HPV E7 antigen-expressing Listeria-based immunotherapy (ADXS11-001) prior to robotic surgery for HPV-positive oropharyngeal cancer enhances HPV-specific T cell immunity (#7632)

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Introduction

Human papilloma virus-associated oropharyngeal cancer (HPV OPC), which accounts for almost 75% of newly diagnosed OPC, is an appealing target for immunotherapy due to the expression of viral antigens1. ADXS11-001, a live attenuated Listeria monocytogenes LLO (LLO) immunotherapeutic agent expressing an HPV-E7 fusion protein, has been shown to induce HPV-specific T cell responses in animal models, and to have clinical activity in cervical cancer. A phase II "window of opportunity" trial was designed to evaluate the effect of ADXS11-001 on anti-tumor immunity in peripheral blood and the tumor immune microenvironment (TIME) of patients with HPV OPC.

ADXS11-001 vaccine

Listeria monocytogenes (Lm)-Listeriolysin O (LLO) immunotherapies have shown to generate antigen-specific T-cell responses and neutralize T-regulatory (Treg) and myeloid-derived suppressor cells (MDSCs) that protect the TIME against immunologic attack3.

ADXS11-001 is an attenuated, genetically modified Lm vector that secretes an HPV-E7 fusion protein; LLO refers to the truncated form of non-hemolytic LLO protein4.

ADXS11-001 can be combined with different treatment modalities and data in cervical cancer supports potential clinical benefit5.

Study design

Window of opportunity, non-randomized, single-arm phase 2 trial of neo-adjunct ADXS11-001 treatment before standard of care TORS in patients with stage II-IV HPV OPDC (NCT02002182).

Preoperative biopsy

Observational arm

Study arm

Adx 11-001 neo-adjunct

HPV test

ADXS11-001

CD8+ TIL

H&E

Analysis of tumor infiltrating lymphocytes (TIL) at the tumor host interface

Current status of the trial

• 6 control patients have been enrolled and completed tumor resection by TORS.
• 8 study patients have been enrolled, completed ADXS11-001 administration and tumor resection by TORS.
• 3 adverse events (AE) grade III have been observed in the study patients (vomiting, hypotension), remaining events were grade I-II.
• Tumor immune microenvironment (TIME) profiling of biopsies before 1st ADXS11-001 administration (preADXS) and of surgical resection specimens after 2nd ADXS11-001 administration (postADXS) has been completed for 8 study patients.
• E6/E7 specific T cell response has been analyzed in 8 study patients preADXS, postADXS and postTORS (after tumor resection).
• Serum cytokines preADXS, postADXS and postTORS have been measured in 7 study patients.

TIME profiling by qIF and H&E analysis

Quantitative multiplex immunofluorescence (qIF) of preADXS biopsies and postADXS surgical resection specimens for CD8, CD4, PD1, PD-L1, VISTA and FOXP3. Single FFPTE tissue sections were stained for multiple antibodies by immunofluorescence and staining intensity was automatically quantified in multicolor images of representative tumor areas.

Summary

• Successful accrual of 8 study patients and 1 obstrucional control patients.
• Detection of E6 and/or E7 specific T cell response in the peripheral blood in 5 of 8 analyzed patients with postADXS increase.
• Increase in E6 response potentially suggests epitope spreading.
• Potential ADXS11-001-induced changes in the TIME with regard to T cell infiltration and immune checkpoint molecule expression.
• Decrease in tumor infiltrating FOXP3+ Tregs observed in 3 patients postADXS.
• Decrease of serum cytokines involved in T cell activation postADXS might suggest increased consumption.
• While few observations reach significance in this small, preliminary patient cohort, overall trends suggest systemic and intratumoral immune activation and enhanced anti-tumor immunity.

Further investigations

• Completion of study arm and control arm patient accrual.
• Immune cell phenotyping of PBMCs at different time points.
• Completion of T cell immune responses and cytokine changes for additional time points.
• T cell receptor diversity profiling by Immunoseq TCR deep sequencing of TIL and PBMCs.

References


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