A Phase 1 Study of INCMGA00012, a PD-1 Inhibitor, in Patients With Advanced Solid Tumors: Preliminary Results for Patients With Advanced Cervical Cancer (POD1UM-101)

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Introduction

Objective: The current study is the fourth most common cause of cancer-related deaths in western adult populations.1 Several studies have demonstrated clinical effectiveness and improved survival for patients with metastatic disease.1-4 Programmed cell death 1 (PD-1) inhibitors have demonstrated clinical activity in human papillomavirus (HPV)-related tumors with a response rate of 14.3% in patients with pretreated locally advanced metastatic cervical cancer.5,6 INCMGA00012 is an investigational monoclonal antibody (mAb) targeting programmed death ligand 1 (PD-L1) with promising activity in solid tumors.7

The ongoing cohort-expansion phase of the first-in-human POD1UM-101 study (NCT03059823) has demonstrated consistent safety and encouraging preliminary antitumor activity in patients with non-small cell lung cancer and metastatic melanoma.8

Methods

Study Design: This was a Phase 1, open-label, dose-escalation, and cohort-expansion study (Figure 1).

Objectives: The objectives were to determine PD-L1 expression and immune cell infiltration and their relationship to clinical outcomes; determine safety and tolerability; and determine antitumor activity in patients with advanced solid tumors.

Results

Patient Population: 35 patients were enrolled in the cervical cancer cohort (Table 1).

Safety and Tolerability: Adverse events of special interest are shown in Figure 2. There were no serious treatment-related adverse events; 28 of 35 patients (80%) discontinued treatment, primarily (60%) owing to progression; 11% discontinued owing to AEs.

Antitumor Activity: The best percentage change from baseline in target lesion size is shown in Figure 3. No complete responses were observed; 10 patients (29%) had partial responses (PR). Median overall survival was not reached (NE). Median duration of response was not reached (NE).

Conclusions

INCMGA00012 demonstrated consistent safety and tolerability with locally advanced metastatic cervical cancer and has shown clinical activity with encouraging median progression-free survival (3.6 months). Further study of INCMGA00012 in cervical cancer is warranted.

1. Eastern Cooperative Oncology Group performance status 0 or 1
2. Patients ≥18 years of age with unresectable, locally advanced, or metastatic cervical cancer who are not candidates for surgical resection or radiotherapy
3. Patients with HPV disease that is positive for 16 or 18
4. No chemotherapy within 12 weeks prior to study
5. Total dose of systemic corticosteroids or immunosuppressant drugs within 14 days prior to study
6. Clinically significant cardiovascular, gastrointestinal, or pulmonary conditions
7. PD-L1 status was determined retrospectively on available tissues by immunohistochemistry (IHC) using the PD-L1 IHC 22C3 pharmDx assay (Ventana, CA)
8. SD: stable disease; TPS: tumor proportion score
9. ORR: objective response rate; CR: complete response; PD: progressive disease; PR: partial response; SD: stable disease; TPS: tumor proportion score; TTP: time to progression
10. AE: adverse event; CR: complete response; PD: progressive disease; PR: partial response; SD: stable disease; TPS: tumor proportion score

References

3. Ochsenreiter: Consultant – AstraZeneca, Bristol-Myers Squibb, Glenmark, Incyte, Ipsen, Macrogenics, ALX Therapeutics, Amgen, ArQule, Ascentage, Apexian, Asana; Employment and stock ownership – AstraZeneca, AstraZeneca Spain, Bristol-Myers Squibb, Lilly, MSD, Pfizer, Roche
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