

P1.199. Persistent N2 After Neoadjuvant Chemoimmunotherapy in Non–Small Cell Lung Cancer: Insights from Three Prospective Cohorts

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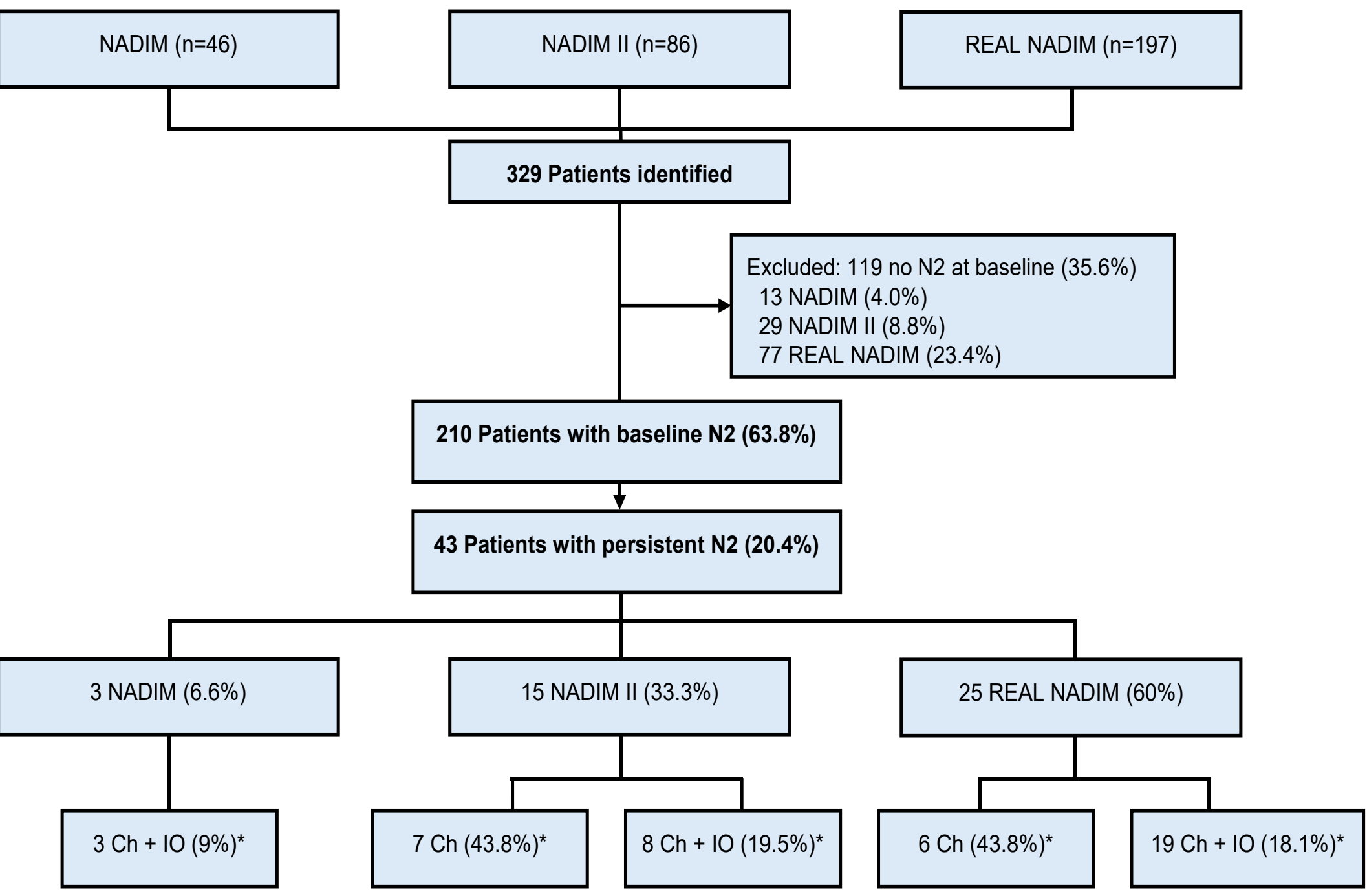
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INTRODUCTION

- Stage III non-small cell lung cancer (NSCLC) with involvement of ipsilateral mediastinal lymph nodes (N2) is a heterogeneous and biologically aggressive disease with poor outcomes.¹
- Around 52% of patients have persistent N2 disease after induction therapy, correlated to lower survival rates compared to nodal downstaging.²
- Neoadjuvant chemoimmunotherapy (Ch + IO) has significantly improved outcomes in resectable NSCLC³, but the prognostic impact of persistent N2 after Ch + IO remains unclear.
- We evaluated the prognostic significance of persistent N2 disease following neoadjuvant Ch + IO in our prospective studies.

METHODS

- Retrospective analysis of NADIM, NADIM II and REAL NADIM cohorts.
- Patients with stage IIIA-N2 NSCLC who underwent surgery after neoadjuvant therapy.
- Persistent N2 defined as viable tumor cells in mediastinal lymph nodes on pathological examination.
- Clinical, surgical, radiological, molecular, and survival outcomes were analyzed.

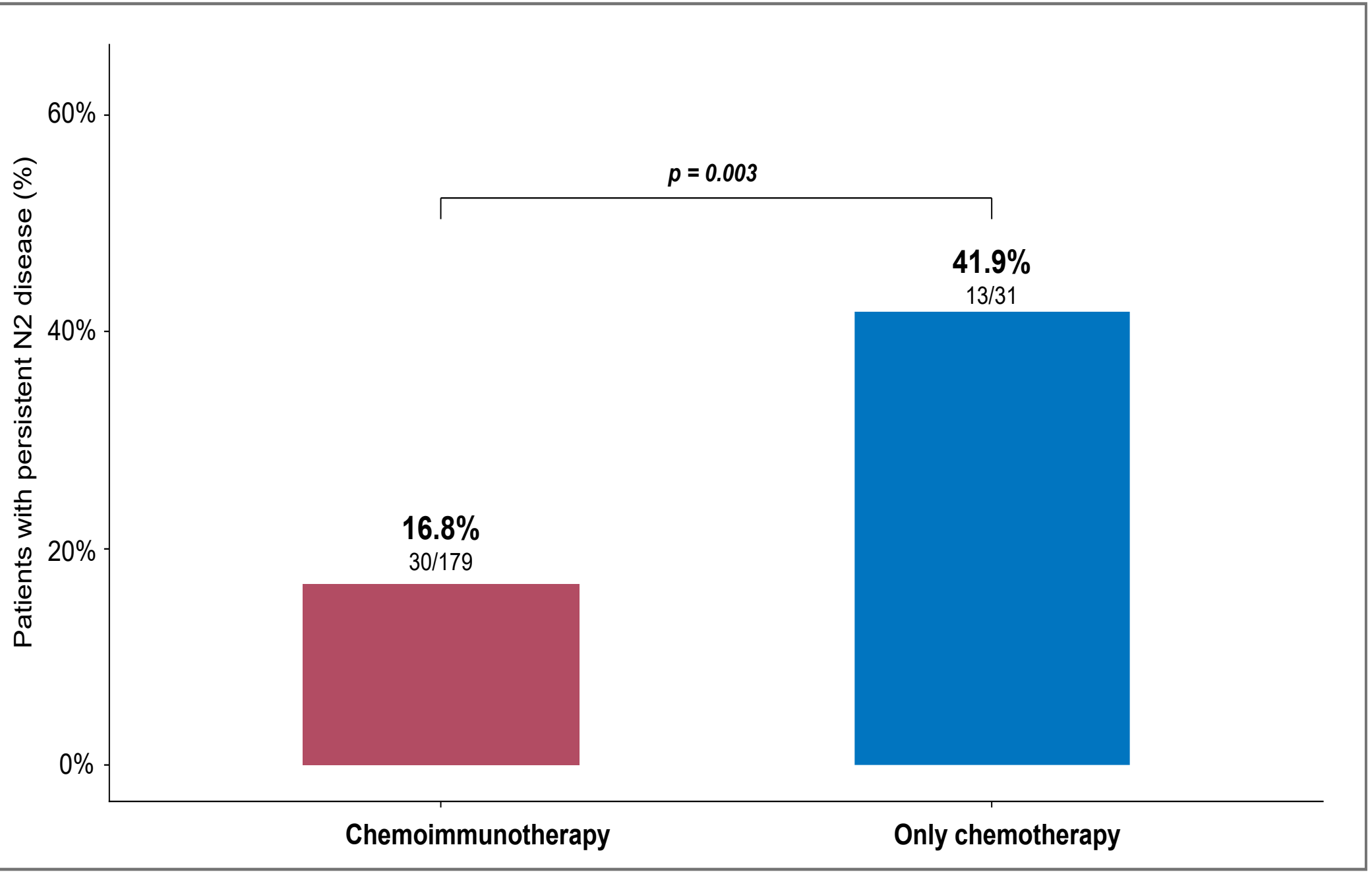


* % of patients with persistent N2 among those with baseline N2, by treatment group.

Figure 1. CONSORT-style flow diagram of patient distribution and treatment in the analysis from NADIM studies. Abbreviations: Ch: chemotherapy; IO: immunotherapy.

RESULTS

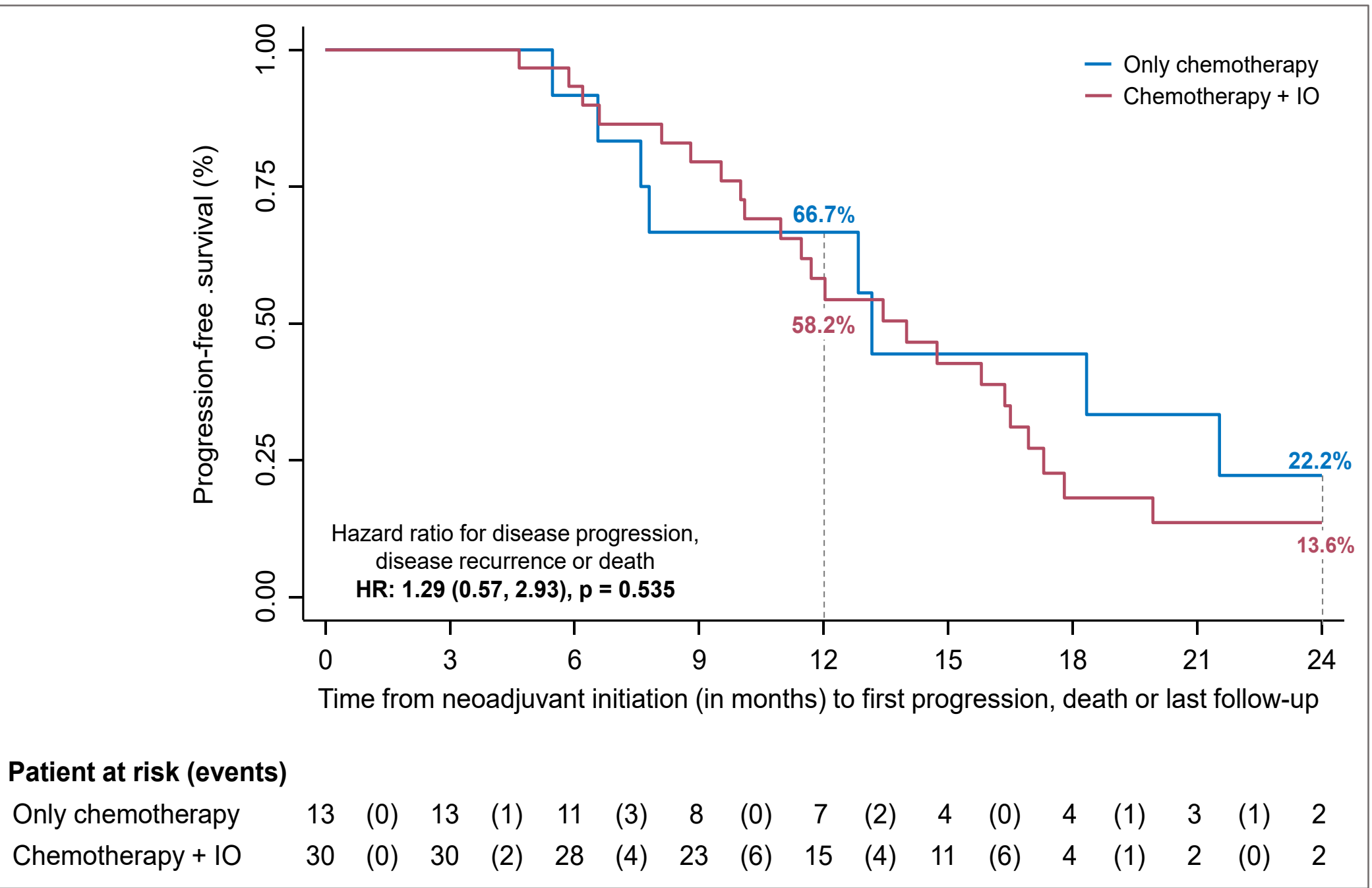
INCIDENCE OF PERSISTENT N2 DISEASE



- Persistent N2 disease on final pathological evaluation was observed in 43 out of 210 patients (20.4%) (Figure 2).
- Persistent N2 disease was less frequent after Ch + IO than after Ch alone (16.8% vs 41.9%).
- Among patients with persistent N2 disease who received Ch + IO (n=30), 25 (83.3%) underwent lobectomy with R0 resection achieved in 80% of cases.

Figure 2. Incidence of persistent N2 disease according to treatment.

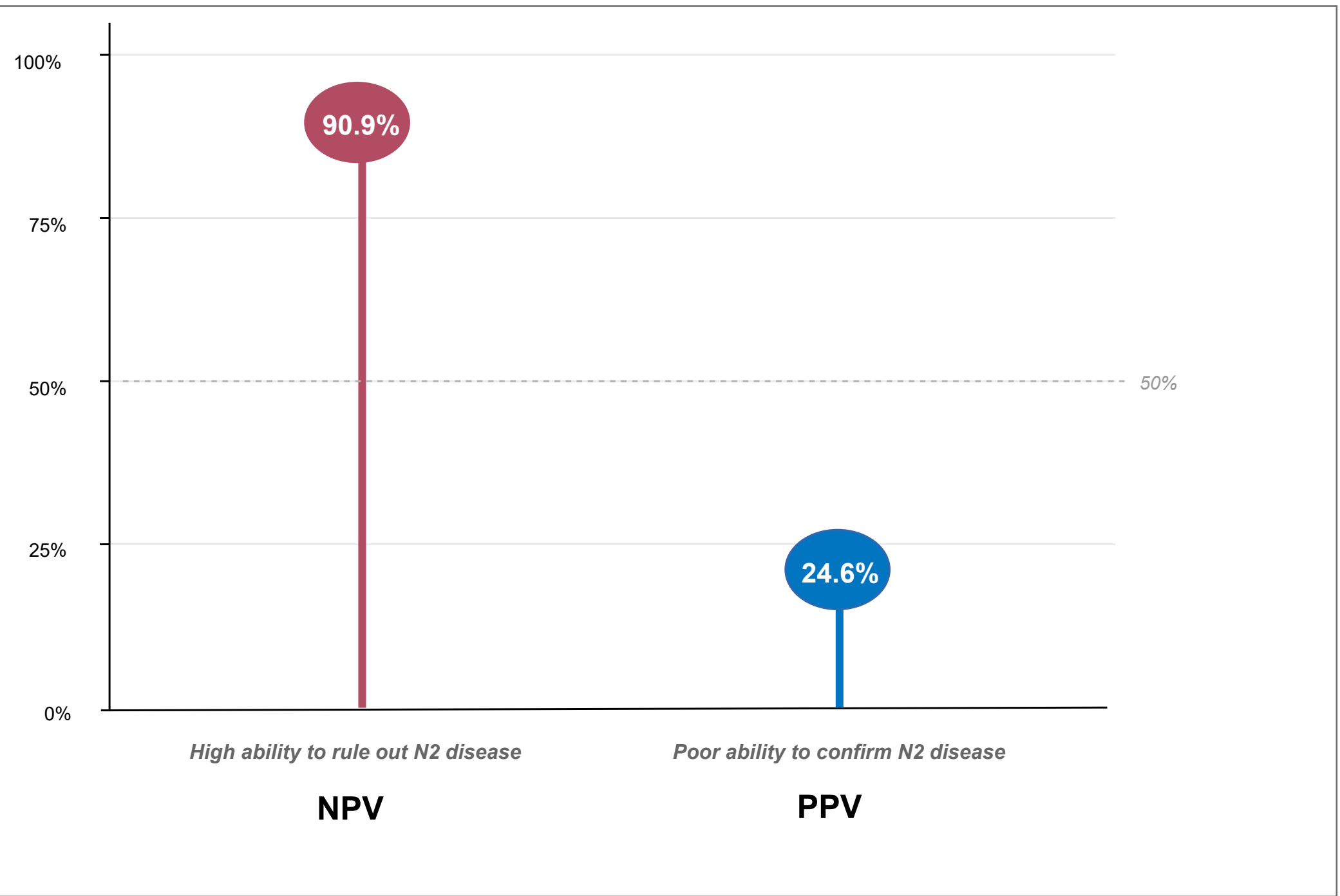
PROGRESSION FREE SURVIVAL (PFS)



- In patients with persistent N2, no significant differences in PFS were observed between the Ch + IO and Ch arms.
- Median PFS was 14.0 months (95% CI, 10.0-17.3) in Ch + IO and 13.2 months (95% CI, 7.6-21.5) in Ch alone (Figure 3).

Figure 3. Progression-free survival among patients with persistent pathological N2 disease according to treatment. Abbreviation: IO: immunotherapy

PREDICTIVE ACCURACY OF PET-CT AND PROGNOSTIC VALUE OF ctDNA



- Post-induction Positron Emission Tomography–Computed Tomography (PET-CT) demonstrated limited ability to identify persistent N2 disease with a positive predictive value (PPV) of 24.6% and a negative predictive value (NPV) of 90.9% (Figure 4). The high NPV indicates a low false-negative rate, while the low PPV suggests potential overestimation of persistent nodal disease.
- No significant differences in circulating tumor (ctDNA) levels or genomic alterations were observed after neoadjuvant chemoimmunotherapy.

Figure 4 Predictive performance of post-induction PET-CT for persistent N2 disease.

DISCUSSION & CONCLUSION

- To our knowledge, this is the first study evaluating persistent N2 disease after neoadjuvant Ch + IO.
- Despite advances in neoadjuvant Ch + IO and high rates of R0 resection, persistent N2 disease is associated with worse outcomes.
- Post-induction PET-CT alone is insufficient to identify persistent N2 disease given its limited accuracy.
- Improved biomarkers are needed to better identify these patients and define optimal management.



TAKE HOME MESSAGE

Persistent N2 disease remains a biological red flag despite modern neoadjuvant chemoimmunotherapy and requires multidisciplinary, multimodal evaluation for optimal management.

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