

EP07.34: Real-World Pathologic Response and Overall Survival After Neoadjuvant Chemoimmunotherapy and Surgery in Stage III NSCLC

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INTRODUCTION

Resectable stage III non–small cell lung cancer (NSCLC) is a clinically heterogeneous disease in which durable cure requires effective control of both locoregional and occult systemic disease. Neoadjuvant therapy offers several potential advantages, including early treatment of micrometastatic disease, assessment of treatment sensitivity, and immune priming in the presence of an intact tumor and regional lymphatic architecture, while pathologic complete response (pCR) and major pathologic response (MPR) provide early measures of antitumor activity. The phase III CheckMate 816 trial established neoadjuvant nivolumab plus platinum-based chemotherapy as an effective strategy for resectable NSCLC, improving event-free survival (EFS), pCR, and subsequently overall survival (OS), while perioperative trials including KEYNOTE-671, AEGEAN, and CheckMate 77T further demonstrated improvements in EFS and pathologic response, with an OS benefit also reported for KEYNOTE-671. However, randomized trials enroll carefully selected patients under protocol-defined criteria and may not fully capture the heterogeneity of stage III NSCLC encountered in routine practice, particularly patients with more advanced nodal or T-stage disease. We therefore evaluated real-world clinicopathologic and survival outcomes among patients undergoing resection after neoadjuvant chemoimmunotherapy, focusing on pretreatment clinical stage III NSCLC and assessing pathologic response, stage change, margin status, OS, and exploratory source-recorded disease-free survival.

METHODS

Study design and population

We conducted a retrospective, two-center cohort study of patients with EGFR- and ALK-negative non–small cell lung cancer (NSCLC) treated at The Ohio State University and National Cheng Kung University. Eligible patients received neoadjuvant platinum-doublet chemotherapy plus PD-1 or PD-L1 blockade followed by surgical resection. Pretreatment clinical stage was assigned according to the eighth edition of the American Joint Committee on Cancer staging system. The primary analytic population comprised patients with stage IIIA–IIIC disease; patients with stage ≤IIB were retained as a contextual comparator to preserve the structure of the supplied dataset and draft abstract.

Outcomes and definitions

Pathologic complete response (pCR) was defined in the source draft as 0% residual viable tumor, and major pathologic response (MPR) as ≤10% residual viable tumor. Response results were summarized using endpoint-specific evaluable denominators because pathology data were incomplete. Overall survival (OS) was measured from diagnosis to death from any cause; patients alive at last follow-up were censored on that date. The higher-precision source OS column was used for time-to-event analysis, while the two-decimal OS(Diagnosis) field was retained as a quality-control cross-check. Exploratory disease-free survival (DFS) used the source-recorded DFS duration because its time origin was not documented; the event was the first recorded recurrence or death from any cause. Event-free survival (EFS) was not estimated.

Statistical analysis

Continuous variables were summarized as medians and interquartile ranges and categorical variables as n/N (%). The age interquartile range used the type 6 quantile definition to reproduce the source draft. Missing data were not imputed. Pathologic response proportions were compared across pretreatment clinical-stage groups with the Fisher–Freeman–Halton exact test. OS and exploratory DFS were estimated using the Kaplan–Meier method with Greenwood log–log 95% confidence intervals; survival distributions were compared with global log-rank tests. All tests were two-sided and exploratory. Analyses used R version 4.5.0 and the survival package version 3.8.3.

DISCUSSION AND CONCLUSION

- In this real-world cohort of patients with surgically resectable NSCLC, neoadjuvant chemoimmunotherapy provided substantial pathologic regression, with a provisional pCR rate of 36.4% and an MPR rate of 64.0%, together with a 4-year disease-free survival and overall survival of 51.4% and 77.9%, respectively.
- Patients with stage IIIC disease had numerically shorter disease-free survival and significantly shorter overall survival compared to the other three groups.

Future Direction for Research

- Multicenter cohorts with standardized treatment regimens, surgical assessment will be warranted to determine the real-world effectiveness of neoadjuvant chemoimmunotherapy across the full spectrum of stage III NSCLC, particularly for patients with stage IIIB and selected IIIC disease, for whom the optimal criteria for surgery remain uncertain.
- Future research should also integrate pathologic response with circulating tumor DNA-based molecular residual disease, radiomics, and tumor/immune biomarkers.

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The author use ChatGPT for English editing.

RESULTS

Cohort characteristics

The cohort included 73 patients, including 18 (24.7%) with stage ≤IIB, 40 (54.8%) with stage IIIA, 12 (16.4%) with stage IIIB, and 3 (4.1%) with stage IIIC disease. Median age was 64.0 years (IQR, 58.0–70.3; n=72), and 22 patients (30.1%) were female. Histology was adenocarcinoma in 34 patients (46.6%), squamous cell carcinoma in 24 (32.9%), and other in 15 (20.5%). PD-L1 status was positive in 36 (49.3%), negative in 16 (21.9%), and unknown in 21 (28.8%) (Table 1).

Pathologic response and surgical outcomes

Within the stage III cohort, provisional pCR was observed in 20 of 55 patients (36.4%) and MPR in 32 of 50 evaluable patients (64.0%). In the source-aligned all-stage analysis, provisional pCR was 28/70 (40.0%) and MPR was 44/65 (67.7%). Stage-specific pCR rates were 53.3%, 40.0%, 25.0%, and 33.3% for stage ≤IIB, IIIA, IIIB, and IIIC, respectively (p=0.515); corresponding MPR rates were 80.0%, 62.9%, 58.3%, and 100% (p=0.422). R0 resection was recorded for 70 of 72 evaluable patients (97.2%), and downstaging for 50 of 72 (69.4%) (Figure 1).

Disease-free survival and Overall survival

The median follow-up of 30.6 months (95% CI, 25.0–36.4). All 73 patients were evaluable, and 22 recurrence-or-death events occurred. The 2-, 3-, and 4-year exploratory DFS estimates were 66.2% (52.0–77.1), 66.2% (52.0–77.1), and 51.1% (28.9–69.5), respectively. Patients with stage IIIC disease had numerically shorter PFS compared to the patients in the other three groups (p=0.056; Figure 2). The 2-, 3-, and 4-year OS estimates were 92.3% (80.7–97.0), 92.3% (80.7–97.0), and 77.9% (50.8–91.2), respectively. Across all four stage groups, 4-year OS ranged from 0% in IIIC to 92.2% in IIIA. Patients with stage IIIC disease had significantly shorter PFS compared to the patients in the other three groups (p=0.002; Figure 3).

Table 1. Baseline and Treatment Characteristics by Pretreatment Clinical Stage

Characteristic	Overall	≤IIB	IIIA	IIIB	IIIC
Patients	73	18	40	12	3
Age, years	64.0 (58.0–70.3)	66.7 (56.6–77.9)	63.9 (56.5–70.4)	64.4 (58.4–68.7)	60.7 (58.5–70.0)
Female sex	22/73 (30.1%)	2/18 (11.1%)	16/40 (40.0%)	3/12 (25.0%)	1/3 (33.3%)
Adenocarcinoma	34/73 (46.6%)	4/18 (22.2%)	22/40 (55.0%)	7/12 (58.3%)	1/3 (33.3%)
Squamous cell carcinoma	24/73 (32.9%)	10/18 (55.6%)	10/40 (25.0%)	3/12 (25.0%)	1/3 (33.3%)
Other histology	15/73 (20.5%)	4/18 (22.2%)	8/40 (20.0%)	2/12 (16.7%)	1/3 (33.3%)
PD-L1 positive	36/73 (49.3%)	11/18 (61.1%)	22/40 (55.0%)	2/12 (16.7%)	1/3 (33.3%)
PD-L1 negative	16/73 (21.9%)	4/18 (22.2%)	11/40 (27.5%)	1/12 (8.3%)	0/3 (0.0%)
PD-L1 unknown	21/73 (28.8%)	3/18 (16.7%)	7/40 (17.5%)	9/12 (75.0%)	2/3 (66.7%)
Three neoadjuvant cycles	47/73 (64.4%)	15/18 (83.3%)	28/40 (70.0%)	3/12 (25.0%)	1/3 (33.3%)
Four neoadjuvant cycles	17/73 (23.3%)	1/18 (5.6%)	8/40 (20.0%)	7/12 (58.3%)	1/3 (33.3%)
Positive resection margin	2/72 (2.8%)	0/18 (0.0%)	2/39 (5.1%)	0/12 (0.0%)	0/3 (0.0%)
Adjuvant treatment	19/73 (26.0%)	4/18 (22.2%)	8/40 (20.0%)	6/12 (50.0%)	1/3 (33.3%)

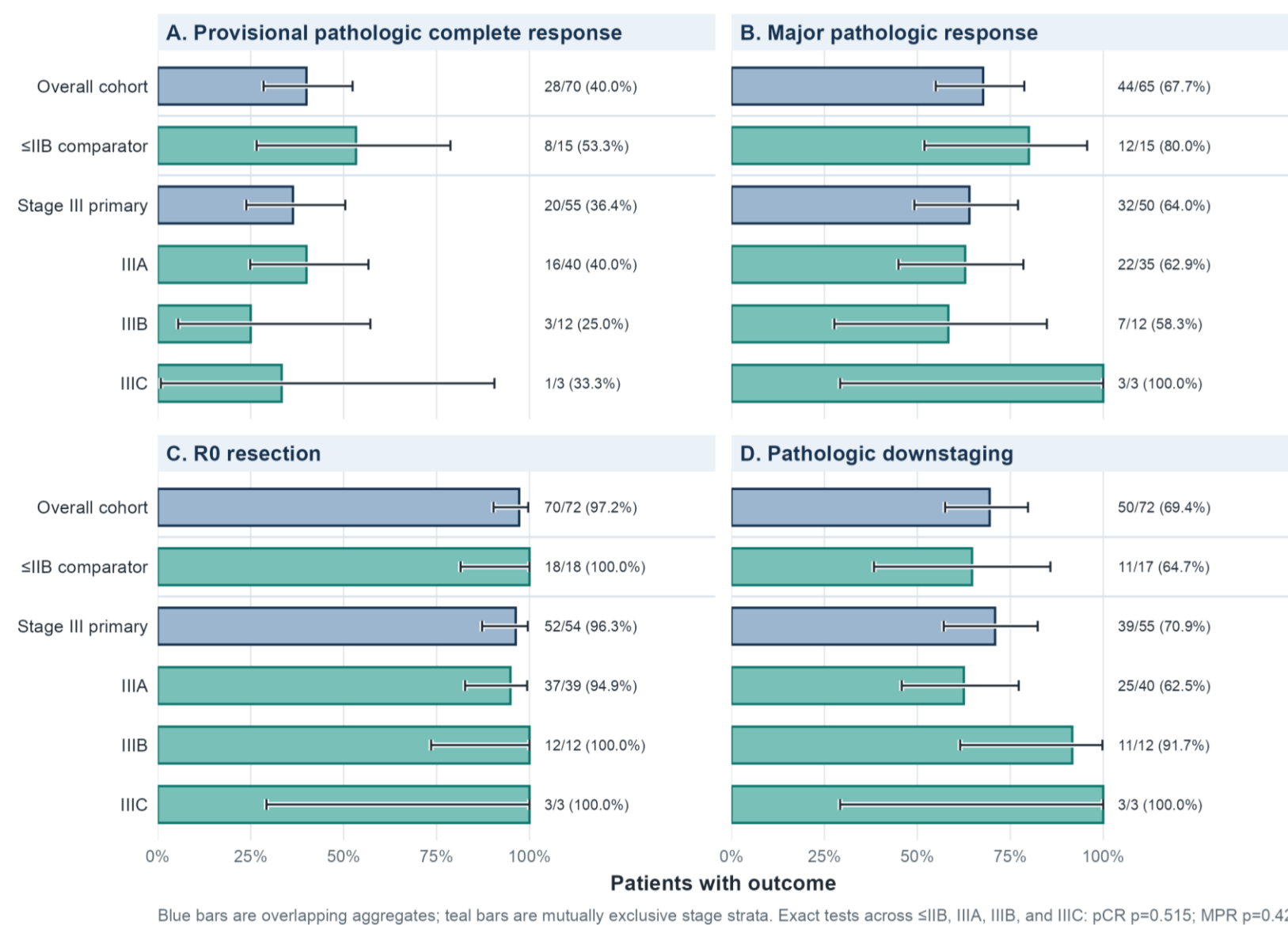


Figure 1. Pathologic response and surgical outcomes by pretreatment clinical stage

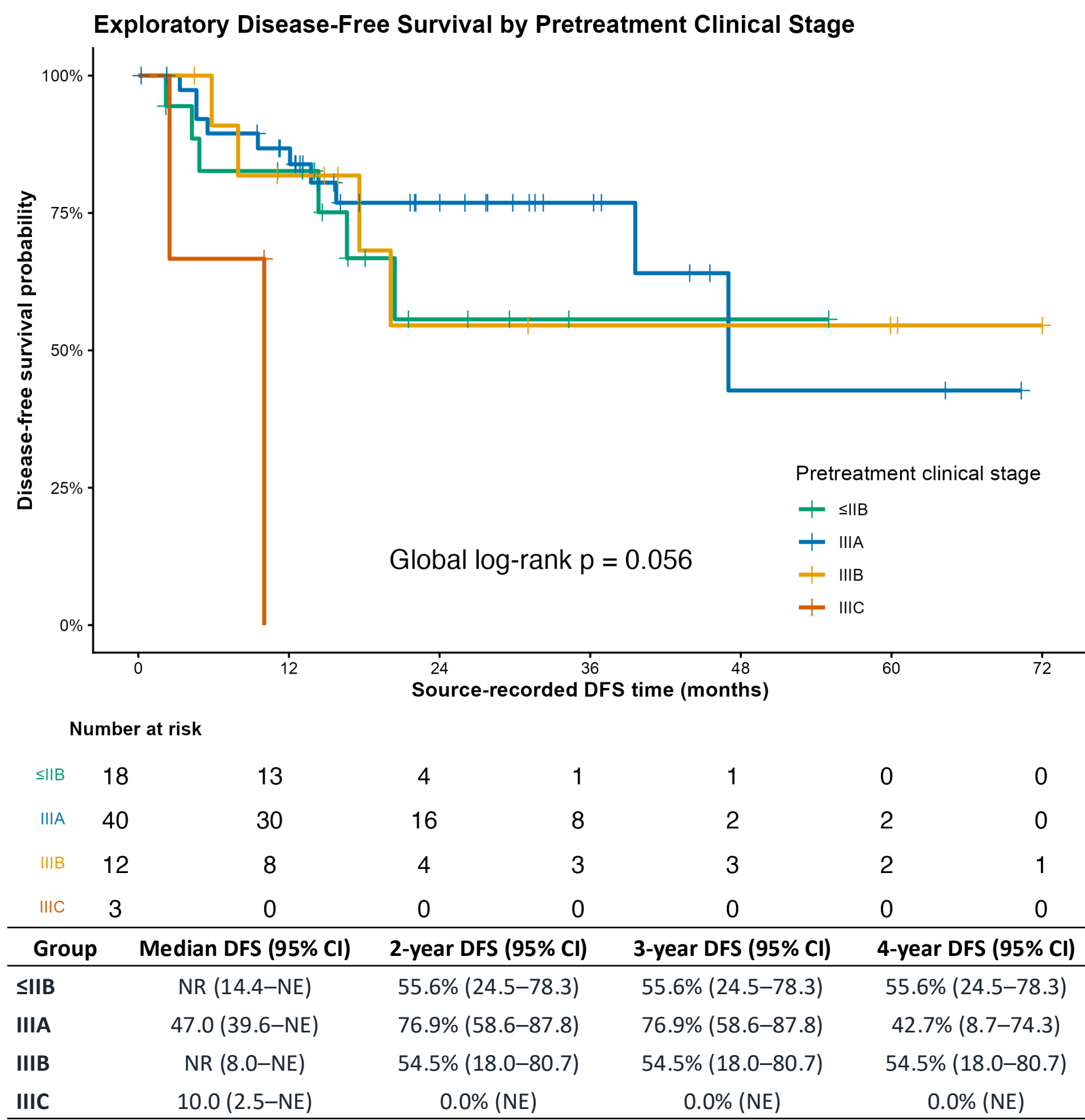


Figure 2. Kaplan–Meier estimates of disease-free survival by pretreatment clinical stage

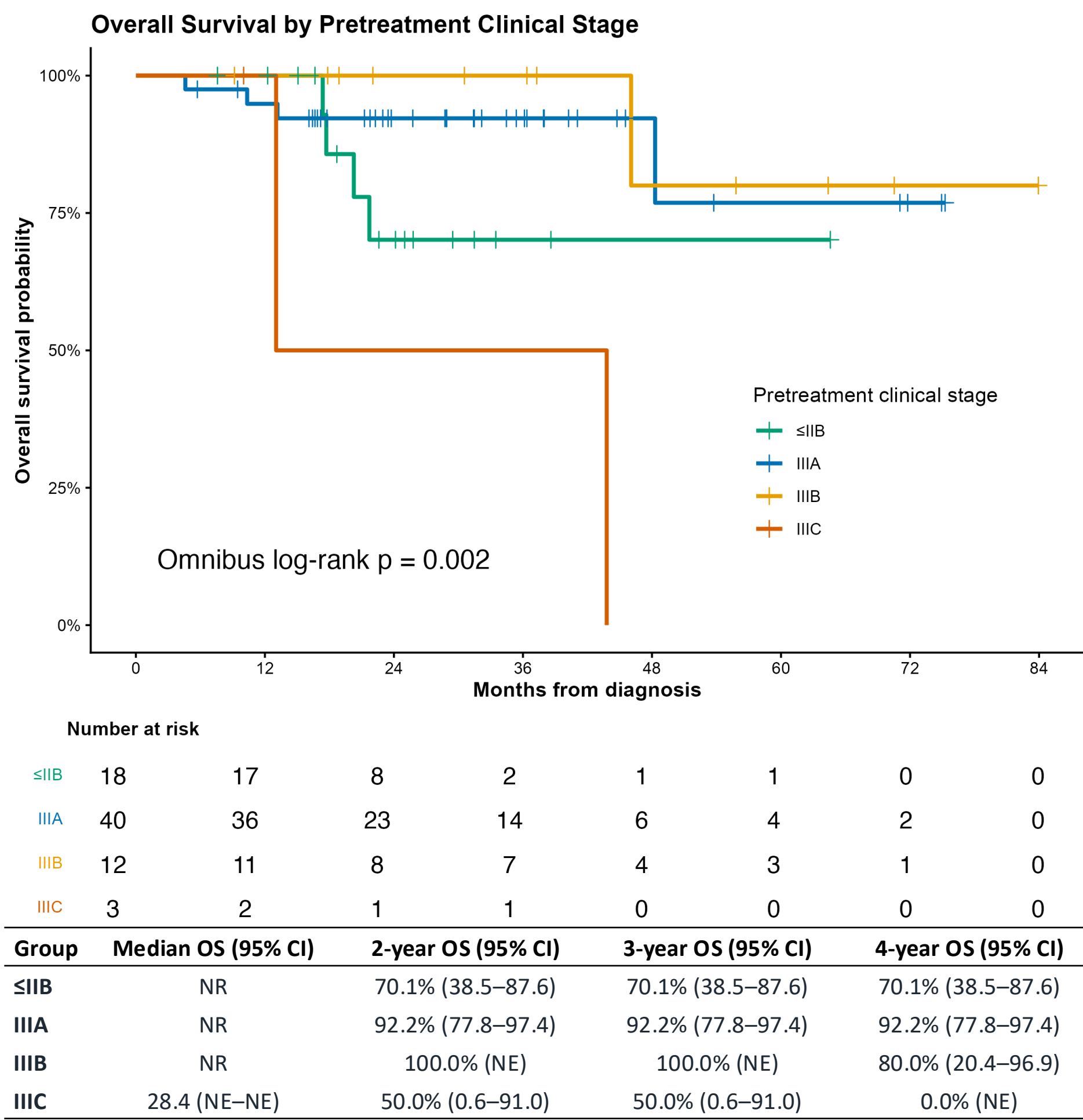


Figure 3. Kaplan–Meier estimates of overall survival by pretreatment clinical stage