INTRODUCTION

- Cervical cancer is the second most common cancer in developing countries, where ~450,000 new cases are diagnosed annually, most at an advanced stage. 1
- Prognosis of women with advanced cervical cancer is poor, with a 5-year survival rate of 15%. 2
- Survival rates are also poor for women who have recurrent cancer, a population that is often resistant to the standard of care, cisplatin. 3
- The primary etiologic agent of cervical cancer is the human papillomavirus (HPV).
  - Approaches that target this virus may have great utility in improving survival in cervical cancer.

PBMCs will be analyzed for the presence and quantitation of HPV-E7– and HPV-E6–specific

Dose-limiting toxicities

- A Phase I study was conducted in order to further explore a possible dose-response relationship that has been identified in preclinical models, and to evaluate whether a higher dose than that used in the ongoing Phase 2 studies is safe and well tolerated in patients with metastatic or recurrent cervical carcinoma.

Figure 1. Step by step Lm-tLLO immunomodulation

OBJECTIVES

- The primary objective is to evaluate the tolerability and safety of ADXS11-001 in patients with persistent, metastatic or recurrent squamous or non-squamous cell carcinoma, adenocarcinoma squamous, or adenocarcinoma of the cervix.
- The secondary objectives are to:
  - Evaluate tumor response and progression-free survival (PFS) by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and immune-related RECIST (irRECIST)
  - Assess correlative immunologic studies of ADXS11-001 treatment

METHODS

STUDY DESIGN

- Phase I, dose-escalation, open-label, multicenter study (NCT02164461).
- Doses will be escalated in the standard 3 + 3 fashion, in 2 doses, starting with 5 x 10⁶ colony-forming units (CFU) to a maximum dose level of 1 x 10⁹ CFU.
  - If no dose-limiting toxicities (DLIs) are observed at Dose Level 1 (5 x 10⁶ CFU), then patients will be enrolled at the next dose level (1 x 10⁷ CFU)
  - If a DLT is seen in 1 of 3 patients, another 3 will be treated at that same dose
  - If a DLT is seen in 2 of 6 patients, then that dose level will be considered the maximum tolerated dose and the previous dose level will be selected as the recommended phase 2 dose (RP2D).
- The RP2D cohort will then be expanded to ~15 patients to further define safety and efficacy

ENDPOINTS

- Primary endpoint:
  - Safety will be assessed by comparing treatment-related adverse events (according to the CTCAE v4.0 criteria), DLTs, changes in physical examinations, vital sign measurements, and laboratory abnormalities
- Secondary endpoints:
  - Tumor assessment will be carried out at baseline, at Week 12 in Cycle 1, then every 12 weeks thereafter. Assessment of disease will be done using RECIST 1.1 and irRECIST
  - Immuneologic effects will be measured and evaluated by collection of peripheral blood preparation of peripheral blood mononuclear cells (PBMCs) and serum immediately prior to each ADXS11-001 infusion

STATISTICAL METHODS

- Descriptive statistics will be used to summarize and evaluate the safety and tolerability of ADXS11-001.
  - All patients who received at least 1 dose of ADXS11-001 will be included in the safety analyses
  - The RP2D of ADXS11-001 will be selected based on an observed DLT rate of <33%
- PFS is defined as the time from first dose of study treatment until objective tumor progression or death. Patients who have not progressed or who are still alive at the time of evaluation will be censored for the analysis.
- Kaplan-Meier curves and descriptive statistics will be used to summarize PFS
  - All patients who completed one 12-week cycle of ADXS11-001 treatment will be considered evaluable for response

TRIAL STATUS

- This phase I study is open and is currently enrolling at Georgia Regents University, Augusta, GA.
- To date, 3 patients have been enrolled at Dose Level 1.

REFERENCES


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Samir Khaleif; Board member; Advaxis; David Mauro; Employee and shareholder; Advaxis; Sharad Ghamande, Cheryl Price; Dona Wheatley; Robin Dobbins; Lisa Marshall and John Janik have no potential conflicts of interest to disclose.