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Adjusted Comparison of Amivantamab in Combination With Carboplatin Plus Pemetrexed From the PAPILLON Study Versus US Real-World Frontline Treatments in Patients With Advanced NSCLC Harboring EGFR Exon 20 Insertions

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Key Takeaway

Amivantamab+CP as 1L therapy demonstrated superior effectiveness compared with other commonly used RWPC 1L therapies in patients with advanced/metastatic NSCLC with EGFR Exon20ins mutations, and further supports the adoption of Amivantamab+CP as the new standard of care for these patients

Conclusions

In RW practice, platinum-based chemotherapies were the most commonly used 1L therapy in patients with advanced/metastatic NSCLC and EGFR exon20ins mutations

In the ITC efficacy analysis, statistically significant differences were observed favoring amivantamab+CP compared with other commonly used RWPC 1L therapies across all endpoints

Acknowledgments

This study utilized ConcertAI (Patient360™ NSCLC) and COTA (NSCLC Vantage), 2 real-world, de-identified databases derived from electronic health records of partnered healthcare providers in the United States.

Disclosures

MS, XL, NN, NP, EC, FG, AH: employees of Johnson and Johnson Innovative Medicine and may hold stocks in Johnson and Johnson.

Introduction

Epidermal growth factor receptor (EGFR) activating mutations are detected in ~10% to 20% of patients with non-squamous non-small cell lung cancer (NSCLC),[1,2] and up to ~10% of these are exon 20 insertions (exon20ins).[3-5] Patients with EGFR exon20ins face poor prognosis compared with other common EGFR mutations, with 5-year real-world survival rates of 8% and 19%, respectively.[3,9]

Prior to July 2024 when amivantamab was included, European Society for Medical Oncology (ESMO) treatment guidelines referred to platinum doublet chemotherapy as the frontline (1L) therapy for advanced/metastatic NSCLC with EGFR exon20ins.[6,7]

Amivantamab, an EGFR MET-receptor bispecific antibody, demonstrated superior efficacy in combination with carboplatin plus pemetrexed (CP) as 1L therapy versus CP alone in patients with advanced NSCLC with EGFR exon20ins.[8]

Amivantamab+CP has not been directly compared in clinical studies to therapies other than CP in the 1L setting in patients with EGFR exon20ins advanced/metastatic NSCLC.

This study aims to assess the comparative effectiveness of 1L amivantamab+CP versus real-world (RW) treatments in the U.S. in this patient population.

Methods

In this retrospective, observational study, routinely-collected individual patient data (IPD) from 2012 to 2023 from 2 U.S. RW databases, ConcertAI (Patient360™ NSCLC) and COTA (NSCLC Vantage), were accessed. Patients aged ⩾18 years with locally advanced/metastatic NSCLC, without prior systemic treatment, with Eastern Cooperative Oncology Group (ECOG) performance status 0-1 (when available), and confirmed EGFR exon20ins were included.

The study objectives were:

- Describe 1L RW treatment patterns and outcomes
- Compare time to next treatment (TTNT; considered as a potential proxy for PFS), progression-free survival (PFS), and overall survival (OS) of amivantamab+CP (from PAPILLON[8]) with RW treatment options (alternatives to platinum-based chemotherapy) in an indirect treatment comparison (ITC) using IPD from RW data sources and the PAPILLON study.

PAPILLON data cut-offs were May 2023 for PFS and TTNT, consistent with the primary and final analysis for PFS[8], and October 2023 for OS.

RW data were pooled from the 2 databases, and all RW treatment classes were combined to form a RW physician choice (RWPC) cohort.

For the ITC, RW data were reweighted to account for potential confounders using inverse probability weighting (IPW) average treatment effect in the treated (ATT) method to balance all prognostic factors (ECOG performance status, history of brain and liver metastases, age, history of smoking, and sex) between the reweighted RWPC cohort and the observed amivantamab+CP cohort from PAPILLON.

Results

Patient characteristics

Data leveraged from 2 RW datasets allowed for analysis of 94 patients. Median follow-up was 50.5 months. Patient demographics and baseline characteristics are described for RW databases and the PAPILLON amivantamab+CP arm in **Table 1**.

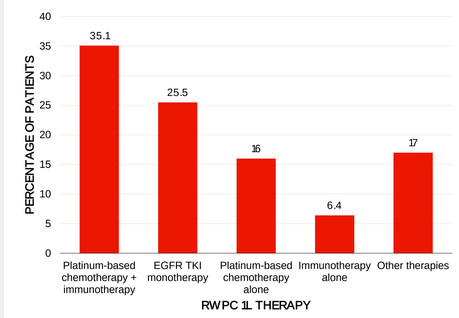
Table 1. Demographics and baseline patient characteristics

Characteristic, N (%)	Overall RW data	PAPILLON amivantamab+CP[8]
N	94	153
Age, years		
< 65	43 (46)	97 (63)
≥ 65	51 (54)	56 (37)
Sex		
Female	56 (60)	85 (56)
Male	38 (40)	68 (44)
ECOG performance status		
0	26 (28)	54 (35)
1	36 (38)	99 (65)
Missing	32 (34)	0
Smoking status		
Current or prior smoker	34 (36)	65 (42)
No smoking history	57 (61)	88 (58)
Missing	3 (3)	0
Metastatic site		
Brain	31 (33)	35 (23)
Liver	25 (27)	18 (12)

Treatment of patients with RWPC 1L therapy

1L treatments included platinum-based chemotherapy + immunotherapy (35.1%), EGFR TKI alone (25.5%), platinum-based chemotherapies (16.0%), immunotherapy alone (6.4%), or others (17.0%). The other treatment group included treatments such as platinum + VEGFi, platinum + EGFR TKI, EGFR TKI combinations, platinum-based chemotherapy alone, non-platinum monotherapy/non-platinum+ non-chemotherapy, platinum + EGFR TKI + IO.

Figure 1: First-line Real-World Treatment Patterns in the U.S.



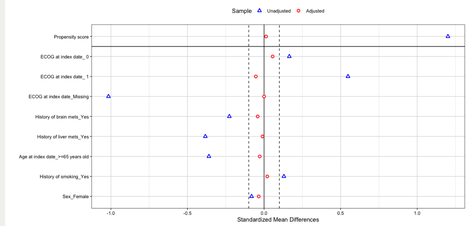
Population adjustment

Table 2. and **Figure 2.** show the unweighted and fully weighted-ATT comparisons of the key variables in the RW data sources and PAPIILON. After adjustment, the RWPC cohort was well balanced with the amivantamab+CP cohort, with all standardized mean differences ⩽0.10.

Table 2. Unweighted and fully-weighted standardized mean differences (SMD) for key weighting variables

Variable	Unweighted SMD	Weighted SMD	Weighted SMD threshold
ECOG at index date (0)	0.165	0.056	Balanced, <0.1
ECOG at index date (1)	0.548	-0.054	Balanced, <0.1
ECOG at index date (Missing)	-1.016	0.000	Balanced, <0.1
History of brain mets (Yes)	-0.227	-0.042	Balanced, <0.1
History of liver mets (Yes)	-0.384	-0.010	Balanced, <0.1
Age at index date (≥65 years old)	-0.360	-0.028	Balanced, <0.1
History of smoking (Yes)	0.130	0.021	Balanced, <0.1
Sex (Female)	-0.081	-0.035	Balanced, <0.1

Figure 2. Unadjusted and fully-adjusted standardized mean differences (SMD) for key weighting variables



Adjusted relative treatment effect of amivantamab+CP versus RWPC 1L therapy

Based on adjusted hazard ratio (HR) estimates of TTNT, statistically significant differences were observed favoring amivantamab+CP compared with pooled RWPC 1L therapy (**Figure 3.** and **Table 3.**).

Figure 3: Kaplan-Meier plot of TTNT for amivantamab+CP 1L versus RWPC 1L therapy

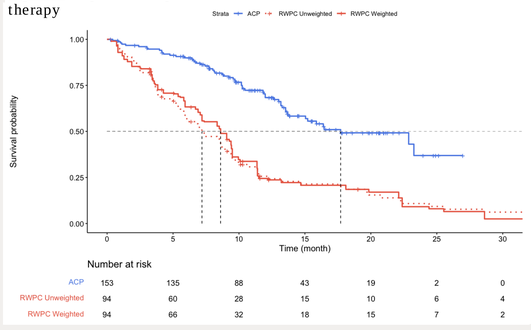


Table 3: TTNT of amivantamab+CP 1L versus RWPC 1L therapy

TTNT ITC	N	Median, months (95% CI)	HR (95% CI)	p value
Amivantamab+CP [a] vs:	153	17.7 (13.5-NE)		
Unadjusted pooled RWPC 1L therapy	94	7.2 (5.8, 9.1)	0.3 (0.2, 0.5)	<0.001
Adjusted pooled RWPC 1L therapy [b]	94	8.6 (5.9, 9.9)	0.3 (0.2, 0.5)	<0.001

TTNT, time to next therapy; NE, not estimable; CI, confidence interval; HR, hazard ratio.
[a]Data from PAPILLON May 2023 data cut
[b]Adjusted with IPW-ATT for: ECOG performance status, history of brain and liver metastases, age, history of smoking, and sex.

Based on adjusted hazard ratio (HR) estimates of PFS (real-world PFS v. PAPILLON PFS-INV), statistically significant differences were observed favoring amivantamab+CP compared with pooled RWPC 1L therapy (**Figure 4.** and **Table 4.**).

Figure 4: Kaplan-Meier plot of PFS for amivantamab+CP 1L versus RWPC 1L therapy

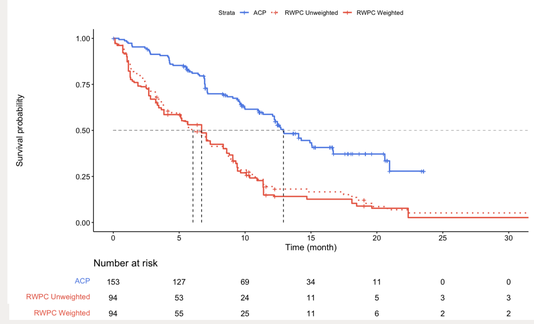


Table 4: PFS of amivantamab+CP 1L versus RWPC 1L therapy

PFS ITC	N	Median, months (95% CI)	HR (95% CI)	p value
Amivantamab+CP [a] vs:	153	12.9 (11.4, 16.7)		
Unadjusted pooled RWPC 1L therapy	94	6.1 (3.8, 8.6)	0.4 (0.3, 0.5)	<0.001
Adjusted pooled RWPC 1L therapy [b]	94	6.7 (3.2, 9.1)	0.4 (0.2, 0.5)	<0.001

PFS, progression-free survival; NE, not estimable; CI, confidence interval; HR, hazard ratio.
[a]Data from PAPILLON May 2023 data cut
[b]Adjusted with IPW-ATT for: ECOG performance status, history of brain and liver metastases, age, history of smoking, and sex.

Based on adjusted hazard ratio (HR) estimates of OS, statistically significant differences were observed favoring amivantamab+CP compared with pooled RWPC 1L therapy (**Figure 5.** and **Table 5.**).

Figure 5: Kaplan-Meier plot of OS for amivantamab+CP 1L versus RWPC 1L therapy

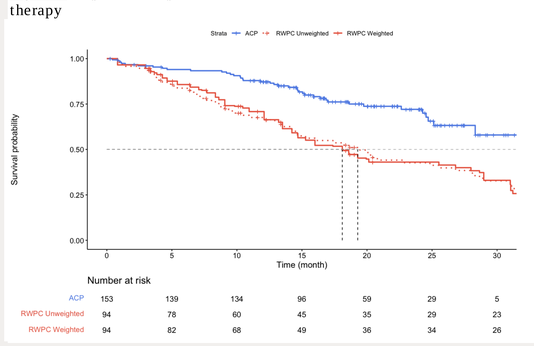


Table 5: OS of amivantamab+CP 1L versus RWPC 1L therapy

OS ITC	N	Median, months (95% CI)	HR (95% CI)	p value
Amivantamab+CP [a] vs:	153	NE (28.3, NE)		
Unadjusted pooled RWPC 1L therapy	94	19.3 (14.2, 26.8)	0.4 (0.3, 0.6)	<0.001
Pooled RWPC 1L therapy [b]	94	18.1 (13.2, 29.0)	0.4 (0.3, 0.7)	0.001

OS, overall survival; NE, not estimable; CI, confidence interval; HR, hazard ratio.
[a]Data from PAPILLON October 2023 data cut
[b]Adjusted with IPW-ATT for: ECOG performance status, history of brain and liver metastases, age, history of smoking, and sex.

References

1. Greenhalgh J, et al. *Cochrane Database Syst Rev*. 2021;3:CD010383. 2. O'Leary C, et al. Pharmaceuticals (Basel). 2020;13:273. 3. Pacini L, et al. *Pharmgenomics Pers Med*. 2021;14:301-317. 4. Takeda M, et al. *Oncotarget*. 2018;9:21132-21140. 5. Vyse S, Huang PH. *Sig Transduct Target Ther*. 2019;4:5. 6. Hendriks LE, et al. *Ann Oncol*. 2023;34:339-357. 7. ESMO Oncogene-Addicted Metastatic NSCLC Living Guidelines, v1.1 July 2024. Accessed September 27, 2024. 8. Zhou C, et al. *N Engl J Med*. 2023;389:2039-2051. 9. Bazhenova L, et al. Lung Cancer. 2021 Dec; 162: 154-161.

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