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Preliminary Results of a Phase 2 Study of INCMGA00012 in Patients With Squamous Carcinoma of the Anal Canal Who Have Progressed Following Platinum-Based Chemotherapy

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Introduction

- Though rare, the incidence of anal cancers has been increasing[1]
  - Risk factors include women with a previous cervical precancer, men who have sex with men, human papillomavirus infection, and immunosuppression after solid organ transplantation or human immunodeficiency virus (HIV) infection[2,3]
  - The majority of anal cancers (85%) have a squamous histology[4]
- No standard treatment has been established following failure of first-line, platinum-based chemotherapy[5]
- Programmed cell death 1 (PD-1) inhibitors have demonstrated encouraging preliminary antitumor activity and a manageable safety profile in patients with advanced squamous carcinoma of the anal canal (SCAC)[6,7]
- INCMGA00012 is an investigational humanized immunoglobulin G4 monoclonal antibody against human PD-1 that prevents the interaction between PD-1 and its ligands to sustain/restore T-cell antitumor function[8]
- We report preliminary interim results on efficacy and safety of INCMGA00012 in patients with locally advanced or metastatic SCAC who have progressed after treatment with platinum-based chemotherapy (POD1UM-202; NCT03597295)

Study Objectives

Primary
- To assess efficacy of INCMGA00012 in terms of objective response rate

Secondary
- To determine additional measures of clinical benefit (duration of response, disease control rate, progression-free survival, and overall survival)
- To evaluate safety and pharmacokinetics of INCMGA00012

Exploratory
- Biomarkers, immunogenicity, efficacy per immune-related response criteria, health-related quality of life, and impact on HIV control. HIV reservoir and other HIV-related markers or mutations will be monitored in patients enrolled in the translational substudy

Methods

Study Design and Treatment
- Phase 2, open-label, single-arm, multicenter study
- Planned enrollment: approximately 81 patients
- Patients receive a 500 mg dose of INCMGA00012 every 4 weeks as an intravenous infusion over 60 (±15) minutes (day 1 of each 28-day cycle)
- Treatment will continue for up to 2 years in the absence of clinical disease progression, intolerable toxicity, death, withdrawal of consent, lost to follow-up, or premature discontinuation for any other reason

Key Eligibility Criteria

Inclusion
- Patients ≥18 years of age with confirmed diagnosis of locally advanced or metastatic SCAC
- Disease progression on or after platinum-based therapy (maximum 2 lines of prior systemic therapies for metastatic SCAC)
- Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- Eastern Cooperative Oncology Group performance status 0 or 1
- Patients known to be HIV-positive met the following criteria: CD4$^+$ count ≥300/µL, undetectable viral load, and receiving highly active antiretroviral therapy

Exclusion
- Previous treatment with any anti–PD-1 or anti–programmed cell death ligand protein 1 (PD-L1) therapy
- Active autoimmune disease requiring systemic immunosuppression in excess of physiologic maintenance doses of corticosteroids (defined as >10 mg of prednisone or equivalent)
- Known active central nervous system metastases and/or carcinomatous meningitis
- Clinically significant cardiovascular or pulmonary conditions
- Active infections requiring systemic therapy

Assessments
- Response is assessed per RECIST v1.1 every 8 weeks during treatment, and at least every 12 weeks for long-term follow-up
- Adverse events, graded by Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, are monitored throughout the study and for 28 (±7) days after the last dose of study treatment (immune-related adverse events are monitored for 90 days after the last dose of study treatment)
- HIV management testing (in patients known to be HIV-positive), including HIV viral load and CD4$^+$ cell count, is performed every 8 weeks during treatment
- Tumor tissues are collected during screening for evaluation of human papillomavirus, microsatellite instability, and PD-L1 expression

Results

Patients
- As of the September 13, 2019 data cutoff, 49 patients with locally advanced or metastatic SCAC were enrolled and treated with INCMGA00012
  - Twenty-six patients either with 2 postbaseline tumor assessments or discontinued the study earlier were included in the efficacy analysis
- Patient demographics and disease characteristics are presented in **Table 1**
- Thirty-five of 49 patients (71%) are ongoing as of this report

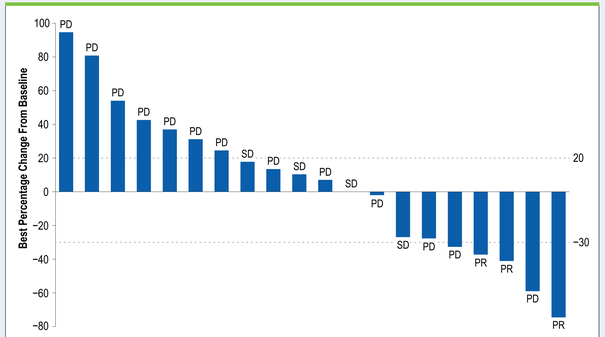
Table 1. Baseline Demographics and Disease Characteristics

Variable	N = 49
Age, median (range), y	64 (39–81)
Sex, n (%)	
Women	30 (61)
Men	19 (39)
Race, n (%)	
White	41 (84)
Other	7 (14)
Missing	1 (2)
ECOG PS,* n (%)	
0	18 (37)
1	30 (61)
HPV positive, n (%)	3 (6)
Known to be HIV-positive, n (%)	3 (6)
Number of prior lines of therapy, n (%)	
<2	25 (51)
≥2	16 (33)
Unknown	8 (16)

*ECOG PS was not reported for 1 patient.
ECOG PS, Eastern Cooperative Oncology Group performance status; HIV, human immunodeficiency virus; HPV, human papillomavirus.

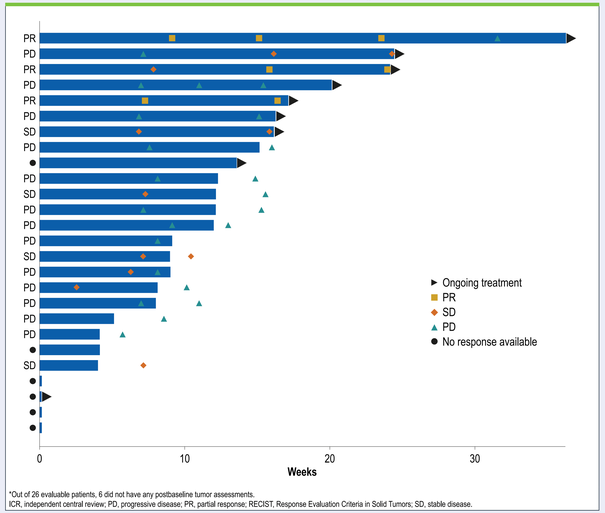
Antitumor Activity

Figure 1. Best Percentage Change From Baseline in Target Lesion Size (Sum of Diameters) for Individual Patients*



*Out of 26 evaluable patients, 6 did not have any baseline or postbaseline tumor assessments. Upper limit of dotted line indicates a criterion for PD (≥20% increase in sum of target lesion diameters) and lower limit indicates a criterion for PR (≥30% decrease in sum of target lesion diameters).
PD, progressive disease; PR, partial response; SD, stable disease.

Figure 2. Duration of Treatment and Response Assessment From ICR (per RECIST v1.1)*



*Out of 26 evaluable patients, 6 did not have any postbaseline tumor assessments.
ICR, independent central review; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Safety and Tolerability

Table 2. Summary of Adverse Events (Safety-Evaluable Population)

Adverse Event, n (%)	N = 49
Adverse event (all grade, treatment-related and -unrelated)	33 (67)
Treatment-related adverse event	20 (41)
Grade ≥3 adverse events (treatment-related and -unrelated)	14 (29)
Grade ≥3 treatment-related adverse event	3 (6)
Serious adverse events (all grade, treatment-related and -unrelated)	14 (29)
Serious treatment-related adverse event	1 (2)
Nonfatal adverse events leading to discontinuation*	1 (2)
Adverse events leading to death†	3 (6)
Potential immune-related adverse events	14 (29)

*Due to pleural effusion (n = 1).
†Due to hypercalcemia, pelvic infection, and pleural effusion (each n = 1).

Table 3. Potential Immune-Related Adverse Events

	N = 49	
Adverse Event, n (%)	Any Grade	Grade ≥3
Rash*	5 (10)	1 (2)
Diarrhea	5 (10)	0
Endocrine disorders†	4 (8)	0
Liver function abnormality‡	2 (4)	0

*Rash includes the following Medical Dictionary for Regulatory Activities (MedDRA) terms: rash, rash erythematous, and rash maculopapular.
†Endocrine disorders includes the following MedDRA terms: hypothyroidism and hyperthyroidism.
‡Liver function abnormality includes the following MedDRA terms: alanine aminotransferase increased and aspartate aminotransferase increased.

Conclusions

- **The POD1UM-202 trial is the largest ongoing assessment of a PD-(L)1 inhibitor in platinum-refractory SCAC**
- **As of this report, 49 of the planned 81 participants have been enrolled**
- **INCMGA00012 at 500 mg every 4 weeks has been generally well tolerated, including in patients with active HIV infection**
- **Evidence of clinical activity, including independently confirmed RECIST responses, has been seen**
- **Further evaluation of INCMGA00012 in earlier-stage SCAC is warranted pending the results of this study**

Disclosures

Rao: Advisor or honoraria – *Amgen, Celgene, Shire*; travel grants – *Bayer, Celgene, Incyte Corporation.* **Capdevila:** Scientific consultancy role (speaker and advisory roles) – *Advanced Accelerator Applications, Amgen, Bayer, Eisai, Exelixis, Ipsen, Merck Serono, Novartis, Pfizer, Sanofi*; research support/research grants – *Advanced Accelerator Applications, AstraZeneca, Bayer, Eisai, Novartis, Pfizer.* **Kim:** Research funding – *Bioproxel Pharma, Novartis, Pfizer, Roche, Sanofi*; adviser or honoraria – *Amgen, Bayer, MSD, Sanofi, Servier.* **Dahan:** Honoraria – *Amgen, Sanofi, Servier.* **Fakih:** Consultant or advisory role – *Amgen, Array BioPharma, Genentech/Roche*; speakers bureau – *Amgen, Taiho Pharmaceutical*; research funding – *Amgen, AstraZeneca, Novartis.* **Cornfeld, Tian, Catlett:** Employment and stock ownership – *Incyte Corporation.* **Spano:** Honoraria – *AstraZeneca, Biogaran, Bristol-Myers Squibb, Gilead Sciences, Leo Pharma, Lilly, Mylan, Myriad Genetics, Novartis, Pfizer, Pierre Fabre*; consulting or advisory role – *MSD, Roche.* **Gilbert, Kayyal, Demols:** Nothing to disclose.

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