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POD1UM-304: Phase 3 Study of Retifanlimab Plus Platinum-Based Chemotherapy as First-Line Therapy for Nonsquamous or Squamous Metastatic Non–Small Cell Lung Cancer

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Abstract #1094

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DECLARATION OF INTERESTS

- **Shun Lu** has received research support from AstraZeneca, BeiGene, Hansoh Pharma, Jiangsu Hengrui Pharmaceuticals, Hutchison MediPharma and Roche; received speaker fees from AstraZeneca, Hansoh Pharma, Jiangsu Hengrui Therapeutics and Roche; has been on an advisory board or been a consultant for AstraZeneca, Boehringer Ingelheim, GenomiCare, Hutchison MediPharma, InventisBio, Menarini, Pfizer, Roche, Yuhan Corporation and Zai Lab; been on an advisory board for Phanes Therapeutics, Shanghai Fosun Pharmaceutical and Simcere Zaiming Pharmaceutical; and been a director/board member for Innovent Bio
- This study was funded by Incyte Corporation (Wilmington, DE, USA)

Background

- Lung cancer is the leading cause of cancer mortality globally, with 1.8 million deaths in 2022[1]; the majority (85%) have NSCLC histology[2]
- Immunotherapy is a major advance in the treatment of 1L NSCLC, but access is not universal[3]
- Retifanlimab is an anti–PD-1 humanised, hinge-stabilised, IgG4k monoclonal antibody approved in the United States and European Union for Merkel cell carcinoma[4-7]
  - Retifanlimab is active in NSCLC, with representative safety for the class[8-11]
- POD1UM-304 is a phase 3, multiregional, placebo-controlled, double-blind randomised trial designed to evaluate retifanlimab in combination with platinum-based chemotherapy in patients with metastatic squamous or non-squamous NSCLC

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4. Chen X, et al. *Cancer Res*. 2019;79(13 suppl):LB-268. **5.** Condamine T, et al. *Cancer Res*. 2019;79(13 suppl):CT085. **6.** Lakhani N, et al. *J Immunother Cancer*. 2017;5:P249.
7. Mehnert, JM, et al. *J Immunother Cancer*. 2018;6:P669. **8.** Di Giacomo AM, et al. *ESMO Open*. 2024;9:102387. **9.** Lakhani N, et al. *ESMO Open*. 2024;9:102254.
10. Rao S, et al. *ESMO Open*. 2022;7:100529. **11.** Rao S, et al. *Front Oncol*. 2022;12:935383.
1L, first-line; IgG4, immunoglobulin G4; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1.

POD1UM-304 Study Design

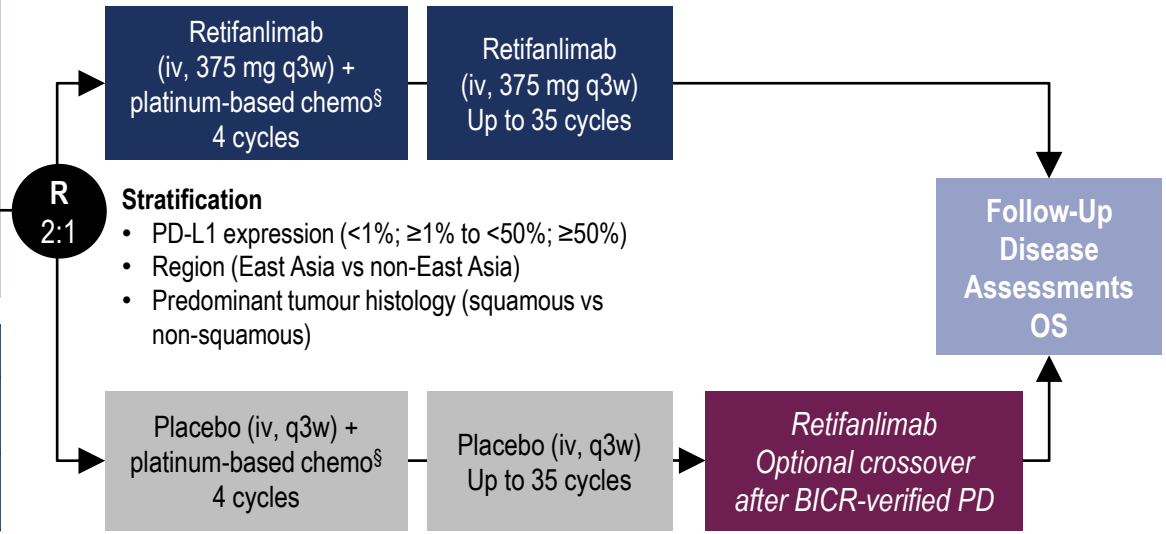
(NCT04205812; EudraCT 2019-003372-39; EU CT# 2022-501987-16-00)

- Enrolment took place from 11 September 2020 to 14 March 2023
- The primary OS analysis was event driven and data cutoff was December 15, 2023

Adult patients with non-squamous or squamous metastatic NSCLC, stage IV

- No prior systemic treatment for advanced disease*
- ECOG PS 0 or 1
- No sensitising driver mutations or rearrangements of *EGFR*, *ALK*, *BRAF* or *ROS1*
- **Planned enrolment: N≈600†**

Study Endpoints‡	
Primary	OS (HR=0.7 at 87% power, 2.5% significance [1-sided])
Secondary	PFS by BICR (HR=0.63 at 90% power, alpha=0.025 [1-sided]), ORR, DOR, safety



*Patients who received (neo)adjuvant therapy that did not include a PD-L1–directed therapy that was completed ≥12 months before diagnosis of metastatic disease were allowed to participate. †<40% squamous NSCLC, representative of disease prevalence while providing adequate population from both disease groups. ‡One interim analysis planned for OS once 60% of events have occurred. §Platinum-based chemo based on tumour histology: non-squamous NSCLC, carboplatin/cisplatin (4 cycles) with pemetrexed until disease progression; squamous NSCLC, carboplatin + paclitaxel/nab-paclitaxel (4 cycles) only.

ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; BRAF, B-Raf proto-oncogene, serine/threonine kinase; chemo, chemotherapy; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; HR, hazard ratio; iv, intravenous; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; q3w, every 3 weeks; R, randomisation; ROS1, receptor tyrosine kinase (encoded by the gene *ROS1*).

Patient Demographics and Characteristics (ITT Population)

Characteristic	Retifanlimab + Chemotherapy (n=391)	Placebo + Chemotherapy (n=192)
Median age (range), years	63.0 (29, 84)	64.0 (36, 84)
Male/female, %	81/19	78/22
White/Asian/other, %	67/32/1	66/32/2
Smoker, %	80	75
East Asia/other, %*,†	32/68	32/68
ECOG PS 0/1, %	26/74	27/73
Squamous/non-squamous, %*	34/66	36/64
Symptomatic brain metastases, %	3	3
Stage IVA/IVB, %	55/45	52/48
PD-L1 TPS, %*,‡		
<1%	27	28
≥1% to <50%	40	40
≥50%	33	33

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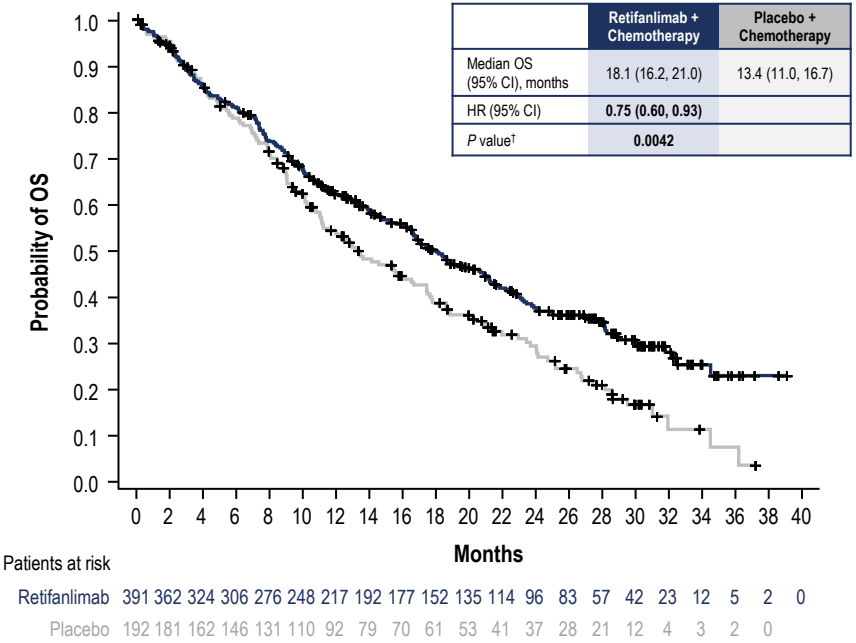
*Stratification factor. †Other includes Black (placebo, n=3; retifanlimab n=3). ‡PD-L1 expression <1% capped at <30% of the total N.
ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intention-to-treat; PD-L1, programmed cell death ligand 1; TPS, tumour proportion score.

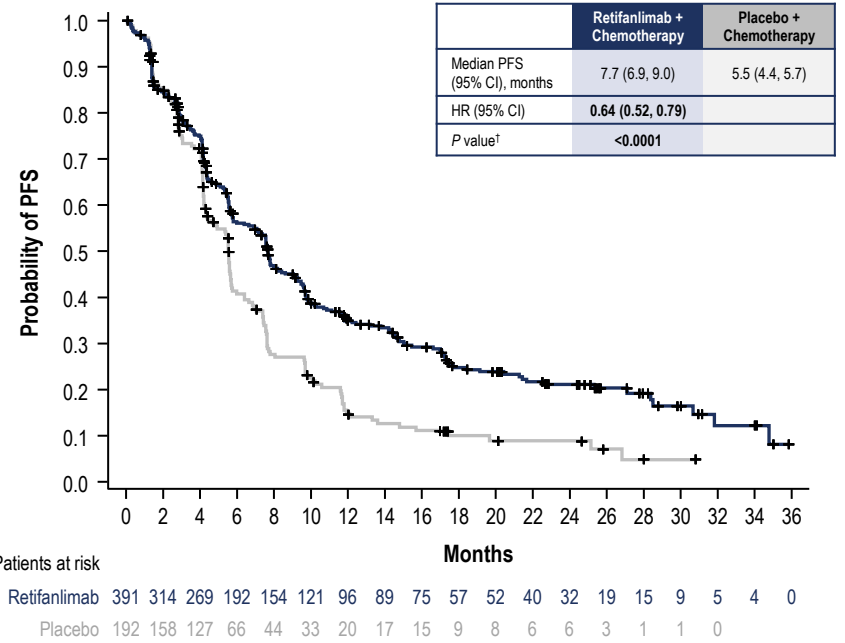
Overall Survival (Primary Endpoint) and Progression-Free Survival by BICR

Overall Survival*



	Retifanlimab + Chemotherapy	Placebo + Chemotherapy
Median OS (95% CI), months	18.1 (16.2, 21.0)	13.4 (11.0, 16.7)
HR (95% CI)	**0.75 (0.60, 0.93)**	
P value†	**0.0042**	

Progression-Free Survival*



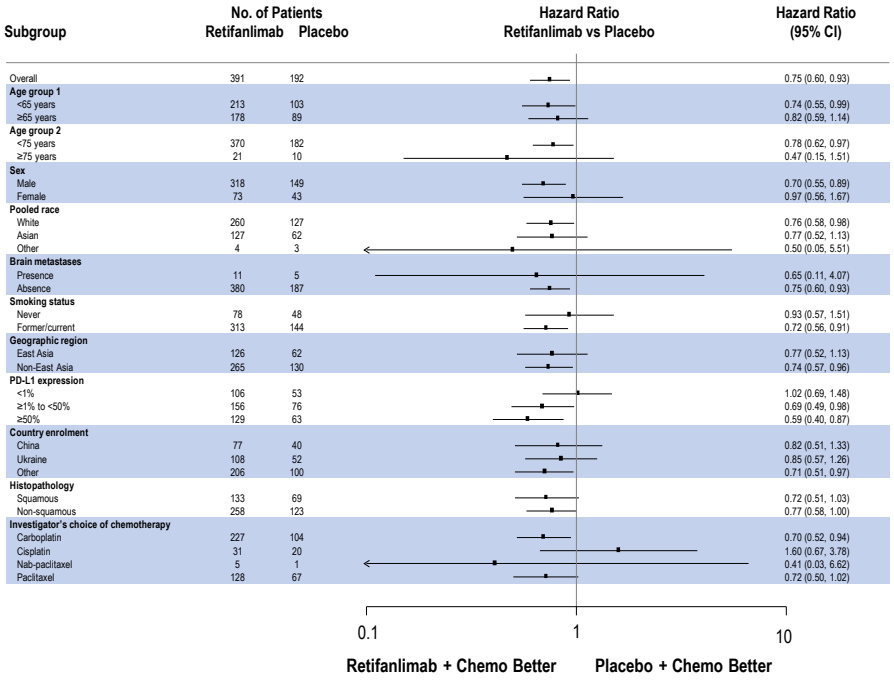
	Retifanlimab + Chemotherapy	Placebo + Chemotherapy
Median PFS (95% CI), months	7.7 (6.9, 9.0)	5.5 (4.4, 5.7)
HR (95% CI)	**0.64 (0.52, 0.79)**	
P value†	**<0.0001**	

*FAS population. †Stratified log rank test with a 1-sided significance level of 2.5%. Stratification factors: PD-L1 expression status (<1%, ≥1% to <50%, ≥50%), geographic region (East Asia vs non-East Asia) and predominant tumour histology (squamous vs non-squamous).

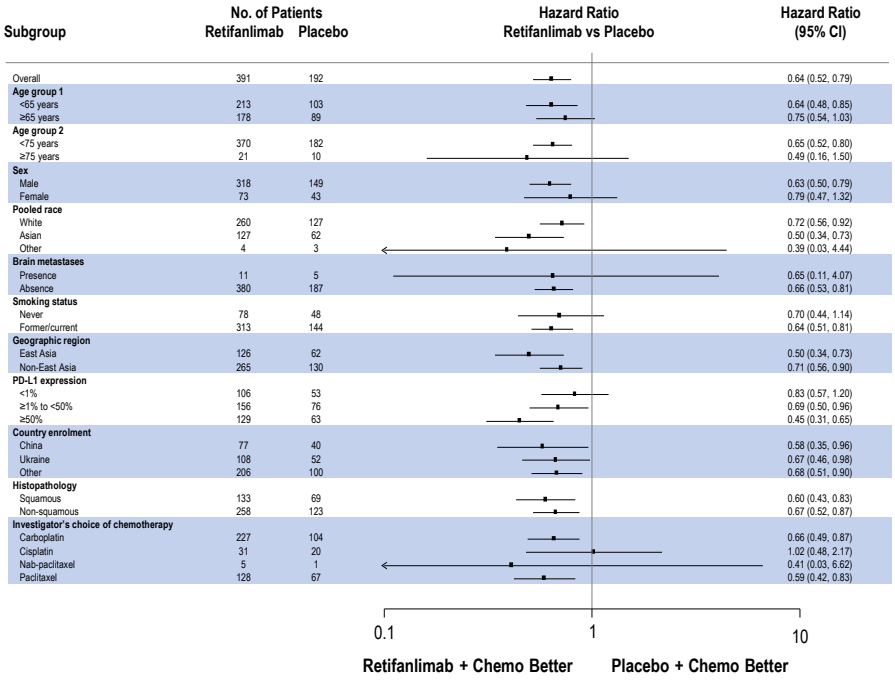
BICR, blinded independent central review; CI, confidence interval; FAS, full analysis set; HR, hazard ratio; OS, overall survival; PD-L1, programmed cell death ligand 1; PFS, progression-free survival.

Overall Survival and Progression-Free Survival (Subgroup Analyses)

Overall Survival*



Progression-Free Survival*



*FAS population; not adjusted for crossover effect.
Chemo, chemotherapy; CI, confidence interval; FAS, full analysis set; PD-L1, programmed cell death ligand 1.

Tumour Response and Durability*

	Retifanlimab + Chemotherapy (n=391)	Placebo + Chemotherapy (n=192)
ORR (95% CI), %	52 (47, 57) ***P*=0.0012**	39 (32, 46)
CR	3	2
PR	49	37
SD	26	39
PD	10	13
DCR	78	78
Median DOR (95% CI), months	12.7 (9.4, 15.2)	6.1 (4.2, 8.3)

*FAS population; results by BICR.

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; FAS, full analysis set; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Summary of Safety (All TEAEs)*

Variable	Retifanlimab + Chemotherapy (n=389)	Placebo + Chemotherapy (n=190)
Patients with any TEAEs	369 (94.9)	183 (96.3)
Patients with treatment-related TEAEs	225 (57.8)	102 (53.7)
Patients with serious TEAEs	158 (40.6)	57 (30.0)
Patients with grade ≥3 TEAEs	238 (61.2)	103 (54.2)
Patients with fatal TEAEs	40 (10.3)	20 (10.5)
Treatment discontinuation due to TEAEs	33 (8.5)	9 (4.7)
Chemotherapy discontinuation due to TEAEs	47 (12.1)	19 (10.0)
COVID-19–related TEAEs†	47 (12.1)	18 (9.5)
Serious	15 (3.9)	8 (4.2)
Fatal	4 (1.0)	5 (2.6)

- No increase in serious or fatal COVID-19–related TEAEs was observed with the addition of retifanlimab

*Safety population. †COVID-19–related TEAEs includes: COVID-19, COVID-19 pneumonia, post-acute COVID-19 syndrome and suspected COVID-19.
COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.

Conclusions

- Retifanlimab improved survival and all secondary measures of efficacy when added to platinum-based chemotherapy for 1L previously untreated metastatic NSCLC
- Magnitude of benefit is comparable with that of the approved PD-(L)1 inhibitors and includes both squamous and non-squamous histologies
- Safety is acceptable and manageable with standard guidelines; no unique safety issues were identified
  - Chemotherapy delivery was not compromised by the addition of retifanlimab
  - Despite an ongoing pandemic, COVID-19–related deaths were uncommon and were not increased by the addition of retifanlimab
- Based on the favourable benefit-risk profile demonstrated in POD1UM-304, retifanlimab in combination with platinum-based chemotherapy is another potential option for treatment of metastatic NSCLC

1L, first-line; COVID-19, coronavirus disease 2019; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

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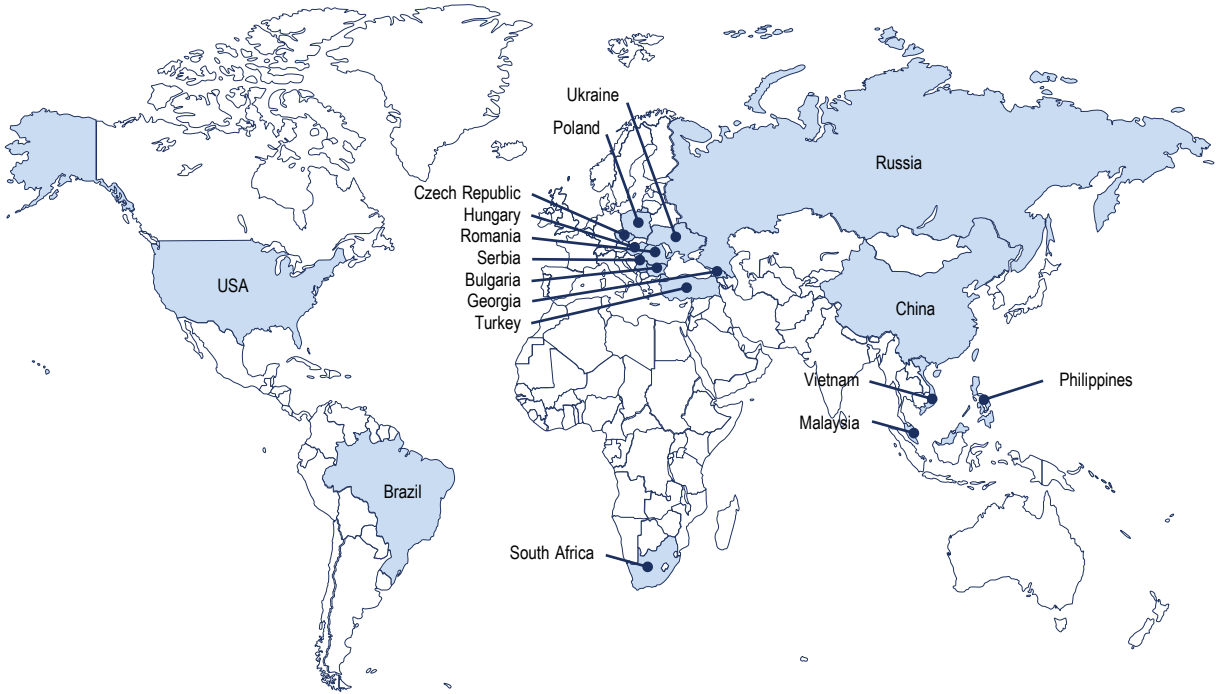

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