



# P2.321 - Perioperative Immunotherapy with Response-Integrated MRD-Guided Execution in Stage II-III NSCLC: The PRIME-MRD Study

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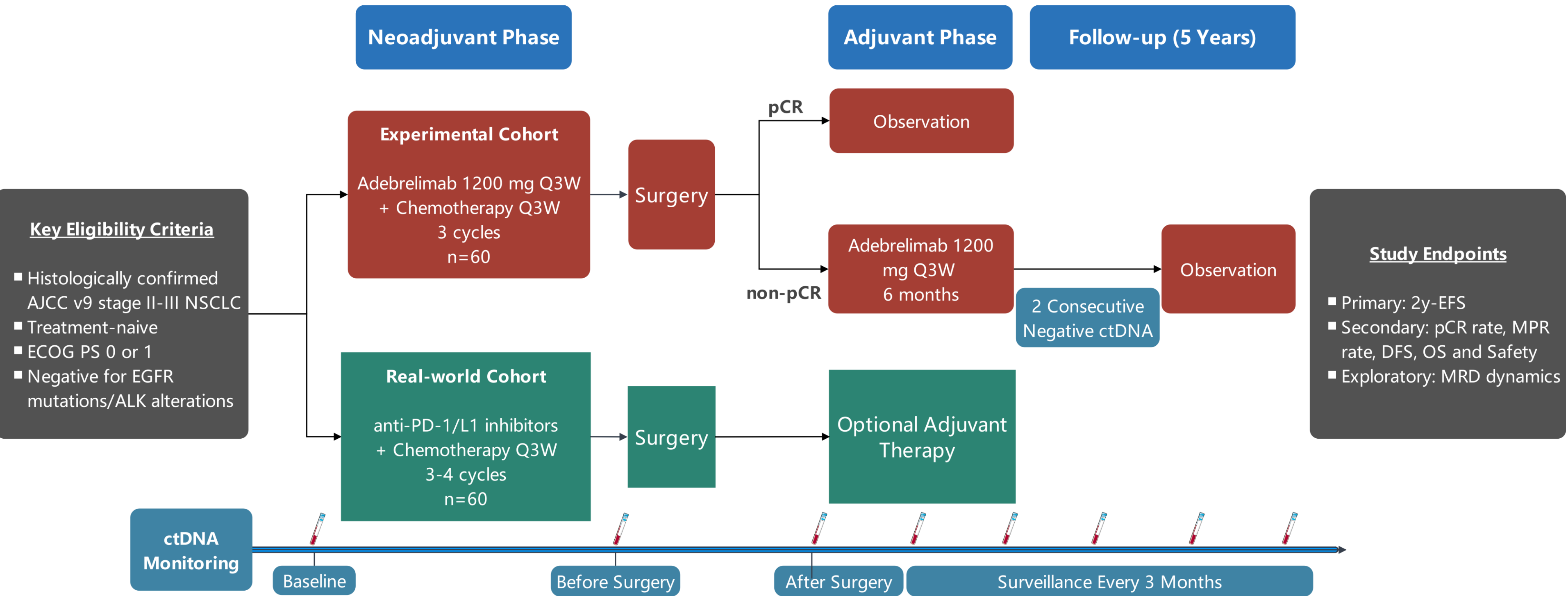
## INTRODUCTION

- Perioperative Immunotherapy Is Now a Standard of Care:** Multiple phase III trials KEYNOTE-671 (pembrolizumab), AEGEAN (durvalumab), CheckMate 77T (nivolumab), RATIONALE-315 (tislelizumab), and the phase III adabrelimab trial (SHR-1316-III-303), have established perioperative chemoimmunotherapy as a standard for resectable stage II–III NSCLC.
- Optimal Adjuvant Duration Remains Unclear:** Current perioperative regimens typically prescribe 1 year of adjuvant immunotherapy, yet real world completion rates are suboptimal (~65% in IMpower010 and ~52% in KEYNOTE 091). Prolonged exposure also increases financial toxicity and immune related adverse events.
- pCR Is Prognostic but Insufficient:** pCR strongly correlates with long term survival. However, outcomes among non-pCR patients remain highly heterogeneous, and pCR alone does not fully capture individual relapse risk.
- MRD Refines Prognostication Beyond pCR:** Recent evidence shows that postoperative MRD positivity identifies patients at heightened recurrence risk, independent of pCR status.
- The critical clinical question: Whether to give adjuvant therapy and How Long**—we aim to evaluate the efficacy and safety of neoadjuvant chemoimmunotherapy followed by a response-adaptive adjuvant strategy based on the integration of pathological response and dynamic MRD monitoring, which may provide the answer by enabling individualised treatment de escalation or continuation.

## METHODS

- The PRIME-MRD study is a prospective, multicenter phase II single-arm study (ChiCTR2600118144).

### Study Design:



- The sample size was calculated based on the 2-year EFS rate, targeting a total of 120 patients across all cohorts.
- pCR is defined as the absence of residual viable tumor cells in both the primary tumor bed and all resected lymph nodes.
- Peripheral blood MRD monitoring will be evaluated through tumor-naïve ctDNA assays.
- Recruitment was activated in November 2025.

### Study Outcomes

- The primary endpoint is the 2-year event-free survival (EFS) rate.
- Secondary endpoints include pCR rate, MPR rate, disease-free survival (DFS), overall survival (OS) and safety, while exploratory endpoints will evaluate the correlation between MRD dynamics and treatment outcomes.

## Eligibility Criteria

### Key Inclusion Criteria

- Male or female aged  $\geq 18$  and  $\leq 80$  years;
- ECOG performance status of 0–1;
- Histologically confirmed NSCLC negative for EGFR/ALK alterations;
- Clinical stage II–III disease according to the 9th edition TNM classification;
- Completed 2–3 cycles of preoperative chemotherapy plus immunotherapy, undergone complete resection of the primary lesion with lymph node dissection per IASLC standards, and undergone pathological assessment for pCR;
- Collected peripheral blood samples at each timepoints required to assess ctDNA status;

### Key Exclusion Criteria

- Active hepatitis B;
- Known HIV antibody-positive status, or presence of other acquired or congenital immunodeficiency diseases, or history of organ transplantation;
- Clinically significant active infection, including active tuberculosis;
- Diagnosis of another malignancy within the past 5 years;
- Surgical specimens confirmed to have histological components of mixed small cell, neuroendocrine tumor, sarcomatoid carcinoma, or large cell carcinoma; exclusion required;
- Patients deemed unsuitable for enrollment by the investigators.

## KEY REFERENCES & ACKNOWLEDGEMENTS

### Key References

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