

BACKGROUND:

Neoadjuvant chemoimmunotherapy has significantly improved pathologic response rates in patients with resectable stage II–III non-small cell lung cancer (NSCLC). However, discordance between primary tumor response and residual nodal disease is increasingly recognized, and the combined prognostic relevance of pathologic response and persistent nodal disease remains incompletely defined.

RESULTS:

The pCR rate was 27.8% (25/90) and the MPR rate was 28.9% (26/90), yielding an overall pathologic response rate of 56.7%. DFS declined significantly with increasing postoperative nodal burden according to the UICC/AJCC 8th edition (global log-rank $p = 0.001$) and was further refined by the 9th edition ($p < 0.001$). Median DFS was not reached for ypN0, compared with 64.8 months for ypN1, 24.4 months for ypN2a, and 9.9 months for ypN2b. Residual mediastinal nodal disease remained independently associated with inferior DFS after adjustment for pathologic response (HR 3.33, 95% CI 1.21–9.11; $p = 0.019$). Integrated tumor–nodal stratification identified low- ($n = 43$), intermediate- ($n = 14$), and high-risk ($n = 33$) groups with significantly different DFS (global log-rank $p = 0.015$); each increase in risk category was associated with a higher recurrence hazard (HR 2.14, 95% CI 1.23–3.71; $p = 0.007$).

METHODS:

In this retrospective single-center study, 90 consecutive patients with clinically node-positive (cN1–2), resectable stage II–III NSCLC treated with neoadjuvant chemoimmunotherapy followed by curative-intent surgery were analyzed. Disease-free survival (DFS) was analyzed according to postoperative nodal status (ypN) using the UICC/AJCC 8th and 9th editions. Pathologic response was classified as pathologic complete response (pCR), major pathologic response (MPR), or no objective response. DFS was evaluated according to integrated risk groups combining pathologic response and postoperative nodal status: low risk (pCR/MPR and ypN0), intermediate risk (pCR/MPR with ypN1 or no response with ypN0), and high risk (ypN2 irrespective of response or no response with ypN1).

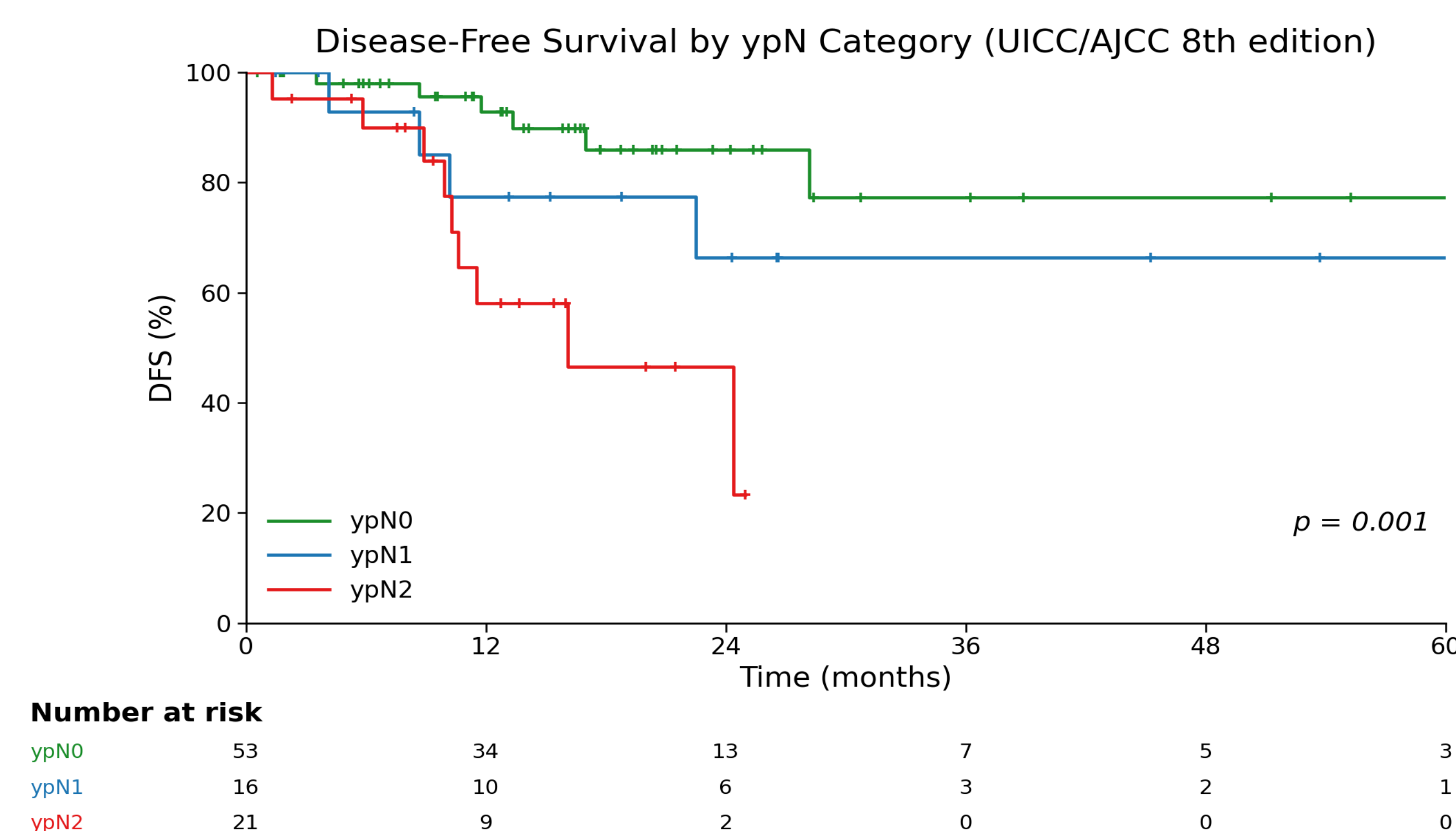


Figure 1. DFS by ypN status according to the 8th staging edition

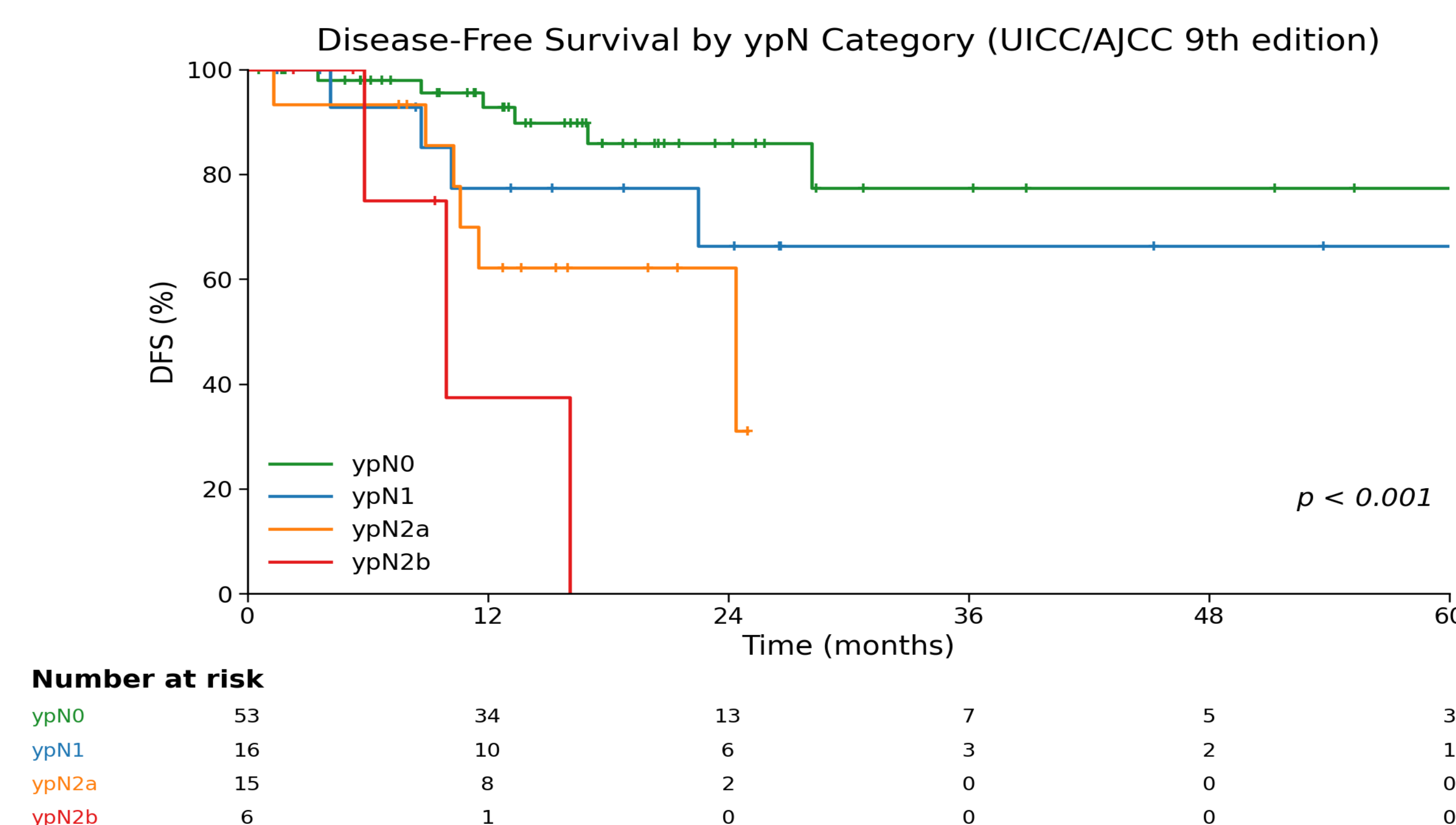


Figure 2. DFS by ypN status according to the 9th staging edition

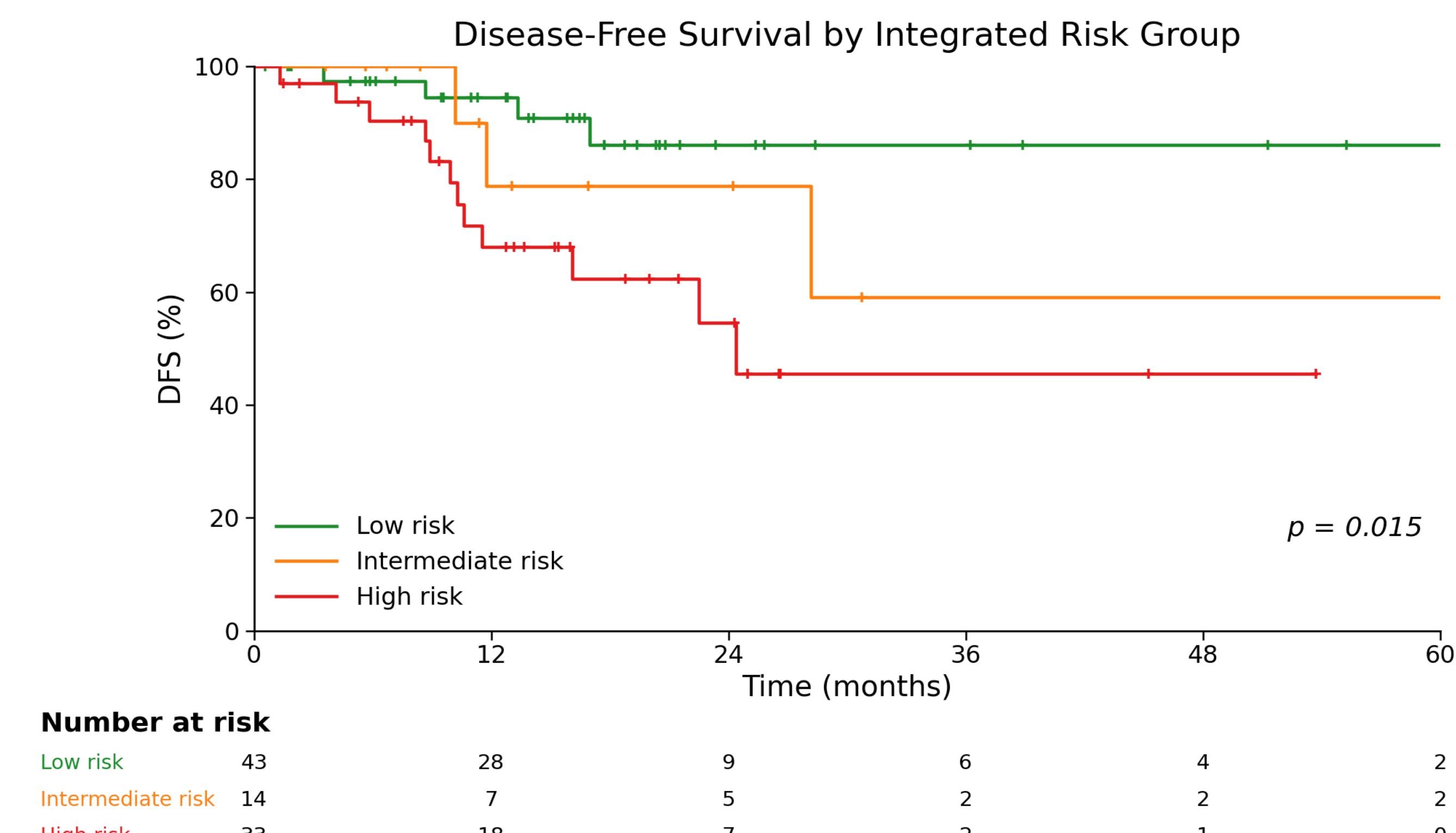


Figure 3. DFS according to integrated tumor–nodal risk stratification

Postoperative nodal status	pCR	MPR	No objective response	Total
ypN0	Low ($n = 25$)	Low ($n = 18$)	Intermediate ($n = 10$)	53
ypN1	Intermediate ($n = 0$)	Intermediate ($n = 4$)	High ($n = 12$)	16
ypN2	High ($n = 0$)	High ($n = 4$)	High ($n = 17$)	21
Total	25	26	39	90

Table 1. Integrated risk stratification combining pathologic response and residual nodal disease

CONCLUSION:

Integrated tumor–nodal assessment enables clinically meaningful risk stratification after neoadjuvant chemoimmunotherapy for resectable NSCLC. Persistent mediastinal nodal disease identifies a high-risk subgroup despite primary tumor response while patients achieving both pathologic response and nodal clearance have the most favorable DFS.