52.8)	17 (44.7)	48 (41.7)	46 (42.2)
≥1%	14 (63.6)	11 (42.3)	25 (47.2)	21 (55.3)	67 (58.3)	63 (57.8)

*ECOG PS value missing for 1 patient in the tislelizumab arm of the 8 cycles subgroup. *Two patients in the tislelizumab arm and 1 patient in the placebo arm of the 8 cycles subgroup were stage IB or IIIB and mistakenly enrolled. *Measured by central laboratory.

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed cell death-ligand 1.

EFS

- The median (range) follow-up for patients completing surgery was 40.0 (2.7-56.8) months
 - At the same data cutoff, the ITT population had a median (range) study follow-up of 38.5 (0.1-57.0) months, with a median (95% confidence interval [CI]) EFS of not reached (50.3-not estimable) months in the tislelizumab arm and 30.6 (16.6-45.3) months in the placebo arm¹
- EFS improvement was greatest in patients who completed 8 cycles of adjuvant tislelizumab versus placebo (**Figure 3**)
 - In the landmark analysis, EFS trended toward improvement with tislelizumab versus placebo in patients who completed 0 cycles (hazard ratio [HR]: 0.75 [95% CI 0.25-2.28]; **Figure 4A**), although small patient numbers limit interpretation
 - Improved EFS was observed in the landmark analysis in patients who completed 1-7 (HR: 0.16 [95% CI 0.07-0.34]; **Figure 4B**) or 8 (HR: 0.48 [95% CI 0.25-0.92]; **Figure 4C**) cycles of adjuvant tislelizumab versus placebo
- Similar results were observed regardless of pCR status or disease stage (**Figure 4**)

Figure 3. EFS by Number of Completed Cycles

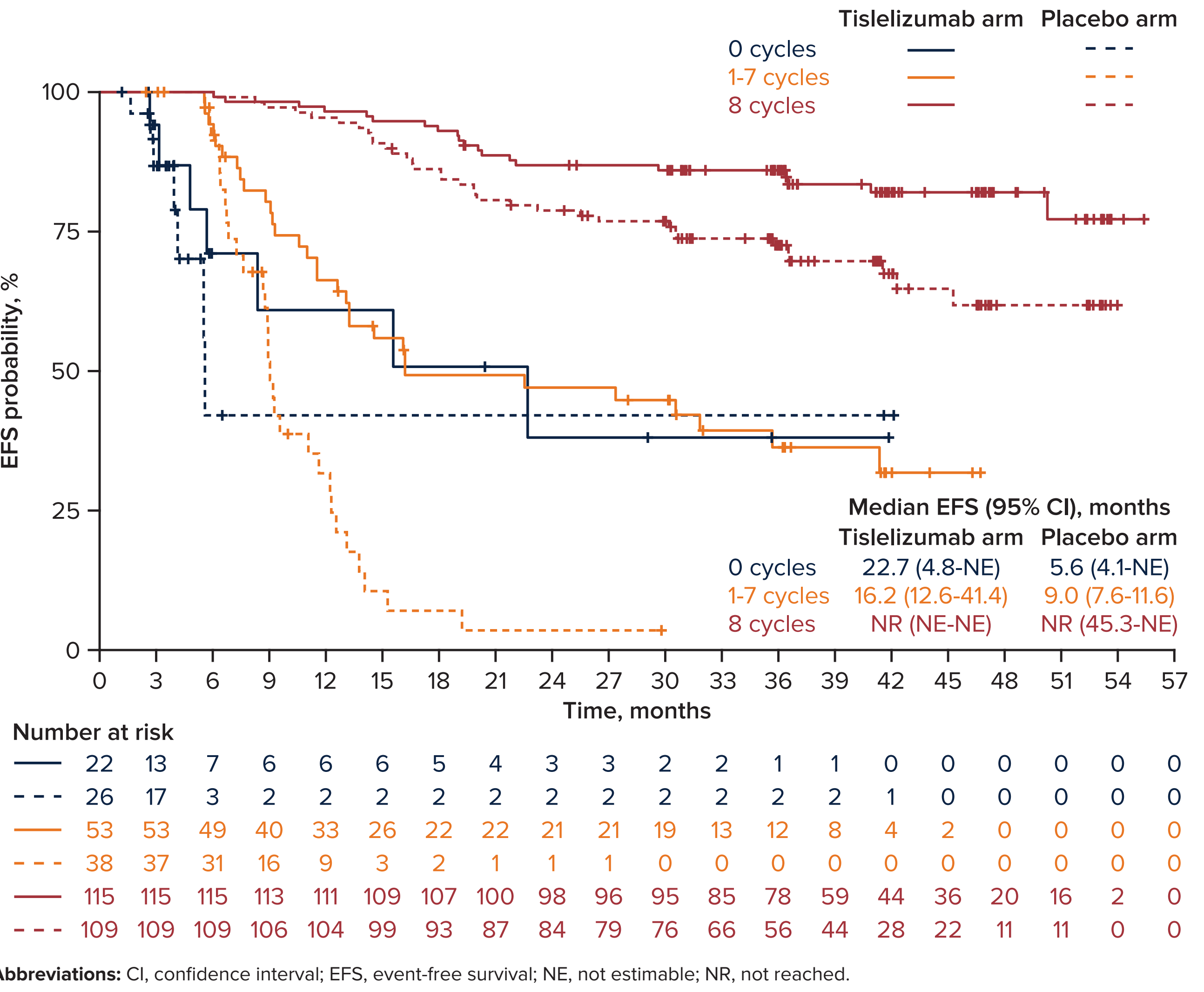
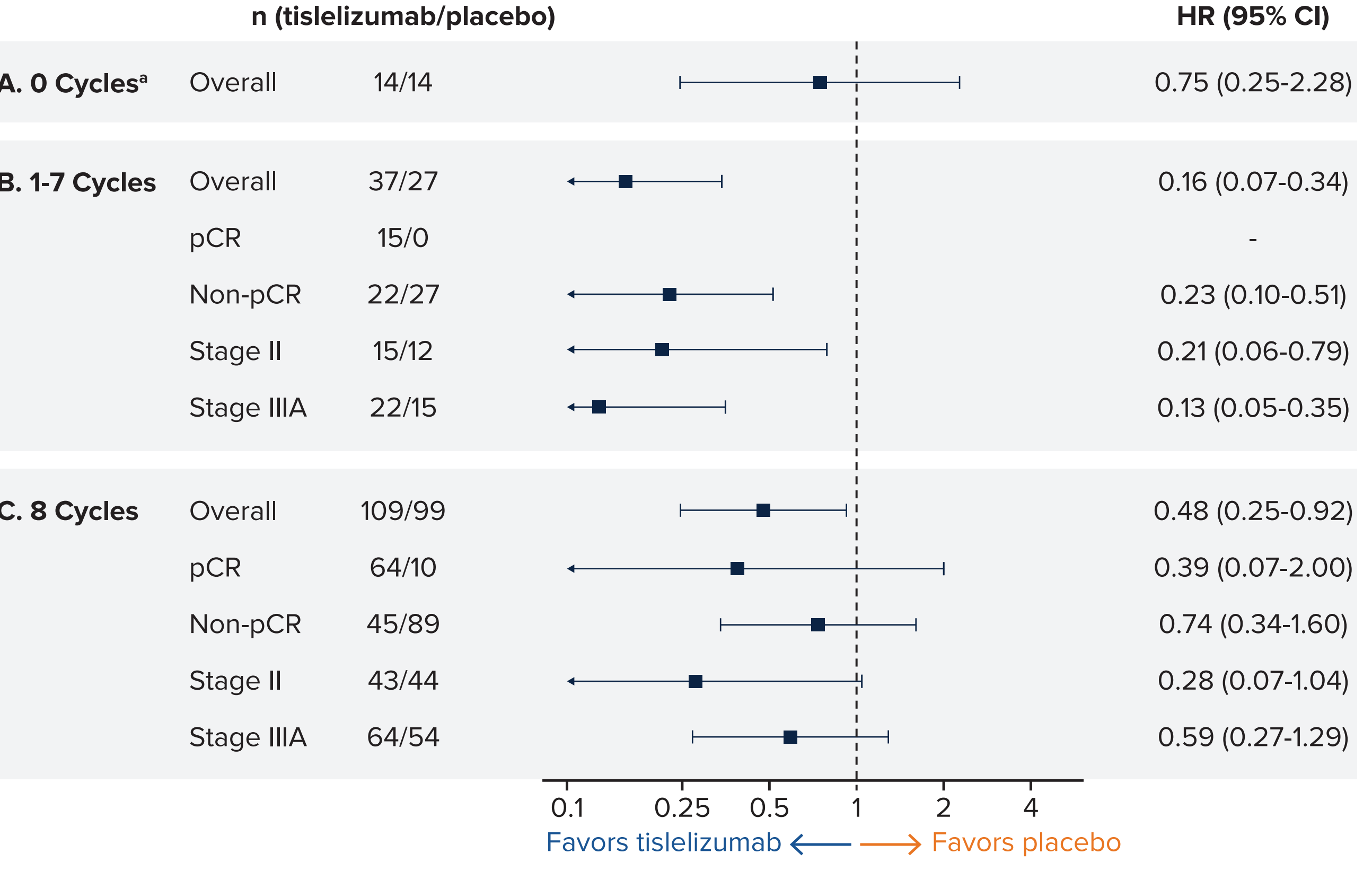


Figure 4. Forest Plot of Landmark EFS HR (Tislelizumab Versus Placebo) by Cycle Completion Subgroup



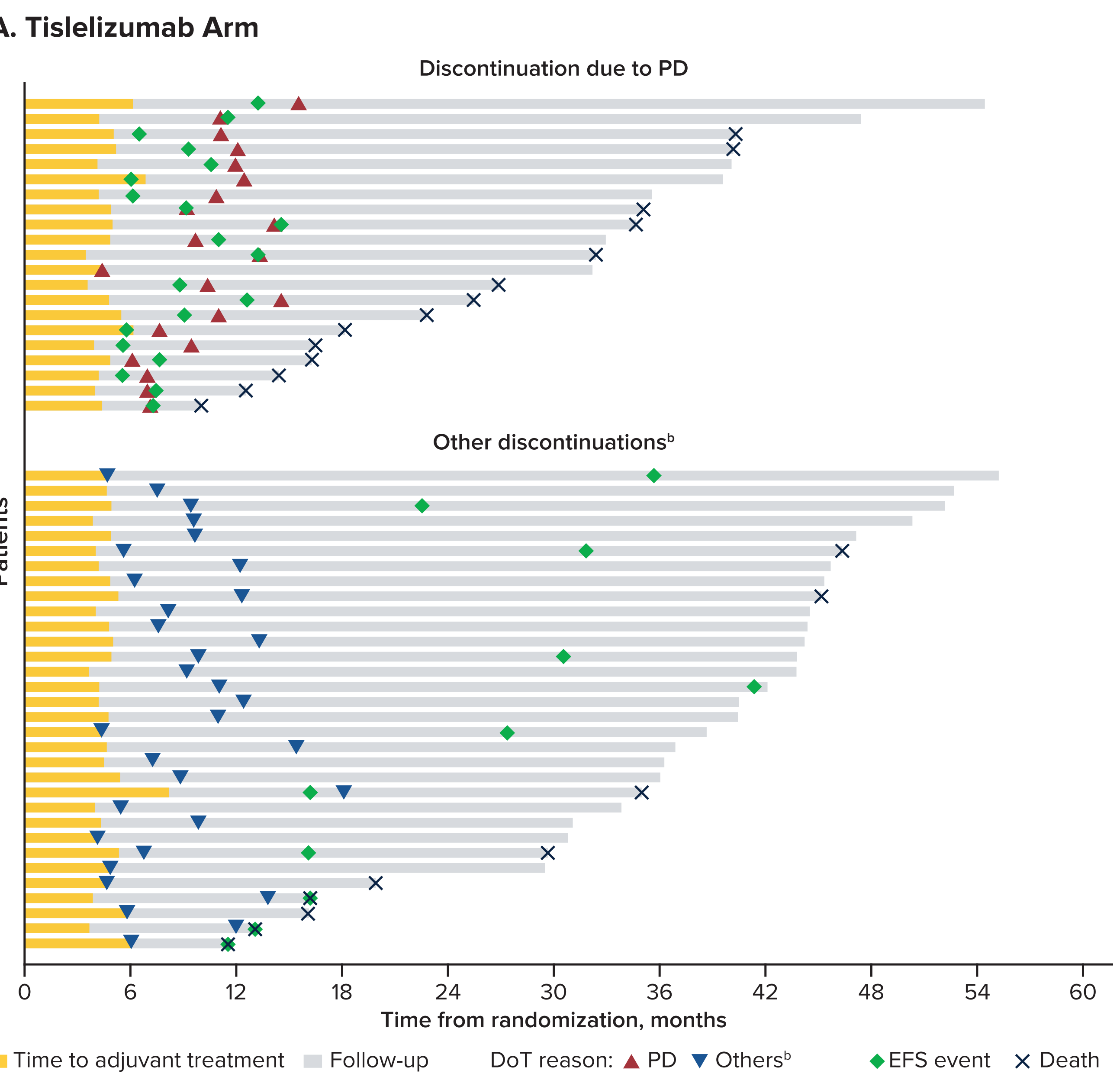
Treatment Discontinuation

- In the placebo arm, most patients who completed 1-7 adjuvant cycles discontinued study treatment due to progressive disease; while in the tislelizumab arm, more patients who completed 1-7 adjuvant cycles discontinued due to adverse events (AEs) (**Table 2** and **Figure 5**)

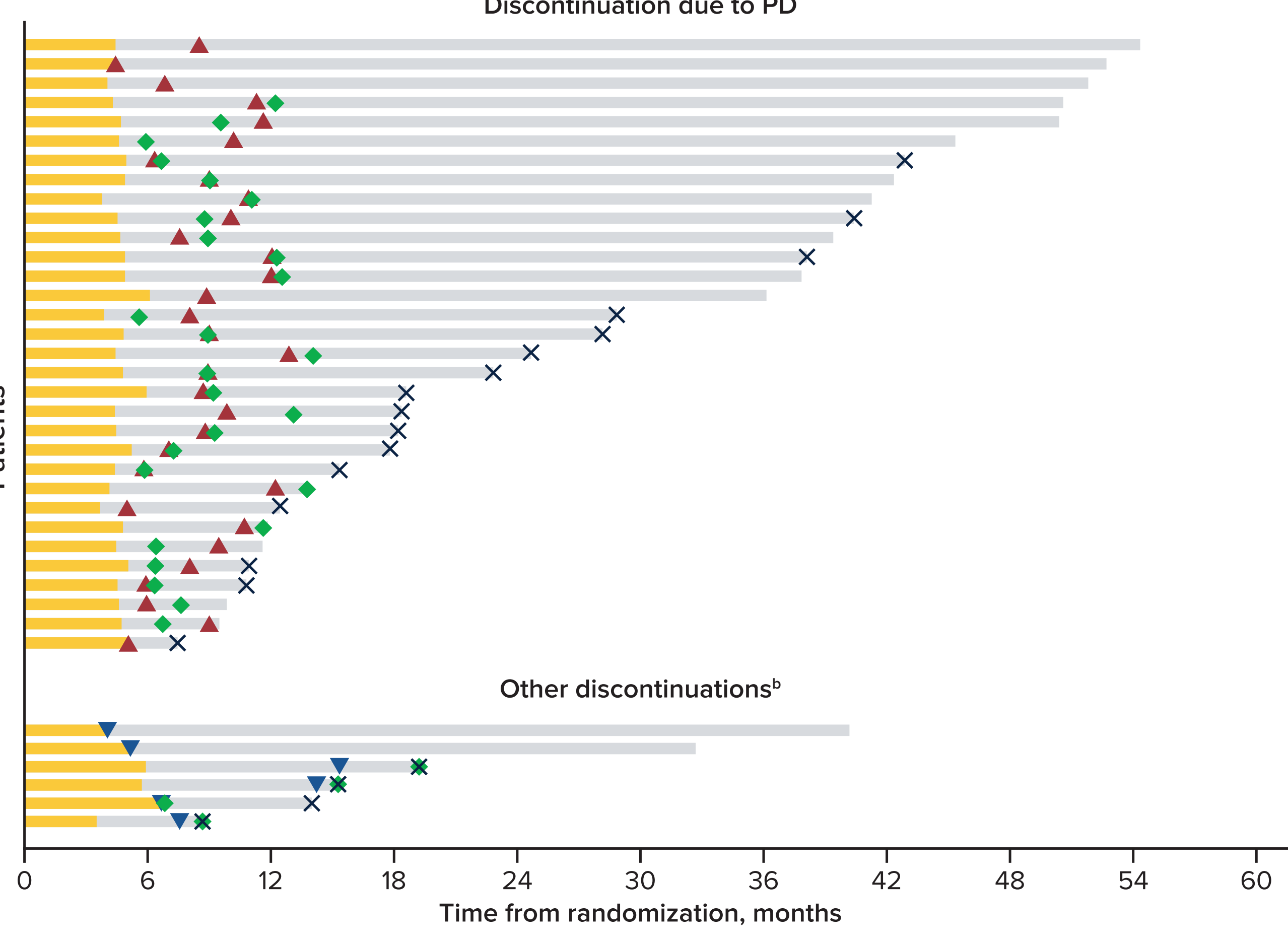
Table 2. Reasons for Discontinuation of Treatment

	0 cycles		1-7 cycles	
n (%)	Tislelizumab n=22	Placebo n=26	Tislelizumab n=53	Placebo n=38
PD	1 (4.5)	2 (7.7)	21 (39.6)	32 (84.2)
AE	7 (31.8)	4 (15.4)	15 (28.3)	4 (10.5)
Patient withdrawal	10 (45.5)	13 (50.0)	9 (17.0)	2 (5.3)
Physician decision	4 (18.2)	7 (26.9)	8 (15.1)	0 (0.0)

Figure 5. EFS Outcomes by Reasons for Treatment Discontinuation in Patients Receiving 1-7 Adjuvant Cycles



B. Placebo Arm



*Sorted by OS time within DoT reason. *Other reasons for discontinuation include AE, patient withdrawal, and physician decision.

Abbreviations: AE, adverse event; DoT, discontinuation of treatment; EFS, event-free survival; OS, overall survival; PD, progressive disease.

Safety

- The incidence of grade ≥ 3 , serious treatment-related treatment-emergent AEs (TRAEs), and TRAEs leading to treatment discontinuation were generally low across treatment cycle groups, but trended to be more frequent in patients receiving 1-7 cycles of adjuvant tislelizumab (**Table 3**)
- Patients receiving 0 adjuvant cycles did not experience any TRAEs during the adjuvant phase

Table 3. Summary of TRAEs From the Adjuvant Phase

	1-7 cycles		8 cycles	
n (%)	Tislelizumab n=53	Placebo n=38	Tislelizumab n=115	Placebo n=109
Any TRAE	23 (43.4)	9 (23.7)	53 (46.1)	35 (32.1)
Grade ≥ 3 TRAE	6 (11.3)	1 (2.6)	7 (6.1)	2 (1.8)
Serious TRAE	6 (11.3)	0 (0.0)	5 (4.3)	2 (1.8)
Leading to death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leading to discontinuation	9 (17.0)	2 (5.3)	0 (0.0)	0 (0.0)
Any imAE	15 (28.3)	0 (0.0)	20 (17.4)	12 (11.0)
Grade ≥ 3 imAE	7 (13.2)	0 (0.0)	2 (1.7)	1 (0.9)

Adverse events were graded for severity using CTCAE v5.0.
Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; imAE, immune-mediated adverse event; TRAE, treatment-related treatment-emergent adverse event.

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DISCLOSURES

EN: Advisory board: Amgen, Apollomics, AstraZeneca, BeOne Medicines, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Genmab, GSK, Janssen, Lilly, Merck Serono, Merck Sharp & Dohme, Pfizer, PharmaMar, Pierre Fabre, Qiagen, Regeneron, Roche, Sanofi, Takeda; Invited speaker: AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Daiichi Sankyo, Illumina, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, Qiagen, Roche, Sanofi, Takeda; Institutional research funding: Bristol Myers Squibb, Merck Serono, Roche; Advisory role: Pfizer, Roche, Transgene; Director of research and innovation: Catalan Institute of Oncology; Steering committee: Spanish Lung Cancer Group (GECIP).

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