



Duo Vitality: Neoadjuvant Tislelizumab Plus Chemotherapy for Resectable EGFR-Mutated, PD-L1–Positive Lung Adenocarcinoma

Phase II Interim Analysis

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BACKGROUND

Standard of Care for EGFR-mutant NSCLC

For patients with EGFR-mutant NSCLC, EGFR-TKIs are the first-line standard of care, effectively blocking tumor cell signaling and significantly prolonging progression-free survival. However, no phase 3 prospective clinical trials have yet demonstrated the superiority of upfront EGFR-TKIs as neoadjuvant therapy for resectable EGFR-mutated NSCLC.

Preoperative Dilemma: Limited Benefit of Chemotherapy

For resectable early-stage patients, traditional neoadjuvant chemotherapy yields limited pathological response and fails to significantly improve long-term survival, highlighting an unmet clinical need.

New Hope: Immunotherapy Combination

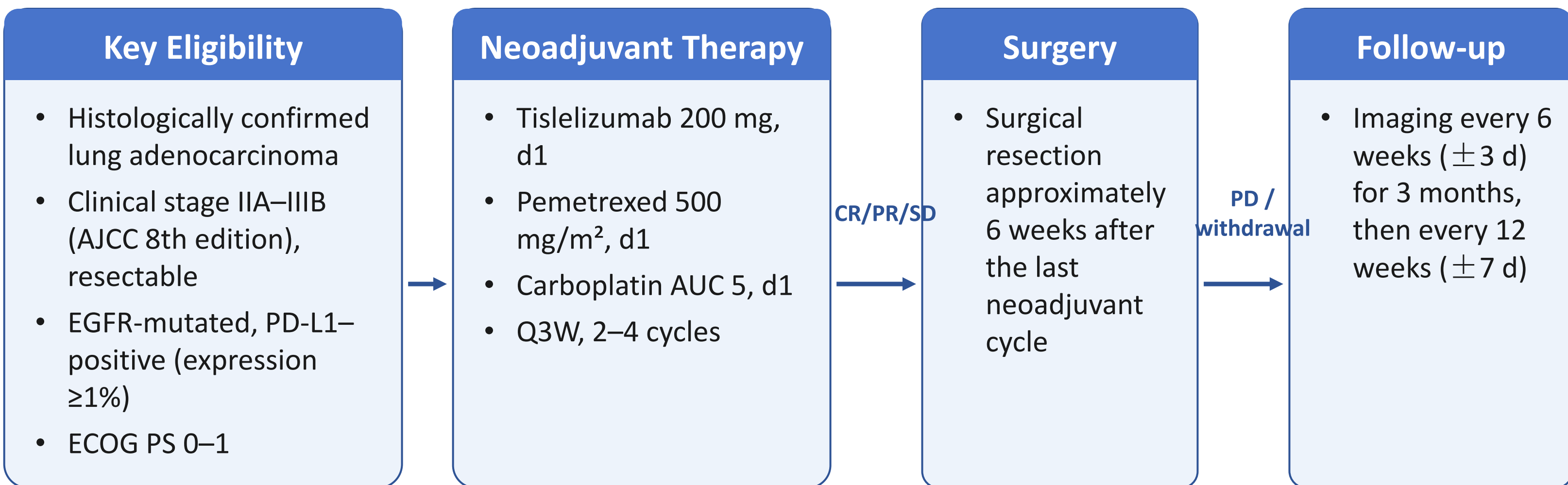
Studies like CheckMate-816 show that immunotherapy plus chemotherapy significantly improves pathological complete response, offering a revolutionary breakthrough for better surgical outcomes.

In this context, we investigated the efficacy and safety of neoadjuvant tislelizumab combined with platinum–pemetrexed chemotherapy for resectable EGFR-mutated, PD-L1–positive lung adenocarcinoma.

METHODS

- This is a single-arm, phase II study (NCT05527808). Eligible patients had EGFR-mutated NSCLC with PD-L1–positive (PD-L1 expression $\geq 1\%$). The study design was detailed in Figure 1.
- Patients received tislelizumab 200 mg IV on day 1 plus pemetrexed 500 mg/m² and carboplatin AUC 5 every 3 weeks for 2–4 cycles.
- Surgical resection was planned approximately 6 weeks after the last neoadjuvant cycle. Postoperative treatment (EGFR-TKI, immunotherapy) was at the physician’s discretion.
- Imaging for disease assessment by the investigator was performed approximately every 6 weeks (± 3 days) within the first 3 months, then every 12 weeks (± 7 days) until disease progression or withdrawal of informed consent and death.
- The primary endpoint was major pathological response (MPR). Secondary endpoints included pathological complete response (pCR), objective response rate (ORR), event-free survival (EFS), overall survival (OS), and safety.
- The planned sample size was 28 using a Simon two-stage design, with an unacceptable MPR rate of 8.9% and a target MPR rate of 27% (one-sided $\alpha=0.05$; power=80%). Stage 1 required 17 patients; enrollment would proceed to stage 2 if ≥ 2 patients achieved MPR.

Figure 1: Study design



RESULTS

Patient characteristics

- This interim analysis includes the 17 patients enrolled in stage 1. Median age was 61 years (range, 41–73).
- Most patients had clinical stage II–III disease (AJCC 8th edition); one patient with stage IV disease was enrolled per patient preference/consent.
- EGFR sensitizing mutations (exon 19 deletion or exon 21 L858R) were present in 82% of patients, and EGFR compound mutations in 18% (Table 1).
- Tumor response**
- As of the data cut-off on December 31, 2025, and excluding 1 patient who withdrew informed consent, the **ORR was 68%** (Table 2).
- The **DCR was 94%** (Table 2).
- 7/16 patients (43.8%) achieved a reduction in target lesion size of $>40\%$ from baseline.(Figure2)

Surgery outcomes

- 16/17 patients (94.1%) underwent surgery, all by VATS lobectomy; **R0 resection was achieved in 15/16 (93.8%)**. N2 nodal downstaging occurred in **66.7%**. No 30-day postoperative complications or deaths occurred (Table 3).

Pathological response

- At a median follow-up of 18.8 months, **MPR and pCR rates were 47% and 12%** in the ITT population (N=17) and **50% and 12.5%** in resected patients (n=16), meeting the criterion to proceed to stage 2 (Table 3). The **2-year EFS rate was 72.6%** (Figure 4).

Safety

- TRAEs were manageable; grade ≥ 3 TRAEs occurred in **5/17 patients (29%)**, most commonly leukopenia and drug-induced liver injury (Table 4).
- Individual treatment courses, including clinical response, antitumour therapy and recurrence/progression patterns, are shown in Figure 3.

Table 2:Tumor response

Total (N=16)	
BOR, n (%)	
CR	0
PR	11(68%)
SD	4(25%)
PD	1(6%)
ORR, n (%)	11(68%)
DCR, n (%)	15 (94%)

Table 1: Demographics and baseline characteristics

N=17	
Median age, years (range)	61 (41-73)
Male, n (%)	8 (47%)
Female, n (%)	9 (53%)
ECOG PS, n (%)	
0	14 (82%)
1	3 (18%)
EGFR mutation*, n (%)	
Sensitive mutations	14 (82%)
19 exon del	7 (41.1%)
19 exon del special	2 (11.7%)
subtype	5 (29.4%)
21 L858R	3 (18%)
Compound mutations	2 (11.7%)
19del+T790M	1 (6%)
21L858R+20S768I	
PD-L1 Expression, n (%)	
PD-L1>50%	7 (41%)
PD-L1 1-49%	10 (59%)
cTNM staging, n (%)	
IIA	1 (6%)
IIB	4 (23.5%)
IIIA	7 (41.1%)
IIIB	2 (11.7%)
IIIC	2 (11.7%)
IVA	1 (6%)

Table 3: Surgery-related outcome assessment.

Surgery outcomes	Patients received surgery N=16
R0 resection rate	15/16(94%)(1 patient had baseline IVA stage)
Operation time,median(range)	2.5h (1.33-3.25)
Surgical approach	
VATS	16/16(100%)
RATS	0
Pathological N downstaging, n (%)	
N3→N2	1(6.25%)
N2→N0	4(25%)
N1→N0	2(12.5%)
No changes	9(56.25%)
N2 nodal downstaging rate	4/6(66.7%)
Median intraoperative blood loss(range)	20ml (5-400)
30-day postoperative complication rate	0
30-day postoperative mortality	0
MPR rate	8(50%)
pCR rate	2(12.5%)

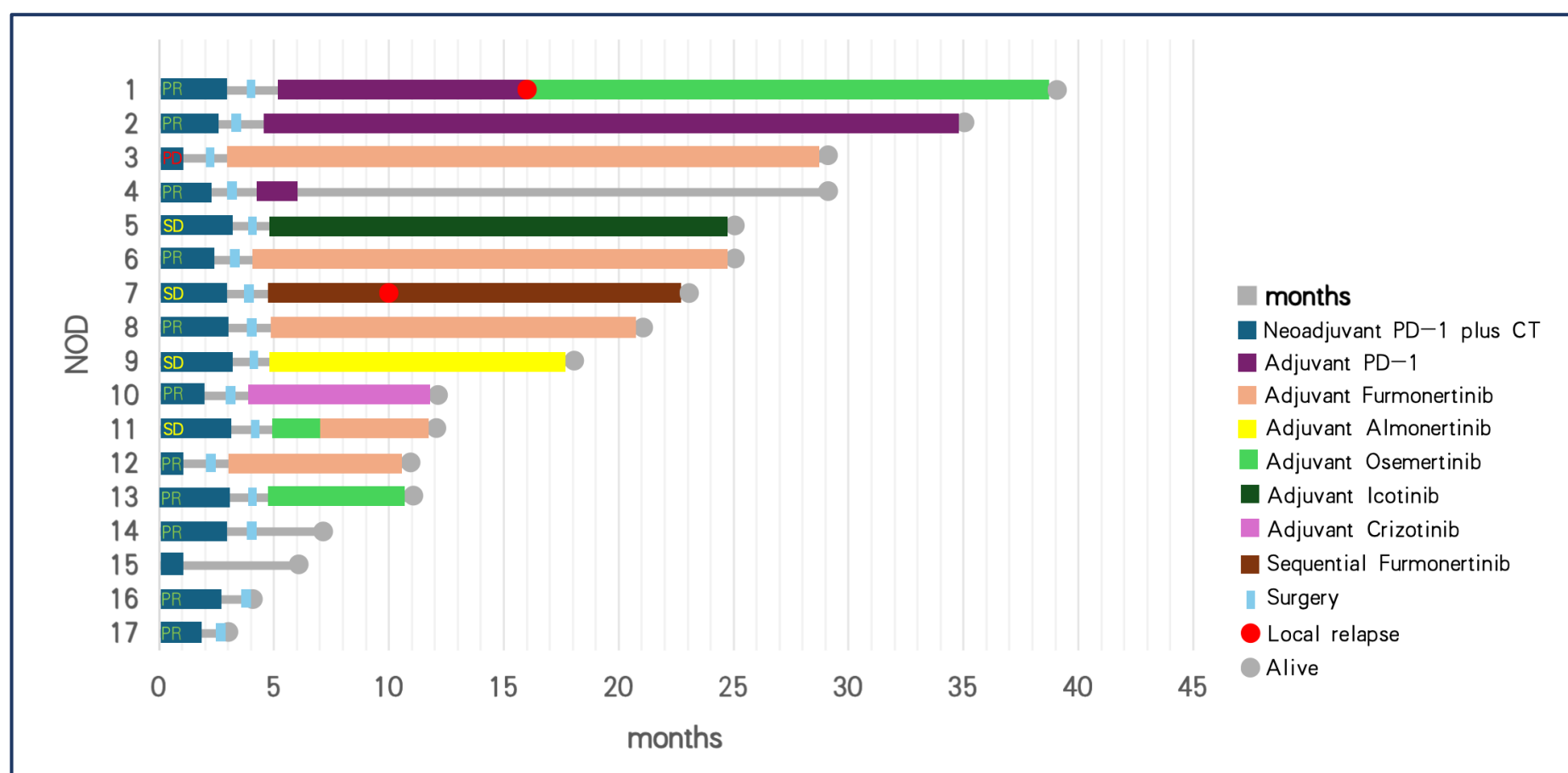


Figure 3:Duration of treatment

Table 4:Safety

Adverse events	Any grade N=17	Grade ≥ 3 N=5(29%)
Liver dysfunction	5(29%)	2(11.8%)
Leukocytopenia	2(11.8%)	2(11.8%)
Granulocytopenia	1(5.9%)	1(5.9%)
Abnormal renal function	1(5.9%)	0
Anemia	1(5.9%)	0

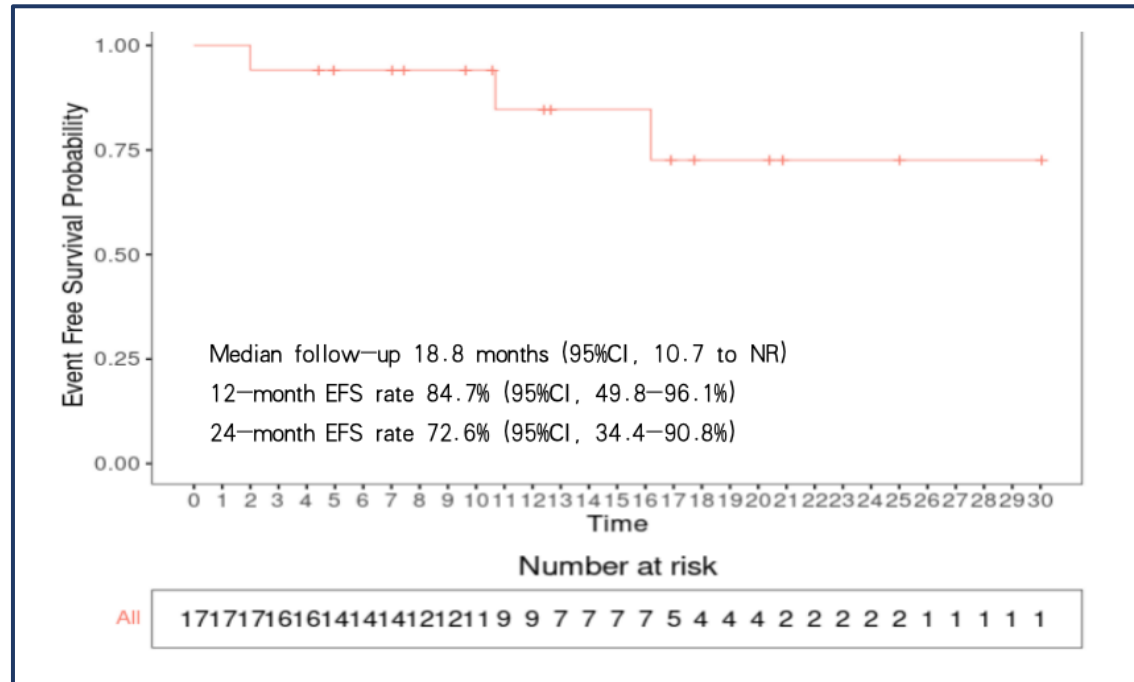


Figure 4: Analysis of survival outcome

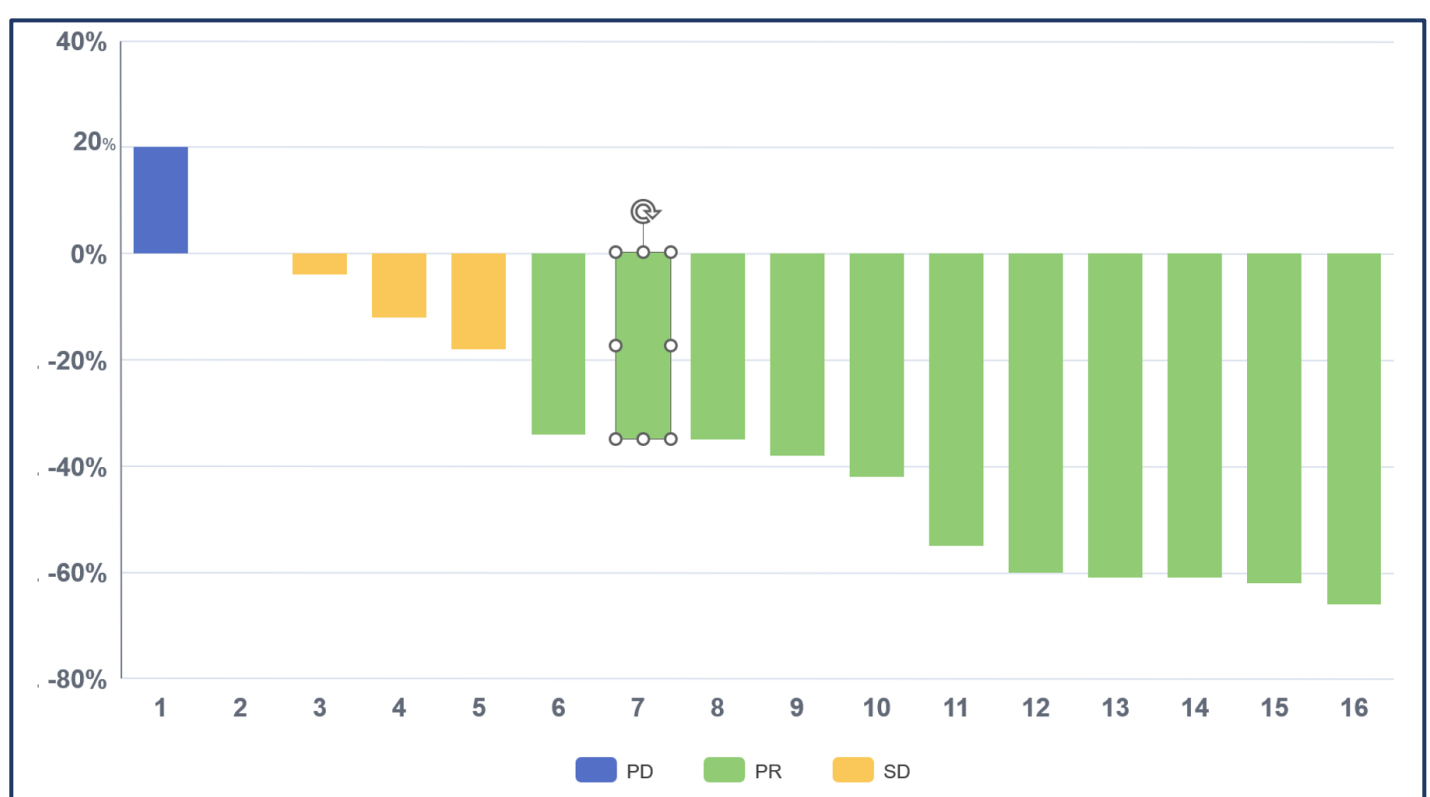


Figure 2:Tumor shrinkage waterfall

Conclusions

- Neoadjuvant tislelizumab plus platinum–pemetrexed chemotherapy demonstrated promising pathological response and manageable safety in EGFR-mutated, PD-L1–positive lung adenocarcinoma in this stage 1 analysis. Further evaluation in the second stage is ongoing.