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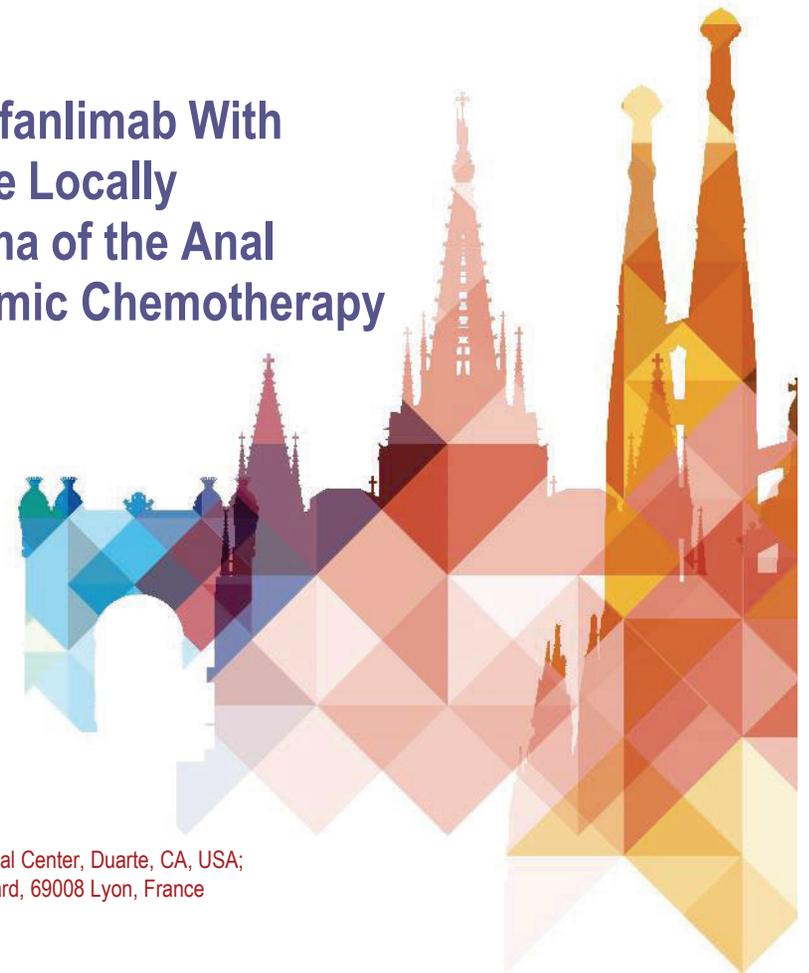
POD1UM-303/InterAACT 2: Phase 3 Study of Retifanlimab With Carboplatin-Paclitaxel in Patients With Inoperable Locally Recurrent or Metastatic Squamous Cell Carcinoma of the Anal Canal (SCAC) Not Previously Treated With Systemic Chemotherapy

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Abstract #5348



DECLARATION OF INTERESTS

- **S Rao** has served as an advisory for AstraZeneca, Bayer, BeiGene, Hookipa, Merck Serono, Seagen, and Servier; been an invited speaker for Bayer, Merck Serono, and Servier; received travel grants from Servier; and has provided expert testimony for Boehringer Ingelheim
- This study was sponsored by Incyte Corporation (Wilmington, DE, USA)

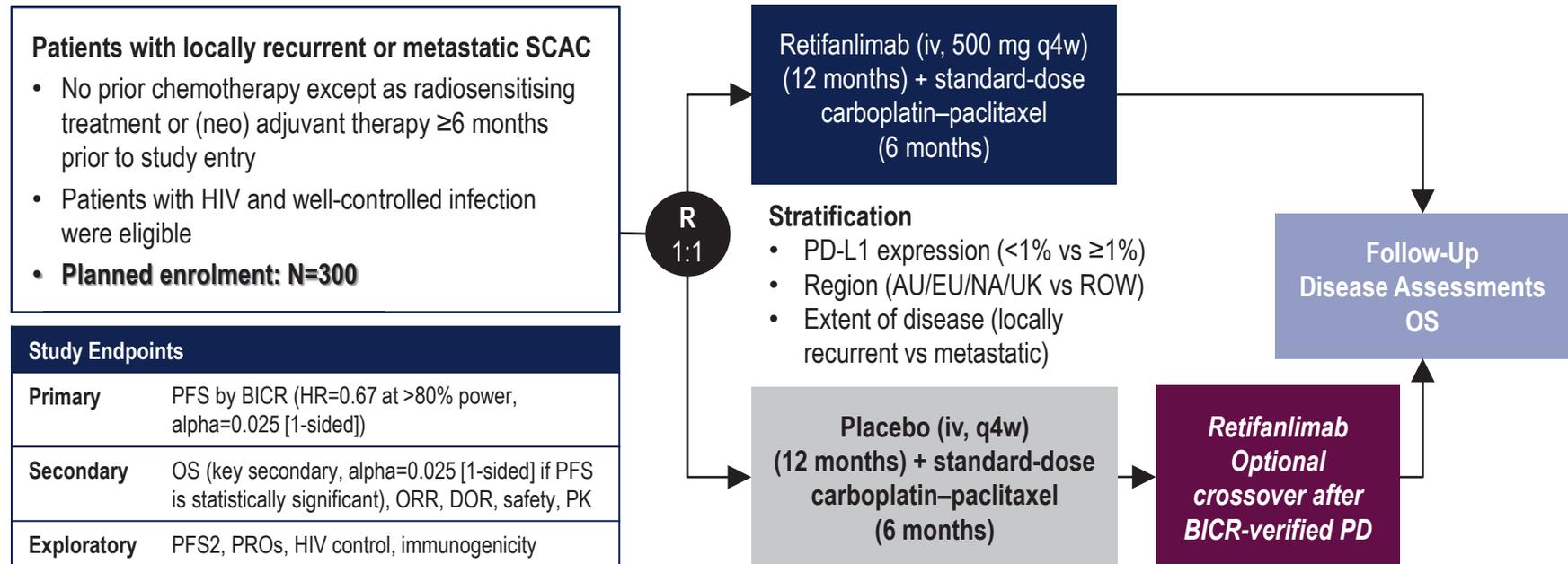
Background

- SCAC is a neglected orphan disease; incidence is increasing ~3% per year mainly due to endemic HPV, the causative agent for most anogenital cancers¹⁻⁴
 - HIV is an important amplifier of SCAC; people with HIV are 25- to 35-fold more likely to develop SCAC^{5,6}
- Relapse after primary therapy (chemo-radiotherapy) is common; standard of care treatment has not changed since the early 1980s⁷
 - Prognosis is poor for patients who relapse or with de novo metastatic disease, and quality of life is greatly diminished⁸
- The InterAACT phase 2 study established carboplatin–paclitaxel as 1L treatment. Responses were meaningful and durable, but overall PFS (8 months) and OS (20 months) remained short⁹
- HPV-driven malignancy is an attractive target for immunotherapy approaches
 - Improved survival in head and neck squamous cell carcinoma¹⁰ and cervical cancer¹¹ serve as proof of concept for SCAC
- Retifanlimab, a humanised anti–PD-1 monoclonal antibody, showed anti-tumour activity in platinum-refractory SCAC in the phase 2 POD1UM-202 study¹²
- The phase 3 POD1UM-303/InterAACT 2 study was designed to evaluate retifanlimab in combination with standard of care chemotherapy in patients with locally advanced or metastatic SCAC not previously treated with systemic therapy

1. Gondal TA, et al. *Curr Oncol*. 2023;30:3232-3250. 2. Islami F, et al. *Int J Epidemiol*. 2017;46:924-938. 3. Giuliano AR, et al. *Int J Cancer*. 2015;136:2752-2760. 4. Morris V, Eng C. *J Gastrointest Oncol*. 2016;7:721-726. 5. Wang C-CJ, et al. *Surg Oncol Clin N Am*. 2017;26:17-31. 6. NCCN Clinical Practice Guidelines in Oncology: Cancer in People with HIV. Version 1.2021. 2021. 7. Pessia B, et al. *Ann Med Surg (Lond)*. 2020;55:36-46. 8. Rao S, et al. *Ann Oncol*. 2021;32:1087-1100. 9. Rao S, et al. *J Clin Oncol*. 2020;38:2510-2518. 10. Ferris RL, et al. *N Engl J Med*. 2016;375:1856-1867. 11. Colombo N, et al. *N Engl J Med*. 2021;385:1856-1867. 12. Rao S, et al. *ESMO Open*. 2022;7:100529.

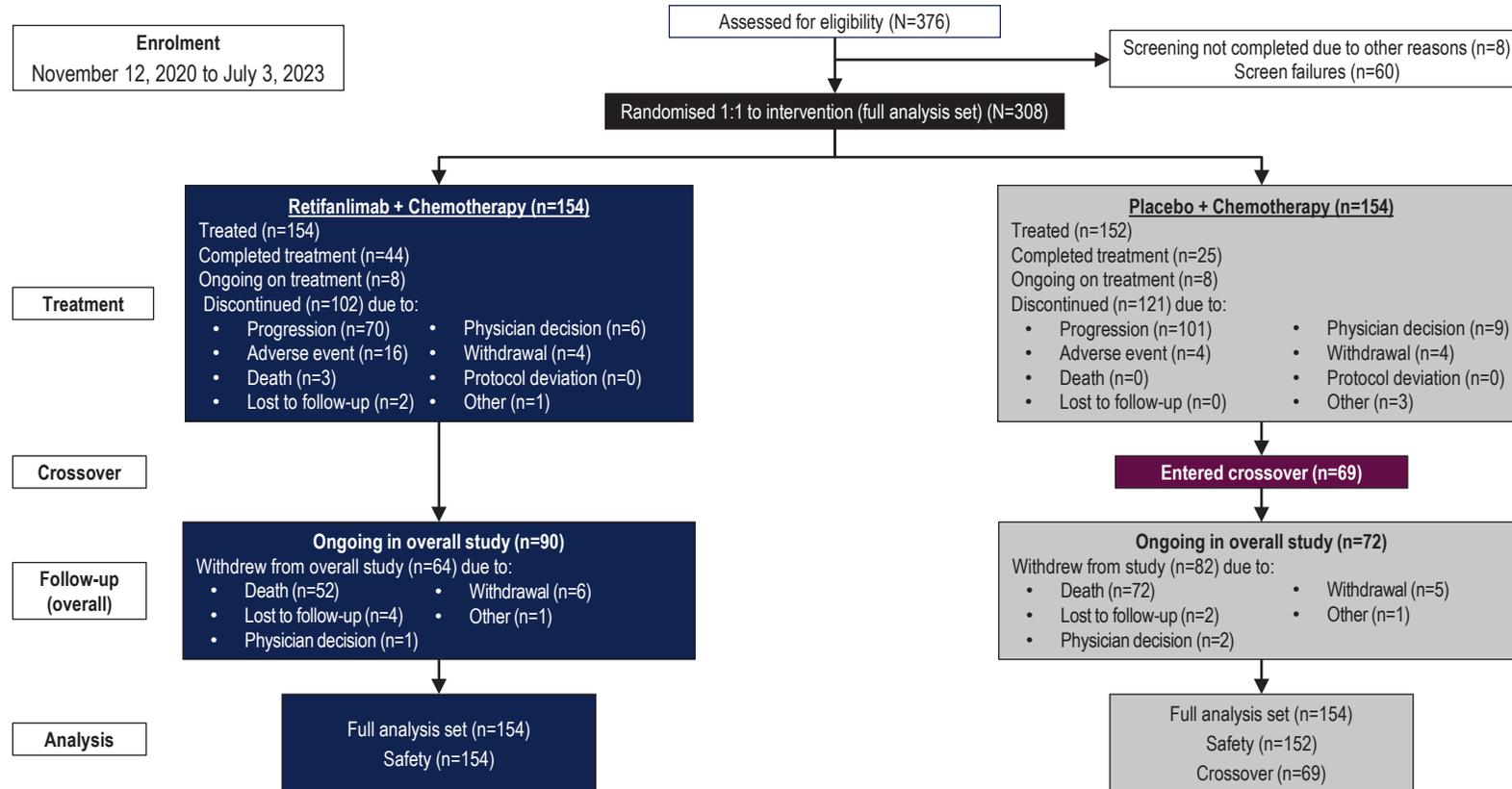
1L, first-line; HIV, human immunodeficiency virus; HPV, human papillomavirus; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; SCAC, squamous cancer of the anal canal.

POD1UM-303/InterAACT 2 Study Design



Standard-dose carboplatin–paclitaxel: carboplatin AUC5 iv: day 1. Paclitaxel 80 mg/m² iv: days 1, 8 and 15. Each cycle = 28 days. 6 months/24 weeks (6 cycles).
 AU, Australia; AUC, area under the curve; BICR, blinded independent central review; DOR, duration of response; EU, European Union; HIV, human immunodeficiency virus; HR, hazard ratio; iv, intravenous; NA, North America; ORR, overall response rate; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; PK, pharmacokinetics; PRO, patient-reported outcome; q4w, every 4 weeks; R, randomisation; ROW, rest of the world; SCAC, squamous cancer of the anal canal; UK, United Kingdom.

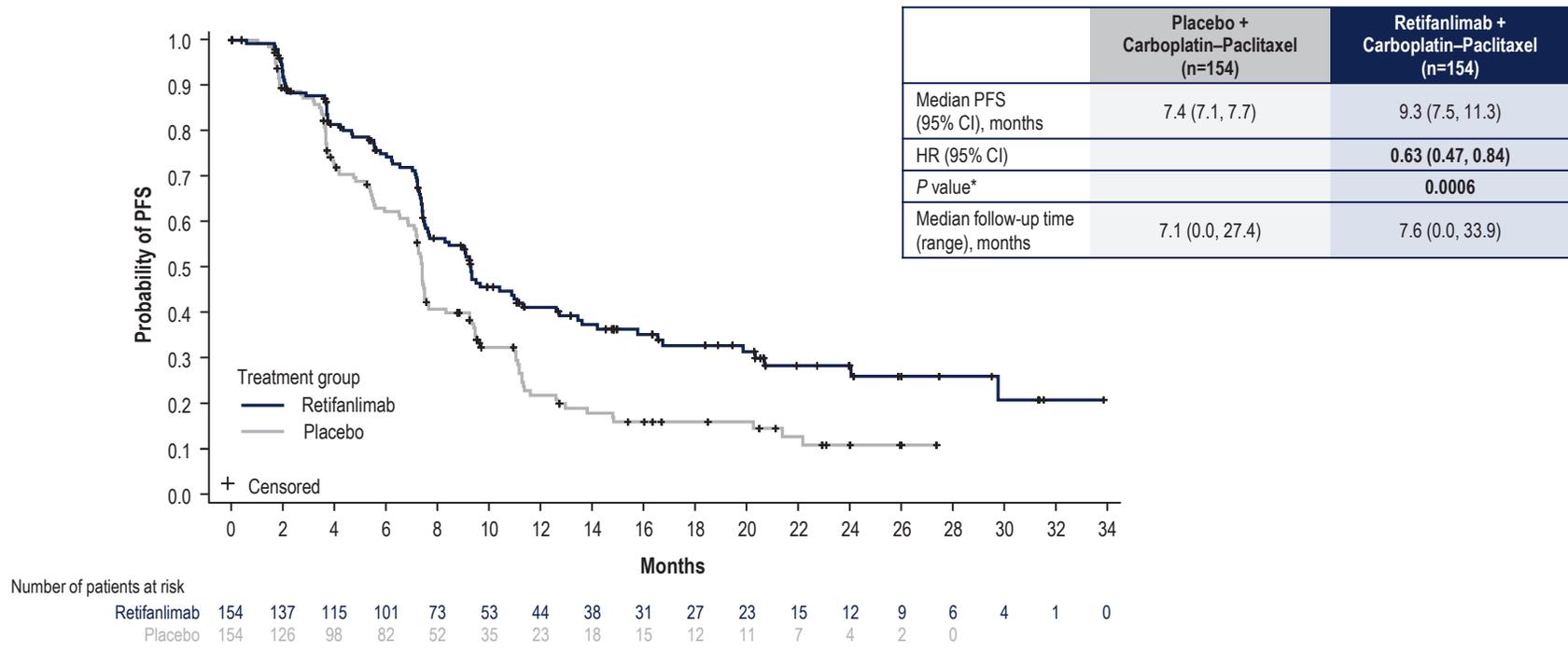
Patient Flow



Patient Demographics and Characteristics (ITT Population)

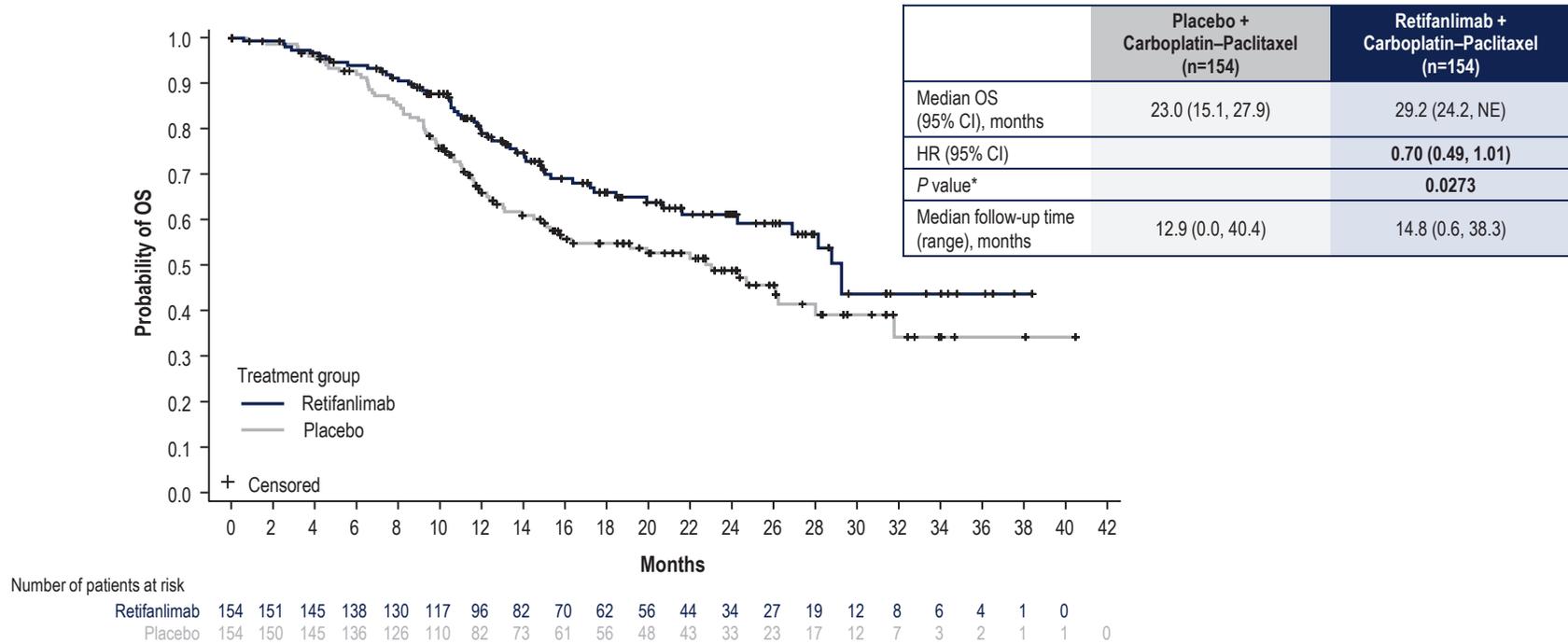
Characteristic	Placebo + Carboplatin–Paclitaxel (n=154)	Retifanlimab + Carboplatin–Paclitaxel (n=154)
Median age, years	61	62
Female, %	77	68
White, %	89	86
Prior RT, %	73	68
Metastatic disease, %*	83	82
Liver, %	36	36
ECOG PS 0, %	56	53
HIV+, %	3	4
PD-L1 expression status ≥ 1, %*,†	91	90

PFS by BICR (Primary Endpoint)



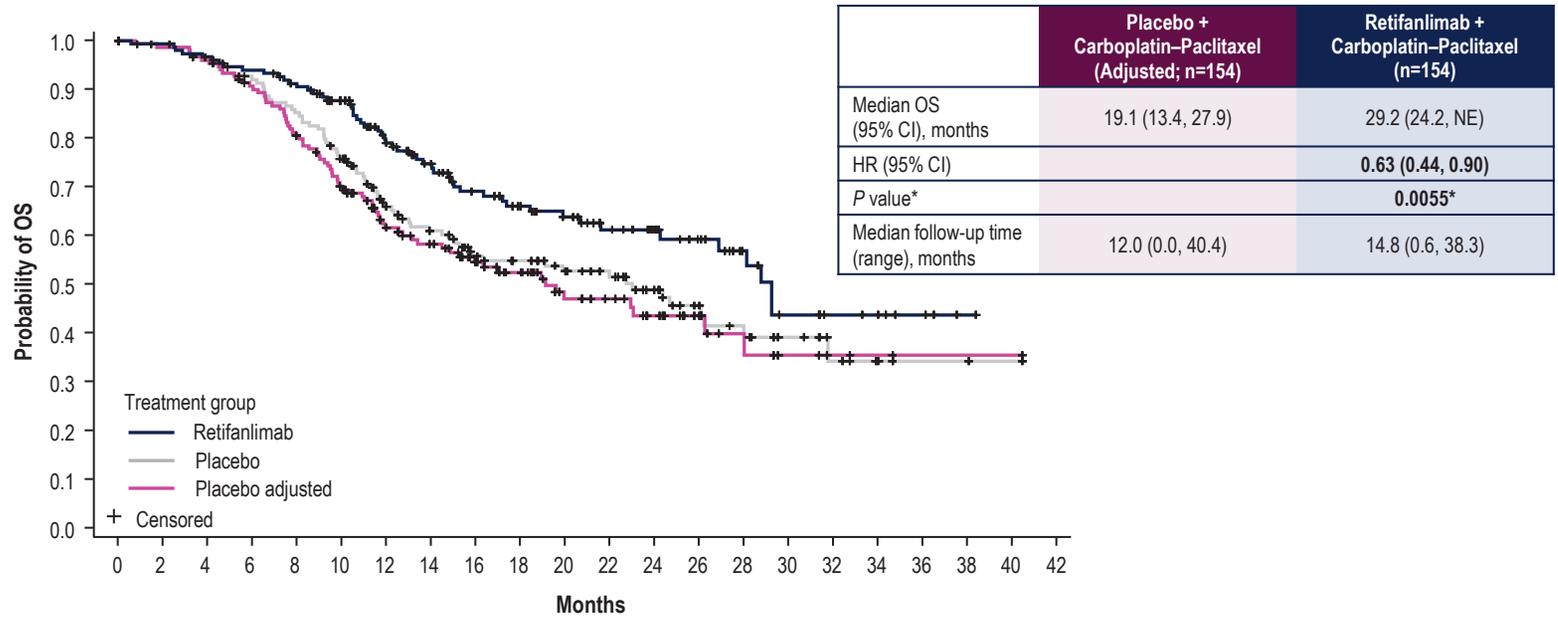
*Stratified log-rank test with a 1-sided significance level of 2.5%. Stratification factors: region of the world, extent of disease and PD-L1 expression status. BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; PD-L1, programmed cell death ligand 1; PFS, progression-free survival.

OS (Interim Analysis)



*Stratified log-rank test with a 1-sided significance level of 1.2% at this interim look. Stratification factors: region of the world, extent of disease and PD-L1 expression status. CI, confidence interval; HR, hazard ratio; NE, not estimable; PD-L1, programmed cell death ligand 1; OS, overall survival.

OS Adjusted for Crossover



Number of patients at risk

	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42
Retifanlimab	154	151	145	138	130	117	96	82	70	62	56	44	34	27	19	12	8	6	4	1	0	
Placebo	154	150	145	136	126	110	82	73	61	56	48	43	33	23	17	12	7	3	2	1	1	0
Placebo adjusted	154	150	145	133	117	99	76	67	54	45	33	29	22	14	8	5	3	2	1	1	1	0

Secondary Efficacy*

	Placebo + Carboplatin–Paclitaxel (n=154)	Retifanlimab + Carboplatin–Paclitaxel (n=154)
ORR (95% CI), %	44 (36, 52)	56 (48, 64)
CR, %	14	22
		<i>P</i>=0.0129[†]
Median DOR (95% CI), months	7.2 (5.6, 9.3)	14.0 (8.6, 22.2)
DCR (95% CI), %	80 (73, 86)	87 (81, 92)

InterAACT vs POD1UM-303/InterAACT 2

Treatment	InterAACT 1 (Rao, 2020*)	POD1UM-303/InterAACT 2	
	Carboplatin–Paclitaxel	Placebo + Carboplatin–Paclitaxel	Retifanlimab + Carboplatin–Paclitaxel
n	91	154	154
Participating countries	UK, AU, Norway, US	EU, AU, JPN, US, PR	
Demographics and disease characteristics [†]			
Median age, years	61		62
Female, %	67		72
White/other, %	NS		87/13
HIV+, %	5		4
Metastatic, %	88		82
ECOG PS 0 or 1	93		100
Median number of chemotherapy cycles	6	6	6
ORR, % (95% CI)	59 (42, 74)	44 (36, 52)	
CR, %	13	14	
Median PFS, months (95% CI)	8.1 (6.6, 8.8)	7.4 (7.1, 7.7)	
Median OS, months (95% CI)	20.0 (12.7, NE)	23.0 (15.1, 27.9)	

*Rao S et al, *J Clin Oncol*. 2020;38(22):2510-2518. [†]Entire study population

AU, Australia, CI, confidence interval; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; EU, European Union; HIV+, human immunodeficiency virus positive; JPN, Japan; NE, not estimable; NS, not shown; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, Puerto Rico; UK, United Kingdom; US, United States.

Safety Summary

Variable	Placebo + Carboplatin–Paclitaxel (n=152)	Retifanlimab + Carboplatin–Paclitaxel (n=154)	Total (N=306)
Median treatment duration, months	6.8	7.4	7.2
Patients with any TEAEs, n (%)	152 (100)	154 (100)	306 (100)
Patients with ≥ grade 3 TEAEs, n (%)	114 (75.0)	128 (83.1)	242 (79.1)
Patients with grade 5 TEAEs, n (%)	1 (0.7)*	4 (2.6)†	5 (1.6)
Patients with SAEs, n (%)	59 (38.8)	73 (47.4)	132 (43.1)
Treatment-related SAEs, n (%)	10 (6.6)	25 (16.2)	35 (11.4)
Immune-related AEs, n (%)	36 (23.7)	71 (46.1)	107 (35.0)
AEs leading to discontinuation, n (%)	4 (2.6)	17 (11.0)	21 (6.9)

- Safety of retifanlimab plus chemotherapy consistent with prior phase 2 data and known CPI literature in SCAC
- No loss of HIV control/viral load observed in patients with HIV
- At data cutoff, 90 patients (58.4%) in the retifanlimab arm remained on study

TEAEs by Preferred Term

Most Common (≥3%) Grade 3 or Higher TEAEs

MedRA Preferred Term	Placebo + Carboplatin–Paclitaxel (n=152)	Retifanlimab + Carboplatin–Paclitaxel (n=154)	Total (N=306)
Neutropenia	45 (29.6)	54 (35.1)	99 (32.4)
Anaemia	31 (20.4)	30 (19.5)	61 (19.9)
Neutrophil count decreased	13 (8.6)	26 (16.9)	39 (12.7)
White blood cell count decreased	13 (8.6)	14 (9.1)	27 (8.8)
Diarrhoea	9 (5.9)	8 (5.2)	17 (5.6)
Leukopenia	6 (3.9)	6 (3.9)	12 (3.9)
Asthenia	5 (3.3)	6 (3.9)	11 (3.6)
Sepsis	6 (3.9)	5 (3.2)	11 (3.6)
Pulmonary embolism	5 (3.3)	5 (3.2)	10 (3.3)
Vomiting	6 (3.9)	4 (2.6)	10 (3.3)

Most Common (≥2%) Immune-Related TEAEs

MedRA Preferred Term	Placebo + Carboplatin–Paclitaxel (n=152)	Retifanlimab + Carboplatin–Paclitaxel (n=154)	Total (N=306)
Peripheral sensory neuropathy	15 (9.9)	17 (11.0)	32 (10.5)
Hypothyroidism	5 (3.3)	22 (14.3)	27 (8.8)
Hyperthyroidism	1 (0.7)	13 (8.4)	14 (4.6)
Pruritus	3 (2.0)	11 (7.1)	14 (4.6)
Adrenal insufficiency	0	8 (5.2)	8 (2.6)
Rash maculo-papular	3 (2.0)	3 (1.9)	6 (2.0)

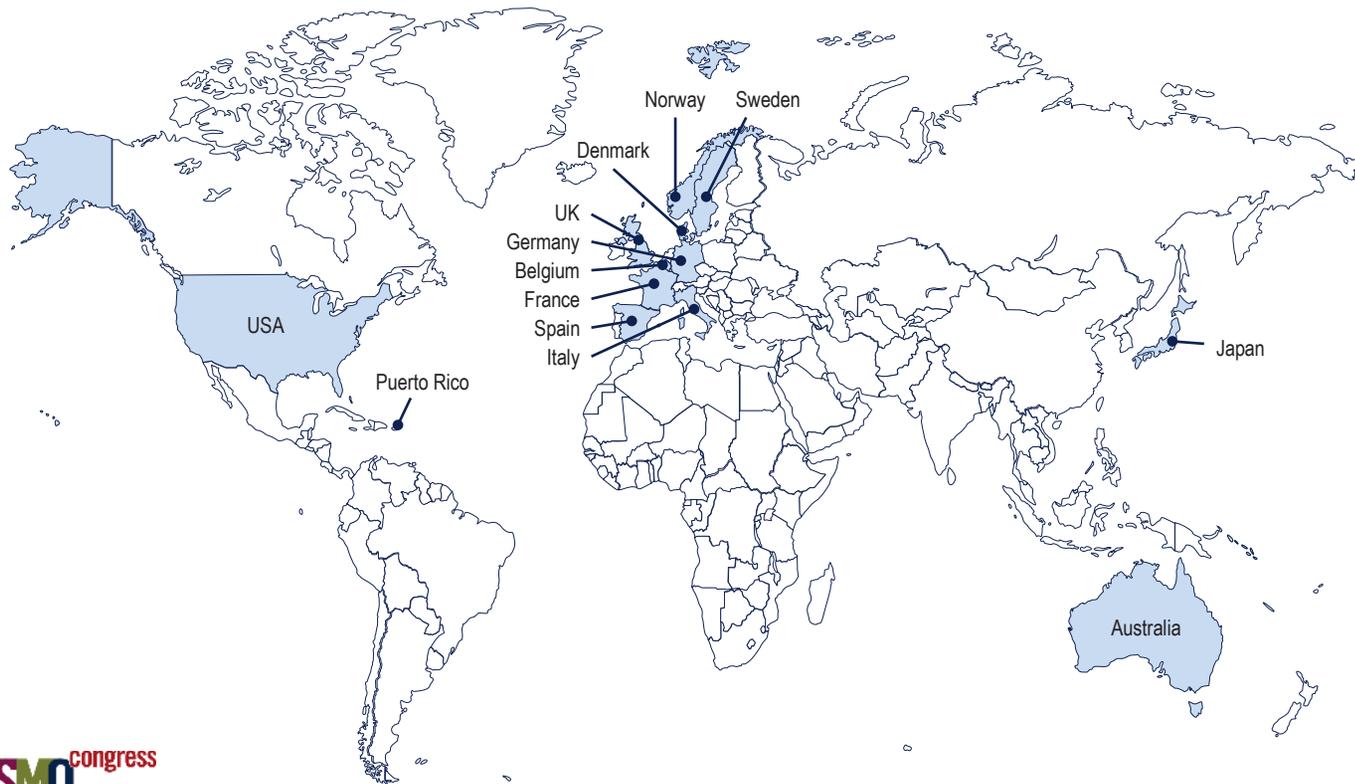
TEAE: any AE either reported for the first time or worsening of a pre-existing event after first dose of study treatment and within 90 days of the last administration of retifanlimab/placebo, or within 30 days of the last chemotherapy.

AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

Conclusions

- This first and largest known phase 3 trial of a checkpoint inhibitor in SCAC, a disease with high unmet medical need, demonstrated benefit of addition of retifanlimab to standard of care chemotherapy
- The study met its PFS primary endpoint:
 - 9.3 months with retifanlimab vs 7.4 months with placebo (HR, 0.63 [95% CI, 0.47, 0.84]; $P=0.0006$)
- Retifanlimab improved OS vs placebo by 6 months, with a strong trend towards statistical significance at data cutoff (OS follow-up ongoing)
- ORR, DOR and DCR all showed improvement with retifanlimab vs placebo
- Treatment was generally well tolerated, and safety was consistent with other chemotherapy plus checkpoint inhibitor regimens
 - Delivery of chemotherapy was not compromised by retifanlimab administration
- Retifanlimab plus carboplatin–paclitaxel represents a potential new reference treatment and standard of care for patients with advanced SCAC

POD1UM-303/InterAACT 2: Countries With Participating Centres



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