11 TRIALS • 5 CANCERS • MONOTHERAPY • COMBINATION THERAPY • NEO-EPITOPES

IMMUNITION

The Intelligent Immune Response

AACR Reception
April 18, 2016

ADVAXIS
IMMUNOTHERAPIES™

Forward-Looking Statements

ADVAXIS IMMUNOTHERAPIES™

Advaxis, Inc. (the “Company”) has filed a registration statement (including a prospectus) and will file a preliminary prospectus supplement with the Securities and Exchange Commission (“SEC”) for the offering to which this presentation relates. Before you invest, you should read the prospectus and the preliminary prospectus supplement in that registration statement and other documents the Company has filed with the SEC for more complete information about the Company and the offering.

This presentation contains forward-looking statements, including, but not limited to: statements regarding Advaxis' ability to develop the next generation of cancer immunotherapies; and the safety and efficacy of Advaxis' proprietary immunotherapy, axalimogene filolisbac. These forward-looking statements are subject to a number of risks, including the risk factors set forth from time to time in Advaxis's SEC filings, including but not limited to its report on Form 10-K for the fiscal year ended October 31, 2015, which is available at http://www.sec.gov.

Advaxis undertakes no obligation to publicly release the result of any revision to these forward-looking statements, which may be made to reflect the events or circumstances after the date hereof or to reflect the occurrence of unanticipated events, except as required by law. You are cautioned not to place undue reliance on any forward-looking statements.

Opening Remarks

ADVAXIS IMMUNOTHERAPIES™

"While our data is preliminary, in several patients we saw increased T cell response, evidence of epitope spreading, and signs of increased immune activation consistent with expansion and infiltration of activated T cells into the tumor. We also saw trends towards a reduction in immuno-suppressive Tregs.

Importantly, in several patients, when compared to pre-treatment tumor tissue, post-treatment tissue analysis showed conversion of the TME into a site of active inflammation characterized by infiltration of activated T cells, and increased expression of activation markers including PD-1, PD-L1.

The fact that we are seeing these trends at this preliminary point in the study is very encouraging, and suggests that AXAL has the potential to generate beneficial immunologic responses in patients with HPV+ head and neck cancer."

Dr. Andy Sikora, Baylor College of Medicine, Advaxis Press Release 4/18/16

Reception Agenda

ADVAXIS IMMUNOTHERAPIES™

Daniel J. O'Connor – President and CEO
Welcome and Opening Remarks

Robert Petit, PhD – Executive Vice President and Chief Scientific Officer
Advaxis Immunotherapies – Not Just a "Vaccine"

Rosemarie Krupar, MD – Baylor College of Medicine
Immunogenicity of Axalimogene Filolisbac in Head and Neck Cancer
(AACR abstract LB-095)

Nicola Mason, PhD, BVetMed – Associate Professor of Medicine and Pathobiology, University of Pennsylvania
Immunogenicity of ADXS-HER2 in Canine Osteosarcoma

Robert Petit, PhD
Effects of Advaxis' Lm Immunotherapy on the STING Pathway

Cancer Neoepitope Immunotherapy: An Update on ADXS-Neo

Advaxis Immunotherapies – Not Just a "Vaccine"

Robert Petit, PhD
Advaxis

ADVAXIS
IMMUNOTHERAPIES™

Here Is a Picture of My "Heater" . . . (No?)

ADVAXIS IMMUNOTHERAPIES™

- Heater?
- Air conditioner?
- Umbrella?
- Radio?
- Storage space?
- Bed?
- Transportation?

- Although it does these things, *together it is much more*
- Advaxis Constructs are:

  Adjuvants, immune stimulators, STING agonists, vaccines, epitope spreading, T-cell infiltration, reduce immune tolerance in tumor microenvironment
- Combination immunotherapy "All-In-One" . . .
- ***Advaxis Constructs are NOT just vaccines***

Fundamental Challenges of Cancer Immunotherapy

ADVAXIS IMMUNOTHERAPIES™

- Immunologic tolerance
  - Multiple mechanisms
  - Peripheral and central
- Weak antigenic targets
- High number of mutations
- Heterologous cell populations
- Suppressive TME
- *Immune system must "see" tumors differently*
  - ***How does biology meet this challenge?***
- Infectious disease: Pathogens trigger multiple signals and pathways that indicate the type of response required to meet and eliminate the infection

Data on file.

Immunotherapy Combination Considerations

ADVAXIS IMMUNOTHERAPIES™

Needed for Effective Immunotherapy	Assoc. Treatment
T cells specific against tumor targets	Therapeutic vaccines
CD8+, CD4+ adjuvants and/or co-stimulators of innate immunity	TLRs, adjuvants, etc
Dendritic cells to present antigen and drive adaptive immunity	Dendritic vaccines
Increased numbers of CTLs against tumors	Vaccines, cytokines, TILs
Overriding peripheral tolerance, without excessive autoimmunity	Checkpoint inhibitors
Accommodation of antigen spreading to help eliminate resistance	Immunogenic death Chemo, RT, onc virus
Infiltration of CTLs into TME, while deactivating TME-specific tolerance (T regs, MDSC, etc)	Chemokines, PD-1, CTLA-4, IDO, CPM
Practical considerations: cost, retreatments, stage of disease, timeliness	Autologous cells $$$ Monoclonals $$ Vaccines $

Data on file.

Immunotherapy Combination Considerations

ADVAXIS IMMUNOTHERAPIES™

Needed for Effective Immunotherapy	Assoc. Treatment	ADVAXIS *Lm*-LLO?
T cells specific against tumor targets	Therapeutic vaccines	**Yes**: Specific CD8+, CD4+
CD8+, CD4+ adjuvants and/or co-stimulators of innate immunity	TLRs, adjuvants, etc	**Yes**: 10 inherent adjuvants
Dendritic cells to present antigen and drive adaptive immunity	Dendritic vaccines	**Yes**: ++ Co-stim
Increased numbers of CTLs against tumors	Vaccines, cytokines, TILs	**Yes**: ++ Co-stim, ++ checkpoints
Overriding peripheral tolerance, without excessive autoimmunity	Checkpoint inhibitors	**Yes**: ++ Checkpoints
Accommodation of antigen spreading to help eliminate resistance	Immunogenic death Chemo, RT, onc virus	**Yes**: Documented
Infiltration of CTLs into TME, while deactivating TME-specific tolerance (T regs, MDSC, etc)	Chemokines, PD-1, CTLA-4, IDO, CPM	**Yes**: Chemokines, STING, dec. Treg, MDSC
Practical considerations: cost, retreatments, stage of disease, timeliness	Autologous cells $$$ Monoclonals $$ Vaccines $	**Yes**: Low COGs, on the shelf, late-stage CRs + adjuvant Rx

Data on file.

What You Will See Today

ADVAXIS IMMUNOTHERAPIES™

- Multiple preclinical studies have shown
  - Potent immune activation
  - Increased T-cell responses to tumor targets
  - Clear evidence of epitope spreading
  - Changes to the tumor microenvironment, which include
    - Increased expression of chemokines and receptors
    - Ability to reverse “tolerant” tumor microenvironment into inflammatory TME
    - Reduced TME suppression by reduction of Tregs and MDSCs
    - Increased infiltration of tumor-killing CD4+ and CD8+ T cells
- Drs Sikora and Krupar are the first to clearly show these same effects in humans
- Dr Mason has demonstrated much of the same data in canine patients
- Some specific data demonstrating the contribution of STING agonism
- Preclinical data on ADXS-Neo

Lm Immunotherapy: Impact Within the Tumor Microenvironment

Immunogenicity of Axalimogene Filolisbac in Head and Neck Cancer
(AACR abstract LB-095)

Rosemarie Krupar, MD
Postdoctoral Fellow
Andrew Sikora Laboratory
Baylor College of Medicine

ADVAXIS
IMMUNOTHERAPIES™

Baylor College of Medicine

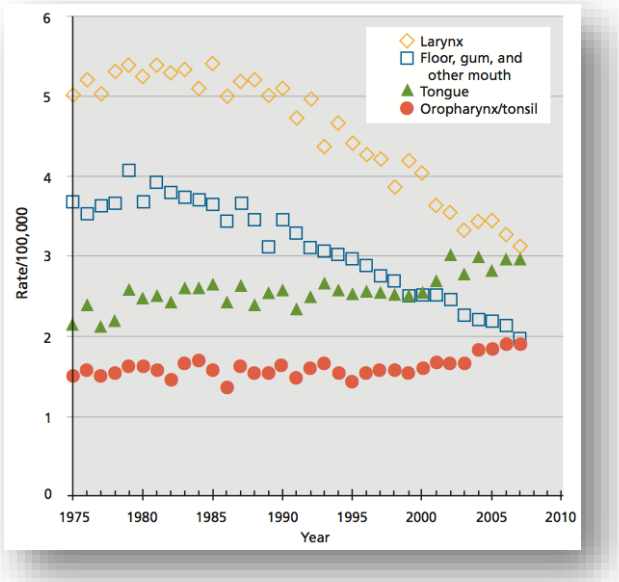
HPV E7 antigen-expressing *Listeria*-based immunotherapy (ADXS11-001) prior to robotic surgery for HPV-positive oropharyngeal cancer enhances HPV-specific T cell immunity

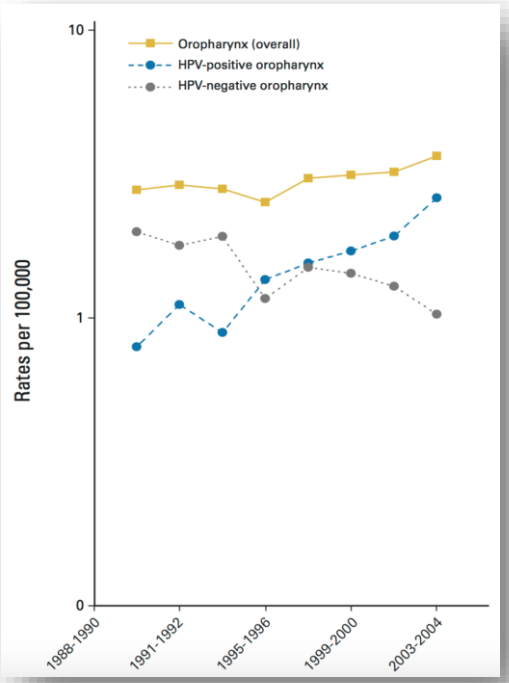
4/18/2016
Rosemarie Krupar, MD
Postdoctoral fellow
Andrew Sikora Laboratory

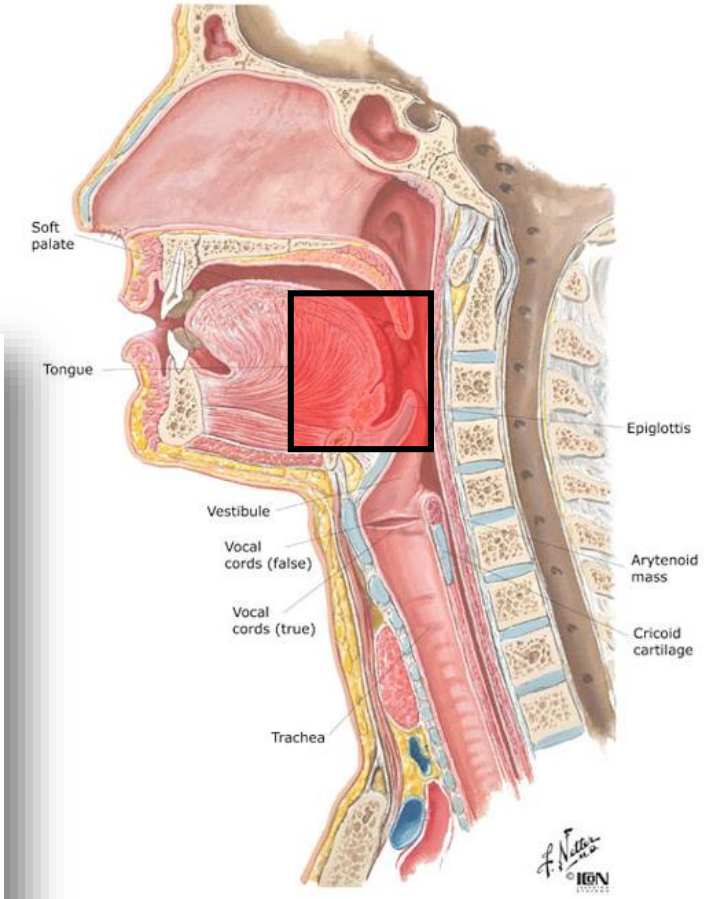
HPV-Related Oropharynx Cancer (HPVOPC)

Baylor College of Medicine

- Rapidly increasing in US
- 225% increase in incidence from 1988–2004
- Much better prognosis (>80% 5 YS)
- HPVOPC patients younger, higher SES
- Expression of the viral oncoproteins E6 and E7







Sturgis EM, et al. J *Natl Compr Canc Netw*. 2011;9:665-673;
Chaturvedi AK, et al. *J Clin Oncol*. 2011;4294-4301.

Rationale for Immunotherapy in HPVOPC

Baylor College of Medicine

Acute and chronic toxicity of intensive chemoradiotherapy

- HPVOPC patients present at “advanced” stage (III, IV)
- Treatment often involves very intense CRT regimens
- Acute effects: Mucositis, neutropenia, malnutrition, dehydration
- Chronic effects: Swallowing, speech, long-term PEG, dry mouth

Paradox: Good-prognosis disease being treated with intensive CRT

Paradox: Poor QOL outcomes in patients who will live for decades

Immunotherapy is one strategy for de-escalating toxicity of CRT

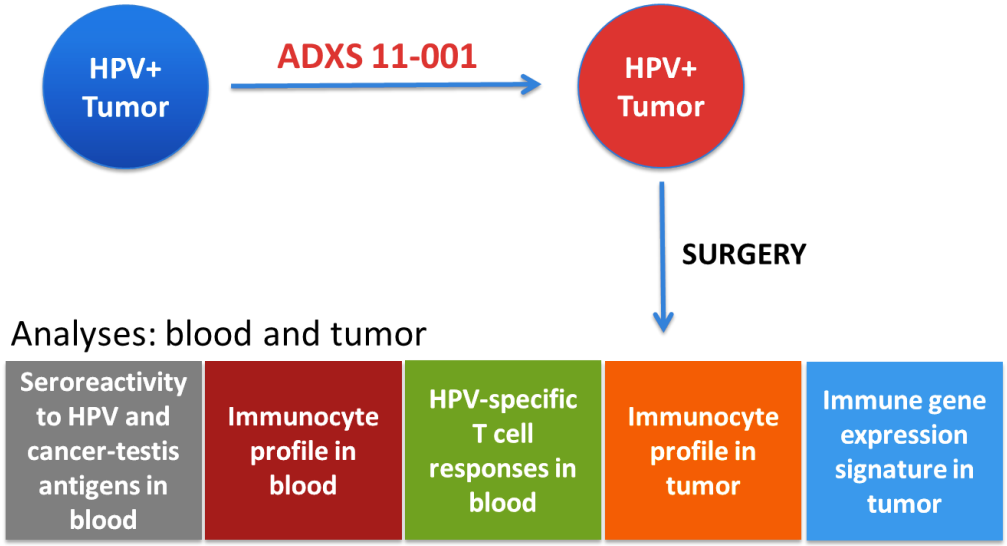
Trial Concept: "Window" Trial in HPVOPC

Baylor College of Medicine

Understand the immune mechanisms of action of ADXS11-001

- Innate immunity (cytokines, etc)
- Adaptive immunity (T-cell responses)
- Blood
- **Tumor**
- Draining lymph nodes

Safety, tolerability, feasibility in HPVOPC population



Window of Opportunity Trial: Neoadjuvant ADXS-HPV Prior to Robot-Assisted Resection (TORS) of HPVOPC

Baylor College of Medicine

Trial Design

- Single-arm Simon's 2-stage design
- Intrapatient comparison of pre- and post-treatment values
- Observational cohort – no ADXS11-001

Primary Aims

- To determine the immunogenicity of ADXS11-001 vaccination in patients with HPVOPC
- To evaluate the tolerability, safety, and nature and degree of toxicity of ADXS11-001 in HPVOPC

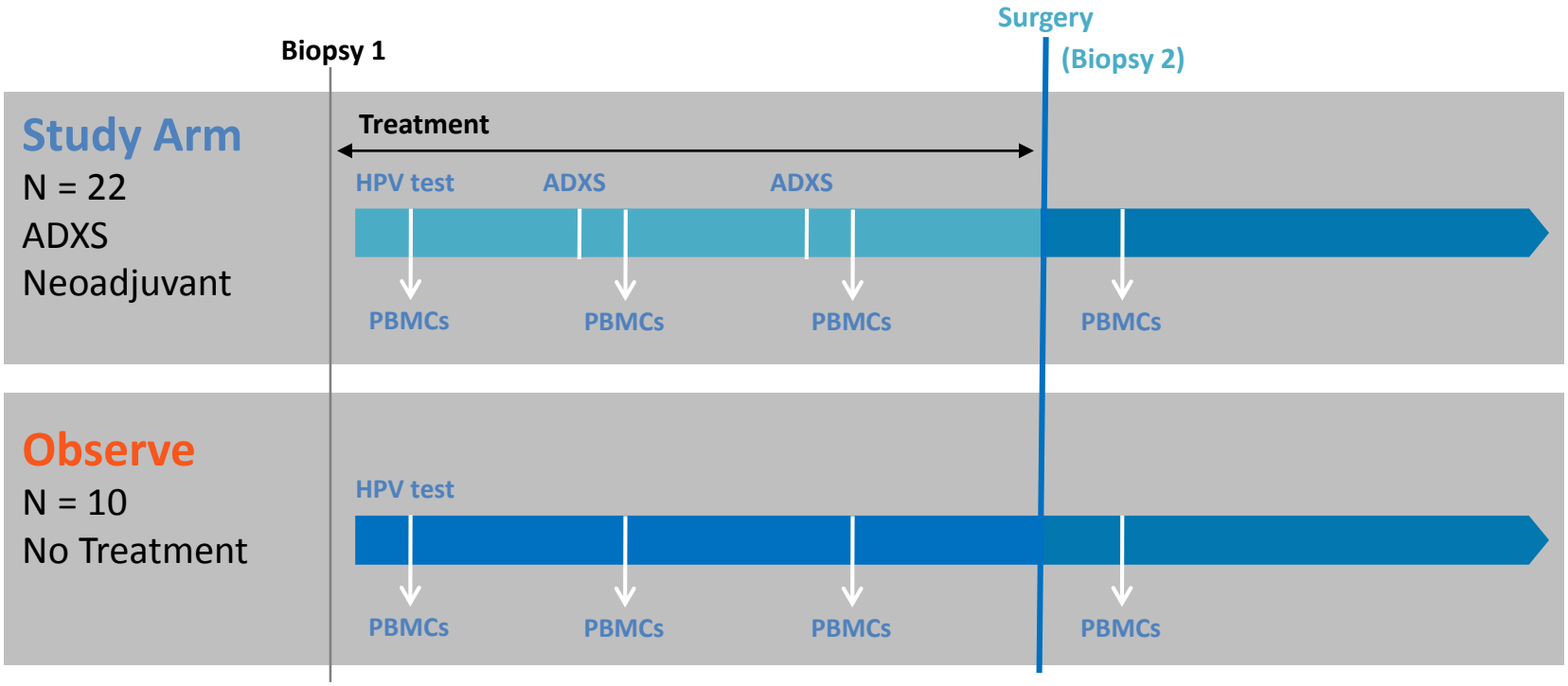
Primary Endpoints

- The change in HPV E6/E7-specific CD8+ cytotoxic T-lymphocyte (CTL) responses in the peripheral blood at time of surgery, with respect to baseline
- Toxicity (NCI Common Terminology Criteria for Adverse Events version 4.0)

Window of Opportunity Trial: Neoadjuvant ADXS-HPV Prior to Robot-Assisted Resection (TORS) of HPVOPC

Baylor College of Medicine

Window of Opportunity Trial
Oropharyngeal Squamous Cell Carcinoma (N = 22)



Mt Sinai Medical Center

- Primary stage 2–4 oropharyngeal squamous cell carcinoma (OPSCC)
- HPV+

Study Arm: ADXS-HPV Alone

- 2 doses of 1 × 10^9 CFU as an 80-mL infusion over 15 minutes

Observational Arm: No Treatment Controls

- Routine surgical preparation

Laboratory Assays

Baylor College of Medicine

Assay	Question Answered
ELISPOT for HPV E7-reactive T cells in blood	Does ADXS11-001 induce robust, systemic antigen-specific immunity?
IHC/IF for tumor-infiltrating CD8+ T cells and other immunocytes	Do vaccine-induced T cells make it into the tumor? Is the overall balance of suppressor and effector immune cells in the tumor microenvironment improved after treatment?
Immunophenotyping of suppressor and effector immune cell subsets in blood by flow cytometry	Does ADXS11-001 improve the systemic balance of suppressor and effector immunocytes?
Seroreactivity to HPV antigens and HNSCCA-associated cancer-testis antigens in blood	Does targeting a foreign viral antigen (E7) lead to epitope spreading and induction of a broad-based response to self-derived tumor antigens?
Immune gene expression signatures in tumor microenvironment by Nanostring	Is ADXS11-001 associated with an “immune-response signature” of altered gene expression? Can we identify potential molecular targets for combination therapy?
Multiplex serum cytokine and soluble immunomodulator levels by Luminex analysis	Does ADXS11-001 induce durable inflammatory/immune cytokine signature?
T-cell receptor diversity profiling by ImmunoSEQ TCR deep sequencing	How does ADXS11-001 treatment affect the depth and breadth of the tumor-infiltrating T-cell repertoire?

Current Status of the Trial

Baylor College of Medicine

- **8 study patients have** completed ADXS11-001 administration and tumor resection by TORS
- **6 observational patients** have completed tumor resection by TORS
- **3 adverse events (AEs) grade III** have been observed in the study patients (vomiting, hypertension)
- **Remaining AEs have been grade I–II**

Current Status of Laboratory Assays

Baylor College of Medicine

- Tumor immune microenvironment (**TIME**) profiling of biopsies before ADXS11-001 administration (**preADXS**) and of surgical resection specimen (**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
- Currently, completion of immunophenotyping for 8 study patients and 3 control patients preADXS, postADXS, and postTORS

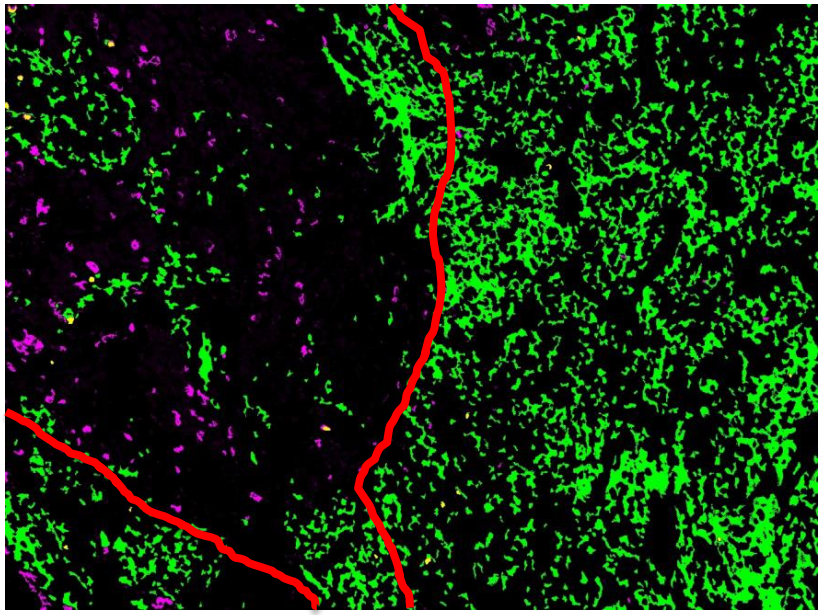
TIME Profiling by Quantitative Immunofluorescence

Baylor College of Medicine

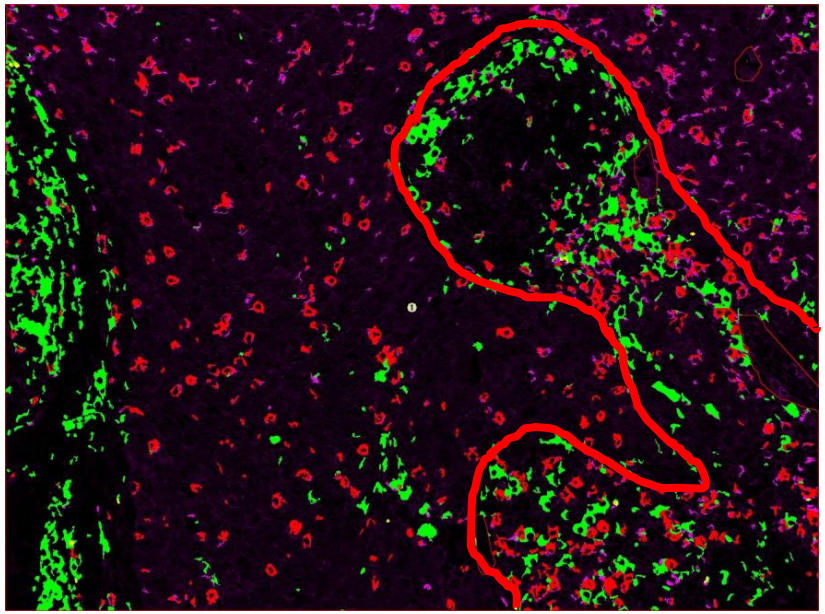
Quantitative multiplex immunofluorescence (qIF)

- preADXS biopsies and postADXS surgical resection specimens
- Evaluation of tumor-infiltrating CD8+, CD4+, and FOXP3+ T cells
- Expression evaluation of negative immune checkpoint molecules PD-1, PD-L1, and VISTA

preADXS

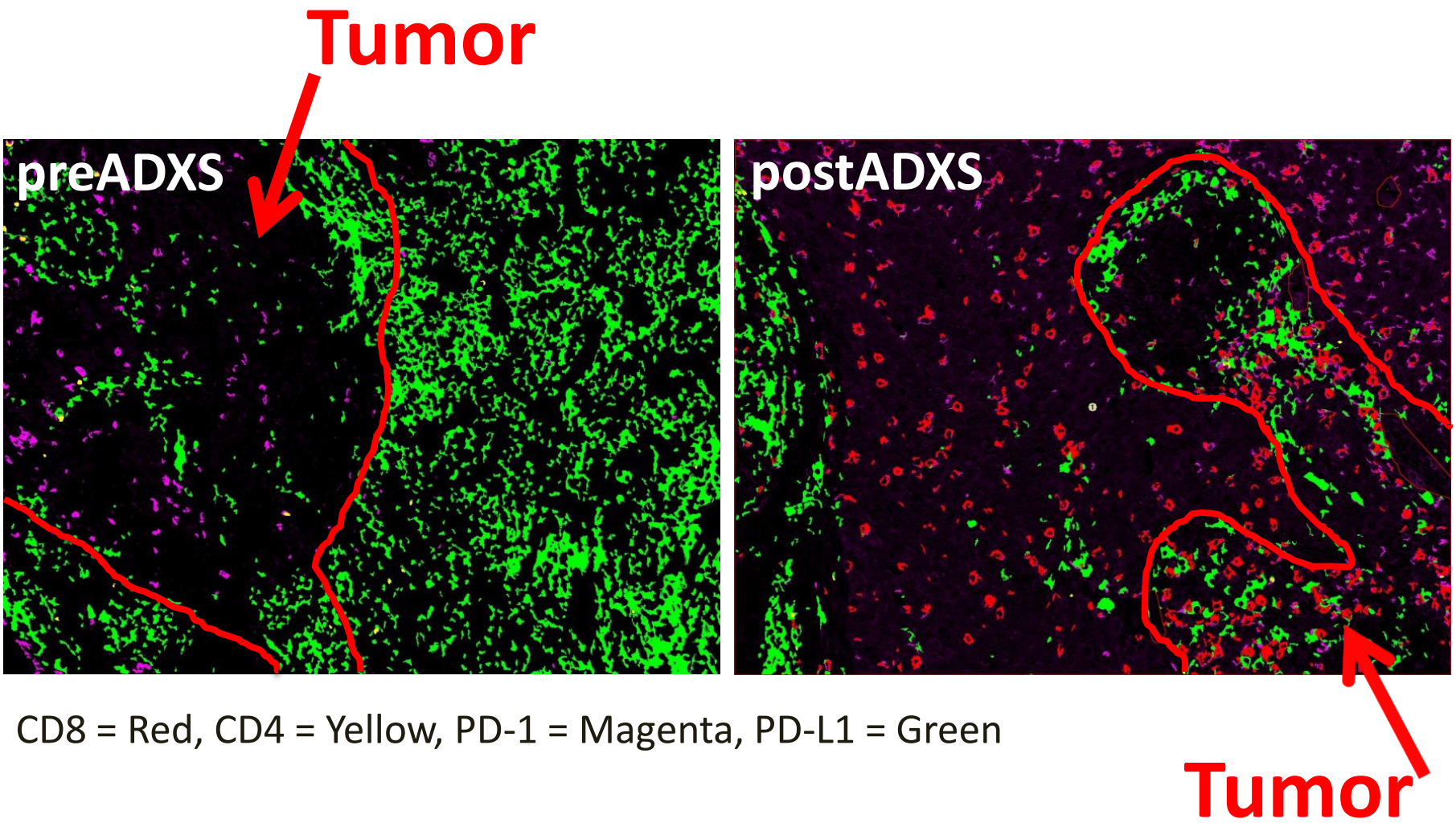


postADXS



TIME Profiling by Quantitative Immunofluorescence

Baylor College of Medicine

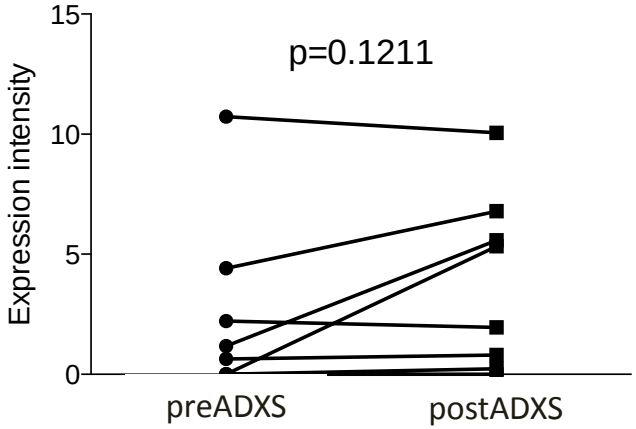


CD8 = Red, CD4 = Yellow, PD-1 = Magenta, PD-L1 = Green

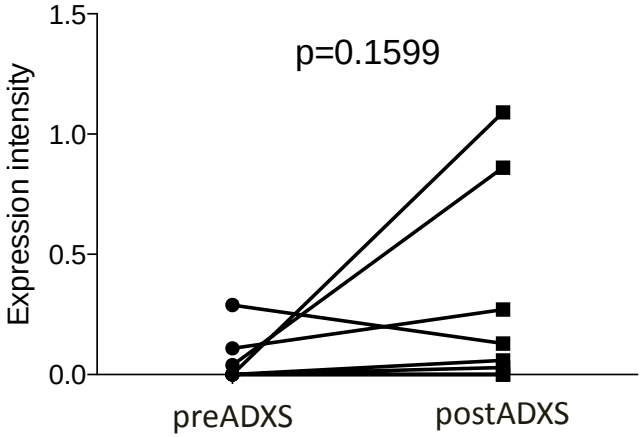
TIME Profiling by Quantitative Immunofluorescence

Baylor College of Medicine

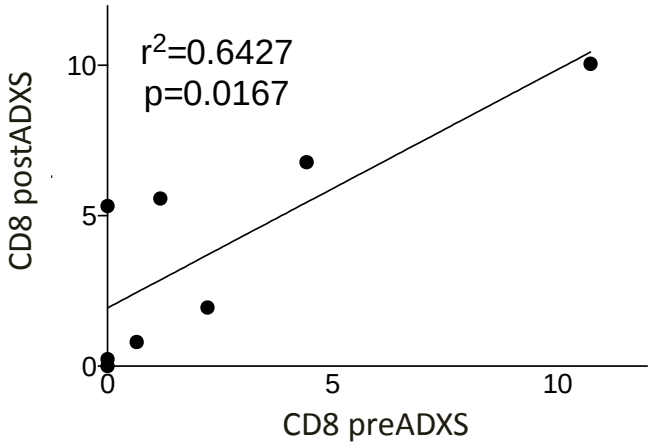
CD8



CD4



CD8 pre/postADXS

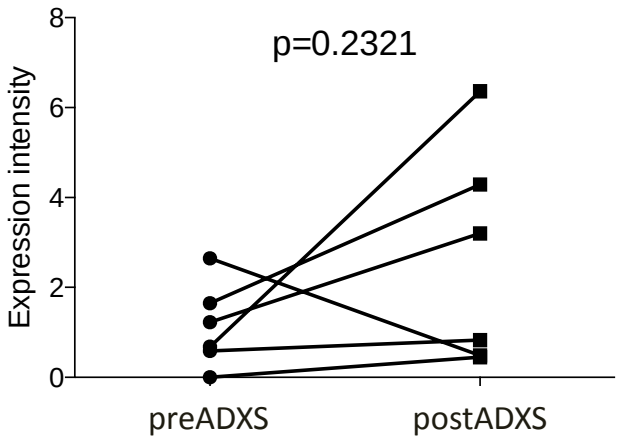


- **CD8 and CD4 T cells increased in 4 of 8 patients** postADXS
- **CD8 T cells** preADXS strongly correlated with **CD8 T cells** postADXS

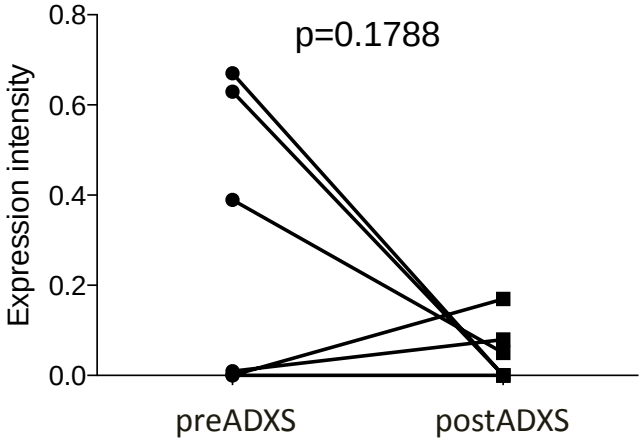
TIME Profiling by Quantitative Immunofluorescence

Baylor College of Medicine

VISTA

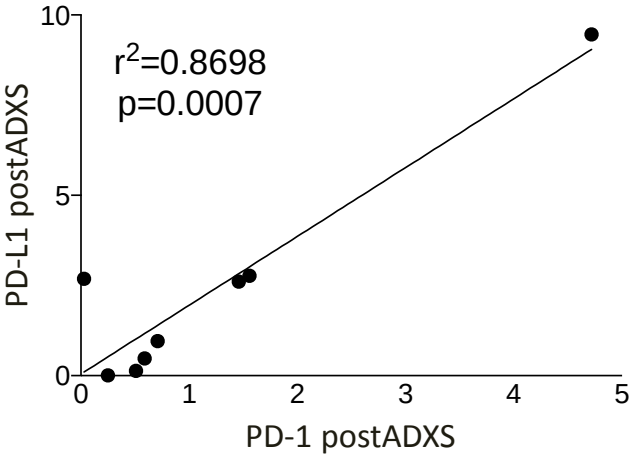


FOXP3



- The immune checkpoint molecule **VISTA increased in 5 of 6 patients** postADXS
- **FOXP3+ regulatory T cells decreased in 3 of 6 patients postADXS**
- **PD-1 strongly correlated with PD-L1** after ADXS11-001 administration

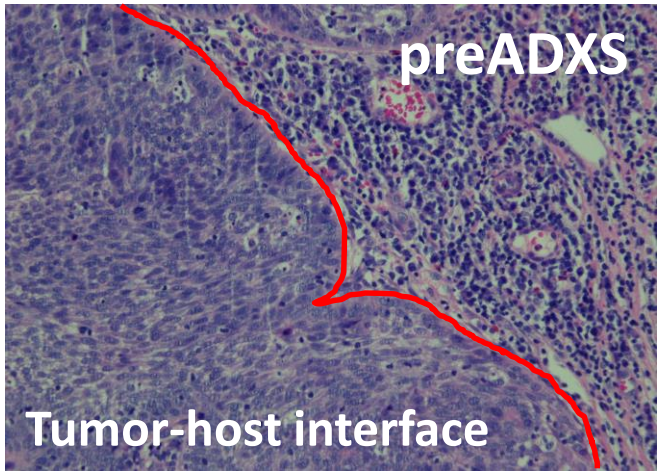
PD-1/PD-L1 postADXS

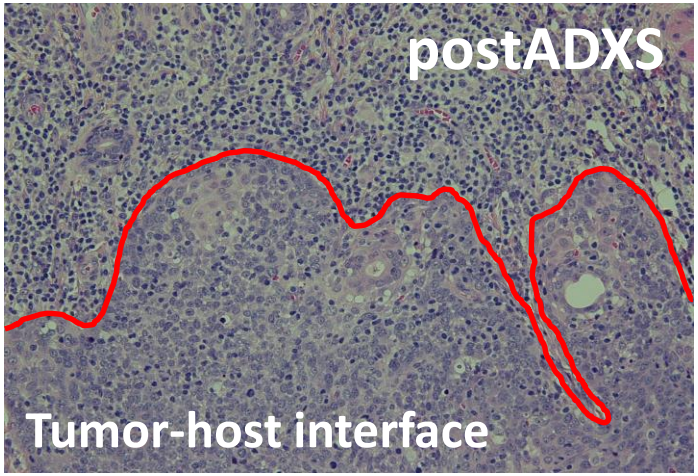


H&E Analysis of Tumor-Infiltrating Lymphocytes

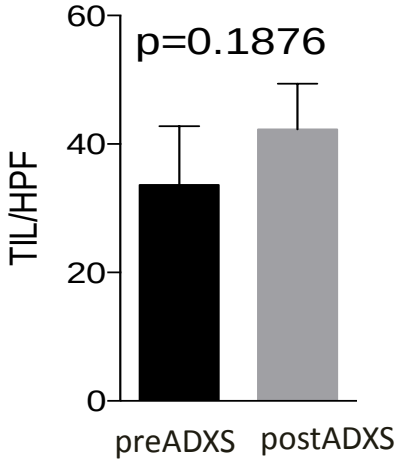
Baylor College of Medicine

Tumor-infiltrating lymphocytes (TIL) at the tumor-host interface

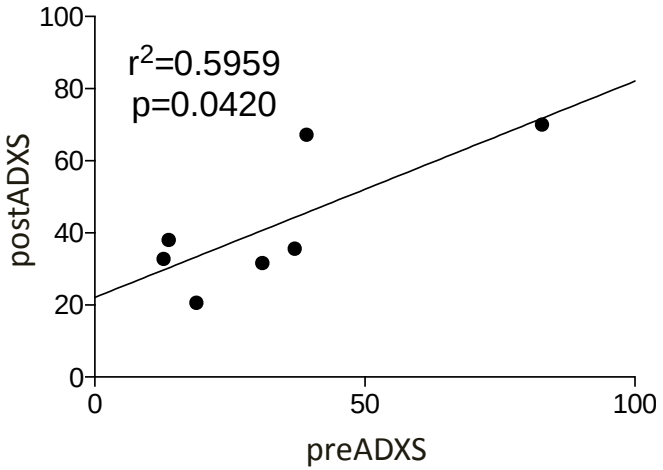




TIL at interface



Pre/postADXS TIL

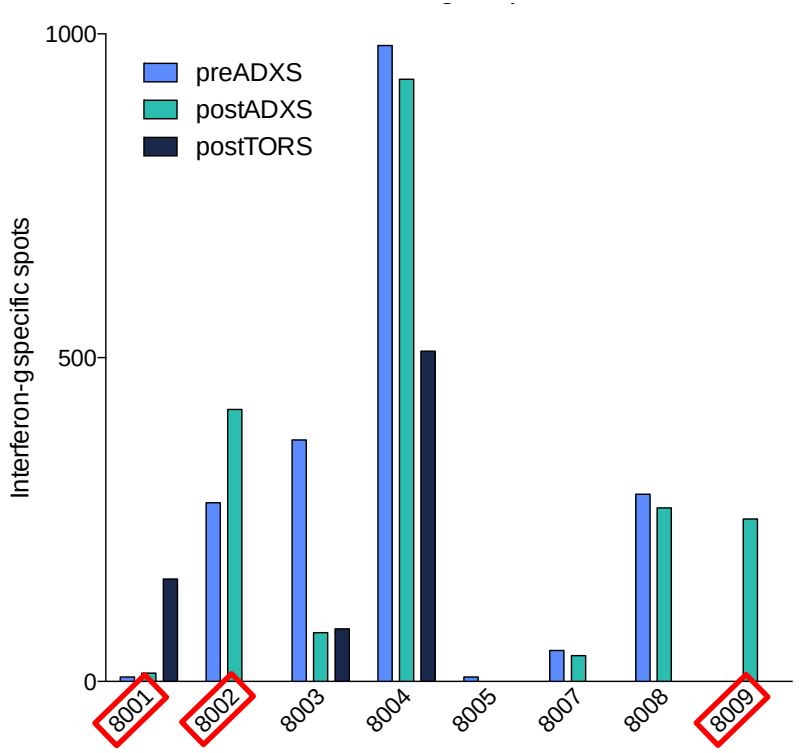


E6/E7-Specific Immune Response in the Blood

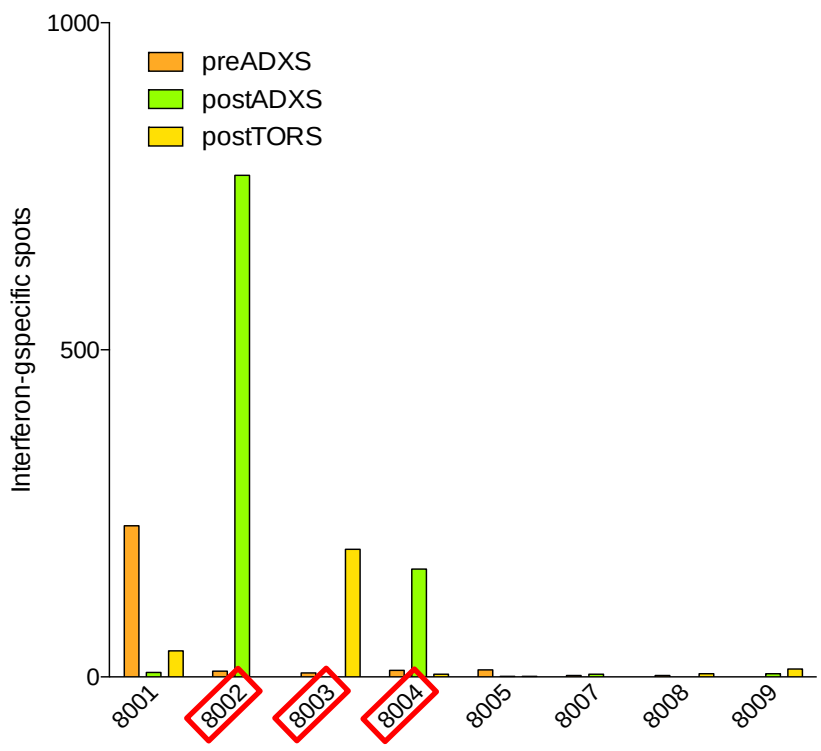
Baylor College of Medicine

Interferon-γ ELISpot assessing IFN-γ–specific response against E6 or E7 in PBMCs of 8 study patients preADXS, postADXS, and postTORS

E6 ELISpot



E7 ELISpot

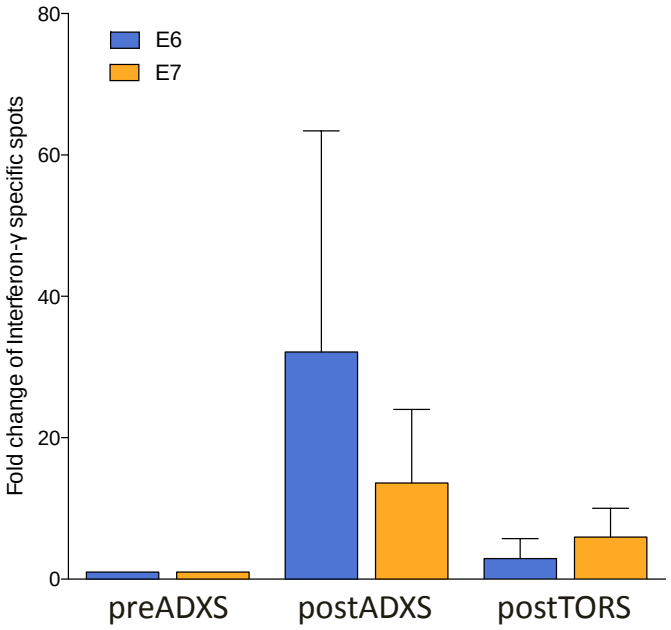


E6/E7-Specific Immune Response in the Blood

Baylor College of Medicine

Interferon-γ ELISpot assessing IFN-γ–specific response against E6 or E7 in PBMCs of 8 study patients preADXS, postADXS, and postTORS

Relative IFN-γ response



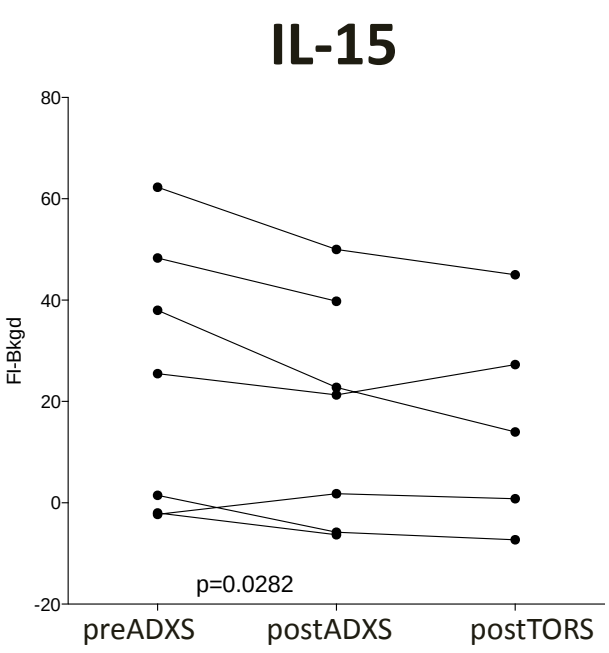
Patient	E6	E7
8001	+	
8002	(+)	+
8003		+
8004		+
8005		
8007		
8008		
8009	+	

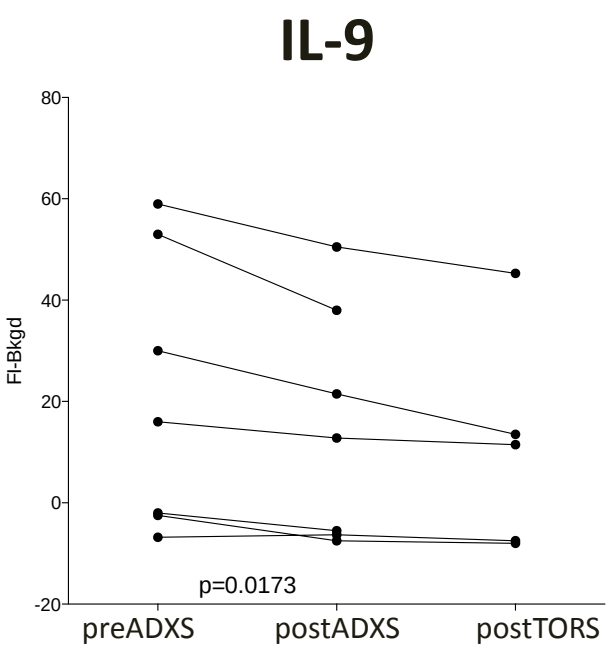
5 out of 8 study patients showed E6 and/or E7-specific T-cell response in the peripheral blood postADXS or postTORS

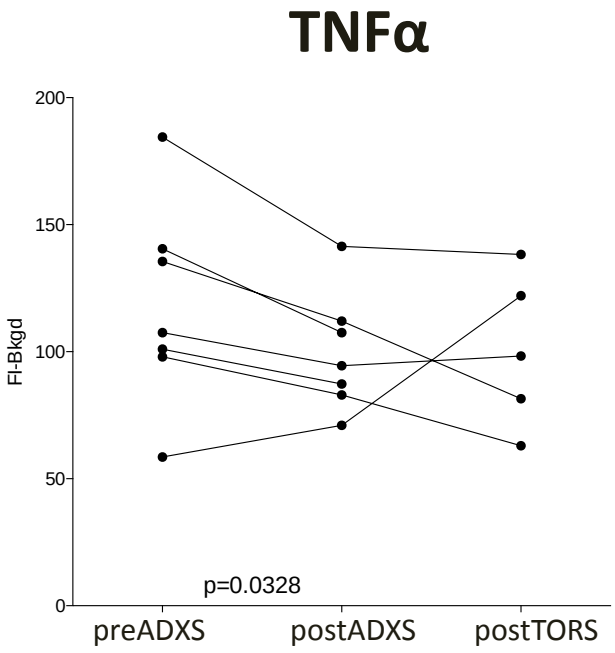
Luminex Multiplex Analysis of Serum Cytokines

Baylor College of Medicine

Analysis of preADXS, postADXS, and postTORS serum for 38 cytokines by Luminex multiplex platform of 7 study patients





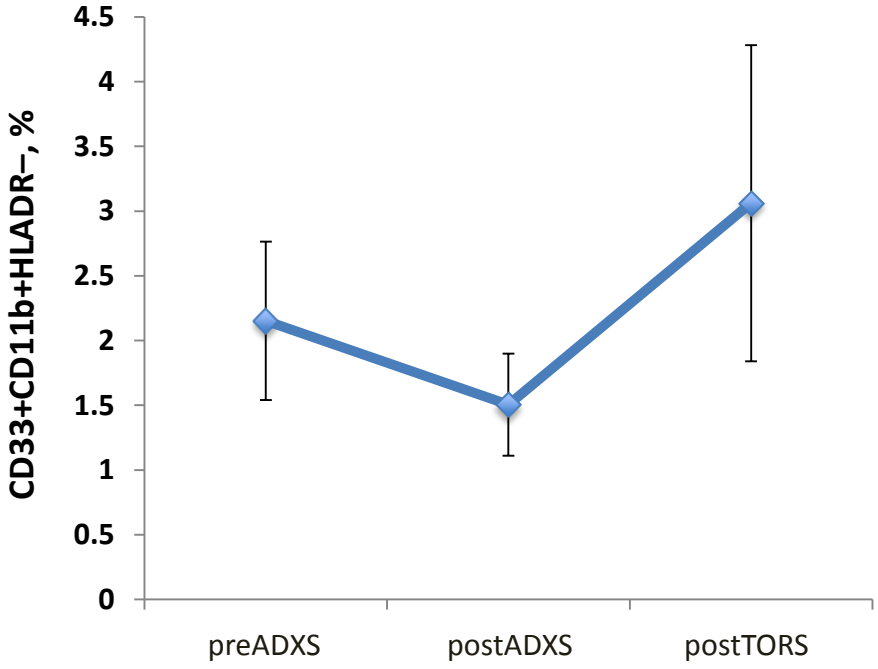


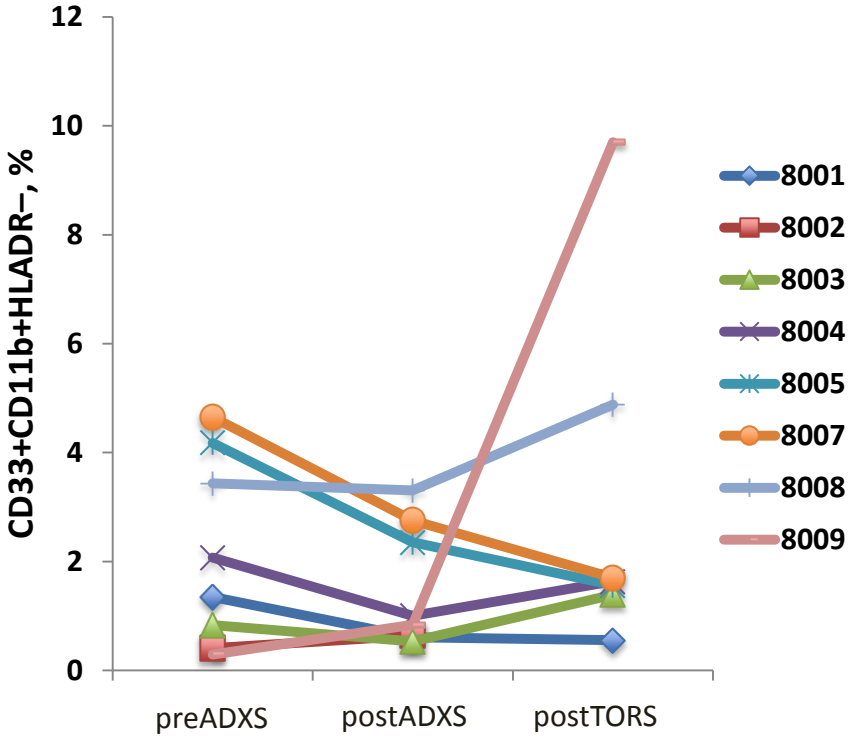
Decrease of serum cytokines **IL-15, IL-9, TNFα, IL-2, and MIP-1b** levels postADXS

Immunophenotyping of the Peripheral Blood

Baylor College of Medicine

MDSC frequency in the peripheral blood preADXS, postADXS, and postTORS in 8 study patients

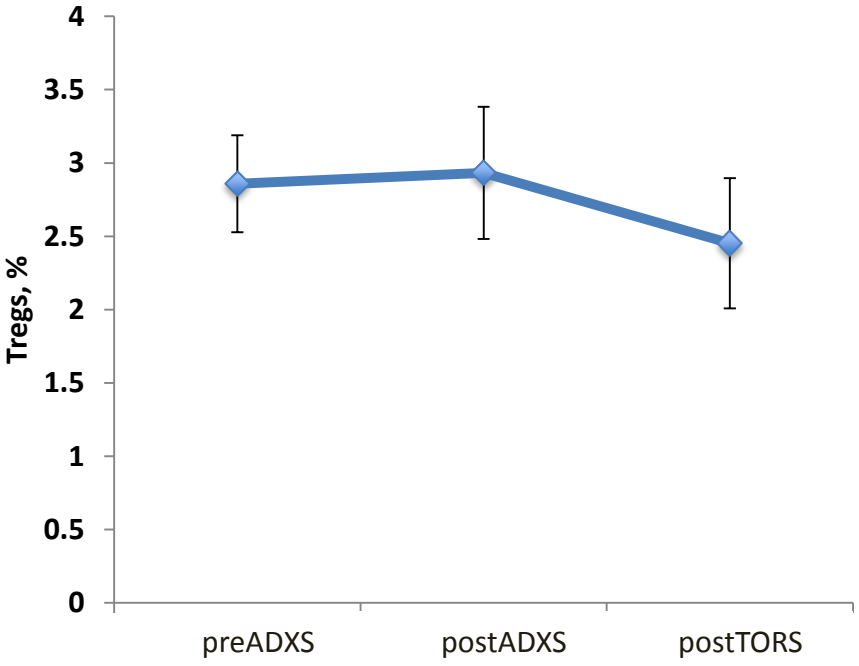


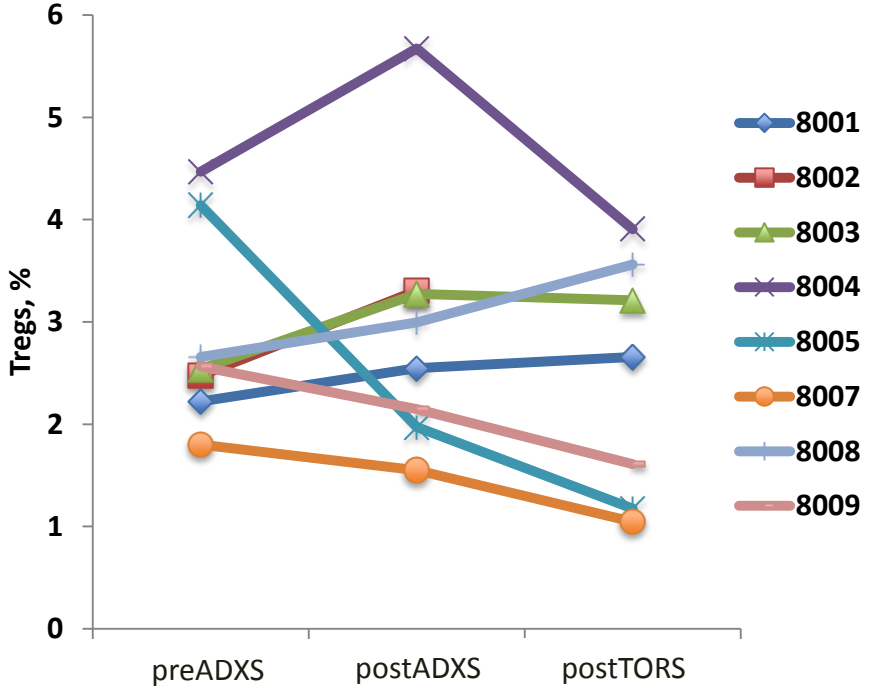


Immunophenotyping of the Peripheral Blood

Baylor College of Medicine

Treg frequency in the peripheral blood preADXS, postADXS, and postTORS in 8 study patients





Summary

Baylor College of Medicine

- Successful accrual of 8 study patients and 6 observational 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 antitumor immunity

Further Investigations

Baylor College of Medicine

- 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

Acknowledgments

Andrew Sikora laboratory

- Falguni Parikh
- Ravi Pathak
- Jigneshkumar Patel

Baylor College of Medicine (BCM)

- Hao Liu

Icahn School of Medicine At Mount Sinai

- Brett Miles
- Marshall Posner
- Eric Genden
- Sacha Gnjatic
- Michael Donovan
- Elizabeth Demicco

Columbia University Medical Center

- Yvonne Saenger

Arizona State University

- Karen Anderson

Funding sources:

ADVAXIS IMMUNOTHERAPIES™

FDA

Lm Immunotherapy: Impact Within the Tumor Microenvironment

Immunogenicity of ADXS-HER2 in Canine Osteosarcoma

Nicola Mason, PhD, BVetMed
Assistant Professor of Medicine and Pathobiology
University of Pennsylvania

ADVAXIS
IMMUNOTHERAPIES™

Effects of Advaxis' *Lm* Immunotherapy on the STING Pathway

Robert Petit, PhD
Advaxis

ADVAXIS
IMMUNOTHERAPIES™

STING Agonism: Inherent in Advaxis Vectors

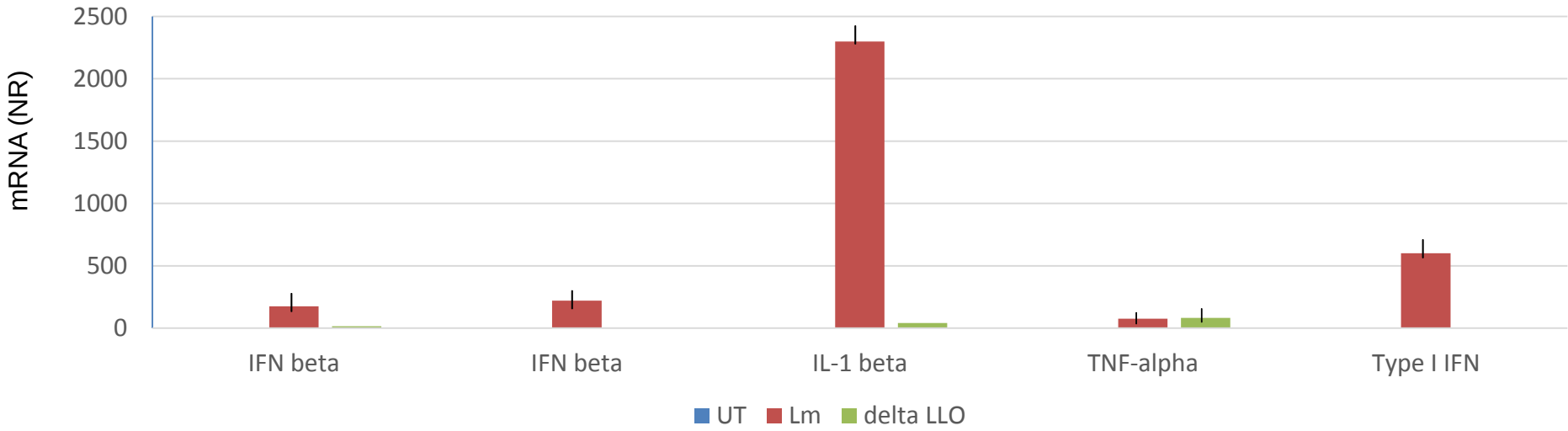
ADVAXIS IMMUNOTHERAPIES™

- **STING** is a cytosolic detector of pathogen DNA and or DNA breakdown products (dicyclic nucleotides) in APCs that triggers secretion of type I interferons and proinflammatory cytokines
- **Human STING triggered primarily by DNA**; mouse STING recognizes both DNA and dicyclic nucleotides
- **STING agonism**
  - **Enhances T-cell immunity, particularly with vaccines**
    - ***Cures PD-1–resistant tumors***
  - **Innate immune "sensing" of tumors leading to adaptive immunity**
  - **Increases TIL infiltration into tumors**
  - **Promotes antitumor immune responses to dying cells (epitope spreading)**
- **Advaxis *Lm* vectors have DNA genomes** and replicate in the cytosol of the APCs
- **Advaxis *Lm* vectors** contain 80–100 copies of **DNA plasmids** per bacterium, potentially triggering more STING than even wild-type *Lm*

Data on file.

STING Is a Component of Advaxis *Lm* Immune Stimulation

ADVAXIS IMMUNOTHERAPIES™



Lm triggers type I interferons through STING in human macrophages

In human cells, *Lm* DNA, rather than cyclic dinucleotides, triggers STING

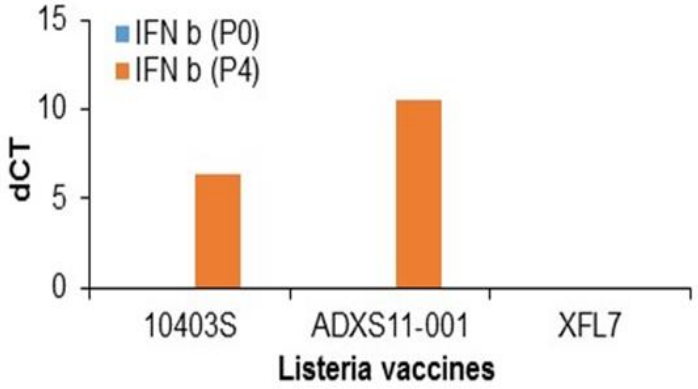
In addition to *Lm* DNA, Advaxis constructs also contain <u>additional</u> DNA in multiple copies of DNA plasmids

Hansen K, et al. *EMBO J.* 2014;33:1654-1666.

Stimulation of the STING pathway by ADXS11-001

ADVAXIS IMMUNOTHERAPIES™

	10403S	ADXS11-001	XFL7
IFN b (P0)	Undetermined	Undetermined	Undetermined
IFN b (P4)	6.32	10.57	Undetermined

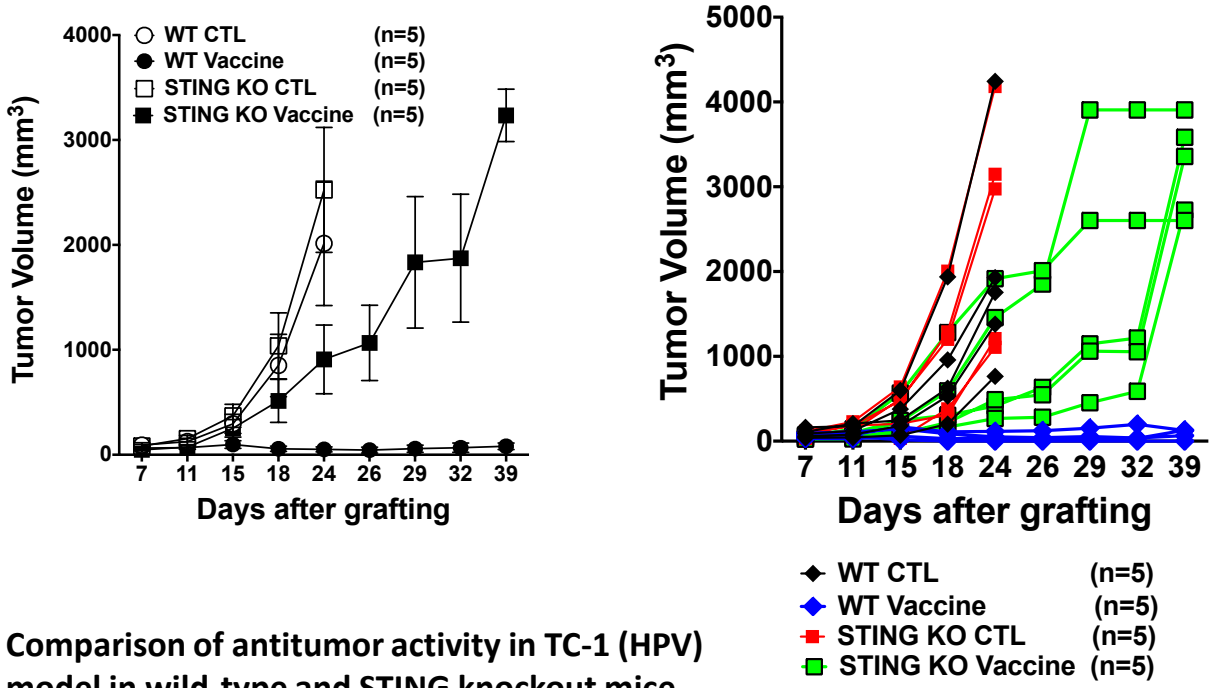


- STING (stimulator of interferon genes) triggered by ds-DNA in the cytoplasm of the APC
- Triggering STING is important to antitumor immunity and immune recognition of tumors
- *Lm* triggers IFN-β secretion via STING pathway
- ADXS11-001 has additional multicopy ds-DNA plasmids that may contribute greater stimulation of the STING pathway than *Lm* without multicopy plasmids

Data on file.

Contribution of STING signaling to ADXS11-001 activity

ADVAXIS IMMUNOTHERAPIES™



Comparison of antitumor activity in TC-1 (HPV) model in wild-type and STING knockout mice

CTL = HPV E7 vaccine control

Vaccine = ADXS11-001 (AXAL)

AXAL activity is reduced, but not eliminated, in a STING knockout model

Potent triggering of STING is built into every Advaxis vector

Data on file.

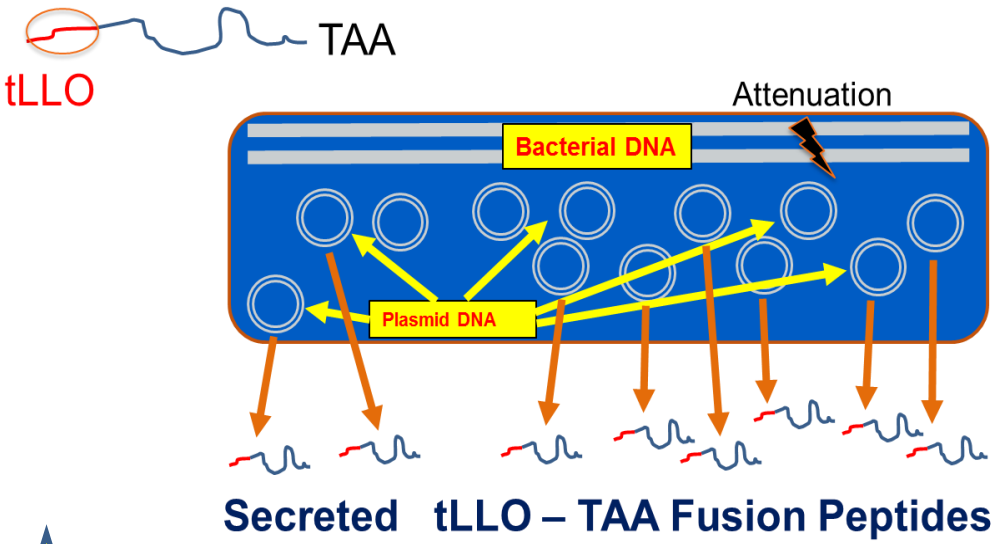
Cancer Neoepitope Immunotherapy: An Update on ADXS-Neo

Robert Petit, PhD
Advaxis

ADVAXIS
IMMUNOTHERAPIES™

Targeting Neoepitopes with *Lm* Technology™
Advantages for Personalized Immunotherapy

ADVAXIS IMMUNOTHERAPIES™



- tLLO-TAA fusion represents multiple precision-selected neoepitopes secreted into the cytoplasm of the APC by ADXS-Neo
- 80–100 plasmid copies per bacterium
- Payload for multiple neoepitopes per construct
- Vector activates innate immune pathways (TLRs, PAMP, STING, DAMP, NOD1, NOD2, CpG)
- Treatments can be given repeatedly without neutralizing antibodies
- Decreases Tregs and MDSCs in the tumor microenvironment
- Can combine tumor driver targets with neoepitope targets

Lm Technology™ has advantages for targeting neoepitopes

- **Bandwidth** – 20+ epitopes possible
- **Feasibility** – affordable COGS, ease of manufacture, rapid turnaround time

Data on file.

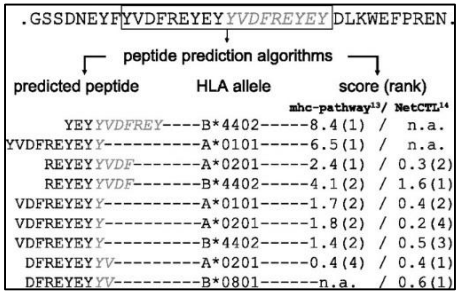
ADXS-Neo Schema: How Does It Work?

ADVAXIS IMMUNOTHERAPIES™

Academic or Commercial Massively Parallel Sequencing

Sequencing to identify non-synonymous mutations

Identify neoepitope targets

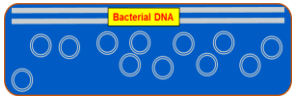


Advaxis Immunotherapies

Advaxis designs vector to target key neoantigens

DNA synthesis – molecular cloning

Transfection into *Lm* vector, QA/QC – OK



Ship to patient's institution

Patient's Hospital or Treating Institution

Treat patient with immunotherapy vector targeting neoantigens

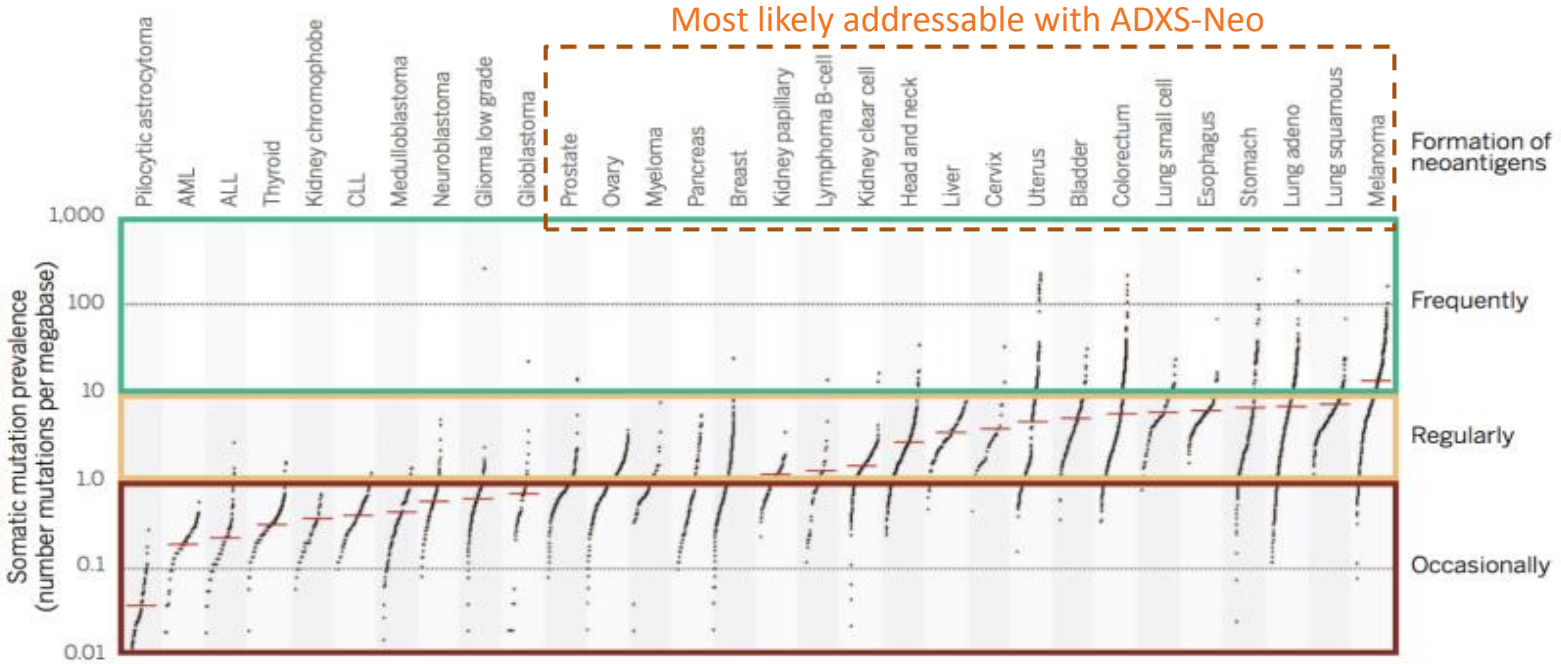
- Multiple cycles of treatment
- Combination with
  - PD-1, co-stims
  - ADXS-tumor driver vectors
  - Other treatments

Time from biopsy to infusion administration ~4–5 weeks

Data on file.

ADXS-Neo: Collaborations and Indications

ADVAXIS IMMUNOTHERAPIES™



Schumacher TN and Schreiber RD. *Science* 2015;348(6230):69-74.

Collaborations and Clinical Indications

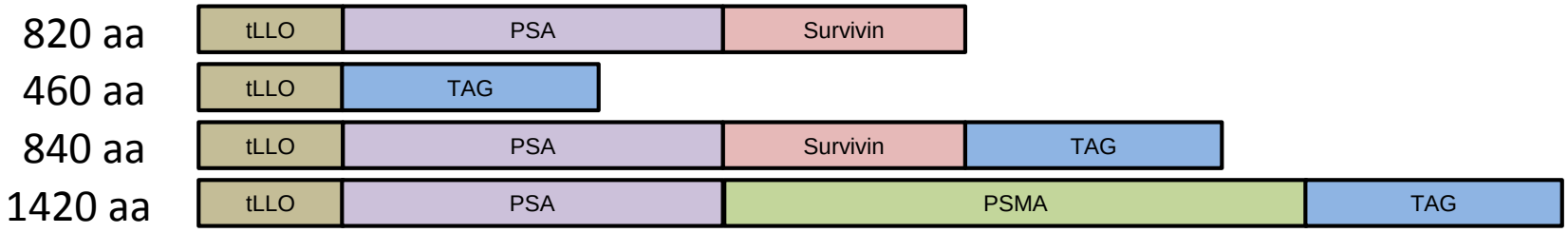
- **Advaxis is actively building close collaborations both in academia and industry in order to drive ADXS-Neo forward as rapidly as possible**
  - MINE™ collaboration with Memorial Sloan Kettering Cancer Center will focus on preclinical and clinical development of neoepitope-based *Lm* treatments
  - Researchers interested in targeting: melanoma, NSCLC, colorectal adenocarcinoma, head and neck cancer, ovarian cancer
- **Clinical strategy will emphasize the broad applicability of *Lm* Technology™ to many different types of cancer through a combination of ISTs and company sponsored trials**

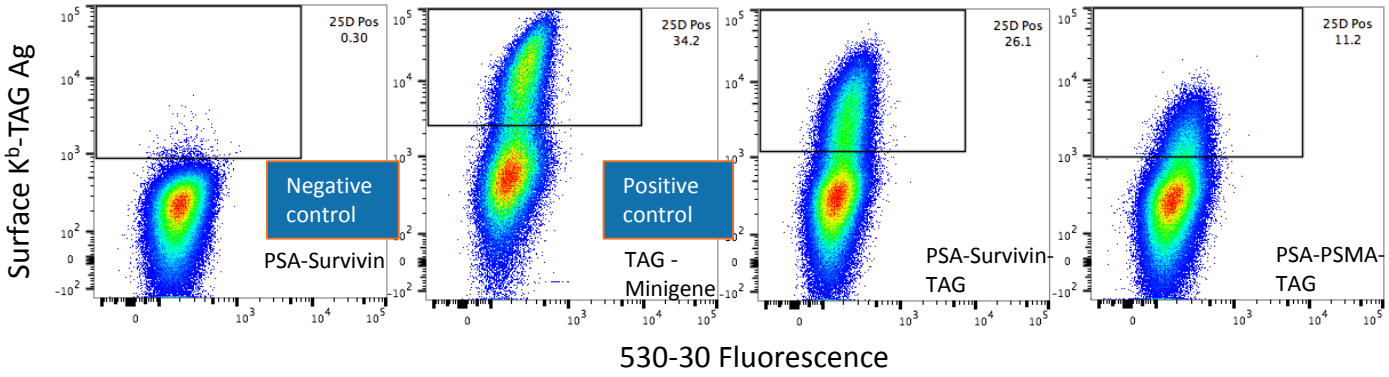
Data on file.

Multi-epitope *Listeria* Vector:
Confirmation of Antigen Production from Polypeptides of Differing Length Using the TAG Antigen Presentation Assay

ADVAXIS IMMUNOTHERAPIES™

Polypeptide length:





Data on file.

Modeling ADXS-Neo

ADVAXIS IMMUNOTHERAPIES™

- B16-F10 tumors were sequenced and compared to normal tissue to identify nonsynonymous mutations (neoepitopes)
- Results compared to Castle et al[1]
  - ~3,570; 50 validated in DNA
  - 12 (16) immunogenic
  - 2 controlled tumor growth

Research Questions

- Can we do it?
- Will Advaxis *Lm* present neoantigens?
- Are ADXS-Neo constructs capable of tumor control?
- Are more neoantigens better than fewer?
- How does it compare to another platform's Neo constructs?

Data on file; 1. Castle J, et al. *Cancer Res.* 2012;72(5);1081-1091.

Two ADXS-Neoantigen Constructs Were Tested in a Mouse Tumor Model (B16F10 Melanoma)

ADVAXIS IMMUNOTHERAPIES™

Sequences containing nonsynonymous mutations used to create 2 neoantigen constructs:

Neo 12

Mutation #	Amino Acid Sequence
MUT30	PSFQEFVDWENVSPELNSTDQ
MUT5	KAYLPVNESFAFTADLRSNTG
MUT17	RNPQFLDPVLAYLMKGLCEKP
MUT20	KAFLHWYTGEAMDEMEFTEAE
MUT22	DFSQLQRNILPSNPRVTRFHI
MUT24	ITPPTTTTKKARVSTPKPATP
MUT25	NYNTSHLNNDVWQIFENPVDW
MUT44	HIKAFDRTFANNPGPMVVFAT
MUT45	ITSNFVIPSEYWVEEKEEKQK
MUT46	GLVTFQAFIDVMSRETTDTDT
MUT48	HWNDLAVIPAGVVHNWDFEPR
MUT50	QPLRRLVLHVVSAAQAERLAR

Tumor control

Tumor control

Neo 20

Mutation #	Amino Acid Sequence
MUT30	PSFQEFVDWENVSPELNSTDQ
MUT2	AENVEQVLVTIIQGAVDYPDP
MUT3	SFKKKFEECQHNIIKLQNGHT
MUT4	SALIESLNQKTQSTGDHPQPT
MUT5	KAYLPVNESFAFTADLRSNTG
MUT6	HTLLEITEESGAVLVDKSDSD
MUT7	SVMCTYSPPLDKLFCQLAKTC
MUT8	ESGKHKYRQTAMFTATMPPAV
MUT9	AAPSAASSPADVQSLKKAMSS
MUT10	SQLFSLNPRGRSLVTAGRIDR
MUT11	SLARGPLSEAGLALFDPYSKE
MUT12	QKKLCHLSSTGLPRETIASLP
MUT13	LTASNMEGKSWPSEVLVCTTS
MUT14	YAAQQHETFLTNGDRAGFLIG
MUT15	QAKVPFSEETQNLILPYISDM
MUT16	CNRAGEKHCFSSNEAARDFGG
MUT17	RNPQFLDPVLAYLMKGLCEKP
MUT18	LECERGKQEAKLLAERSRFED
MUT19	APLEWLRYFDKKELELMLCGM
MUT20	KAFLHWYTGEAMDEMEFTEAE

Tumor control

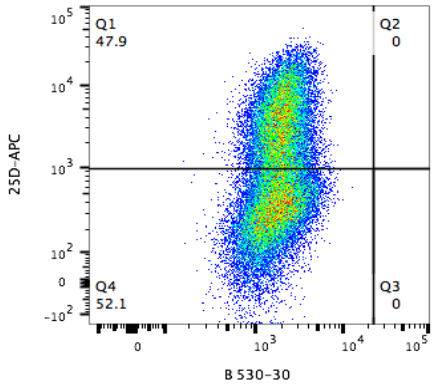
- Antigens in Neo 12 selected based on T-cell response to Peptide + Poly I:C demonstrated by Castle et al
- Mut30 and Mut44 associated with tumor control in Castle et al

Castle J, et al. *Cancer Res.* 2012;72(5); 1081-1091.

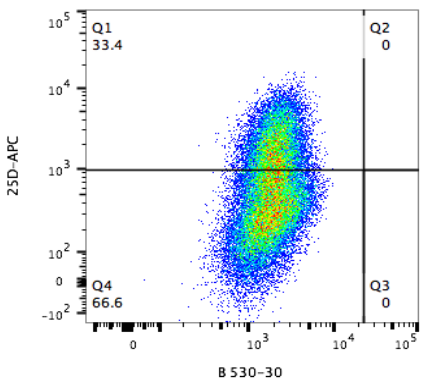
Confirmation of Antigen Presentation from a Neoepitope Construct

ADVAXIS IMMUNOTHERAPIES™

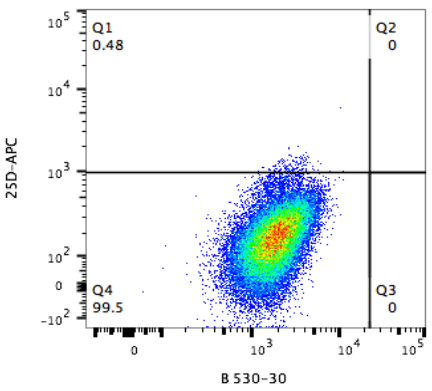
PSA-SVN-TAG



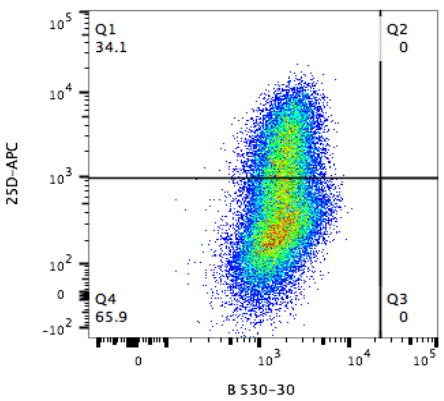
PSA-PSMA-TAG



PSA-SVN-No Tag



Lm Neo 20 TAG



Protein secretion and antigen processing and presentation are confirmed for a representative multiepitope (20 × 21-mers) construct using TAG presentation assay

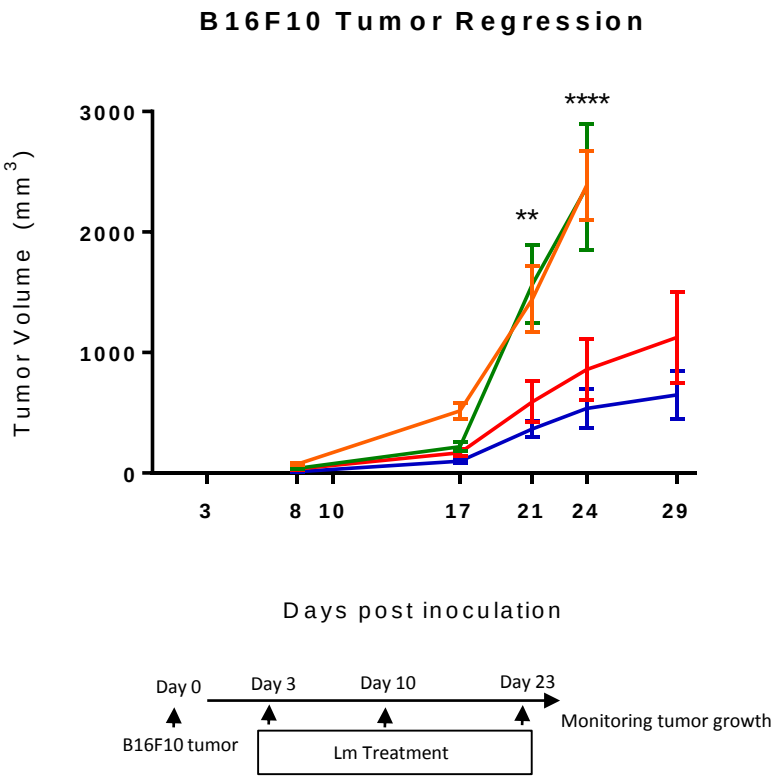
Data on file.

Lm Neoepitope Constructs Expressing Multi-epitope 21-mers Control Tumor Growth

ADVAXIS IMMUNOTHERAPIES™

Experimental Design

- B16F10 tumors were implanted
- Mice (C57BL/6) received 3 doses of ADXS-Neo vectors expressing neoepitopes
- Control mice received either PBS or *Listeria* without neoantigen (LmddA274)



Data on file; data discussed are from Castle J, et al. *Cancer Res.* 2012;72(5); 1081-1091.

ADXS Neo: Summary

ADVAXIS IMMUNOTHERAPIES™

- Can Advaxis create tumor-specific ADXS-Neo constructs? YES
- Can ADXS-Neo vectors present neoantigens? YES
- Are ADXS-Neo constructs capable of tumor control? YES
- Are more neoantigens better than fewer? Perhaps
- How does it compare to another platform's Neo constructs? TBD
- Next steps?
  - Prepare for IND and clinical trials

305 College Road East
Princeton, NJ
www.advaxis.com
ir@Advaxis.com

Thank you

ADVAXIS
IMMUNOTHERAPIES™