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AIM2CERV: a randomized phase III study of adjuvant AXAL immunotherapy following chemoradiation in patients who have high-risk locally advanced cervical cancer (HRLACC)

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Background
Patients with HRLACC experience a 50% chance of disease recurrence/death following cisplatin-based chemoradiation (CCRT) plus brachytherapy, and represent a group with a significant unmet need for new treatments. Persistent infection with oncogenic strains of human papillomavirus (HPV) is the most common cause of CC, and provides rationale for therapeutic targeting of HPV. Axalimogene filolisbac (AXAL/ADXS11-001) is an irreversibly attenuated *Listeria monocytogenes*-listeriolysin O immunotherapy that secretes a HPV E7 fusion protein that induces HPV-specific cytotoxic T cell generation and reduces immune tolerance in the tumor microenvironment. Previous studies demonstrated AXAL was well tolerated and associated with objective tumor response and survival benefits in patients with recurrent/metastatic CC. AXAL has received FDA Fast Track Designation for the treatment of HRLACC.
Methods
This double-blind, placebo-controlled, multinational, multicenter randomized phase III trial is being conducted under a Special Protocol Assessment agreement with the FDA. The study will evaluate adjuvant AXAL in patients with HRLACC, defined as histologically confirmed squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix and ≥1 of the following: 1) FIGO stage IB2, IIA2, IIB with biopsy-proven pelvic nodes, or ≥2 positive nodes by MRI/CT ≥1.5-cm diameter, or ≥2 positive pelvic nodes by PET; 2) all FIGO stage IIIA, IIIB, IVA; 3) any FIGO stage with para-aortic lymph node metastases criteria, defined by biopsy-proven para-aortic node(s), or ≥1 positive para-aortic node(s) by MRI/CT >1.5-cm shortest dimension, or ≥1 positive para-aortic node(s) by PET with SUV >2.5. Eligible patients must be disease free per RECIST 1.1 following completion of CCRT with curative intent and aged ≥18 with GOG performance status 0–1. Patients will be randomized 2:1 to AXAL (1×10^9 colony-forming units) or placebo and receive a 60-minute infusion of treatment every 3 weeks for 3 doses (weeks 1, 4, and 7) for the first 3 months (Induction Phase). Thereafter, patients will receive treatment every 8 weeks for 5 doses or until disease recurrence (Maintenance Phase); patients will receive a 7-day course of oral antibiotics/placebo 72 hours after completion of each treatment in both phases. Primary objective is to compare disease-free survival (DFS) of AXAL with placebo; secondary objectives are safety and overall survival (OS). Exploratory objectives will determine if there is an association between HPV subtypes and DFS/OS, and patient-reported outcomes. The design provides 85% power for a sample size of 450 to demonstrate a reduction in the hazard of recurrence by 38%.
Trial Registration
ClinicalTrials.gov identifier NCT02853604.