

Amivantamab Plus Chemotherapy vs Chemotherapy as First-line Treatment Among Patients with EGFR Exon 20 Insertion-mutated Advanced Non-small Cell Lung Cancer (NSCLC): PAPILLON Chinese Subgroup Analysis

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Background

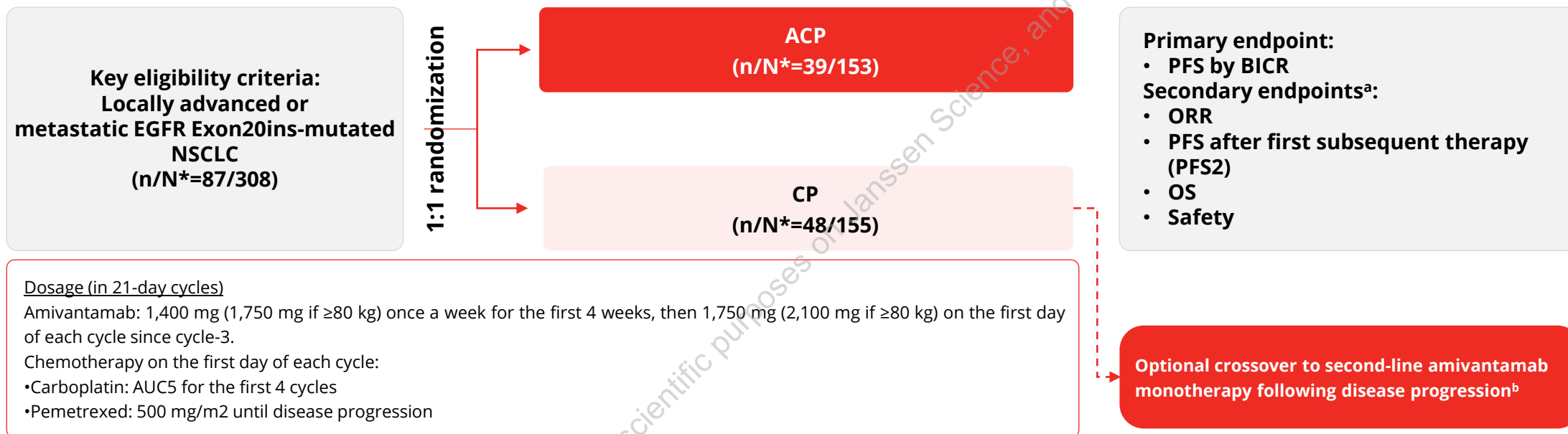
- **Amivantamab is a bispecific antibody targeting EGFR and MET tyrosine kinase receptors with immune cell-directing activity. The phase 3 PAPILLON study (NCT04538664) investigated the combination of amivantamab with chemotherapy (carboplatin and pemetrexed) (ACP) vs chemotherapy (carboplatin and pemetrexed) (CP) as first-line treatment in patients (pts) with advanced EGFR Exon20ins-mutated NSCLC.**
- **In PAPILLON study, ACP significantly improved PFS versus CP in patients with treatment-naïve, EGFR Exon20ins-mutated advanced NSCLC^[1,2].**
- **The FDA has recently approved ACP for the first-line treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.**
- **Herein, the results of Chinese subgroup analysis from PAPILLON study is reported**

EGFR, epidermal growth factor receptor; FDA, Food and Drug Administration; MET, mesenchymal-epithelial transition; NSCLC, non-small cell lung cancer; PFS, progression-free survival.

1. Girard N, Park K, Tang K, et al. Amivantamab plus chemotherapy vs chemotherapy as first-line treatment in EGFR Exon 20 insertion-mutated advanced non-small cell lung cancer (NSCLC): Primary results from PAPILLON, a randomized phase III global study. *Annals of Oncology*, 2023, 34: S1304.

2. Zhou C, Tang K J, Cho B C, et al. Amivantamab plus chemotherapy in NSCLC with EGFR exon 20 insertions. *New England Journal of Medicine*, 2023, 389(22): 2039-2051.

Phase 3 PAPILLON Study Design



*The lowercase “n” and uppercase “N” in the study design diagram indicate number of patients in the Chinese subgroup and overall population, respectively

PAPILLON (ClinicalTrials.gov Identifier: NCT04538664) enrollment period: December 2020 to November 2022; data cut-off: May 3, 2023.

^aDetailed list of secondary endpoints is available in the protocol. ^bCrossover was only allowed after BICR confirmation of disease progression; amivantamab monotherapy on Q3W dosing per main study.

ACP, Amivantamab-Chemotherapy; AUC, area under the curve; BICR, blinded independent central review; CP, Chemotherapy; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, PFS after first subsequent therapy.

Study population

- Among the 308 pts enrolled, 87 were Chinese, with 39 receiving ACP and 48 receiving CP. Among the Chinese subgroup, median age was 57/57 years, 15%/25% history of brain metastases for pts in ACP/CP arms
- Baseline characteristics were generally balanced between arms

Table 1. Baseline characteristics of patients

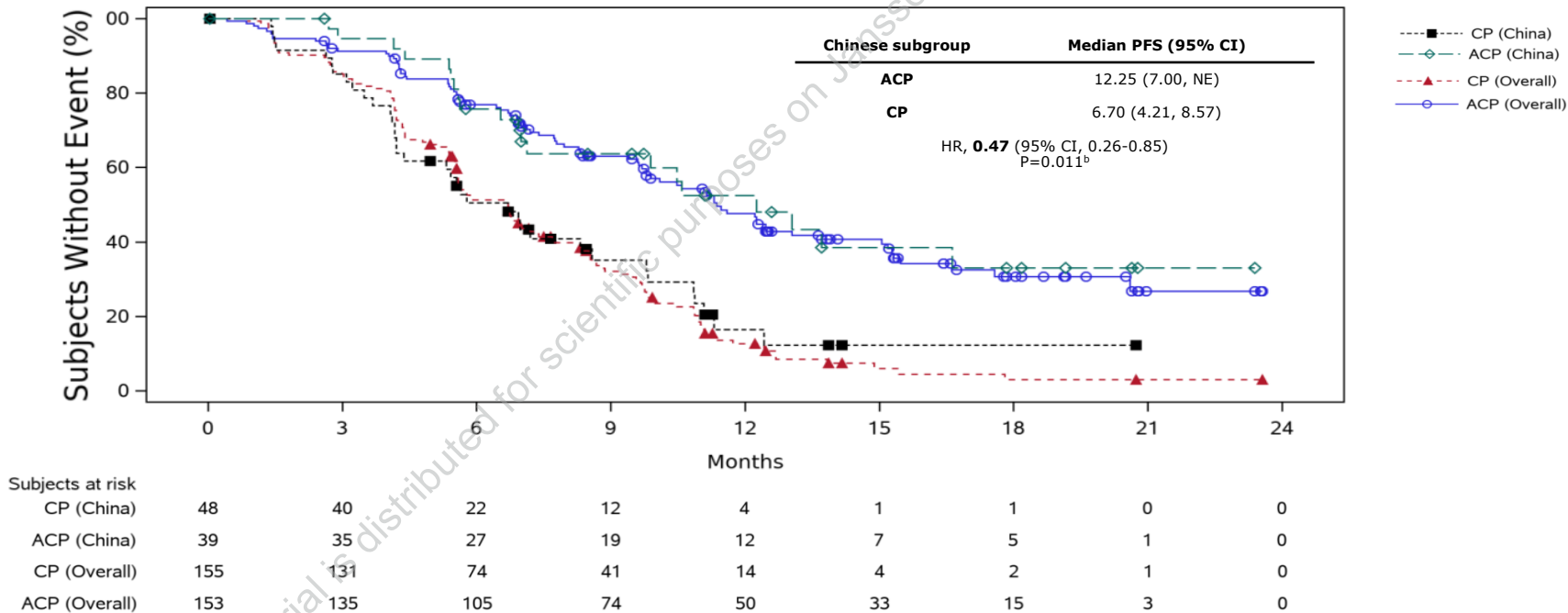
	Chinese subgroup (N=87)		Overall population (N=308)	
	CP (n=48)	ACP (n=39)	CP (n=155)	ACP (n=153)
Age, median, years	57.0	57.0	62.0	61.0
Sex, female/male, %	62.5/37.5	46.2/53.8	60.0/40.0	55.6/44.4
Weight, ≥80kg/<80kg, %	8.3/91.7	7.7/92.3	17.4/82.6	13.7/86.3
ECOG performance score, 0/1, %	25.0/75.0	20.5/79.5	35.5/64.5	35.3/64.7
History of brain metastasis, %	25.0	15.4	23.2	22.9
Prior EGFR TKI use, %	2.1	0	1.9	0.7
NSCLC histology, adenocarcinoma,%	100.0	100.0	98.7	98.7

ACP, Amivantamab-Chemotherapy; CP, Chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex20ins, Exon 20 insertion; TKI, tyrosine kinase inhibitor; NSCLC, non-small cell lung cancer.

Progression-free Survival by BICR Among China Patients

- After a median follow-up of 16.4 months (mo), median PFS was 12.3 mo (95% CI: 7.00, NE) in ACP arm compared with 6.7 mo (95%CI: 4.21, 8.57) in CP arm (HR, 0.47; 95% CI, 0.26-0.85; $P=0.011^a$)
- PFS among China patients were consistent with results from the overall PAPILLON population¹

Figure 1a. Kaplan-Meier plot of progression-free survival



^aNominal P-value; endpoint is not part of hierarchical hypothesis testing.

ACP, Amivantamab-Chemotherapy; BICR, blinded independent central review; CI, confidence interval; CP, Chemotherapy; HR, hazard ratio; mo, months; PFS, progression-free survival.

1. Zhou C, et al. N Engl J Med. 2023;10.1056/NEJMoa2306441.

Best Response, ORR, and DoR by BICR Among China Patients

- **ORR was 71.8% (95% CI, 55.1%-85.0%) for ACP, and 48.9% (95% CI, 34.1%-63.9%) for CP (odds ratio, 2.46; 95% CI, 1.01-5.98; $P=0.048^a$)**
- **Pts in ACP arm reached a duration of response of 12.3 mo versus 6.9 mo of pts in CP arm**

Table 3. Summary of tumor response outcomes

	Chinese subgroup (N=87)		Overall population ¹ (N=308)	
	CP (n=48)	ACP (n=39)	CP (n=155)	ACP (n=153)
ORR, %	48.9	71.8	47.4	73.0
Duration of response, mo	6.9	12.3	5.6	10.1
Best Overall Response				
CR, %	2.1	5.1	0.7	3.9
PR, %	46.8	66.7	46.7	69.1
SD, %	40.4	23.1	40.8	19.1
PD, %	8.5	2.6	10.5	2.6
NE, %	2.1	2.6	1.3	5.3

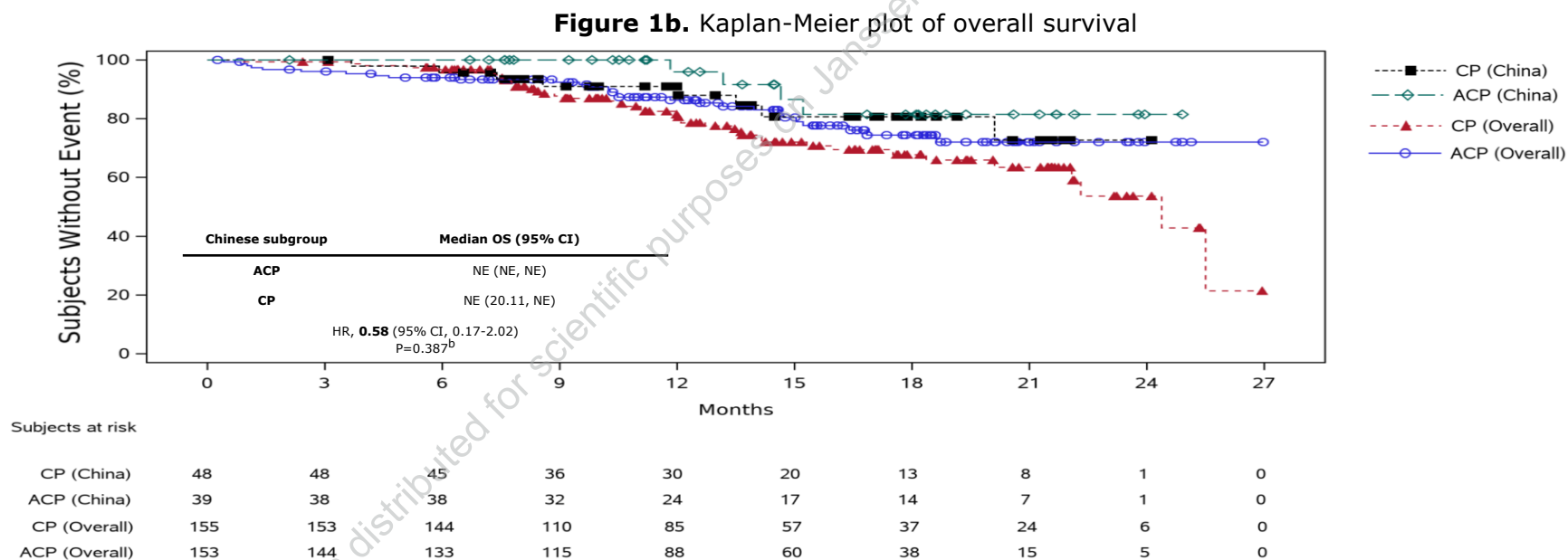
^aNominal P-value; endpoint is not part of hierarchical hypothesis testing.

ACP, Amivantamab-Chemotherapy; BICR, blinded independent central review; CI, confidence interval; CP, Chemotherapy; CR, complete response; HR, hazard ratio; mo, months; NE, not evaluable; OR, odds ratio; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters.

1. Zhou C, et al. N Engl J Med. 2023;10.1056/NEJMoa2306441.

PFS2 and Interim OS Among China Patients

- Interim OS showed a trend favoring ACP, (HR, 0.58; 95%CI, 0.17-2.02; $P=0.387^a$), despite crossover of 43.8% (21/48) subjects to receive monotherapy amivantamab
- Median PFS2^b was not estimable (NE) for ACP vs 18.8 mo for CP (HR, 0.32; 95% CI, 0.11-0.88; $P=0.021^a$)



^aNominal P-value; endpoint is not part of hierarchical hypothesis testing.

^bPFS2 is defined from the time of randomization until the time of second objective disease progression (based on investigator assessment) or death, whichever comes first, after the initiation of the first subsequent systemic anticancer therapy.

ACP, Amivantamab-Chemotherapy; CI, confidence interval; CP, Chemotherapy; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival; PFS2, progression-free survival after first subsequent therapy.

1. Zhou C, et al. N Engl J Med. 2023;10.1056/NEJMoa2306441.

Summary of Adverse Events Among China Patients

- No pts had discontinuation of amivantamab due to an AE
- Most common AEs (all grades) (>50%) in ACP arm were rash, paronychia, hypoalbuminemia, neutropenia, anemia, leukopenia and thrombocytopenia which were consistent with the known safety profile of the individual agents

Table 4. Summary of TEAEs among Chinese patients

Treatment-emergent AEs, n (%)	CP (n=48)	ACP(n=39)
Any AEs	47 (97.9%)	39 (100%)
Grade ≥3 AEs	26 (54.2%)	27 (69.2%)
Serious AEs	14 (29.2%)	9 (23.1%)
AEs leading to death	1 (2.1%)	0
AEs leading to discontinuation of any agent	3 (6.3%)	3 (7.7%)
AEs leading to interruption of any agents	13 (27.1%)	21 (53.8%)
AEs leading to discontinuation of amivantamab	NA	0

Data included from the safety population, which included all randomized patients who received ≥1 dose of study treatment. AE, adverse event; EGFR, epidermal growth factor receptor.

Most common AEs by preferred term (≥30%), n (%)	CP (n=48)		ACP(n=39)	
	All grades	Grades≥3	All grades	Grades≥3
Associated with EGFR inhibition				
Paronychia	0	0	25 (64.1%)	2 (5.1%)
Rash	2 (4.2%)	0	28 (71.8%)	7 (17.9%)
Associated with MET inhibition				
Hypoalbuminemia	9 (18.8%)	0	22 (56.4%)	0
Other				
Neutropenia	31 (64.6%)	13 (27.1%)	31 (79.5%)	15 (38.5%)
Anemia	33 (68.8%)	5 (10.4%)	31 (79.5%)	3 (7.7%)
Leukopenia	29 (60.4%)	4 (8.3%)	29 (74.4%)	8 (20.5%)
Thrombocytopenia	19 (39.6%)	6 (12.5%)	21 (53.8%)	5 (12.8%)
Constipation	11 (22.9%)	0	13 (33.3%)	0
Aspartate aminotransferase increased	28 (58.3%)	0	17 (43.6%)	0
Alanine aminotransferase increased	28 (58.3%)	1 (2.1%)	16 (41.0%)	0
Decreased appetite	16 (33.3%)	0	12 (30.8%)	0
Nausea	18 (37.5%)	0	6 (15.4%)	0

Conclusions

- ✓ **Amivantamab-chemotherapy represents the new standard of care for first-line EGFR Exon20ins NSCLC.**
- ✓ **Amivantamab-chemotherapy demonstrated superior PFS versus chemotherapy in Chinese patients in first-line EGFR Exon20ins advanced NSCLC (12.3 mo vs 6.7 mo; HR, 0.47; P=0.011b).**
- ✓ **The safety profile was manageable and tolerable. Notably, no pts had discontinuation of amivantamab due to an AE.**

KEY TAKE AWAY

Amivantamab-chemotherapy demonstrated superior PFS compared to chemotherapy as first-line treatment in Chinese patients with EGFR Exon20ins advanced NSCLC.

