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POD1UM-202: Phase 2 Study of Retifanlimab in Patients With Squamous Carcinoma of the Anal Canal Who Progressed Following Platinum-Based Chemotherapy

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Disclosures

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Background

- The incidence of SCAC is increasing worldwide, especially in women[1]
  - SCAC shares common etiologic features with other HPV-related malignancies, including cervical cancer and HNSCC[2]
  - Risk is markedly increased with concurrent HIV infection[1]
  - Median survival in advanced/metastatic disease is only 20 months with standard treatment[3,4]
- PD-1 inhibitors have shown encouraging preliminary antitumor activity in previously treated, advanced SCAC[5–7]
- Retifanlimab (INCMGA00012) is an investigational humanized immunoglobulin G4 monoclonal antibody against human PD-1, which has shown preliminary activity against a broad variety of solid tumors, including cervical cancer (another HPV-driven malignancy)[8]

HNSCC, head and neck squamous cell carcinoma; HIV, human immunodeficiency virus; HPV, human papillomavirus; PD-1, programmed cell death-1; SCAC, squamous carcinoma of the anal canal.

1. Symer MM, et al. *F1000Res*. 2018;7. **2**. Schiffman, M *J Natl Cancer Inst Monogr.* 2003;31:14–9; **3.** Rao S, et al. *J Clin Oncol*. 2020;38:2510–2518; **4.** Marabelle A, et al. *J Clin Oncol*. 2020;38 (4 suppl): Abstract 1; **5.** Morris VK, et al. *Lancet Oncol*. 2017;18:446–453; **6.** Ott PA, et al. *Ann Oncol*. 2017;28:1036–1041; **7**. Lonardi S, et al. *J Clin Oncol*. 2020;38:15 (Suppl), Abstract 4051; **8**. Mehnert JJ, et al. *J ImmunoTherapy Cancer*. 2018;6 (Suppl 1) 115; Abstract 669.

POD1UM-202: Phase 2, Open-label, Single-arm, Multicenter Study of Retifanlimab (NCT03597295)

Patients

- ≥18 years with confirmed locally advanced or metastatic SCAC
- Disease progression on or after platinum-based therapy (≤2 lines of prior systemic therapies for metastatic SCAC)
- Measurable disease per RECIST v1.1
- ECOG PS 0 or 1
- HIV-positive patients eligible: CD4+ count ≥300/μL, undetectable viral load, and receiving HAART

Enrollment

- 94 patients enrolled in US and EU

Treatment

- Retifanlimab 500 mg IV infusion Q4W (28-day cycle) for up to 2 years

Primary endpoint

- ORR by ICR (RECIST v1.1)

Secondary endpoints

- DOR, DCR, PFS, and OS
- Safety (CTCAE v5.0)
- **Data cutoff date:** June 8, 2020
  - Median duration of follow-up is 7.1 months

CTCAE, Common Terminology Criteria for Adverse Events; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; ICR, independent central review; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q4W, every 4 weeks; RESIST, Response Evaluation Criteria in Solid Tumors; SCAC, squamous carcinoma of the anal canal.

Patient Characteristics

Characteristic	N = 94
Age, median (range), y	64 (37–94)
≥65	46 (49)
≥75	10 (11)
Female, n (%)	61 (65)
Race, n (%)	
White	72 (77)
Other/Missing	22 (23)
ECOG PS, n (%)	
0	39 (42)
1	55 (59)
Prior therapy, n (%)	
Chemoradiation therapy	69 (73)
Radiotherapy (no chemotherapy)	16 (17)
Platinum-based therapy*	91 (97)
Current M1 staging, n (%)	76 (81)
Known HIV-positive status, n (%)	9 (10)
Liver metastases, n (%)	39 (42)

* 3 patients were ineligible or intolerant of platinum-based chemotherapy.
ECOG PS, Eastern Cooperative Oncology Group performance status.

Summary of Overall Responses (RECIST v1.1)

Objective Responses by ICR

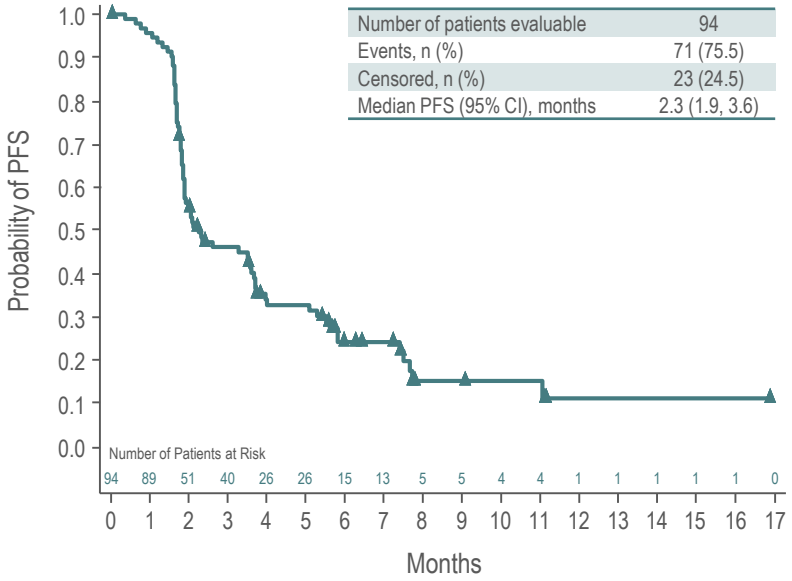
Variable	N = 94
ORR (95% CI), %	13.8 (7.6–22.5)
Best overall response, n (%)	
CR	1 (1.1)
PR	12 (12.8)
SD	33 (35.1)
PD	43 (45.7)
Missing	5 (5.3)
DCR, n (%)	46 (48.9)

- Median (95% CI) duration of response was 9.5 (5.6–not estimable) months
- Responses were observed in patients regardless of age, sex, HIV status, liver metastases, and PD-L1 expression

CI, confidence interval; CR, complete response; DCR, disease control rate; HIV, human immunodeficiency virus; ICR, independent central review; ORR, objective response rate; PD-L1, programmed cell death ligand-1; PR, partial response; PD, progressive disease; SD, stable disease.

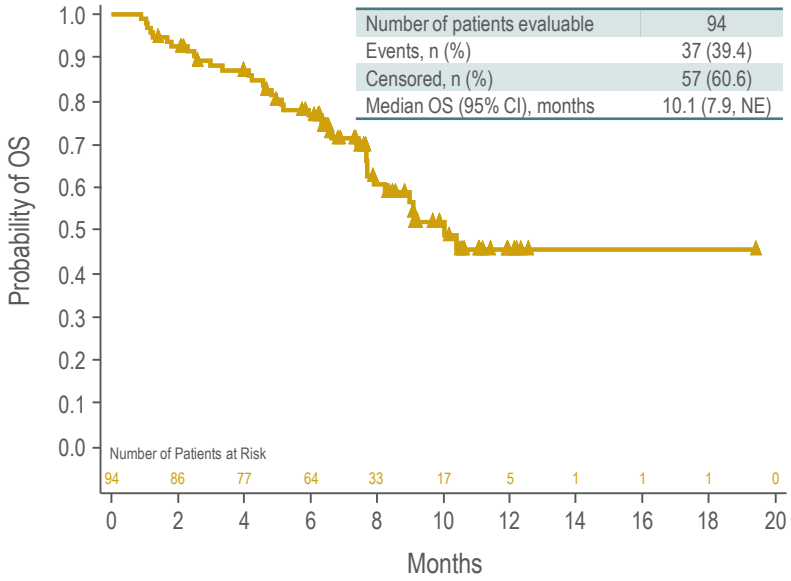
Kaplan-Meier Estimate of PFS by ICR and OS

PFS



Number of patients evaluable	94
Events, n (%)	71 (75.5)
Censored, n (%)	23 (24.5)
Median PFS (95% CI), months	2.3 (1.9, 3.6)

OS



Number of patients evaluable	94
Events, n (%)	37 (39.4)
Censored, n (%)	57 (60.6)
Median OS (95% CI), months	10.1 (7.9, NE)

ICR, independent central review; NE, not estimable; PFS, progression-free survival; OS, overall survival..

Summary of Adverse Events

Patients With AE, n (%)	All Patients (N = 94)
Any treatment-related AE	55 (58.5)
Grade ≥3	11 (11.7)
Led to treatment discontinuation	4 (4.2)
Any immune-related AE*	24 (25.5)
Grade ≥3†	6 (6.4)
Led to treatment discontinuation	2 (2.1)
Infusion reactions (none grade ≥3)	4 (4.3)

- No loss of HIV control in any HIV-positive patient (n = 9), as assessed by serial CD4+ counts and viral load measurements

* Group terms: Immune-related AEs identified using predefined preferred terms regardless of investigator's assessment of causality.
† Adrenal insufficiency (n = 1), nephritis (n = 1), pneumonitis (n = 2), skin reactions (n = 2).
AE, adverse event.

Conclusions

- Retifanlimab has promising activity in patients with platinum-refractory SCAC, including those known to be HIV-positive
  - ICR-assessed ORR of 14% is comparable to that seen previously with PD-1 inhibitors in other HPV-driven malignancies[1–6]
  - Median DOR of 9.5 months compares favorably to historical experience with salvage chemotherapy[7]
- The retifanlimab safety profile was as expected for a PD-1 inhibitor
  - Well tolerated in HIV-positive patients and not associated with any loss of HIV control
- These promising results warrant further investigation of retifanlimab in phase 3 trials, as a potential new therapeutic option for SCAC
  - A phase 3 trial in combination with carboplatin and paclitaxel in patients with inoperable locally recurrent/metastatic SCAC is ongoing (POD1UM-303/InterAACT 2; NCT04472429)

1. Morris VK, et al. *Lancet Oncol*. 2017;18:446–453. **2.** Ott PA, et al. *Ann Oncol*. 2017;28:1036–1041. **3.** Marabelle A, et al. *J Clin Oncol*. 2020;38:1–10. **4.** Bauml J, et al. *J Clin Oncol*. 2017;35:1542–1549. **5.** Ferris RL, et al. *N Engl J Med*. 2016;375:1856–1867. **6.** Chung HC, et al. *J Clin Oncol*. 2019;37:1470–1478. **7.** Saint A et al. *Cancer Med*. 2019;8:6853–6859..

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