

P2.385: ATHENEA, a Phase II study of Atezolizumab as Neoadjuvant, Adjuvant and Maintenance treatment for stage IIIA-IIIB NSCLC patients

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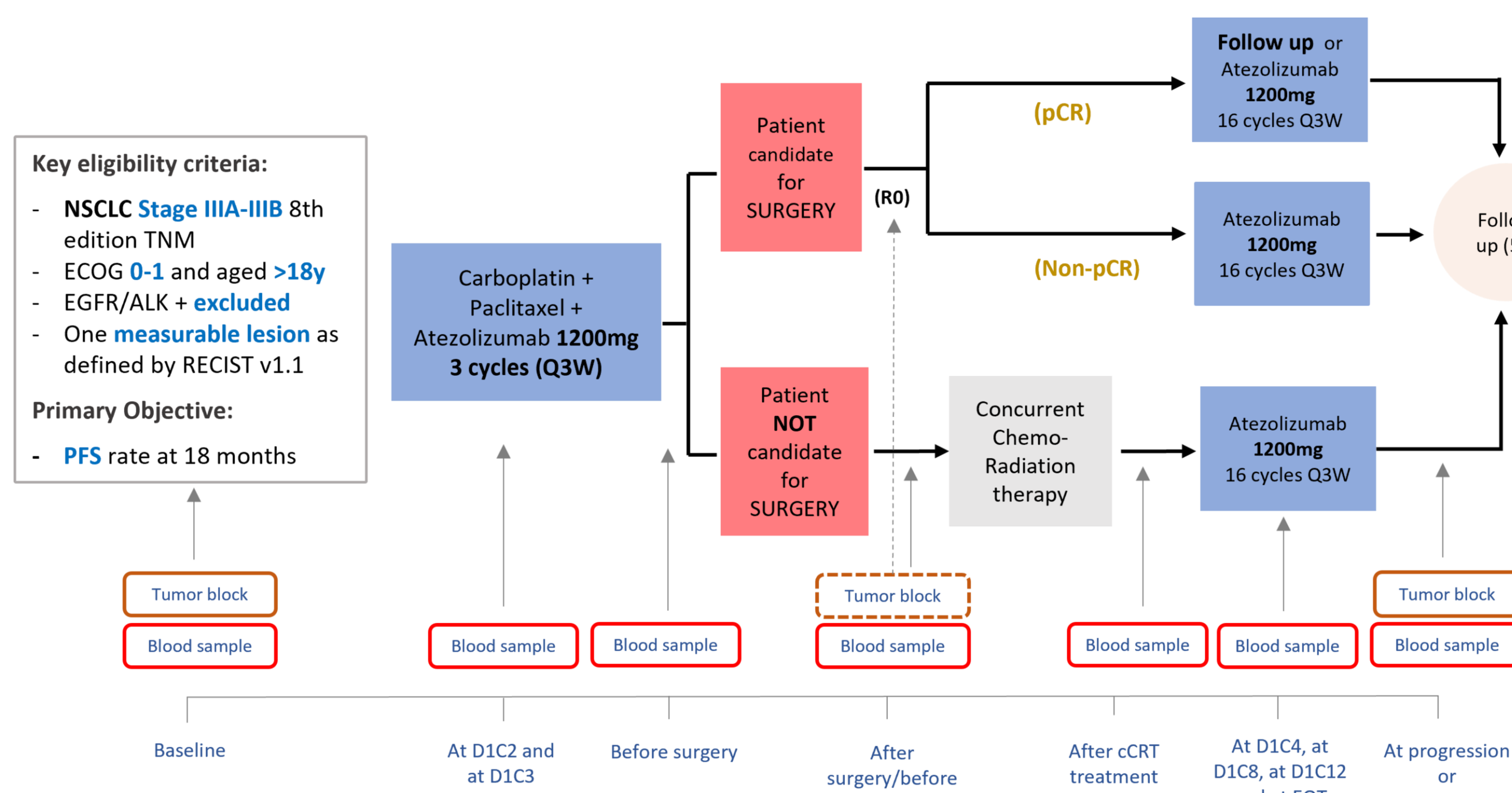
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INTRODUCTION

The choice of treatment for locally advanced non-small cell lung cancer (NSCLC) is based on clinical factors, and there are several therapeutic options available. Neoadjuvant treatment reduces tumor burden and may allow complete tumor resection (R0). The NADIM trials and the subsequent phase III CheckMate 816 trial have proven that neoadjuvant treatment based on chemotherapy plus immunotherapy has a synergistic impact on clinical outcomes [1-3]. The standard treatment for unresectable stage III patients without actionable genomic alteration is cCRT followed by durvalumab for 1 year (PACIFIC regimen) [4]. **The present study aimed to explore the results of treating all stage III (8th edition TNM) NSCLC patients with chemo-immunotherapy in a neoadjuvant phase, regardless of their initial resectability assessment.**

TRIAL DESIGN AND PROCEDURES



ATHENEA: open-label, phase II, multicenter clinical trial (EUCT No.: 2024-515984-68-00)

Overall, 97 patients with previously untreated stage IIIA-IIIB NSCLC will be recruited. All patients will receive 3 cycles of neoadjuvant/induction therapy with atezolizumab 1200 mg plus carboplatin AUC6 and paclitaxel 200mg/m². Thereafter, eligibility for surgery will be assessed by the multidisciplinary team at each participating hospital. Depending on the decision, each patient subset will receive different treatment:

- Eligible for surgery → R0 resection with pCR: will either be followed for survival or receive adjuvant atezolizumab 1200 mg for 16 cycles, according to the physician's decision.
- Eligible for surgery → R0 resection with non-pCR: will receive adjuvant treatment with atezolizumab 1200 mg for 16 cycles.
- Not eligible for surgery → will be treated with cCRT, followed by atezolizumab 1200 mg for 16 cycles if stable disease or partial response is achieved after cCRT.

Patients with R1 or R2 resection will be treated as per local guidelines. Patients will undergo CT-SCAN tumor assessments at baseline and post-neoadjuvant treatment (pre-surgery or cCRT). Post-treatment scans will follow surgery (resectable) or cCRT (non-resectable). During adjuvant atezolizumab/post-cCRT, scans occur every 12 weeks; thereafter, follow-up scans are scheduled every 3 months for 2 years, then every 6 months until year 5. A PET-SCAN will also be required at baseline. Tumor response will be evaluated by PET-SCAN and CT-SCAN after neoadjuvant or induction treatment following RECIST v1.1 criteria.

KEY ELEGIBILITY CRITERIA

Key Inclusion Criteria:

- Previously untreated patients with histologically- or cytologically- documented stage IIIA–IIIB NSCLC (according to 8th version of the IASLC Staging Manual in Thoracic Oncology).
- Presence of at least one measurable lesion by CT-SCAN, as defined by RECIST v1.1
- PET-SCAN and brain CT or MRI at baseline to confirm the absence of distant disease.
- ECOG Performance status: 0-1.
- Adequate hematologic, organ and lung function.

Key Exclusion Criteria:

- Known EGFR sensitizing mutation, EGFR amplification or ALK fusion oncogenes.
- Known STK-11 alterations, MDM2 amplifications or ROS1 translocations.
- Weight loss >10% within the previous 3 months.
- Received treatment with antineoplastic drugs, chest radiotherapy, or previous surgery for lung cancer.
- Malignancies other than NSCLC within 3 years prior to enrolment.
- Pleural or pericardial effusion.
- History of autoimmune disease or significant cardiovascular disease.
- History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced pneumonitis, idiopathic pneumonitis or evidence of active pneumonitis.
- Positive test for HIV. Patients with active HBV or HCV.
- Active severe infections and active tuberculosis.
- Symptomatic neuropathy (sensory) grade >1 according to the NCI CTCAE v5.0 and that were not related to the tumor.
- Received therapeutic oral or IV antibiotics within 2 weeks prior to be included in the study.

OBJECTIVES

Primary Endpoint: to evaluate PFS rate at 18 months in the ITT population. PFS is defined as the time from initiation of treatment to the occurrence of disease progression or death.

Secondary Endpoints: to determine resectability rate, proportion of R0 resections, pCR rate in the ITT population, MPR rate and downstaging rate. Also, PFS and OS rate at 12 and 18 months for patient subsets: patients eligible for surgery with pCR, surgical candidates with pCR and clinical follow up, surgical candidates with pCR and adjuvant treatment, surgical candidates with no pCR and patients not eligible for surgery.

Exploratory Endpoints:

- Association between baseline levels of ctDNA and OS and PFS.
- Association between ctDNA clearance (no detection of ctDNA) after neoadjuvant treatment and OS and PFS.
- To identify molecular alterations that may lead to treatment failure.
- To measure minimal residual disease after surgery and evaluating its capacity to predict PFS and OS.
- To describe the levels, relationships and changes of molecular markers related to the immune response at diagnosis and during treatment, as well as, whether they are predictive for pathological response, ORR, ctDNA clearance, adverse events, sites of first failure, PFS and OS.

STATISTICAL CONSIDERATIONS

Based on data from PACIFIC study, we assume a 40% PFS at 18 months as null survival probability, and 55% as the alternative PFS probability at 18 months. Test will be performed with a statistical power of 80% and with a one-sided type I error of 2.5%. On these bases and considering a drop-out rate of 10%, 97 patients will be included.

To ensure representativeness of theoretically unresectable patients, at least 40% of the recruited patients will be N3, T4 N1-2, N2 multiple or N2 bulky.

It will be performed an analysis of the ITT population following Cox proportional hazard models, log-rank test and Kaplan-Meier method to estimate the survival curves for primary and secondary endpoints. Also, it will be used Pearson's chi-squared or Fisher's exact tests and Kruskal-Wallis tests for the categorical and numerical variables, respectively.

RECRUITMENT

- **Regulatory approval:** 17 Feb 2025
- **Participating sites:** 21
- **First patient enrolled:** 08 Jul 2025
- **Enrollment:** 92 of 97 patients (as of 04 Aug 2026)
- **Status:** currently enrolling

REFERENCES, ACKNOWLEDGEMENTS & FUNDING

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