

# Indirect comparison of tarlatamab vs chemotherapy for previously treated platinum-refractory or resistant extensive stage small cell lung cancer

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## INTRODUCTION

- Extensive-stage small cell lung cancer (ES-SCLC) is an aggressive cancer that has poor survival and limited treatment options, particularly for patients with relapsed disease
- Treatment options for relapsed ES-SCLC can be guided by platinum-sensitivity status
- Clinical guidelines differ in terms of the threshold used to define platinum-resistant or refractory disease, with the European Society for Medical Oncology (ESMO) defining it as progression within 90 days of the last dose of first-line treatment (chemotherapy-free interval [CFI] <90 days) and the German S3 guideline defining it as CFI <180 days
- Tarlatamab is a new treatment option for SCLC that was recently shown to provide clinically meaningful improvements in overall survival (OS; hazard ratio [HR] with a 95% confidence interval [95% CI]: 0.60 [0.47, 0.77]) and progression-free survival (PFS; HR [95% CI]: 0.71 [0.59, 0.86]) relative to chemotherapy (topotecan, lurbinectedin, or amrubicin) for patients with relapsed ES-SCLC in the Ph3 DeLLphi-304 trial (NCT05740566)<sup>1</sup>
- While paclitaxel and cyclophosphamide/doxorubicin/vincristine (CAV) are treatment options for platinum-refractory or resistant ES-SCLC, there is a lack of head-to-head data comparing these treatments to tarlatamab

## OBJECTIVES

- To estimate the relative effect of tarlatamab vs. paclitaxel and CAV in terms of OS and PFS among patients with platinum-refractory/resistant ES-SCLC (defined as CFI <180 days and CFI <90 days for the paclitaxel and CAV comparisons, respectively)

## METHODS

- Unanchored matching adjusted indirect comparisons (MAIC) were conducted following methodology guidance from the National Institute for Health and Care Excellence (NICE)<sup>2</sup>
- The analyses leveraged individual patient-level data (IPD) for tarlatamab (DeLLphi-304) and published aggregate-level data for paclitaxel (Owonikoko 2020, NCT02038647)<sup>3</sup> and for CAV (GFPC 0501, NCT00418743)<sup>4</sup>
- IPD from DeLLphi-304 were restricted to align with key eligibility criteria of Owonikoko 2020 (CFI <180 days & ECOG PS <2) and GFPC 0501 (CFI <90 days)
- Key prognostic factors and effect modifiers reported in DeLLphi-304 and in the comparator trials were controlled for in the MAIC, including age, sex, smoking, time since initial diagnosis, ECOG PS, disease stage at initial diagnosis, brain metastases, and CFI (data availability permitting)
- HRs for OS and PFS were estimated using a weighted Cox proportional hazards model with robust variance estimation for the 95% confidence intervals (CIs)
- E-values were estimated to assess the robustness of the results to potential unmeasured or residual confounding
- Sensitivity analyses were conducted to explore the impact of alternative covariate selection (i.e., excluding balanced covariates and disease-stage at diagnosis) and different adjustment methods (i.e., controlling for mean and standard deviation of continuous variables vs. mean only)

**Table 1. Baseline characteristics before MAIC weighting**

Baseline characteristics	Tarlatamab (DeLLphi-304)		Paclitaxel (Owonikoko 2020)	CAV (GFPC 0501)
	CFI <180 & ECOG <2 N = 188	CFI <90 N = 108	N = 89	N = 66 <sup>a</sup>
Age, mean (SD)	64 (9.9)	62.7 (10.4)	62 (8.1)	60.6 (8.7)
Male, n (%)	137 (72.9)	82 (75.9)	50 (56.2)	50 (75.8)
Current smoker, n (%)	38 (20.2)	22 (20.4)	29 (33.0)	NR
Former smoker, n (%)	134 (71.3)	74 (68.5)	52 (59.1)	NR
Months since diagnosis, mean (SD)	8.3 (4.0)	7.4 (4.7)	7.8 (4.6)	NR
ECOG PS 1, n (%)	129 (68.6)	79 (73.1)	71 (79.8)	33 (50.0)
ECOG PS 2, n (%)	0 (0.0)	1 (0.9)	0 (0.0)	10 (15.2)
Extensive stage <sup>b</sup> , n (%)	143 (76.1)	86 (79.6)	62 (88.6)	39 (59.1)
Brain metastases	87 (46.3)	49 (45.4)	26 (29.2)	NR
CFI < 90, n (%)	105 (55.9)	108 (100.0)	49 (58.3)	66 (100.0)

**Abbreviations:** CAV, cyclophosphamide, doxorubicin, and vincristine; CFI, chemotherapy-free interval; ECOG PS, Eastern Cooperative Oncology Group Performance Score; NR, not reported; SD, standard deviation; **Footnotes:** a) Smoking, time since diagnosis and brain metastases were not reported in GFPC 0501, and therefore, these variables were not adjusted in the MAIC analysis; b) In the DeLLphi-304 trial, extensive vs limited stage disease at initial diagnosis was approximated using the AJCC TNM information; GFPC 0501 reported the number of patients who did not have localized disease at diagnosis

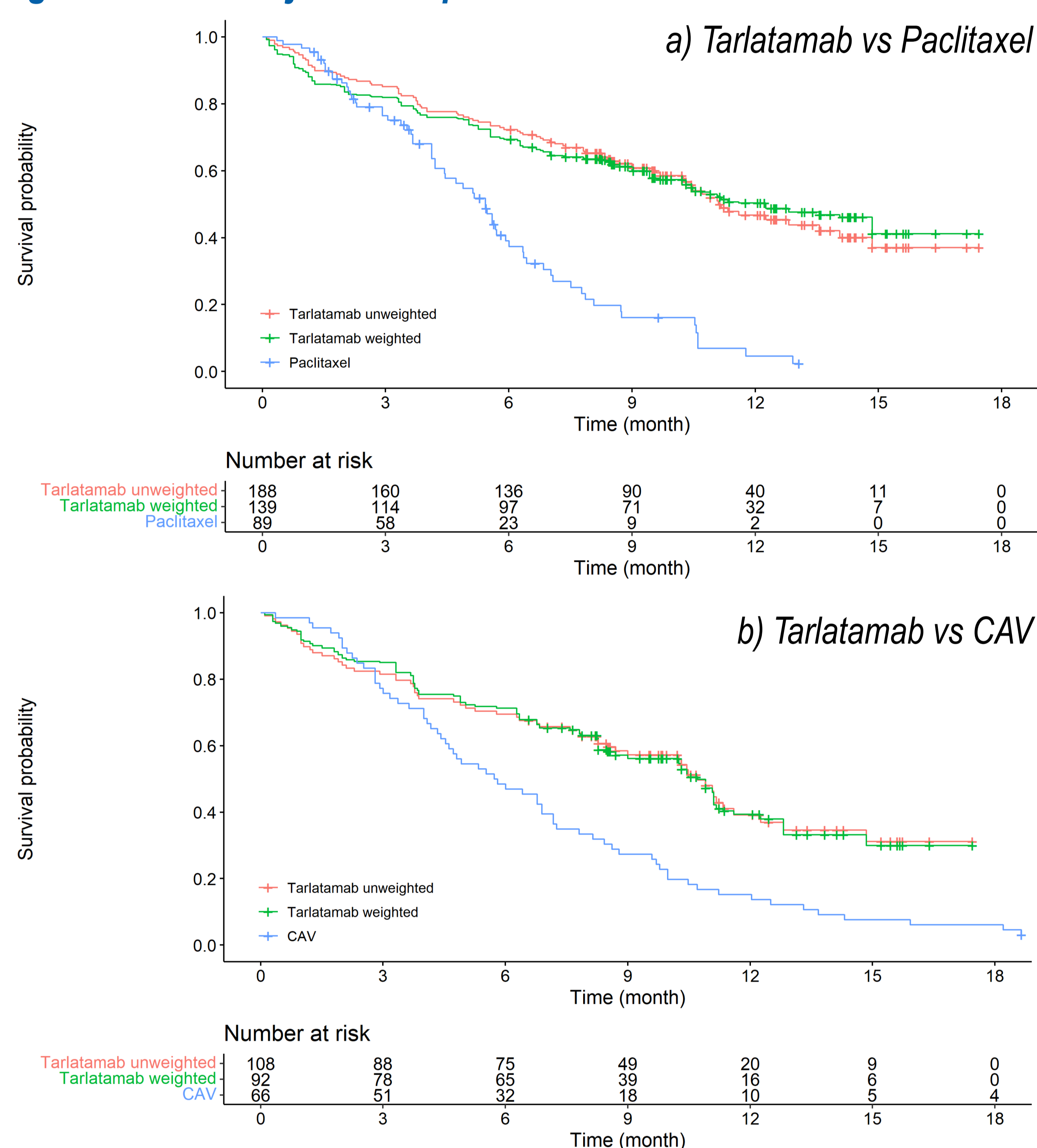
## REFERENCES

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## RESULTS

- After MAIC weighting, the baseline characteristics from DeLLphi-304 and the comparator trials were well balanced (data not shown)
- Tarlatamab was associated with significantly improved OS compared to paclitaxel (HR [95%CI]: 0.35 [0.23, 0.52]) and to CAV (0.48 [0.32, 0.70]) (table 2; figure 1)
- PFS was also significantly higher for tarlatamab compared to paclitaxel (HR [95%CI]: 0.59 [0.44, 0.78]) but was comparable to CAV (0.89 [0.63, 1.26]; table 2)
- The observed E-values (>2) indicated that the results were robust to unmeasured or residual confounding (table 2)
- The HRs and 95% CIs from the sensitivity analyses were not meaningfully different from those of the primary analyses (data not shown)

**Figure 1. MAIC-adjusted Kaplan-Meier curves for OS**



**Table 2. Results from MAIC analyses for OS and PFS**

Outcome	Treatment	ESS	Median Survival, Months (95% CI)	Hazard Ratio (95% CI)	P-value	E-value
<b>Tarlatamab vs paclitaxel (CFI &lt;180 days)</b>						
OS	Tarlatamab	109.9	12.26 (9.43, NE)	0.35 (0.23, 0.52)	<0.001	3.55
	Paclitaxel	89	5.42 (NR)	Reference	-	-
PFS	Tarlatamab	109.9	3.02 (2.83, 4.27)	0.59 (0.44, 0.78)	<0.001	2.25
	Paclitaxel	89	2.17 (NR)	Reference	-	-
<b>Tarlatamab vs CAV (CFI &lt;90 days)</b>						
OS	Tarlatamab	78.4	10.71 (8.28, 12.81)	0.48 (0.32, 0.70)	<0.001	2.73
	CAV	66	5.8 (NR)	Reference	-	-
PFS	Tarlatamab	78.4	2.92 (1.68, 4.17)	0.89 (0.63, 1.26)	0.502	1.39
	CAV	66	3.1 (NR)	Reference	-	-

**Abbreviations:** CAV, cyclophosphamide, doxorubicin, and vincristine; CFI, chemotherapy-free interval; CI, confidence interval; ESS, effective sample size; MAIC, matching adjusted indirect comparison; NE, not estimable; NR, not reported; OS, overall survival; PFS, progression-free survival

## CONCLUSIONS

- Tarlatamab offers significant survival benefit relative to paclitaxel and CAV in patients with platinum-refractory or resistant ES-SCLC
- These findings complement the results of the DeLLphi-304 trial and further support tarlatamab as the second-line standard-of-care treatment for patients with relapsed ES-SCLC

## DISCLOSURES

Umit Tapan reports personal fees for consulting from Amgen. Franziska Dirnberger, Sachin Patel, Jessie Wang, Seoyoon Cho, Ian Bridges, and Lucy DeCosta are employees of Amgen Inc. and hold stock/options. Devon Boyne, Tommy Lan, and Jenny Uyei are employees of IQVIA Inc. which received funding from Amgen Inc. for the conduct of this study.