Matching-Adjusted Indirect Comparison of Amivantamab vs. Mobocertinib in EGFR Exon 20 Insertion-Mutated Non-Small Cell Lung Cancer

Abstract # 115347

[1]Janssen Belgium, Beerse, Belgium; [2]Janssen-Cilag, Issy-les-Moulineaux, France; [3]Janssen-Cilag, Lagoas Park, Portugal; [4]Evidera, Waltham, MA USA; [5]Evidera, London, UK; [6]Janssen Global Services, Bridgewater, NJ, USA

Suzy Van Sanden[1], Nora Rahhali[2], Claudio Schioppa[1], Joris Diels[1], Bernardo Rodrigues[3], Conor Chandler[4], Venediktos Kapetanakis[5], Ruhee Jain[6], Tracy Li[6]

INTRODUCTION

- National Comprehensive Cancer Network clinical practice guidelines for non-small cell lung cancer (NSCLC) recommend Amivantamab and mobocertinib as second-line therapies for patients with epidermal growth factor receptor (EGFR) exon20ins with disease progression after first-line chemotherapy or immunotherapy[1]
- In the absence of clinical studies providing a head-to-head comparison of Amivantamab vs. mobocertinib, an indirect treatment comparison is needed to evaluate the relative efficacy and safety between these two treatments

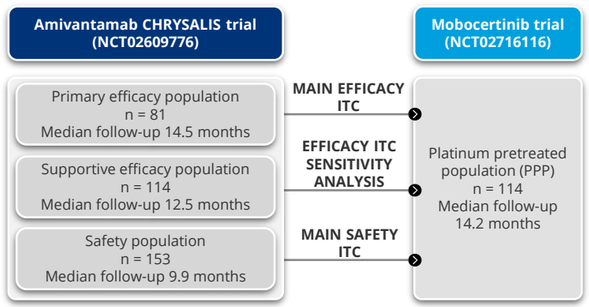
OBJECTIVES

- To assess the relative efficacy and safety of Amivantamab vs. mobocertinib in patients with NSCLC with EGFR exon 20 insertion (exon20ins) mutations who had progressed on prior platinum-based chemotherapy

METHODS

- Unanchored matching-adjusted indirect comparisons (MAIC) were conducted by reweighting patient-level data from the CHRYSALIS study[2] (multi-center, open-label, multi-cohort study of Amivantamab) to match baseline summary data from a single-arm phase I/II mobocertinib trial[3]
- Key aspects of the two trials—including inclusion/exclusion criteria, general study designs, outcome definitions, and baseline characteristics—were broadly comparable and suitable for unanchored MAICs

FIGURE 1: Amivantamab and mobocertinib populations used in the analysis



ITC, indirect treatment comparison; PPP, platinum pretreated patients

- Populations were matched on all factors reported for NCT02716116[3]: the number and type of prior therapies, Eastern Cooperative Oncology Group (ECOG) performance status, brain metastases, age, race, sex, smoking history and histology
- The efficacy outcomes included in the MAIC were:
  - Overall response rate (ORR) assessed by an independent review committee (ORR-IRC) and investigator (ORR-INV)
  - Progression-free survival (PFS) assessed by an IRC (PFS-IRC)
  - Overall survival (OS)
  - Clinical benefit rate (CBR) assessed by an IRC (CBR-IRC) and INV (CBR-INV); a post-hoc version of CBR was derived using the CHRYSALIS trial data to align with the NCT02716116 outcome definition
- The safety outcomes included in the MAIC were those reported for mobocertinib[3]
- Adjusted relative efficacy for Amivantamab vs. mobocertinib on binary outcomes were estimated by relative risks (RR) using weighted logistic regression models and time-to-event outcomes were analyzed using weighted Cox proportional hazards regression models

REFERENCES:

1. NCCN Clinical Practice Guidelines in Oncology. NCCN Guidelines Version 7.2021 NSCLC; 2021.; **2.**Park K, et al. *J Clin Oncol.* 2021;39:3391-3402.; **3.**Zhou C, et al. *JAMA Oncol*. 2021; 1;7(12):e214761.

RESULTS

TABLE 1: Baseline characteristics before matching*

Baseline Characteristic	CHRYSALIS (Ami)			PPP Cohort (Mobo)
	Primary Efficacy	Supportive Efficacy	Safety	
Number of patients, N	**81**	**114**	**153**	**114**
Number of prior systemic anti-cancer therapies, %				
1	38	42	39	41
2	30	30	31	32
3+	32	28	30	27
ECOG, %				
0	32	29	27	25
1 or 2	68	71	73	75
Presence of brain metastasis, %	22	25	24	35
Prior immunotherapy, %	47	44	42	43
Prior EGFR/HER2 TKI therapy, %	23	20	22	25
Age, median	62	62	61	60
Race, %				
Asian	56	57	66	60
White	42	40	31	37
Other	3	3	2	3
Female, %	59	61	61	66
Smoking history, %	47	43	39	29
Histology, %				
Adenocarcinoma	95	96	96	98
Large cell carcinoma	4	3	3	1
Squamous cell carcinoma	1	2	1	1

ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; ESS, effective sample size; HER2, human epidermal growth factor receptor 2; PPP, platinum pretreated patients; TKI, tyrosine kinase inhibitor
*Matching was carried out on all variables of Table 1 and was successful (i.e., patient characteristics after weighting matched those reported in the PPP cohort)

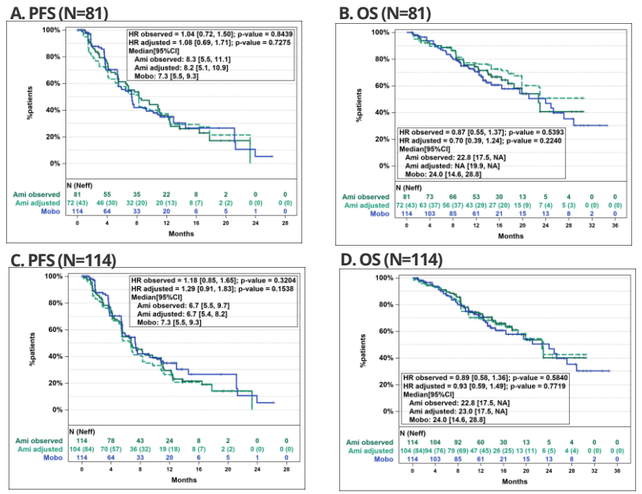
- Baseline characteristics of both studies are presented in **Table 1**. Matching was carried out on all variables, populations were comparable after matching
- Based on the adjusted comparisons in the primary efficacy population, Amivantamab provided a more favorable ORR-IRC in comparison with mobocertinib (RR, 1.44; 95% CI, [0.90,2.29] (**Table 2**). In the larger supportive population, the RR was statistically significant in favor of Amivantamab (1.55 [1.05,2.27])
- Both treatments had similar efficacy for all other outcomes in the primary and supportive efficacy population, including ORR-INV , CBR-IRC, CBR-INV, PFS, and OS (**Table 2** and **Figure 2**)

TABLE 2: Naïve and population-adjusted estimates of efficacy outcomes for Amivantamab (primary and supportive population) and mobocertinib

Outcome	N (ESS)	Ami	Mobo	Ami vs. Mobo	
		ORR	ORR	RR (95% CI)	*p* value
ORR-IRC					
Naïve (N=81)	81	43.2%	28.1%	1.54 [1.04,2.27]	0.029
Adjusted (N=81)	72* (43)	40.3%	28.1%	1.44 [0.90,2.29]	0.137
Naïve (N=114)	114	43.0%	28.1%	1.53 [1.06,2.20]	0.019
Adjusted (N=114)	104* (84)	43.4%	28.1%	1.55 [1.05,2.27]	0.026
ORR-INV					
Naïve (N=81)	81	38.3%	35.1%	1.09 [0.75,1.59]	0.649
Adjusted (N=81)	72* (43)	36.5%	35.1%	1.04 [0.65,1.66]	0.866
Naïve (N=114)	114	36.8%	35.1%	1.05 [0.74,1.49]	0.783
Adjusted (N=114)	104* (84)	35.8%	35.1%	1.02 [070,1.49]	0.921
CBR-IRC					
Naïve (N=81)	81	85.2%	78.1%	1.09 [0.95,1.25]	0.214
Adjusted (N=81)	72* (43)	76.9%	78.1%	0.98 [0.80,1.22]	0.883
Naïve (N=114)	114	84.2%	78.1%	1.08 [0.95,1.22]	0.238
Adjusted (N=114)	104* (84)	80.0%	78.1%	1.03 [0.88,1.19]	0.746
CBR-INV					
Naïve (N=81)	81	81.5%	78.1%	1.04 [0.90,1.20]	0.561
Adjusted (N=81)	72* (43)	79.1%	78.1%	1.01 [0.85,1.21]	0.882
Naïve (N=114)	114	83.3%	78.1%	1.07 [0.94,1.21]	0.315
Adjusted (N=114)	104* (84)	78.2%	78.1%	1.00 [0.86,1.17]	0.979

Ami, Amivantamab; CBR, clinical benefit rate; CI, confidence interval; ESS, effective sample size; INV, investigator; IRC, independent review committee; Mobo, mobocertinib; ORR, overall response rate; RR, risk ratio
*Before-matching sample size of patients with available data on all matching factors

FIGURE 2: Amivantamab vs. mobocertinib in the primary and supportive efficacy populations



Ami, Amivantamab; CI, confidence interval; HR, hazard ratio; Mobo, mobocertinib; NEff, effective sample size
Above the x-axis, the sample size is presented for all three groups (N). Additionally, the NEff is provided in parentheses at each timepoint for the adjusted Amivantamab population.

- Any grade TRAEs leading to dose reduction and grade 3+ treatment related, treatment-emergent, and serious AEs were significantly less frequent with Amivantamab. (**Table 3**)
- Additionally, 15 of the 23 all-grade TRAE reported for mobocertinib[3] occurred significantly less with Amivantamab: diarrhea (RR=0.12 [0.07,0.23]), decreased appetite (0.23 [0.11,0.49]), nausea (0.52 [0.31,0.88]), vomiting (0.24 [0.11,0.52]), dry skin (0.42 [0.42,0.73]), increased levels of creatinine (0.02 [0.00,0.12]), lipase (0.04 [0.01,0.30]), amylase (0.04 [0.01, 0.32]), anemia (0.40 [0.16,0.98]), weight decreased (0.16 [0.04, 0.66]), alopecia (0.05 [0.01,0.41]), gastro reflux disease (0.03 [0.00,0.25]), mouth ulceration (0.18 [0.05,0.68]), electrocardiogram QT prolonged (0.04 [0.00,0.30]), rhinorrhea (0.04 [0.00,0.30]). Dermatitis (2.55 [1.64,3.97]) and increased ALT (2.24 [1.05,4.77]) occurred significantly more with Amivantamab
- Sensitivity analyses from different data cuts with different duration of follow-up showed consistent results

TABLE 3: Naïve and population-adjusted safety outcomes for Amivantamab in the safety population and mobocertinib in the PPP population

Outcome	Probability			Ami vs. Mobo		
	Ami Observed	Ami Adjusted	Mobo	Naive RR (95% CI)	Adjusted RR (95% CI)	Adjusted *p* value
Any grade						
Any TRAE	98.0%	97.7%	99.1%	0.99 [0.96,1.02]	0.99 [0.95,1.02]	0.421
Serious AE	28.8%	36.4%	49.1%	0.59 [0.43,0.80]	0.74 [0.53,1.03]	0.066
AE leading to dose reduction	14.4%	13.4%	25.4%	0.57 [0.34,0.93]	0.53 [0.29,0.95]	0.030
AE leading to discontinuation	11.8%	18.5%	16.7%	0.71 [0.39,1.29]	1.11 [0.60,2.04]	0.740
Grade ≥3						
Any TEAE	41.8%	49.6%	69.3%	0.60 [0.48,0.76]	0.72 [0.57,0.91]	0.004
Any TRAE	19.6%	20.7%	47.4%	0.41 [0.28,0.60]	0.44 [0.28,0.68]	<0.001
Serious AE	20.9%	28.0%	45.6%	0.46 [0.32,0.66]	0.61 [0.42,0.91]	0.011

AE, adverse event; Ami, Amivantamab; CI, confidence interval; Mobo, mobocertinib; RR, risk ratio; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event

Presented at ISPOR US; May 15-18, 2022; Washington, D.C., US.

DISCUSSION

- Relative efficacy and safety of Amivantamab vs. mobocertinib were assessed in both the primary (n=81) and supportive (n=114) efficacy populations for Amivantamab. After matching, Amivantamab was found to have a higher ORR versus mobocertinib, and the results for other efficacy endpoints were similar
- Amivantamab also had a significant favorable safety profile vs. mobocertinib for most all grade TRAE outcomes (15 of the 23) and was associated with a significantly lower risk of any grade TRAEs leading to dose reduction, grade ≥3 TEAEs, grade ≥3 TRAEs, and grade ≥3 SAEs
- The exposure time to treatment differed in the comparison of safety outcomes. Although the CHRYSALIS safety population provided shorter median follow-up vs. the PPP cohort, the comparative safety results for the CHRYSALIS primary efficacy population (median follow-up=14.5 months) vs. PPP cohort (median follow-up=14.2 months) were similar

Limitations

- The MAIC method cannot adjust for trial design differences that may affect the study outcomes, such as the timing of tumor assessments
  - The schedule of disease assessments differed between the two trials, which may result in assessment time bias for unanchored comparisons of PFS. In CHRYSALIS, progression-free status was assessed every six weeks. Conversely, in NCT02716116, disease assessments were conducted every eight weeks for the first 56 weeks, and every 12 weeks thereafter
- As in any non-randomized comparison, residual confounding cannot be excluded. However, commonly available baseline characteristics allowed to adjust for the most important clinical prognostic factors, which minimized the risk of biased comparisons to the extent possible

CONCLUSIONS

- Higher ORRs (IRC-assessed) were observed in Amivantamab and results on other efficacy endpoints were similar
- Amivantamab offers a better safety profile in comparison with mobocertinib in EGFR Exon20ins NSCLC

ACKNOWLEDGMENTS

Writing and editorial assistance was provided by Brooke Middlebrook, CMPP of Evidera, Inc. and funded by Janssen

DISCLOSURES

CC and VK are employees of Evidera, Inc., which received funding from Janssen

Scan the QR code for the full digital presentation

https://www.congresshub.com/Oncology/ISPOR2022/Amivantamab/Li