Analyst and Investor Day Meeting

NewLink Genetics Corporation

Nasdaq: NLNK
October 25, 2016

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Today's Agenda

Science, Clinical Trials and Future Opportunities

IDO, GDC-0919 and Indoximod

- Immuno-oncology is the future of cancer treatment
- IDO is an increasingly validated immuno-oncology target
- Two IDO pathway inhibitors – GDC-0919 and indoximod
- Two distinct mechanisms of action

Clinical Trials and Timelines

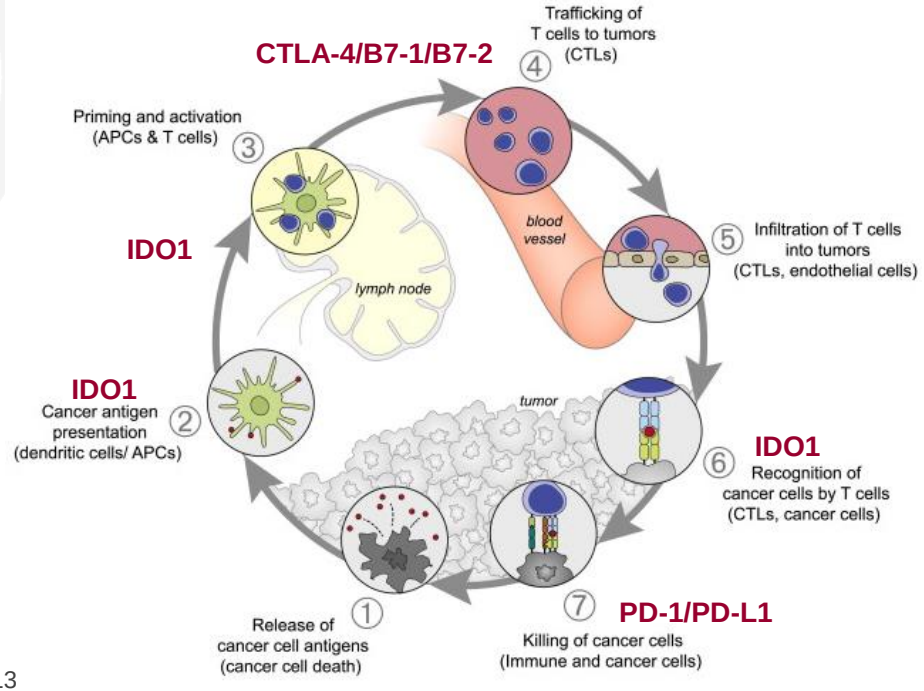
- GDC-0919 – NewLink partnership with Genentech/Roche, opportunity for milestones
- Indoximod – proprietary to NewLink, update on clinical progress

Future R&D and Financials

- PTEN R&D
- In-licensing
- Financial update

IDO is a Central Pathway in Tumor Immuno-Oncology

Applicable Across a Wide Range of Malignancies



From DS Chen, Ira Mellman: Immunity 2013

IDO overexpression is central to immune escape

Today's Presenters – Distinguished Speakers

IDO Combinations with Checkpoint Inhibitors

George C. Prendergast, PhD, President & Chief Executive Officer, Lankenau Institute for Medical Research (LIMR), Editor-in-Chief, Cancer Research

Immunoregulatory Role of Tryptophan Metabolism

David H. Munn, MD, Medical College of Georgia, Augusta University

Understanding Current Melanoma Clinical Data

Montaser Shaheen MD, Associate Professor, University of New Mexico Cancer Center

Indoximod in Treatment of Patients with Acute Myeloid Leukemia (AML)

Ashkan Emadi, MD, PhD, Associate Professor of Medicine, Pharmacology & Experimental Therapeutics, University of Maryland

Today's Presenters – NewLink Management Team

Clinical Strategy and Key Collaborations

Nicholas N. Vahanian, MD, Co-Founder, President, Chief Medical Officer

Indoximod Clinical Development Update

Eugene Kennedy, MD, FACS, Vice President, Clinical and Medical Affairs

Discovering New Immuno-Oncology Products

Mario Mautino, PhD, Senior Vice President, Drug Discovery, Intellectual Property Officer

Financial Update

John B. Henneman III, Executive Vice President, Chief Financial Officer

Opening & Closing Remarks

Charles J. Link, Jr., MD, Co-Founder, Chairman, Chief Executive Officer

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Key Points for Today's Program

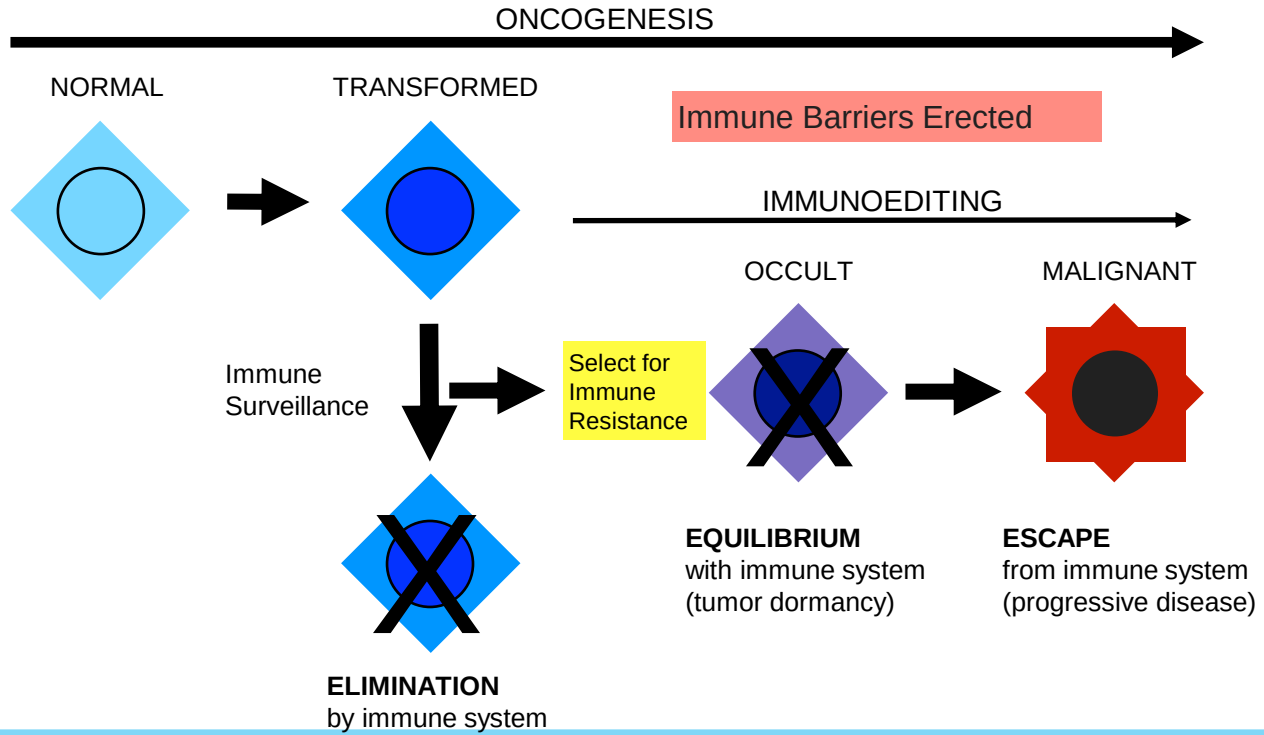
- Indoleamine 2,3-dioxygenase (IDO) pathway is central to immune escape
- IDO is an increasingly validated immuno-oncology target
- Two promising candidates that target the IDO pathway, with distinct mechanisms of action
  - GDC-0919, which targets the enzyme directly (partnered with Genentech)
  - Indoximod, which inhibits the effects of IDO by supplying a "tryptophan-sufficiency" signal
- Scientifically visionary, with "over-the-horizon" programs, such as PTEN
- Proven track record in both in- and out-licensing of products
- Strong balance sheet to execute our current clinical programs

IDO Combinations with Checkpoint Inhibitors

George C. Prendergast, PhD, President & Chief Executive Officer, Lankenau Institute for Medical Research (LIMR), Editor-in-Chief, Cancer Research

Immuno-Oncology (I-O): Restoring Immune Defenses to Eradicate Cancer

Immunity & Oncogenesis: The Grand Battle of Cancer



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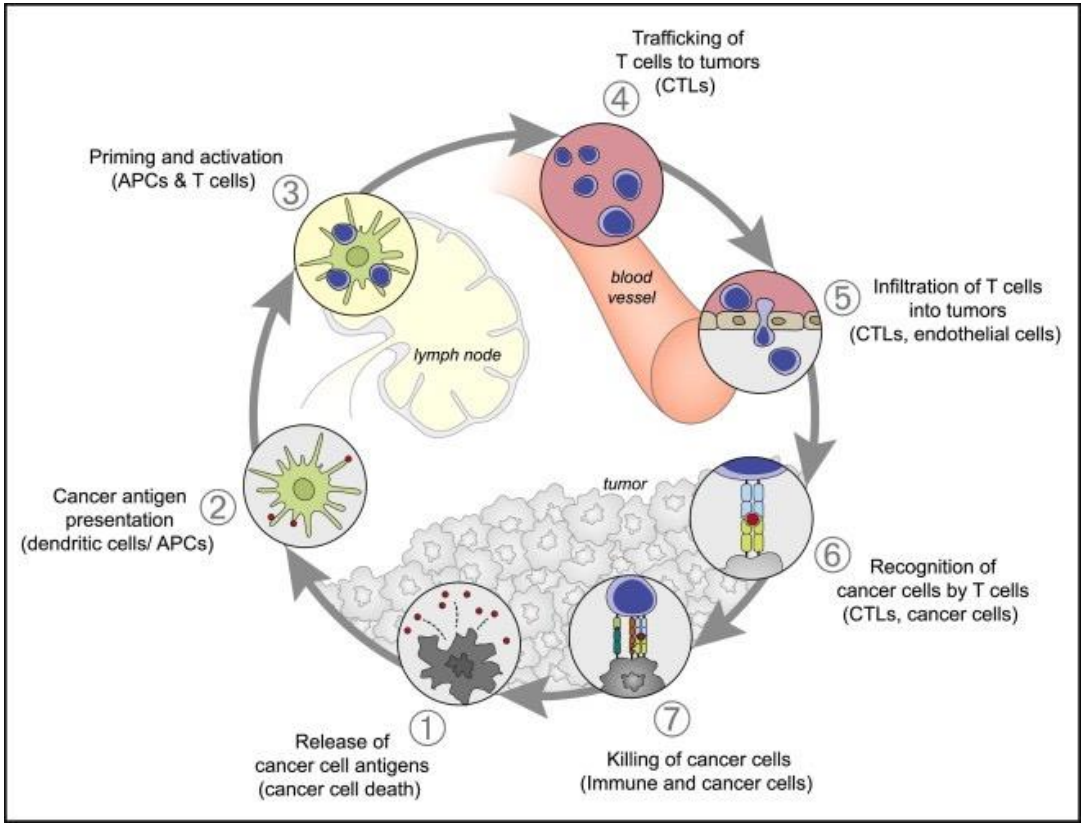
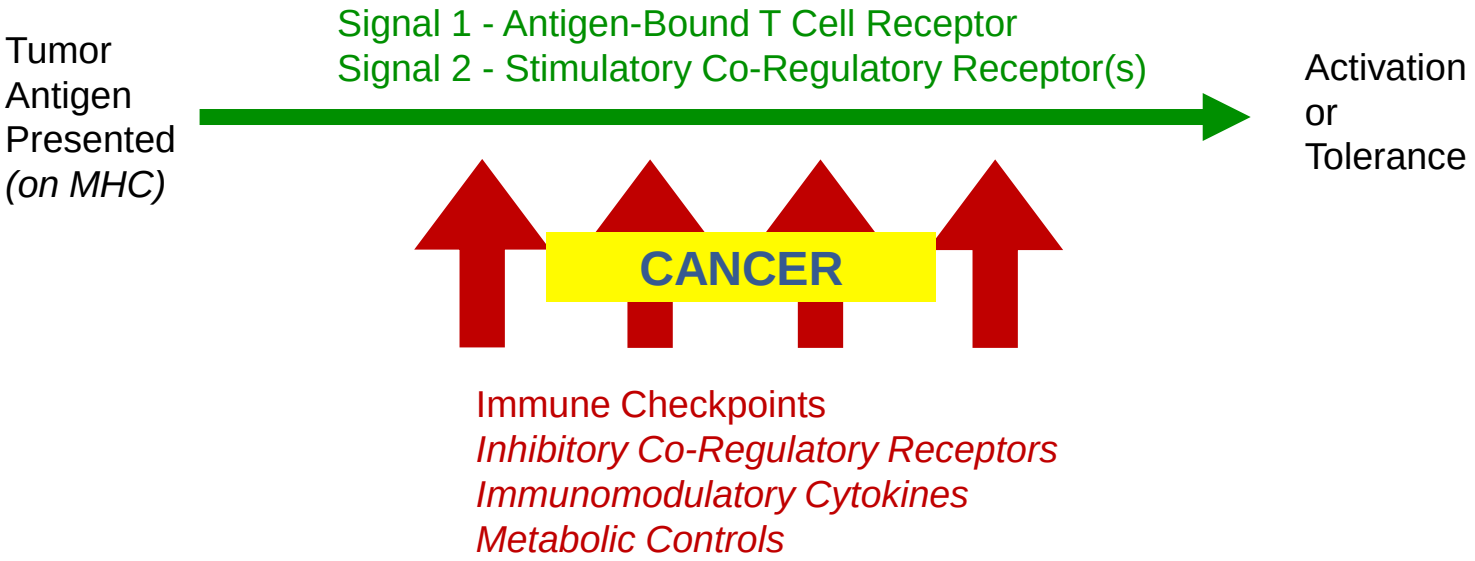
INFLAMMATORY MICROENVIRONMENT

Immuno-Oncology Landscape: Cycle of Skirmishes in the Battle

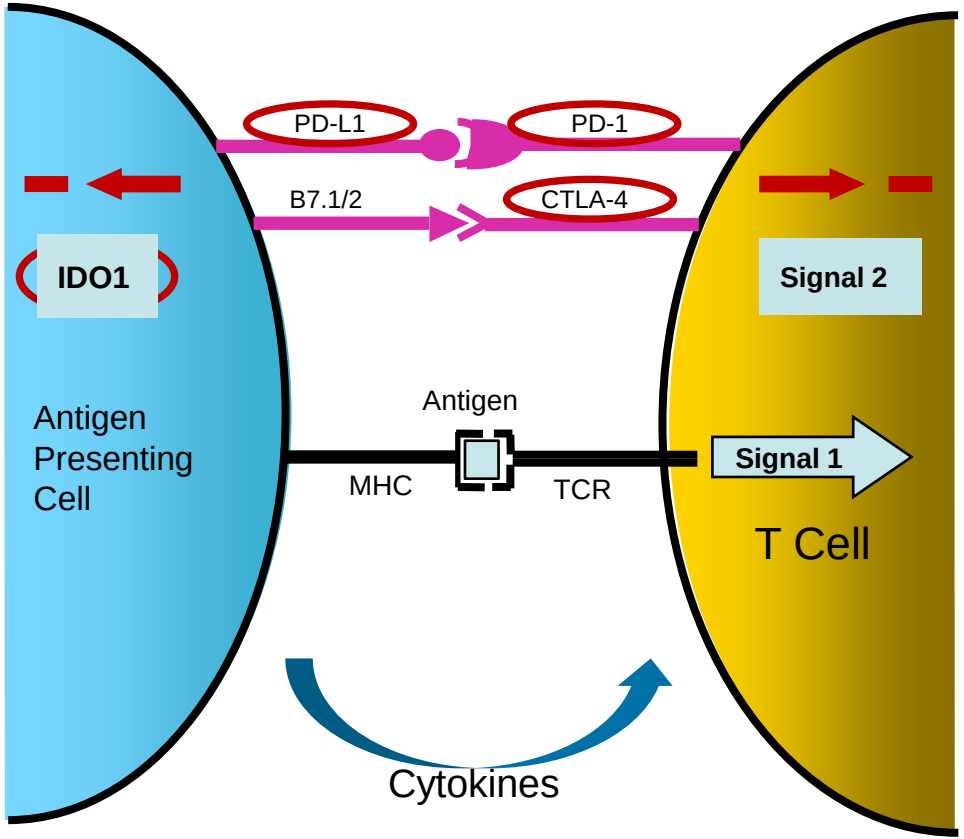


Chen and Mellman, Immunity (2013)

T Cells in Immuno-Oncology: Restoring Function



Key Immuno-Oncology Targets



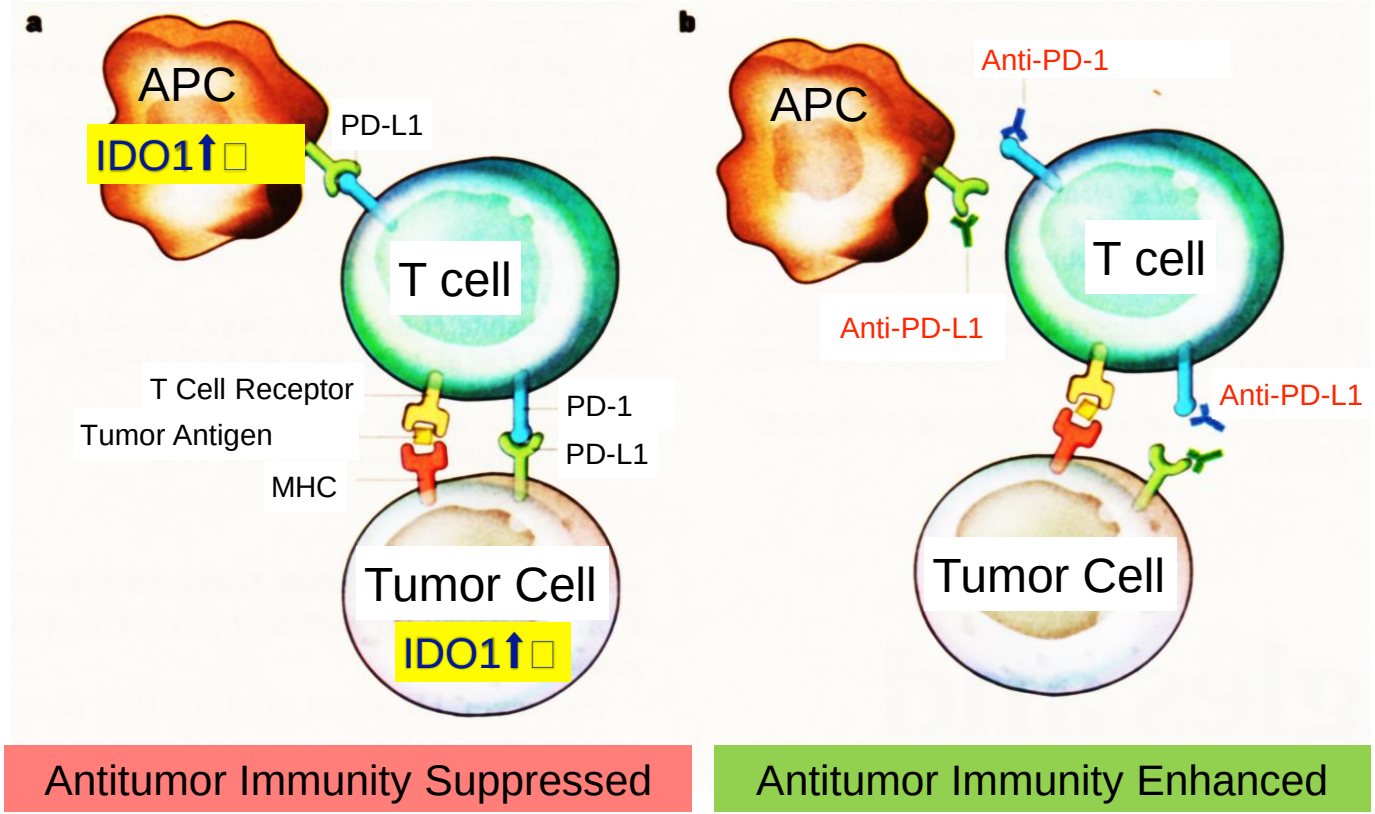
IDO Pathway Inhibitors in Clinical Trials

IDO Pathway Inhibitors	Clinical Trials
Indoximod	Phase II (multiple)
Epacadostat (INCB024360)	Phase II (multiple)
GDC-0919 (NLG-919)	Phase I/II (multiple)
BMS-986205	Phase I Entry
PF-06840003	Phase I Entry

Where Does IDO Fit In?
Broad Role Based Upon Action at Multiple Sites

Lymph Node	• Adaptive Immune Cells – *T Cell - Antigen Presenting Cell Interface*
Tumor Sites	• Cancer Cells • Cancer Stem-Like Cells
Tumor & Metastasis Microenvironment	• Innate Immune Cells – *MDSC - Major Immune Suppressor* – *TAM - Inflam Mediator* • Connective Tissue Cells – *MSC - Inflam Mediator* – *CAF - Invasion-Inflam Mediator*

IDO Blockade Acts at Two Sites to Leverage PD-1 Disruption

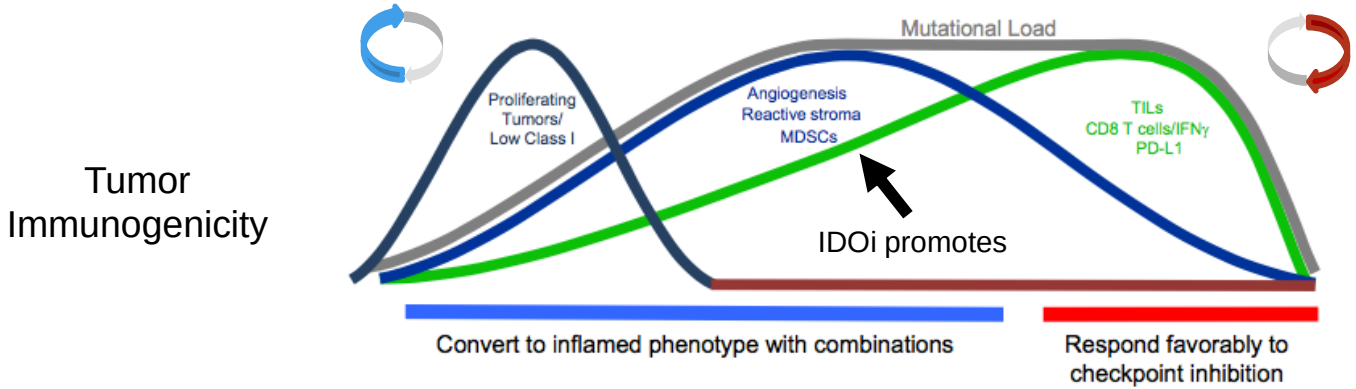


Antitumor Immunity Suppressed

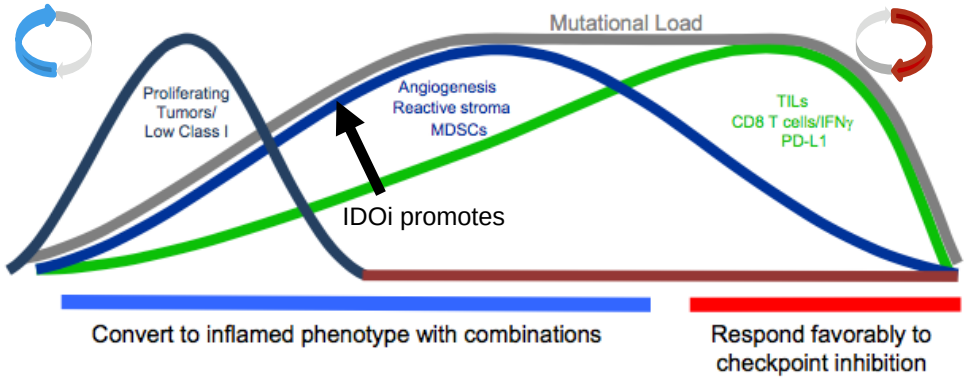
Antitumor Immunity Enhanced

IDO Pathway Inhibitor Combinations: Checkpoint Therapy

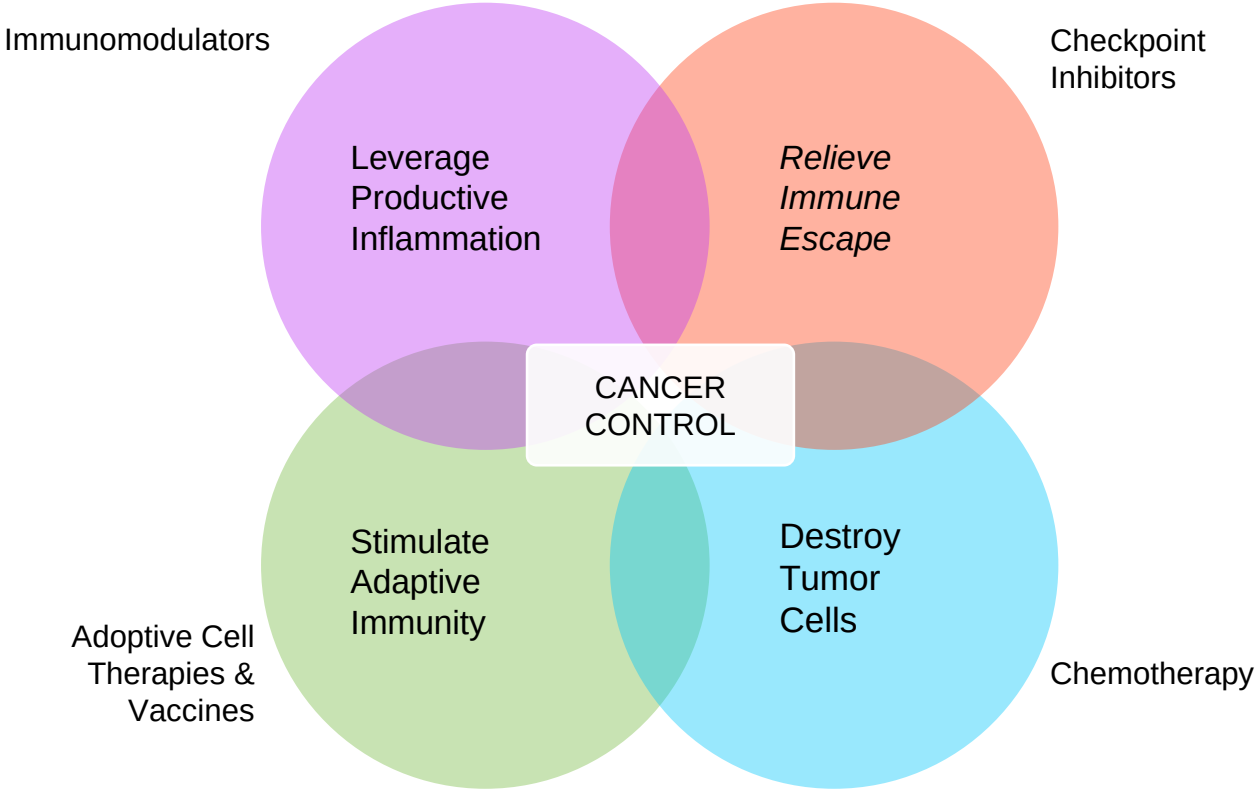
Checkpoint Responses in Tumor Types	Checkpoint virgin territory	Checkpoint weak response	Checkpoint favorable
	• Non-MMR deficient colorectal (<5%) • Pancreatic • P53/KRAS mut tumors • Others	• NSCLC (~15-20%) • SCLC (~15-25%) • RCC (~15-30%) • Squamous H&N (~20%) • HCC (~20%) • TNBC (~20%) • Ovarian (~10-15%)	• Hodgkin lymphoma (~65-85%) • PD-L1 high urothelial (~45%) • MMR deficient colorectal (~40%) • Melanoma (~30%) • B/T-cell NHL (~30%)



IDO Pathway Inhibitor Combinations: Chemotherapy

Chemotherapy That Cooperates with IDO Blockade	Immunogenic Drug Classes		
	Platins	Anthracyclines	Taxanes
Tumor Immunogenicity			
Leveraging Chemotherapy-Induced Inflammation	Non-Inflammatory	Weak/Non-Productive Inflam.	T Cell Inflamed
	• Chemotherapy puts inflammation “On Board”	• Chemotherapy increases / converts inflammatory phenotype	• Chemotherapy converts inflammatory phenotype

IDO Blockade to Leverage Checkpoint Therapy & Chemotherapy



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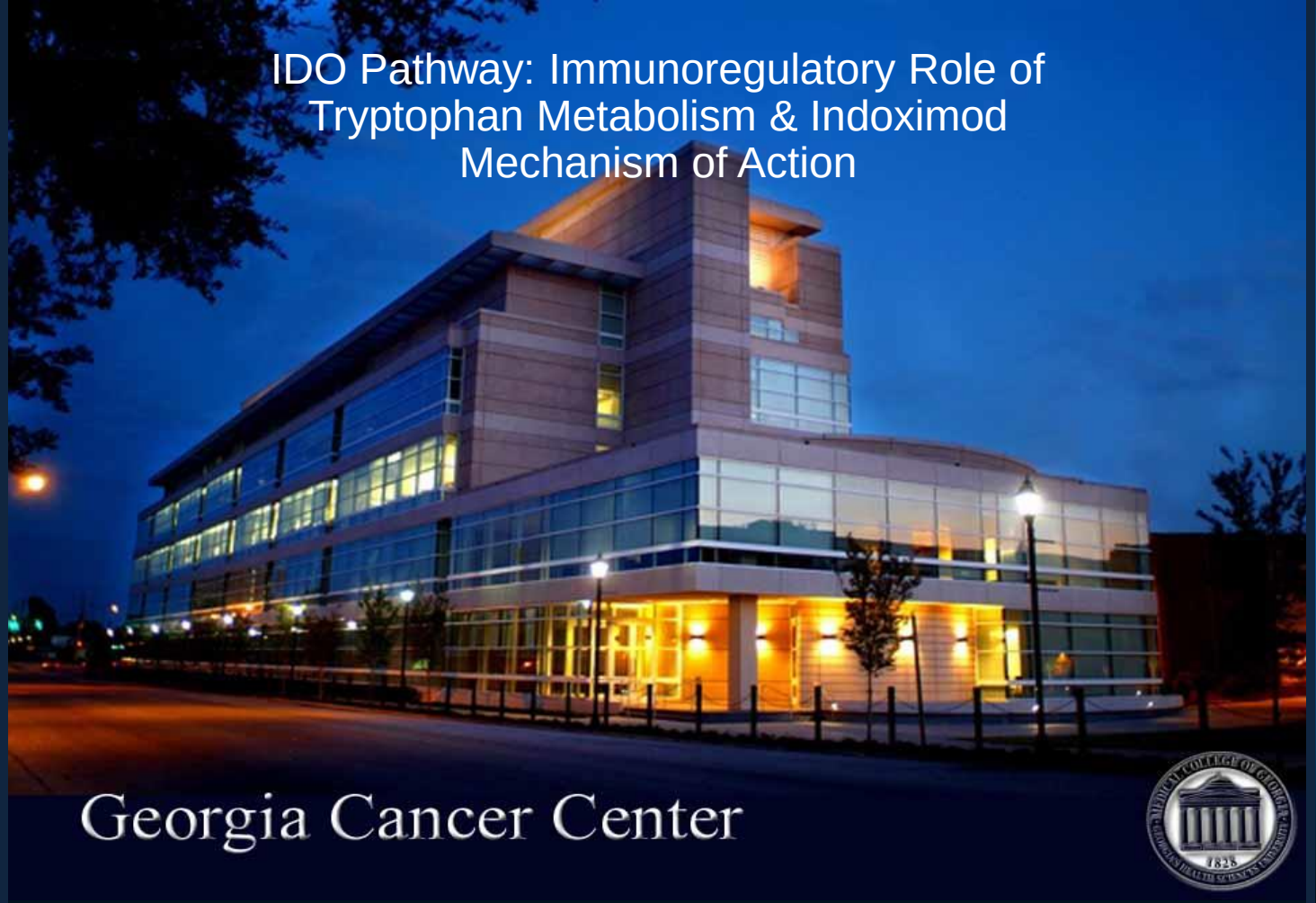
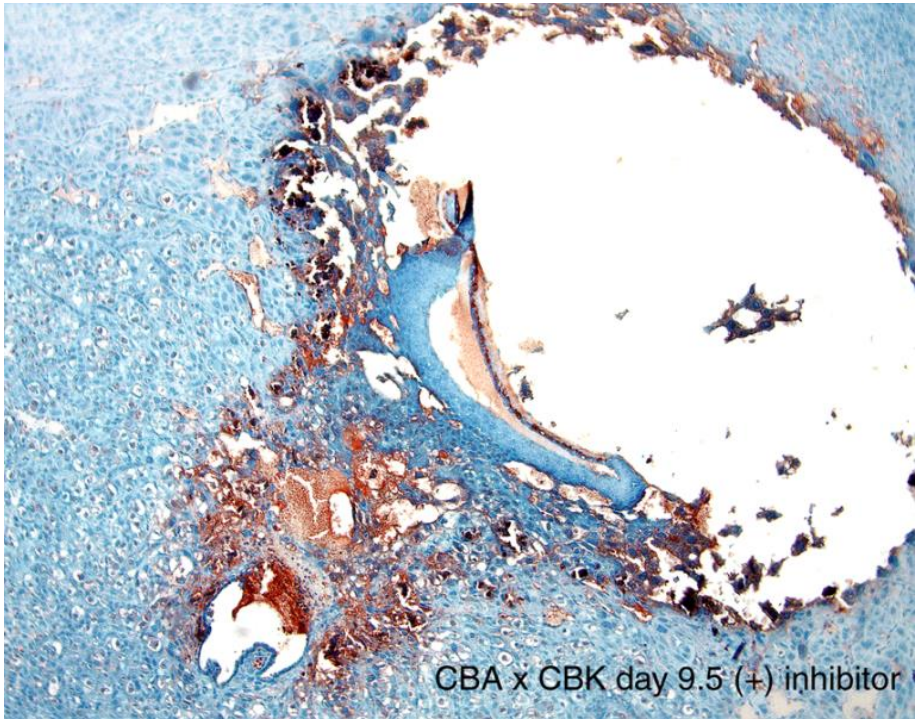
Immunoregulatory Role of Tryptophan Metabolism

David H. Munn, MD, Medical College of Georgia, Augusta University

IDO Pathway: Immunoregulatory Role of Tryptophan Metabolism & Indoximod Mechanism of Action



IDO Is a Natural Molecular Mechanism of Immune Suppression and Tolerance

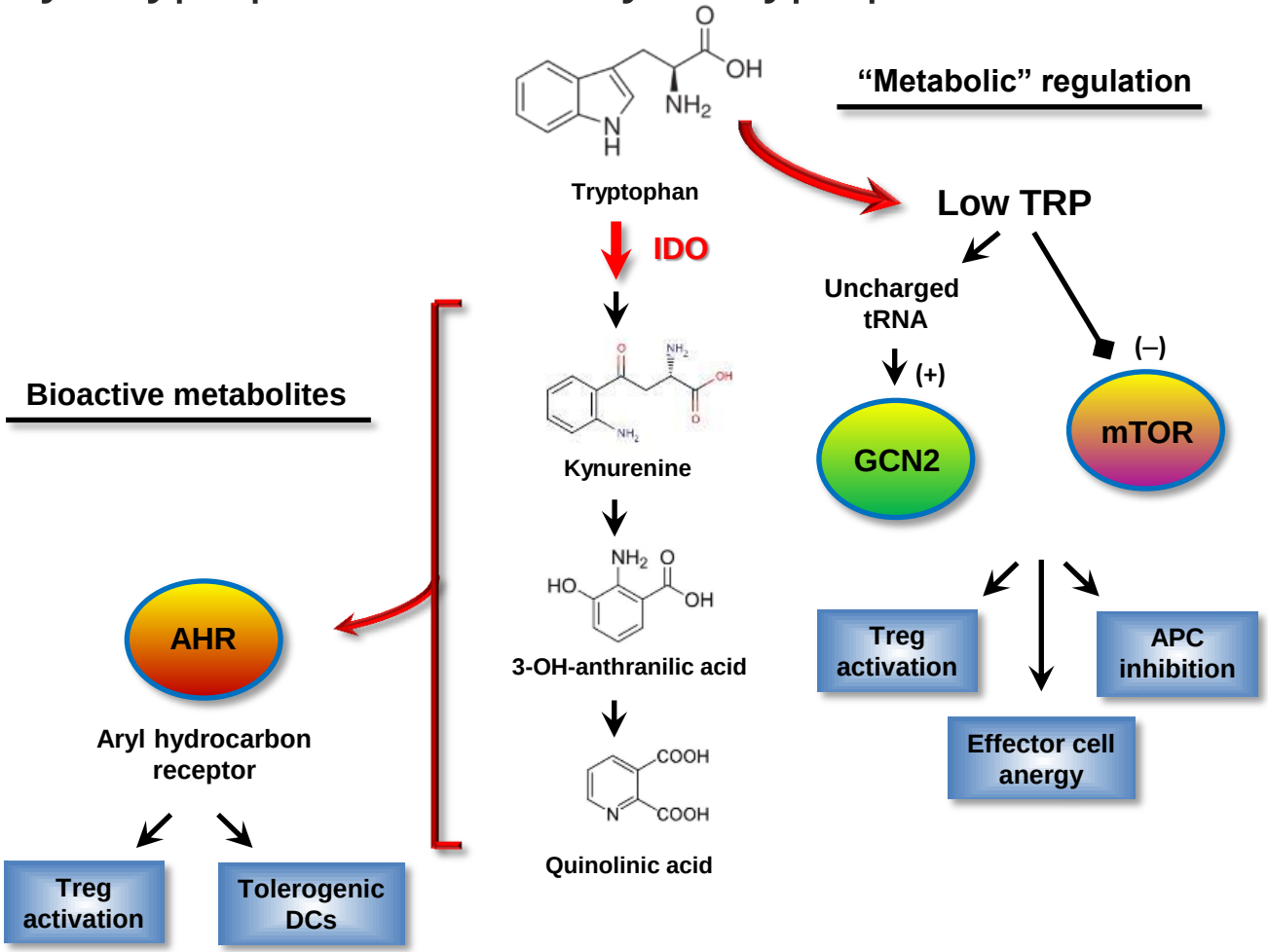


IDO-inhibitor drugs: mechanism of action

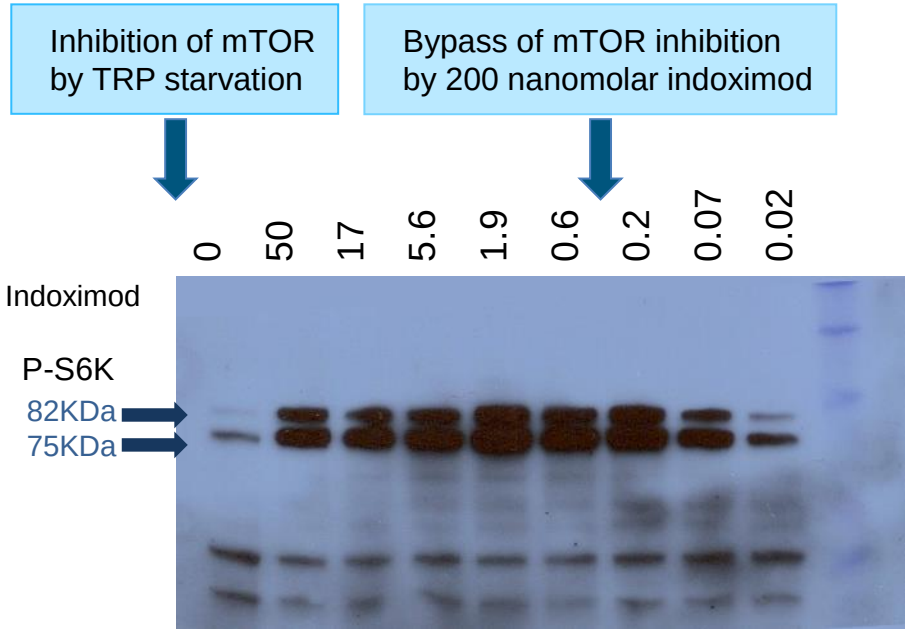
IDO Pathway
A Key Checkpoint in the Immune System

- **Regulates innate and adaptive immune response**
  - Part of the natural mechanism of immune tolerance to dying cells
  - Inhibits effector T cells, activates suppressive Tregs
  - Is also counter-regulatory (induced by inflammation)
- **Dominant suppressive role**
  - Maternal tolerance; prevents autoimmune disorders; creates transplant tolerance
  - Tumor induced immunosuppression
- **Overexpressed in cancer**
  - Can be expressed by tumor cells – to suppress effector T cells in the tumor
  - Can be expressed by host antigen presenting cells – to create systemic acquired peripheral tolerance to tumor associated antigens (TAAs)

IDO Pathway: Tryptophan Sufficiency & Tryptophan Metabolism



Indoximod Can Directly Bypass mTOR Block Induced by Low Tryptophan

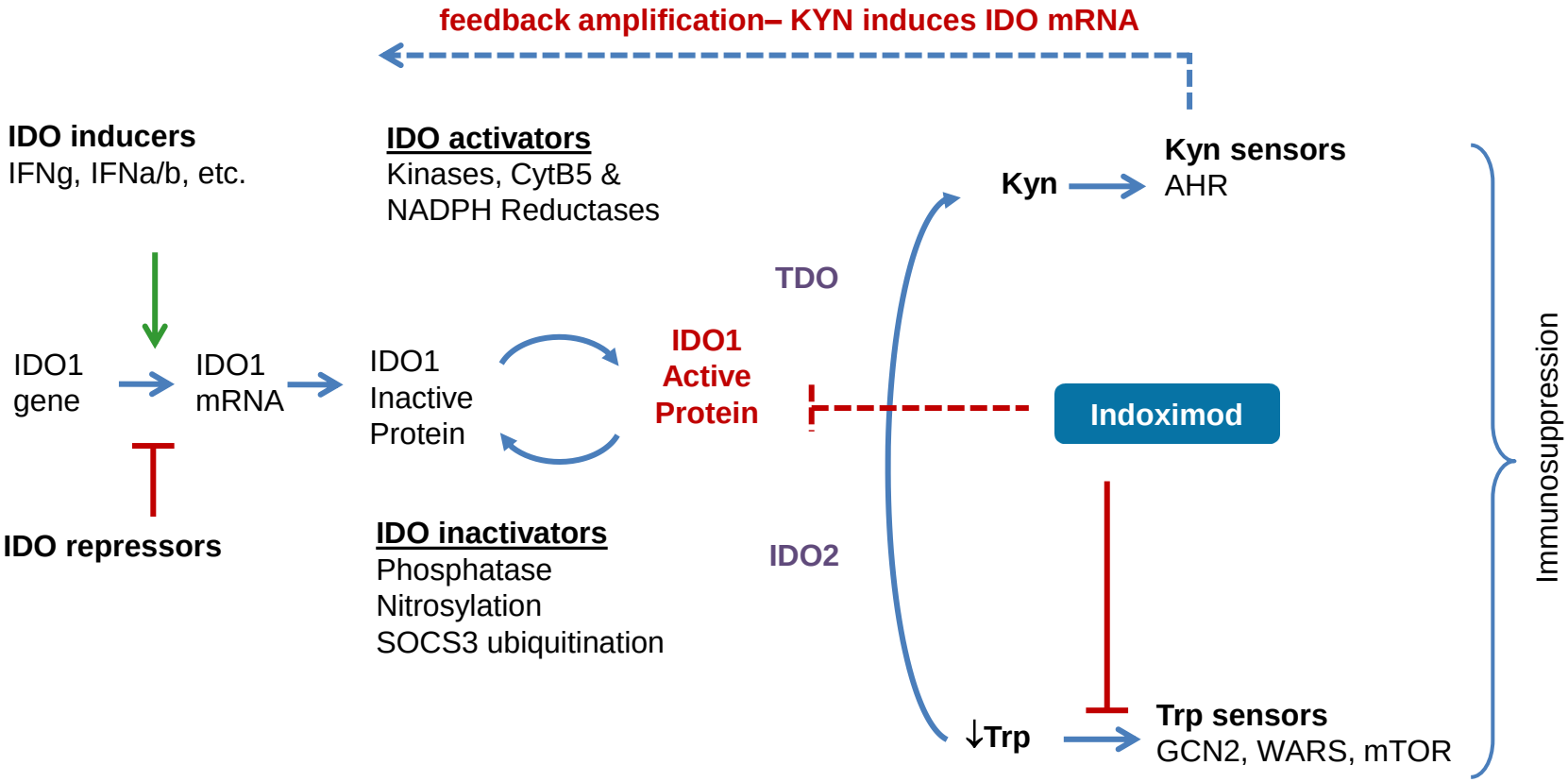


Cells were Starved of Type for 18 hours and then stimulated for 2 hours with Varying amounts of Indoximod

From Metz et al, Oncoimmunology (2012)

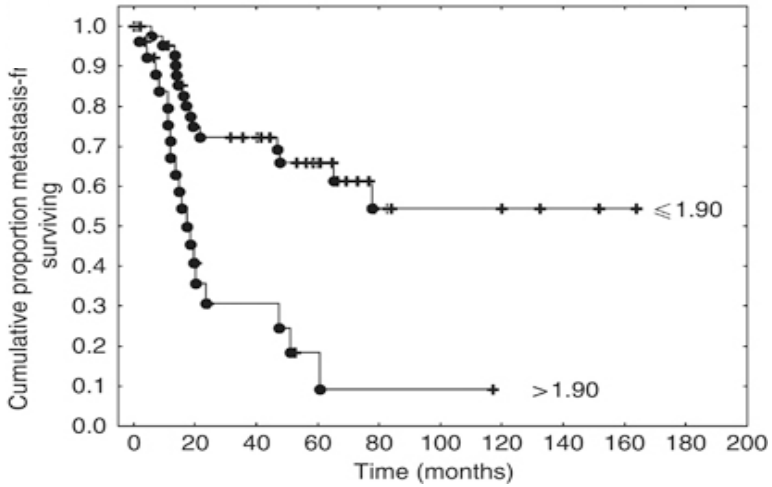
Indoximod Bypasses Tryptophan Insufficiency Signal

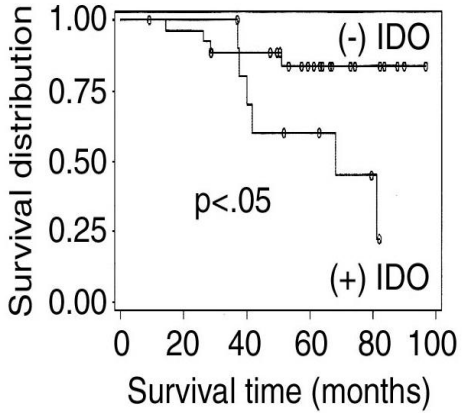
IDO Pathway & Immunosuppression



IDO Over-Expressed by Many Cancers Correlates with Poor Prognosis

- Prostate Cancer[1]
- Osteocarcinoma[2]
- Ovarian Cancer[3]
- Lung Cancer[4]
- Melanoma[5]
- Cervical Cancer[6]
- Endometrial Cancer[7]
- Colorectal Cancer[8]
- AML[9]



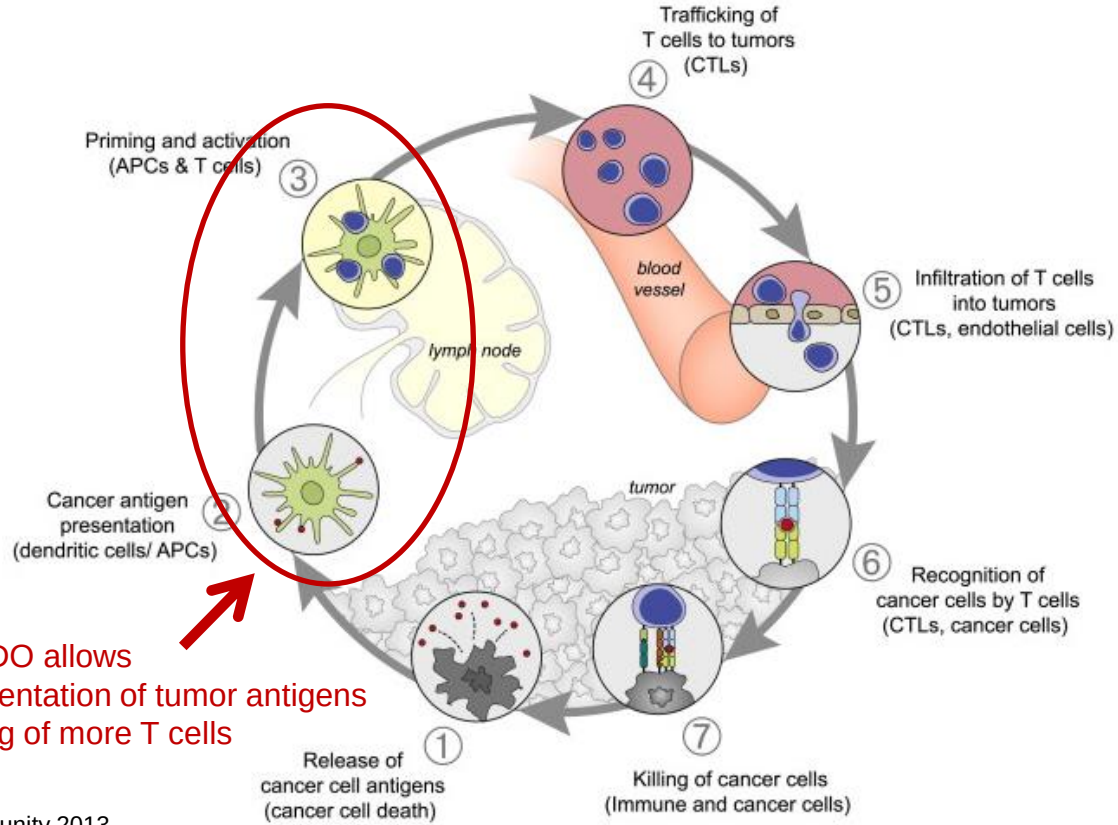


1. *Eur. J. Cancer, 2008, (44): 2266-75;* **2.** *Clin Exp Metastasis (2009) 26 :1005–12;* **3.** *Gyn Oncol., 2009, (115): 185-92; Clin Cancer Res, 2005, (11): 6030-39;* **4.** *Lung Cancer, 2010, (67): 361-65.* **5;** *J. Clin. Invest.(2004) 114:280.;* **6.** *Gyn. Oncol, 2010, (117): 423-28;*
7. *British J. Cancer, 2006, (95): 1555-61;* **8.** *Clin Cancer Res, 2006, (12): 1144-51;* **9.** *Leukemia Res, 2009, (33): 490-94.*

Considerations of IDO Expression as a Biomarker

1. Lack of validated antibodies for *in vitro* diagnostic use
2. IDO can be expressed in either tumor or host (e.g., the relevant site may be the draining lymph node)
3. A small number of host cells may have a powerful systemic effect
4. IDO can be induced by therapy

Blocking IDO Allows Cross-Presentation of Tumor Antigens



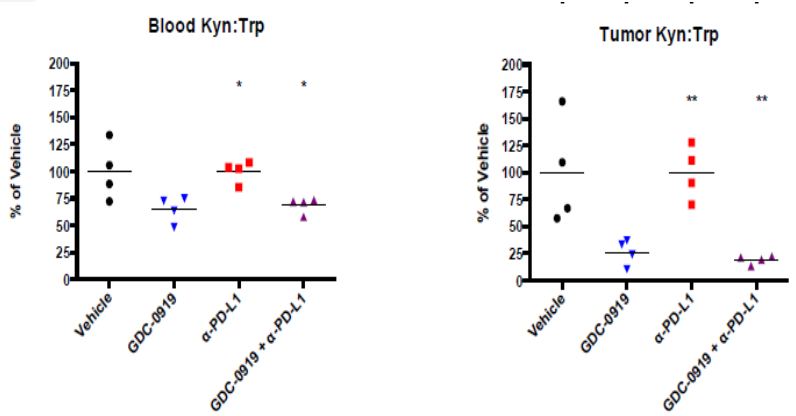
From DS Chen, Ira Mellman: Immunity 2013

IDO-Inhibitors Are Inherently Team Players

1. IDO-inhibitors are optimal in combination – you have to kill some tumor cells to start the amplification cycle, e.g., combination with:
   - Chemotherapy/radiation
   - Immunotherapy (e.g., pembrolizumab)
   - Checkpoint blockade (if patients have pre-activated T cells)
   - Adoptive T cell therapy (CARs, etc)
2. Blocking IDO helps change the **tumor microenvironment** so that tumor antigens are now presented in an immunogenic fashion

Combination of GDC-0919 and Anti-PDL1 Ab Improved Anti-tumor Immunity and Efficacy

GDC-0919 alters tumor microenvironment favorably

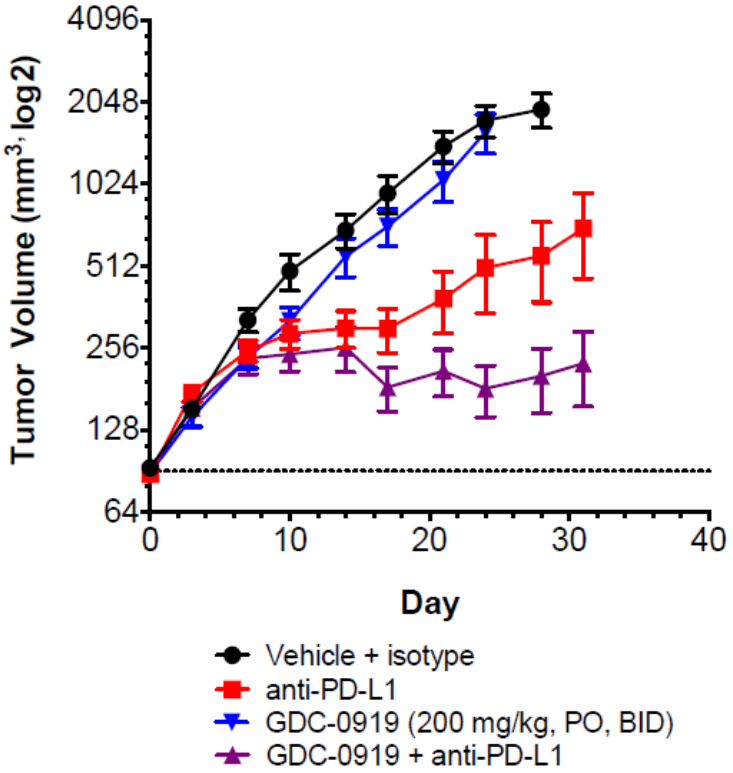


GDC-0919 decreases blood and tumor kynurenine levels in the EMT6 model.

Balb/c mice were injected with EMT6 cells followed by treatment with α-PD-L1 alone (10 mg/kg, 2x/week), GDC-0919 alone (200 mg/kg twice daily), or a combination of the two. At 2 hrs post-last-dose, blood and tumors were assessed for kyn/trp.

From Spahn et al, SITC 2015

Improved Depth and Duration of Tumor Growth Inhibition with GDC-0919 and anti-PDL1 Ab



From Spahn et al, SITC 2015

Two Basic Approaches to Immunotherapy
Not Mutually Exclusive

1. Take the brakes off the **T cells**
    - Conventional checkpoint blockade
        - PD-1 and CTLA-4 are expressed on activated **T cells**
    - Activate T cells in vitro and transfer them
2. Change the **tumor microenvironment** so that endogenous tumor antigens are presented in an immunogenic fashion
    - Immunogenic chemotherapy and radiation
    - Inhibit the IDO pathway
    - Block the activated Tregs (e.g., PTEN-inhibitors)


Georgia Cancer Center

Q & A

IDO Science

- Charles J. Link, Jr., MD
- George C. Prendergast, PhD
- David H. Munn, MD

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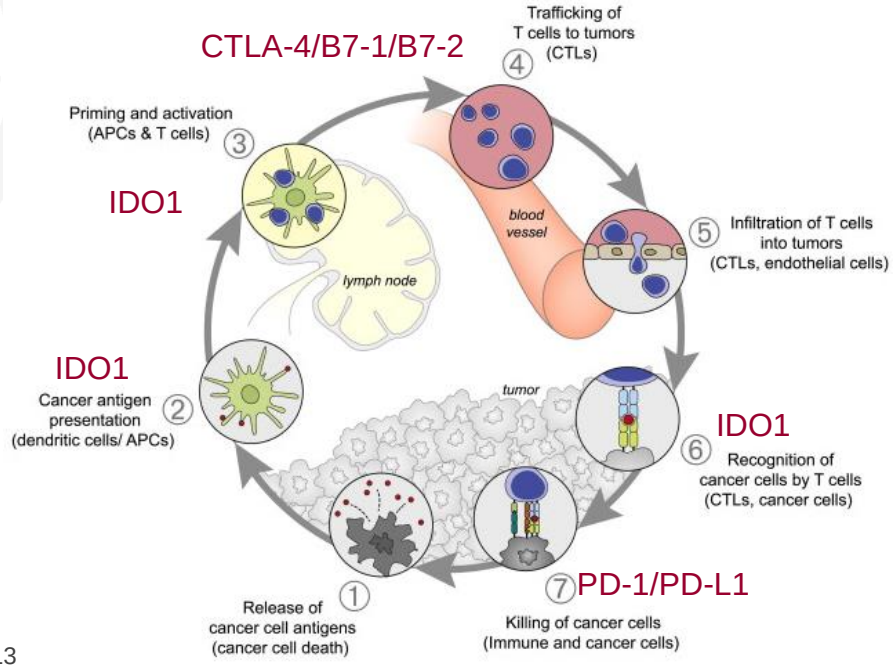
Clinical Strategy and Key Collaborations

Nicholas N. Vahanian, MD, Co-Founder, President, Chief Medical Officer

IDO is a Central Pathway in Tumor Immuno-Oncology

Applicable Across a Wide Range of Malignancies



From DS Chen, Ira Mellman: Immunity 2013

IDO, PD-1/PD-L1 and CTLA-4 are all validated pathways

IDO Pathway Plays Key Role in Immune Regulation

Current IDO Landscape

- Three IDO pathway inhibitors with early clinical data
  - GDC-0919 (NewLink in partnership with Genentech/Roche)
  - Indoximod (NewLink)
  - Epacadostat (Incyte)
- GDC-0919 is currently Phase 1b studies
- Indoximod is in multiple Phase 2 studies
- Epacadostat has advanced as far as Phase 3 in melanoma
  - Positive melanoma update at ESMO
  - Encouraging clinical activity in other indications
- Continued increase in investment by multiple groups in IDO science
  - In-licensing/acquisition of pre-clinical assets

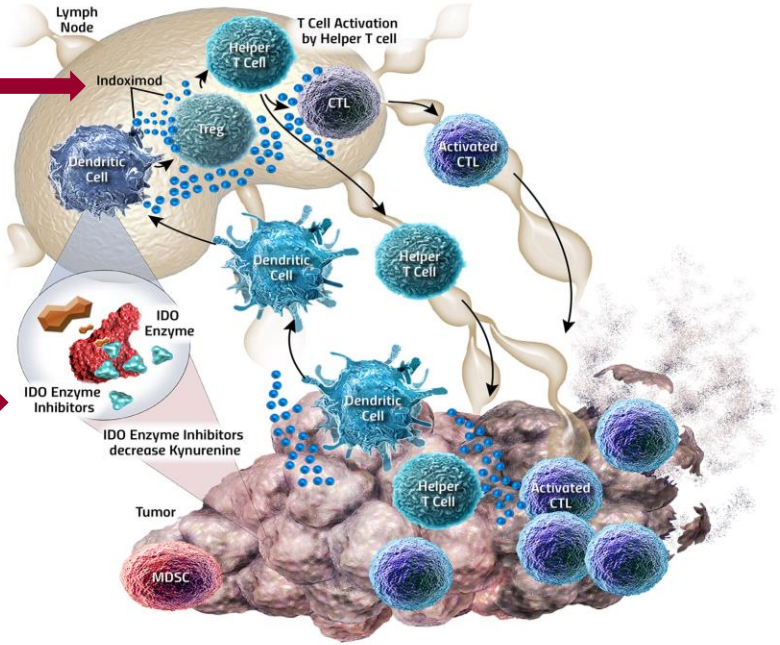
NewLink has two of the three most advanced IDO pathway inhibitors

NewLink Clinical Programs Targeting IDO Pathway

Two Small Molecules with Distinct Mechanisms of Action

Indoximod
Interferes with
IDO mediated
TRP signaling

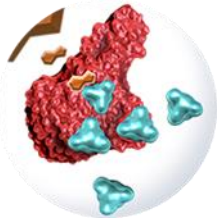
GDC-0919
Direct inhibitor
of IDO enzyme



Potential for combination of GDC-0919 and indoximod

GDC-0919 is a Potent and Selective IDO Inhibitor

Roche Presentation at Cowen Healthcare Conference, March 9, 2016

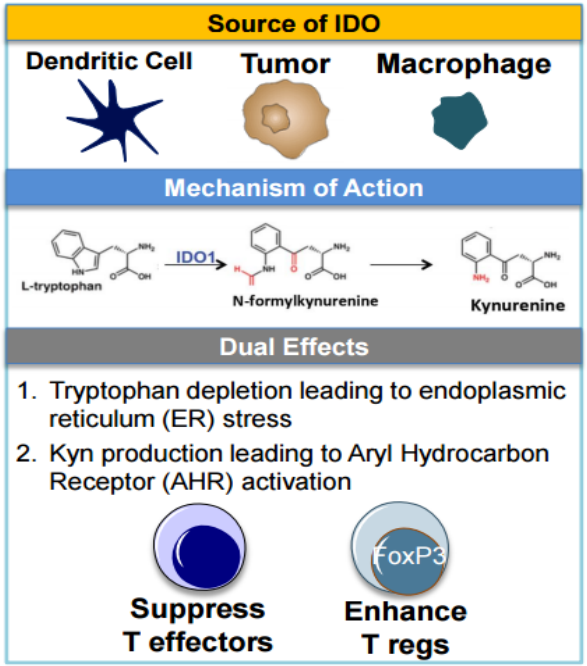


IDO1:

- IDO1 activity contributes to maternal-fetal tolerance and tumor immune escape
- Expression correlates with poor patient survival across a range of tumors
- **MOA**: Catabolizes Tryptophan to Kynurenine, suppresses effector T cells and enhances Tregs function

IDO1 Inhibitor GDC0919 (NLG919):

- Oral small molecule inhibitor of IDO1
- Being tested in Ph1b in combination with **atezolizumab**



gRED Roche

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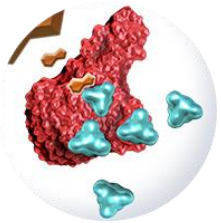
NewLink Genetics and Genentech/Roche Partnership

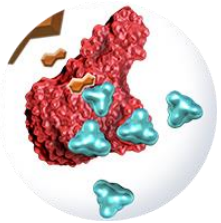
IDO and TDO Pathway Inhibitors



- Exclusive worldwide license agreement
- $150M upfront payment; >$1B in potential milestones
- Clinical collaboration for GDC-0919
- Joint research collaboration for IDO and TDO pathway inhibitors
- Escalating double-digit royalties on net sales
- NewLink retains U.S. co-promote option, with royalty escalation
- NewLink retains exclusive rights to indoximod

NewLink Genetics and Genentech/Roche Partnership

GDC-0919 Clinical Development Overview

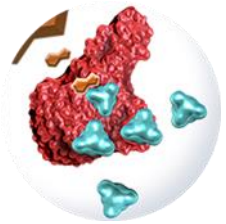


- Joint Development Committee for clinical development activities
- Phase 1 single agent of GDC-0919
  - Dose escalation in solid tumors
  - Target enrollment of 36 patients
- Phase 1b combination of GDC-0919 (IDO) and atezolizumab (PD-L1)
  - Initiated Q3 2015
  - Dose escalation and expansion study in solid tumors
  - Target enrollment of 276 patients
- Plans to combine with additional immuno-oncology agents (i.e. OX 40)

Leading oncology partner, future opportunities

GDC-0919 Phase 1a Results

Safety in Patients with Recurrent/Advanced Solid Tumors



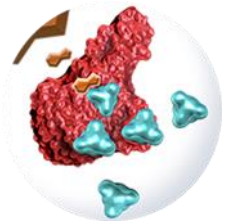
- Well tolerated up to 800mg BID, MTD not reached
- Best response was limited to stable disease (SD) in 7 out of 17 patients
- No AEs requiring withdrawal of study drug were reported
- Grade ≥3 AEs regardless of attribution were reported in 11 (58%) of patients
- Grade ≥3 AE drug related in 1 patient with Grade 4 lower GI hemorrhage
- Grade 4 lower GI hemorrhage, only SAE possibly related to study drug

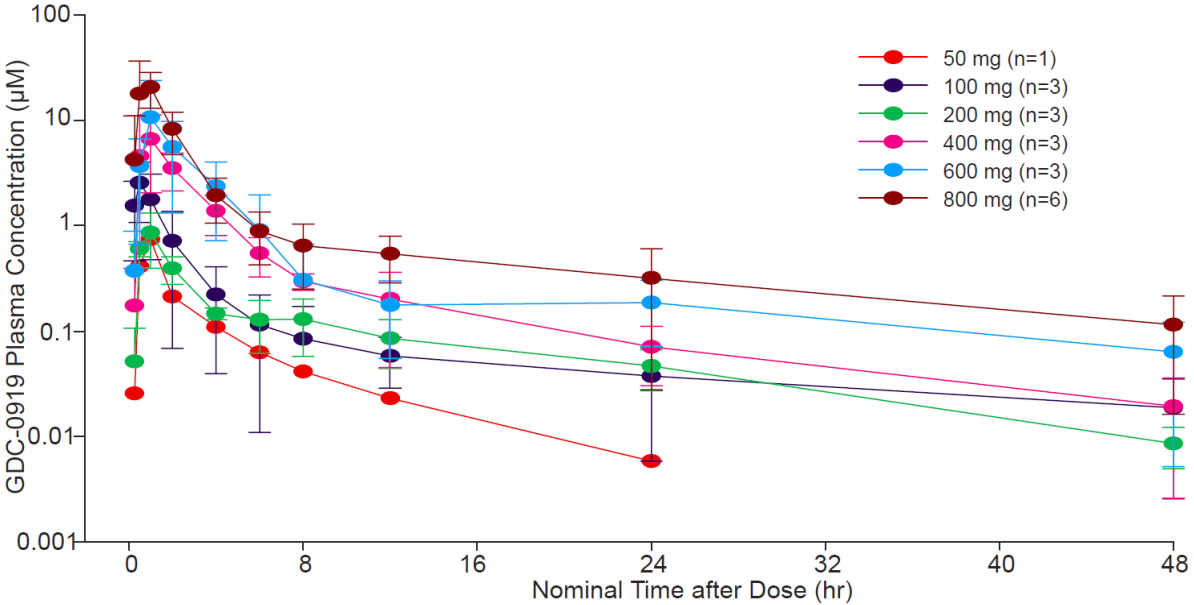
Nayak, A, et al, European Cancer Congress, September 2015, Abstract 346

GDC-0919 is generally well tolerated; a good candidate for potential combinations

GDC-0919 Pharmacokinetic Results

Linear and Dose Proportional, Rapidly Absorbed



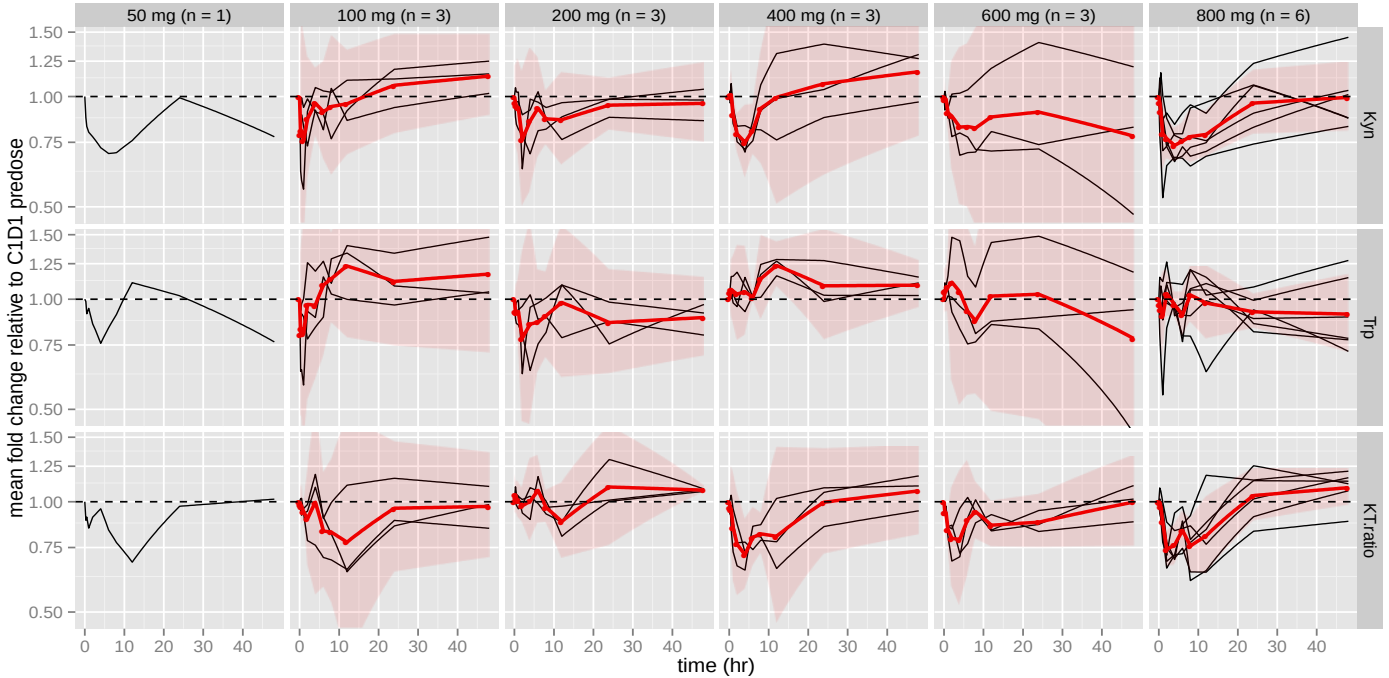


Nayak, A, et al, European Cancer Congress, September 2015, Abstract 346

~12 hour half-life supports BID dosing

GDC-0919 Pharmacodynamic Results

Significant Decrease in Plasma Kynurenine (Kyn) at Higher Dose Levels

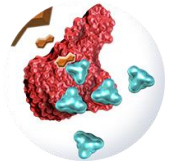


black line: individual patients; red line: cohort mean red ribbon = 95% CI

Nayak, A, et al, European Cancer Congress, September 2015, Abstract 346

GDC-0919 Clinical Development

Phase 1b Trial Design



Dose Escalation

- **GDC-0919 50 mg** Atezo 1200 mg
- **GDC-0919 100 mg** Atezo 1200 mg
- **GDC-0919 200 mg** Atezo 1200 mg
- **GDC-0919 400 mg** Atezo 1200 mg

Expansion cohorts at or below MTD/MAD

- Advanced solid tumors
- Combination treatment
- 3+3 escalation design
- DLT window: 21 days
- Mandatory archival tissue

Disease Specific Expansion Cohorts

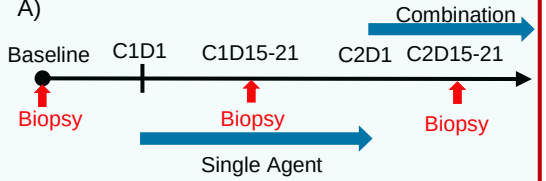
- **NSCLC**
- **Renal**
- **Bladder**
- **Triple Neg Breast**

- Selection by PD-L1 IHC:
- Optional tumor biopsies

Biopsy Expansion Cohorts

- **SCCHN**
- **Melanoma**
- **Gastric**

- Mandatory serial biopsies
- Selection by PD-L1 IHC and/or IDO1 (cohort A)



Cohort A: GDC-0919 run-in
Cohort B: MPDL3280A run-in

Trial NCT02471846

Estimated enrollment up to 276 patients in multiple indications

GDC-0919 Summary

Promising Early Results with Combination Trial Underway

- Well tolerated up to 800 mg BID as a single agent on a 21/28 day cycle
- No immune-related AEs evident
- Higher doses decrease plasma Kyn consistent with half-life
- Evaluating safety, PK, activity, and pharmacodynamics at a continuous dosing schedule (BID 28/28 days) to enable greater flexibility in future dosing regimens
- Phase 1b combination with atezolizumab (PD-L1 inhibitor) currently underway
- Phase 1 combination with OX40 (MOXR0196) currently planned

IDO Pathway Inhibitor Clinical Development

AGENT	INDICATION	DESIGN	STATUS
Indoximod	Melanoma (advanced)	Indoximod + ipilimumab or anti-PD-1 Ab	Phase 2 Enrolling
	Pancreatic cancer (metastatic)	Indoximod + gemcitabine and nab-paclitaxel	Phase 2 Enrolled
	Glioblastoma multiforme	Indoximod + temozolomide	Phase 2 Enrolling
	Breast cancer (metastatic)	Indoximod + taxane	Phase 2 Enrolled
	Acute myeloid leukemia (AML)	Indoximod + Standard Frontline Chemotherapy	Phase 1b Enrolling
	Advanced NSCLC	Indoximod + tergenpumatucel-L + chemotherapy	Phase 1b Enrolling
GDC-0919*	Solid tumors	GDC-0919	Phase 1 Enrolling
	Solid tumors	GDC-0919 + atezolizumab	Phase 1b Enrolling
	Solid tumors	GDC-0919 + anti-OX40	Planned

*Partnered with Genentech/Roche

Indoximod Strategy

Optimize Formulation, Enhance Commercial Opportunity and Extend Lifecycle

Current State

IDO target increasingly validated with early clinical data*

- Clinical results support preclinical combination data
- Promising data in melanoma, brain and pancreatic cancers
- Distinct mechanism of action
- Potential for IP extension

Next 6-12 Months

Emerging IDO data may provide additional validation

- Updated clinical data for indoximod in melanoma, brain and pancreas cancers
- Formulation improvements to optimize clinical and commercial potential

2018 and Beyond

IDO combination data may support multiple indications

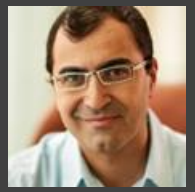
- Potential for large scale indoximod trials
- Commercial formulation established
- Potential for regulatory exclusivity

*Includes indoximod, epacadostat and GDC-0919

NewLink GENETICS

Understanding Current Melanoma Clinical Data

Montaser Shaheen, MD, Associate Professor, University of New Mexico Cancer Center



Melanoma Facts

- Fifth most common cancer in men and the seventh in women in U.S.
- Estimated 2016 U.S. incidence of 76,380
- Estimated 2016 U.S. mortality of 10,130
- Incidence is increasing (1.9% annually 2000-2009)
- 1 in 50 persons diagnosed with melanoma of the skin during their lifetime

ACS, Cancer Facts & Figures 2016

FDA Approved Immune Checkpoint Inhibitors for Metastatic Melanoma

- **Ipilimumab** (anti-CTLA-4)
  - Shown to improve OS when administered as monotherapy compared to a peptide vaccine[1]
- **Nivolumab** (anti-PD1)
  - Shown to improve OS vs dacarbazine in patients with BRAF wild-type, previously untreated advanced melanoma[2]
- **Pembrolizumab** (anti-PD1)
  - Shown to improve OS vs ipilimumab in previously untreated patients3 and vs chemotherapy in patients who previously received ipilimumab4
- **Combination of IPI and Nivolumab**
  - Shown to improve ORR, PFS, and OS vs ipilimumab[5,6]

1. Hodi et al. *NEJM* 2010;363:711-723; 2. Robert et al. *NEJM* 2015;372:320-330, 3.Robert C, et al. N Engl J Med 2015; 372:320-330 4. Ribas Lancet Oncol. 2015 Aug;16(8):908-18. 5.Larkin J, et al N Engl J Med. 2015 Jul 2;373(1):23-34 6. Hodi et al Lancet Oncol. 2016 Sep 9. pii: S1470-2045(16)30366

OVERALL Response Rate (ORR) to Currently Approved Frontline Melanoma Immunotherapies

- Ipilimumab renders an ORR of 10.9%[1]-19%[2]
- Nivolumab ORR 40%[2]-43%[3]
- Pembrolizumab ORR 32.9%[4]
- Ipilimumab and nivolumab combination ORR 57.6%[3]

[1]Hodi FS, et al. N Engl J Med 2010; 363:711-723
[2]Robert C, et al. N Engl J Med 2015; 372:2521-2532
[3]Larkin J, et al. N Engl J Med 2015;373(1):23-34
[4]Robert C, et al. N Engl J Med 2015; 372:320-330

Selected Adverse Events Associated with Combination Immunotherapy in Melanoma

	Nivolumab	Nivolumab + Ipilimumab
	All Grades (Grade 3/4)	All Grades (Grade 3/4)
Diarrhea	19.2% (2.2%)	44.1% (9.3%)
Rash	25.9% (0.6%)	40.1% (4.8%)
Pneumonitis	2%	6%
Hepatitis	3.8% (1.3%)	17.6% (8.1%)
Hypophysitis	<1%	>10%

Larkin J, et al. N Engl J Med. 2015;373(1):23-34
Hodi, FS, et al. Lancet Oncol 2016; S1470-2045(16)30366

Rationale for Combining an IDO Pathway Inhibitor with Anti-PD-1 Antibody

- An effective immunotherapy combination that can rival anti-PD-1 (nivolumab) plus anti-CTLA-4 (ipilimumab) antibody combination in terms of efficacy with a lower toxicity profile to be adapted in a community oncology setting is clearly needed in the frontline setting for metastatic melanoma management

- Anti-PD-1 antibody (pembrolizumab) was shown to be more effective and less toxic than ipilimumab in the frontline setting

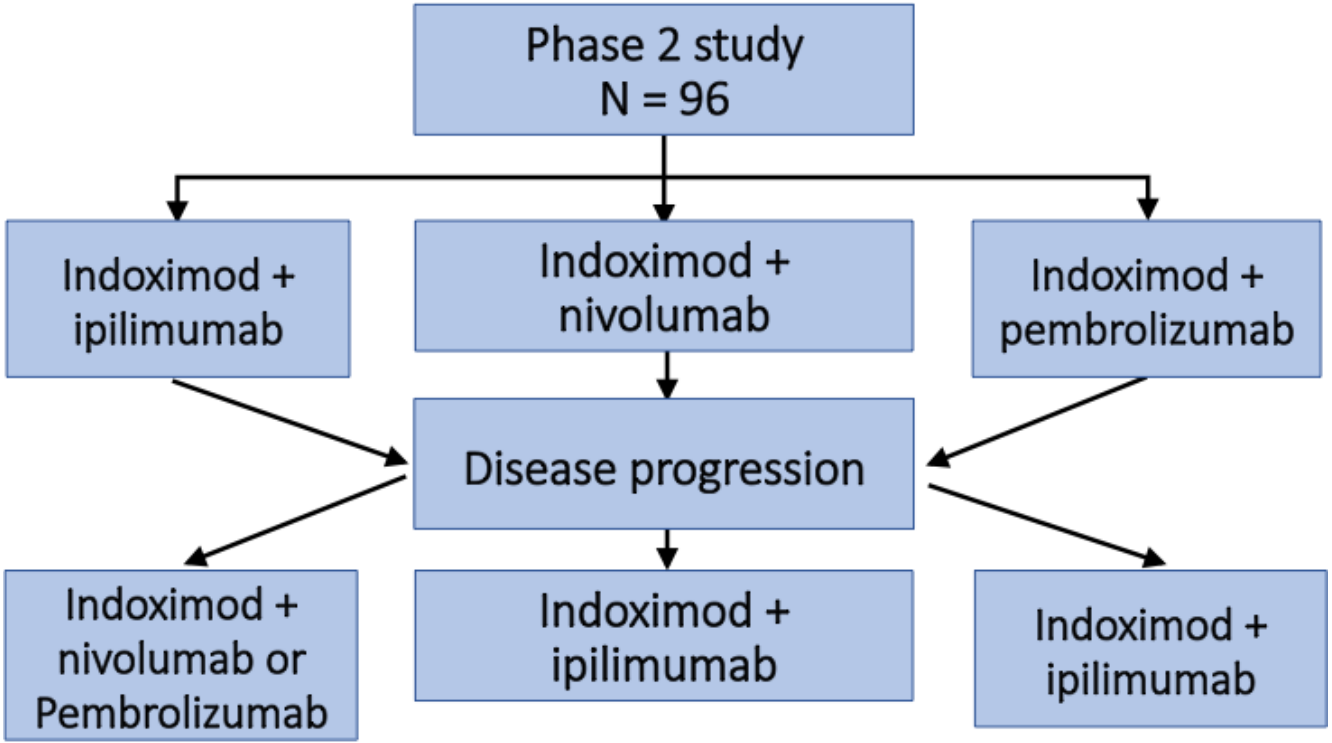
Robert C, et al. N Engl J Med 2015

Indoximod Plus Ipilimumab
Phase 1b Clinical Trial Results

- Patients with untreated metastatic melanoma in standard 3+3 design
- Indoximod (twice daily orally) was dose escalated in combination with ipilimumab (standard dosing) in four 21-day cycles; treatment with indoximod continued beyond treatment with ipilimumab in 28-day cycles until toxicity or disease progression.
- Indoximod and ipilimumab well tolerated without potentiation of immune-mediated adverse events and with no dose-limiting toxicities (DLT).
- Nine patients treated in Phase 1
- 1 complete response by RECIST criteria at 13 months.
- Most common (observed in 33% of patients) AEs, regardless of attribution, were fatigue (7 patients, 78%), pruritus (6 patients, 67%), diarrhea and rash (4 patients each, 44%), and abdominal pain and headache (3 patients each, 33%).

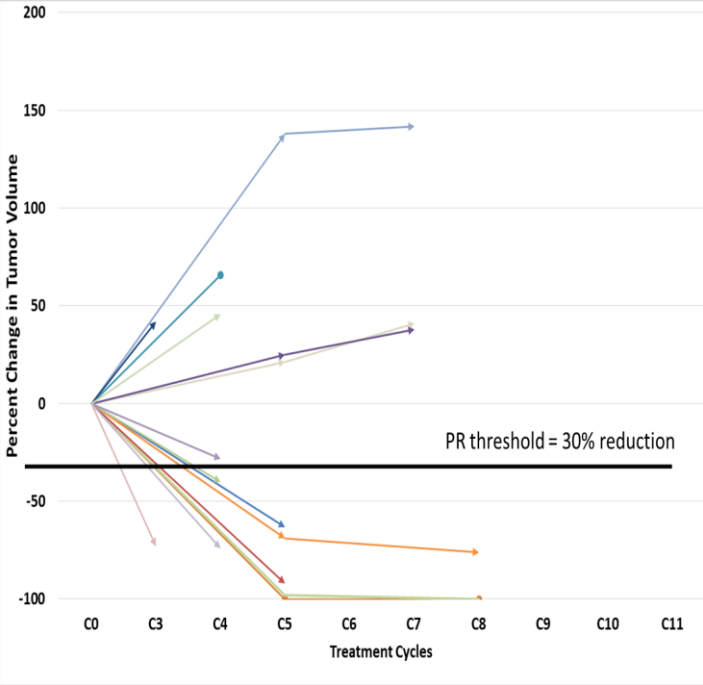
Zakharia Y, et al. ESMO 2015, Abstract 514

NLG-2103: Open-label Phase 2 combination of indoximod plus checkpoint inhibitors for the treatment of unresectable stage 3 or stage 4 melanoma



Zakharia Y, et al. ASCO 2016, Abstract 3075

Responses with Indoximod and Pembrolizumab



- 15 patients in Phase 2 that received pembrolizumab in combination with indoximod as initial therapy
- Response per site reported imaging
- Response rate is 53% (8/15) with two CRs
- Data only available at this time on one patient who received nivolumab

Zakharia Y, et al. ASCO 2016, Abstract 3075

Pembrolizumab Combination with An IDO Pathway Inhibitor

- NLG-2103 (indoximod plus pembrolizumab)
  - Patients with advanced melanoma
  - 15 patients in Phase 2, site reported imaging
  - Overall Response Rate (ORR) is 53% (8/15)

- ECHO-202/KEYNOTE-037 (epacadostat plus pembrolizumab)
  - Patients with advanced melanoma and select solid tumors
  - 19 treatment naïve melanoma patients in Phase 2
  - Melanoma ORR 58% (11/19)

Zakharia Y, et al. ASCO 2016, Abstract 3075
Gangadhar TC, et al. ESMO 2016, Abstract 1110PD

Indoximod Clinical Development Update

Eugene Kennedy, MD, Vice President, Clinical and Medical Affairs

NewLink Genetics IDO Pathway Inhibitors

Leading Position in IDO Development

- NewLink Genetics responsible for the initial development work on 2 of the first 3 IDO pathway inhibitors to advance in human studies
- Two drug approach balances potentially complementary but distinct mechanisms of action within IDO pathway
- GDC-0919 directly inhibits the IDO enzyme
  - Program partnered with Genentech/Roche
- Indoximod works downstream from the IDO enzyme
  - Early development work coming to fruition
  - Indoximod is being positioned to enter late stage development in 2H:17

Leading IDO pathway development position

GDC-0919 Summary

Clinical Development

- Two clinical trials currently underway
  - Single agent dose escalation trial initiated by NewLink Genetics and continued by Genentech/Roche
    - Phase 1 study to establish initial safety data
    - Trial identifier NCT02048709
  - Combination study of GDC-0919 with atezolizumab
    - Phase 1b trial with multiple cohorts
    - Estimated enrollment 276 patients
    - Trial identifier NCT02471846

Productive partnership positioning GDC-0919 for further development

Indoximod Clinical Development

Current Status

- Indoximod has successfully completed Phase 1 and Phase 1b studies
- Established the safety and initial trial dosing of indoximod
  - Current dose set by maximum amount that can be absorbed
- Established evidence of clinical activity in conjunction with chemotherapy
- Current series of Phase 2 trials initiated in 2013 and 2014

Indoximod well positioned for subsequent development

IDO Pathway Inhibitor Clinical Development

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	Pancreatic cancer (metastatic)	Indoximod + gemcitabine and nab-paclitaxel	Phase 2 Enrolled
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GDC-0919*	Solid tumors	GDC-0919	Phase 1 Enrolling
	Solid tumors	GDC-0919 + atezolizumab	Phase 1b Enrolling
	Solid tumors	GDC-0919 + anti-OX40	Planned

*Partnered with Genentech/Roche

Indoximod

Clinical Development in Melanoma

NLG2103 – Advanced Melanoma	
Primary Endpoint	▪ Best Overall Response Rate
Key Secondary Clinical End-Points	▪ Progression Free Survival ▪ Overall Survival
Trial Design	▪ Phase 2 single arm study ▪ Indoximod in combinations with checkpoint inhibitors
Trial Size	▪ 96 patients in Phase 2
Status	▪ Greater than 75% enrolled ▪ Report results 2H:17 ▪ NCT02073123

Available data indicate clinical activity in PD-1 combination

Indoximod

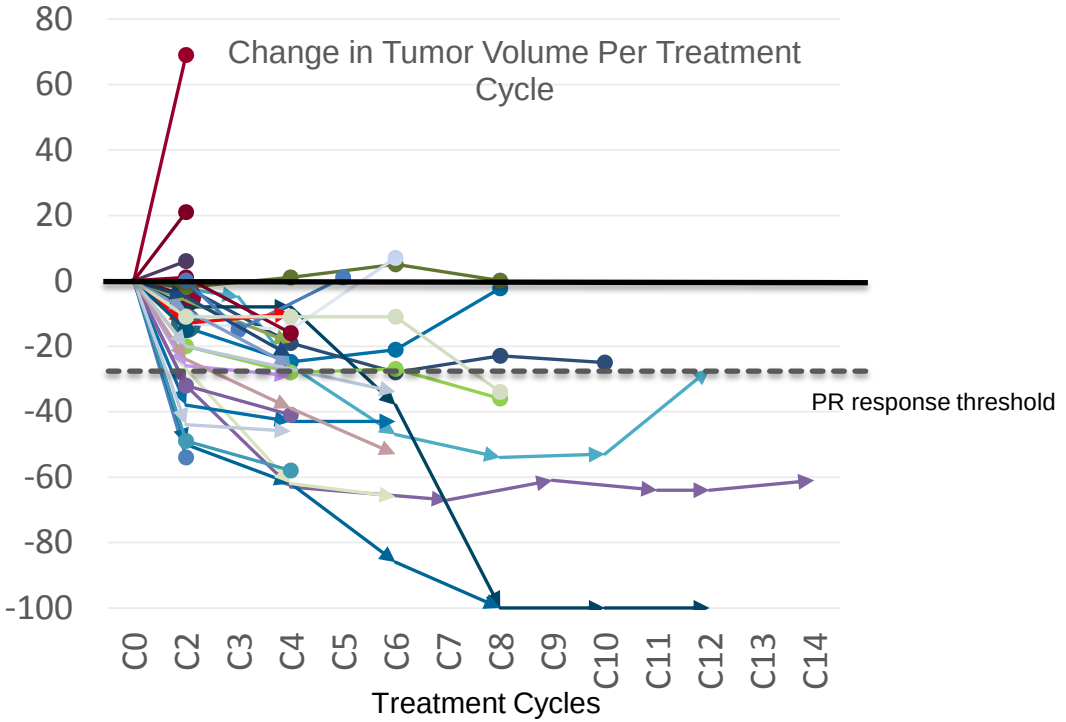
Clinical Development in Pancreatic Cancer

NLG2104 – 1st line Metastatic Pancreatic Cancer	
Primary Endpoint	▪ Overall survival
Key Secondary Clinical End-Points	▪ Objective response rate ▪ Progression free survival
Trial Design	▪ Phase 2 single arm study ▪ Indoximod in combination with gemcitabine / nab-paclitaxel
Trial Size	▪ 80+ patients in Phase 2 ▪ 40 patients in biopsy expansion cohort
Status	• Initial cohort fully enrolled ▪ Anticipate data 1H 2017 ▪ Biopsies cohort enrolling ▪ NCT02077881

Indoximod

Clinical Development in Metastatic Pancreatic Cancer

- Overall, combination of indoximod and gemcitabine / nab-paclitaxel was well tolerated
- 45 patients enrolled 4 months or longer
  - 45% ORR (14/31 PR or CR)
  - Response data per site reports
- Objective responses include 2 CR's
- Kinetics and durability of responses suggest immune mediated mechanism



Bahary et al, ASCO 2016 Abstract #3020

Depth and duration of response suggest immune mediated mechanism

Indoximod

Clinical Development in Malignant Brain Tumors

NLG2102- Refractory GBM	
Primary Endpoint	▪ Progression free survival
Key Secondary Clinical End-Points	▪ Objective response rate ▪ Overall survival
Trial Design	▪ Phase 2 single arm trial ▪ In combination with temozolomide in temozolomide refractory patients
Trial Size	▪ 132 patients in Phase 2
Status	▪ Primary subgroups fully enrolled ▪ Report results 2H:17 ▪ NCT02052648

Preliminary responses observed, await further data

Indoximod

Clinical Development in Breast Cancer

NLG2101 – 1st line Metastatic Breast Cancer	
Primary Endpoint	▪ Progression free survival
Key Secondary Clinical End-Points	▪ Overall survival ▪ Objective response rates
Trial Design	▪ Phase 2 randomized, double blind ▪ In combination with taxane chemotherapy
Trial Size	▪ 154 patients
Status	▪ Fully enrolled fully enrolled end of 2015 ▪ Report results 2017 ▪ NCT01792050

Demonstrated to be a difficult indication for immunotherapy

Indoximod

Clinical Development in AML

NLG2106 – 1st line Acute Myeloid Leukemia	
Primary Endpoint	▪ Safety of combination
Key Secondary Clinical End-Points	▪ Evidence of minimal residual disease
Trial Design	▪ Phase 1b dose escalation ▪ In combination with standard chemotherapy
Trial Size	▪ Up to 18 patients
Status	▪ Anticipate full enrollment in 1H:17 ▪ Opportunity to expand into Phase 2 in 2H:17 ▪ NCT02835729

Strong preclinical data and great unmet need

Indoximod + Tergenpumatucel-L

Clinical Development in NSCLC

NLG0401 – Advanced NSCLC	
Primary Endpoint	▪ Progression free survival
Key Secondary Clinical End-Points	▪ Objective Response Rate ▪ Overall Survival ▪ Correlative scientific studies ▪ Safety
Trial Design	▪ Phase 1b / 2 single arm study ▪ Indoximod in combinations with cellular immunotherapy
Trial Size	▪ 103 patients in Phase 2 ▪ Evaluates PD-1 naïve and PD-1 prior therapy patients
Status	▪ Enrolling ▪ NCT02460367

Combines two proprietary platforms
Evaluates dosing of tergenpumatucel-L and indoximod

Indoximod Clinical Development Plan

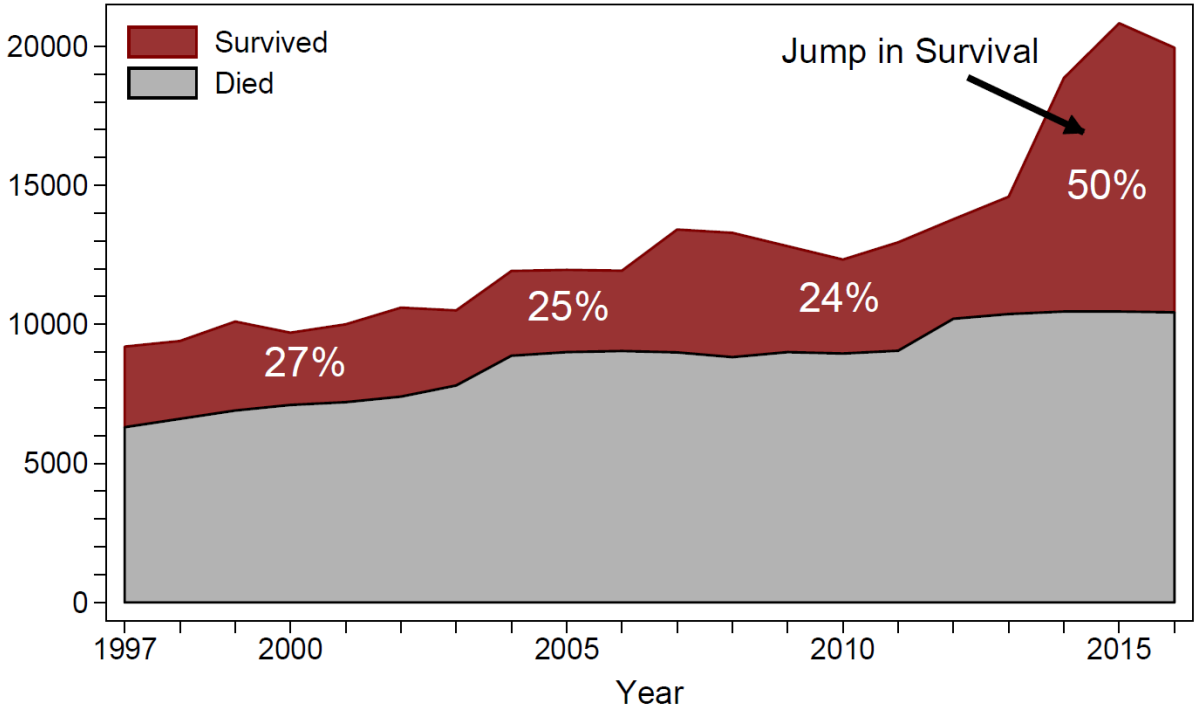
- Evidence of clinical activity justifies moving indoximod into late-stage development
- Clinical investigation and formulation efforts in mid-2017
- Planning for confirmatory randomized trials to start in 2H:17

NewLink GENETICS

Indoximod in Treatment of Patients with Acute Myeloid Leukemia (AML)

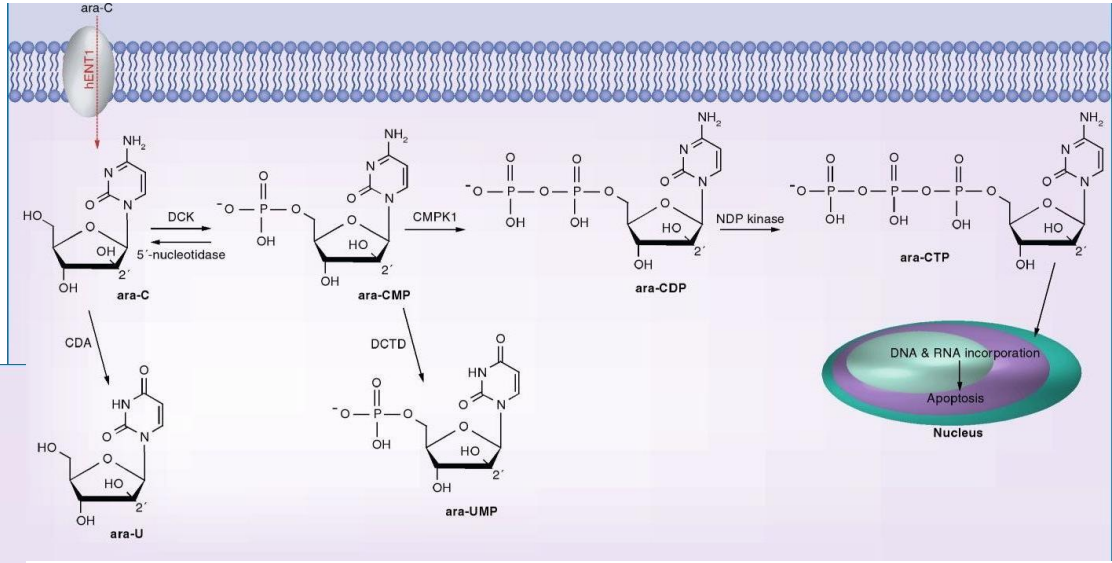
Ashkan Emadi, MD, PhD, Associate Professor of Medicine, Pharmacology & Experimental Therapeutics, University of Maryland

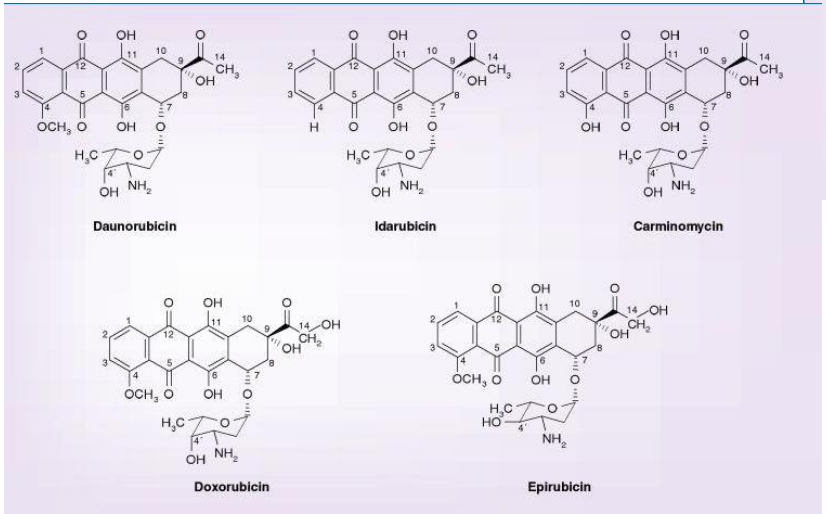
AML: Epidemiology



- Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015 Jan-Feb;65(1):5-29.
- Emadi A, Karp JE. The state of the union on treatment of acute myeloid leukemia. Leukemia & lymphoma 2014;55:2423-5

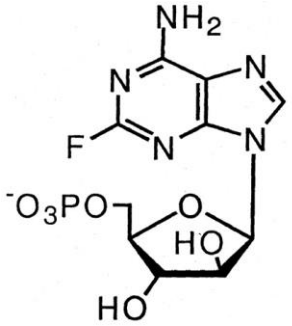
AML Treatment for Young and Medically Fit Patients



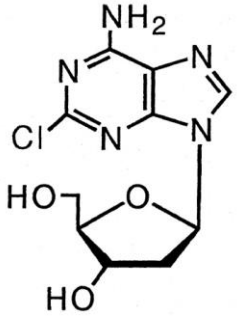


Emadi A, Karp JE. The clinically relevant pharmacogenomic changes in acute myelogenous leukemia *Pharmacogenomics.* 2012;13(11):1257-69

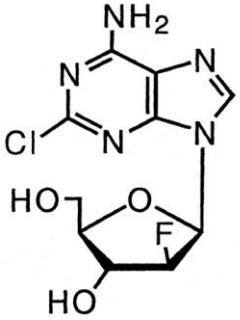
Attempts to Find a 3rd Conventional Cytotoxic Agent



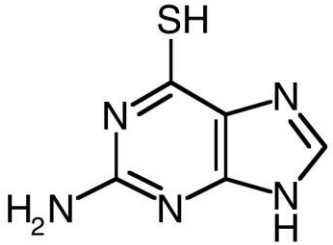
Fludarabine



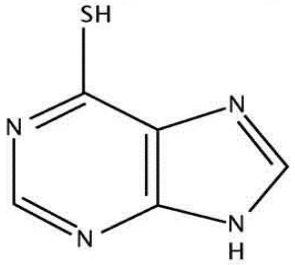
Cladribine



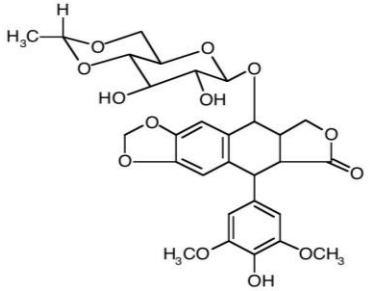
Clofarabine



Thioguanine



6-MP

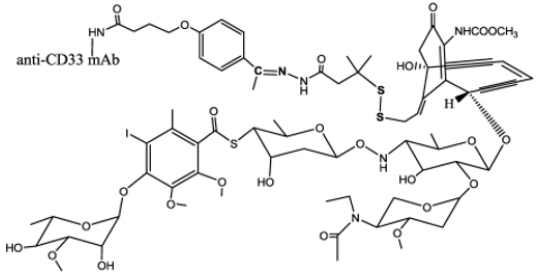


Etoposide

FDA Approved Drugs for Different Hematologic Neoplasms: 1995-2016

- **CML**: busulfan, imatinib, dasatinib, nilotinib, bosutinib, ponatinib, omacetaxine
- **CLL**: alemtuzumab, bendamustine, ofatumumab, obinutuzumab, ibrutinib, idelalisib
- **NHL (B-&T-):** rituximab, Zevalin (ibritumomab tiuxetan), Bexxar (Tositumomab), pralatrexate, romidepsin, brentuximab vedotin, lenalidomide, mechlorethamine gel, SAHA, belinostat, ibrutinib, idelalisib, obinutuzumab
- **Hodgkin Lymphoma**: brentuximab vedotin, nivolumab
- **Multiple Myeloma**: thalidomide, lenalidomide, bortezomib, carfilzomib, pomalidomide, panobinostat, daratumumab (11/6/15), ixazomib (11/20/16), elotuzumab (11/30/16)
- **MDS**: azacitidine, decitabine, lenalidomide
- **ALL**: clofarabine, nelarabine, asparaginase Erwinia chrysanthemi, Marqibo (vinCRIStine sulfate LIPOSOME injection), blinatumomab
- **AML??**

Gemtuzumab ozogamicin (Myelotarg)



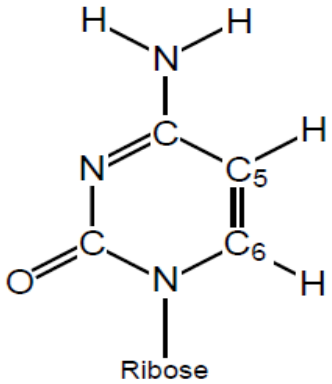
- Gemtuzumab ozogamicin was approved by the FDA in May, 2000 under the Accelerated Approval regulations for the treatment of patients 60 years of age or older with CD33-positive AML in first relapse

- A confirmatory clinical trial began in 2004 to determine whether adding gemtuzumab ozogamicin to standard chemotherapy would improve survival of patients with AML

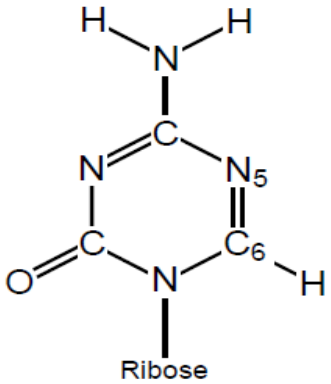
- The trial was stopped early when no clinical benefit was observed, and after a greater number of deaths occurred in patients who received gemtuzumab ozogamicin compared with those who received chemotherapy alone (5.7% with gemtuzumab and 1.4% without the agent (16/283 = 5.7% vs 4/281 = 1.4%; P = 0.01))

- **Gemtuzumab ozogamicin was withdrawn from the market in June, 2010.**

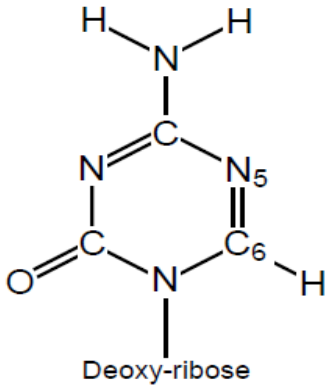
DNMTIs, Hypomethylating Agents FDA & EMA Approved for MDS



Cytidine



5-aza-cytidine
(Azacitidine)
No hydrogen (H)
is attached to
nitrogen 5 (N_5)



Decitabine
No hydrogen (H)
is attached to
nitrogen 5 (N5)

Leukemia & Lymphoma, 2014; Early Online: 1–5

ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2013.856425

informa
healthcare

ORIGINAL ARTICLE: CLINICAL

Ten-day decitabine as initial therapy for newly diagnosed patients with acute myeloid leukemia unfit for intensive chemotherapy

Bhavana Bhatnagar[1,2], Vu H. Duong[1,2], Theodore S. Gourdin[1,2], Michael L. Tidwell[1], Ching Chen[1,3], Yi Ning[1,3], Ashkan Emadi[1,2], Edward A. Sausville[1,2] & Maria R. Baer[1,2]

[1]*University of Maryland Greenebaum Cancer Center, Baltimore MD, USA and* [2]*Division of Hematology and Medical Oncology, Department of Medicine and* [3]*Department of Pathology, University of Maryland School of Medicine, Baltimore, MD, USA*

RESEARCH ARTICLE

AJH

Presence of isocitrate dehydrogenase mutations may predict clinical response to hypomethylating agents in patients with acute myeloid leukemia

Ashkan Emadi,[1*] Rawan Faramand,[1] Brandon Carter-Cooper,[1] Seda Tolu,[1] Laurie A. Ford,[2] Rena G. Lapidus,[1] Meir Wetzler,[2] Eunice S. Wang,[2] Arash Etemadi,[3] and Elizabeth A. Griffiths[2*]

Boulevard of Broken Dreams, Significant Opportunity Exists

- **Five-year survival: 35-40% in younger patients and only 3-8% in patients older than 60 years of age**
- **AML Therapy is Challenging**
  - An extremely heterogeneous disease with various leukemogenic mutations with poorly understood interplay among them
  - when one particular mutation is inhibited in an individual patient, the leukemic cells may survive and proliferate through other mutations which they harbor
- **One solution to this issue is to target a broad and more fundamental characteristic that is common among all AML cells, is agnostic about specific mutation, and is sufficiently different from normal tissues**

Sekeres MA, Steensma DP. Boulevard of broken dreams: drug approval for older adults with acute myeloid leukemia. J Clin Oncol. 2012 Nov 20;30(33):4061-3.

Science Supporting Targeting IDO Pathway in AML

Immune Response in AML

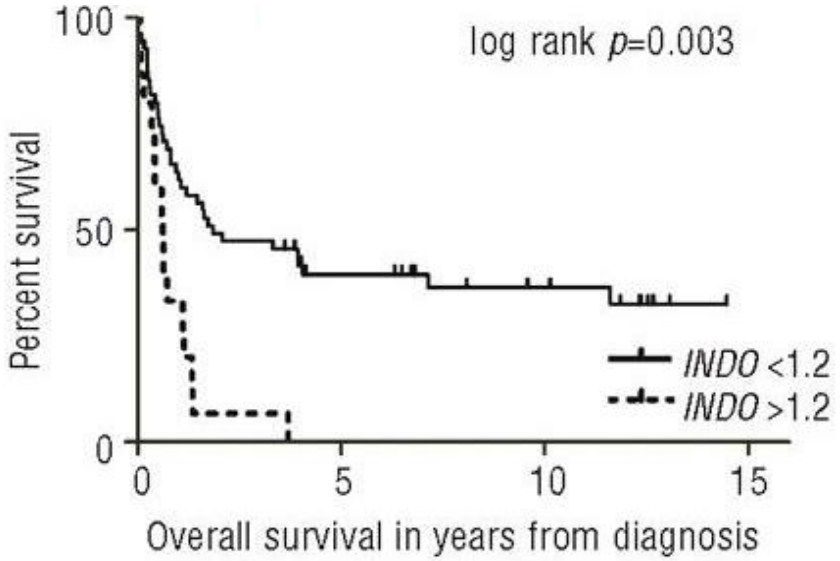
- Well established that T cell and NK cell responses after completion of chemotherapy are crucial to eventual leukemia-free survival

- Specifically, abnormal or diminished T cell and NK-cell responses have been implicated in increased risk of relapse in these patients

- The majority of evidence supporting the role of T cells in AML comes from experience in patients receiving allogenic hematopoietic stem cell transplant (allo-HSCT)

IDO in Bone Marrow Aspirate of AML Patients

INDO Expression by Microarray and by qPCR Correlated to Clinical Outcome in Patients with Adult AML



- IDO was a more significant predictor of survival than FAB morphology or white count
- IDO was more predictive even than FLT3-ITD

Chamuleau, M. E.D. et al. Haematologica 2008;93:1894-1898

Preclinical evidence of indoximod activity in AML

- Curti et al. demonstrated that 52% of a cohort of 76 patients with AML had IDO expression in their leukemic blasts
- IDO expression correlated with increased numbers of T_{reg} cells
- Indoximod induced the ability of IDO-expressing blasts to stimulate a helper T cell

- El Kholy et al. also demonstrated that 52% of peripheral mononuclear cells of patients in a cohort of 25 patients with AML expressed IDO
- They demonstrated that co-culture of blasts with doxorubicin led to a decrease in blast proliferation, an effect that was amplified when the blasts were exposed to the combination of doxorubicin and indoximod

- Curti A, Pandolfi S, Valzasina B, et al. Modulation of tryptophan catabolism by human leukemic cells results in the conversion of CD25- into CD25+ T regulatory cells. Blood 2007;109:2871-7
-- El Kholy NM, Sallam MM, Ahmed MB, et al. Expression of indoleamine 2,3-dioxygenase in acute myeloid leukemia and the effect of its inhibition on cultured leukemia blast cells. Med Oncol 2011;28:270-8

Clinical Trial Protocol NLG2106

A Phase 1b / Randomized Phase 2a Trial of Indoximod in Combination with Idarubicin and Cytarabine in Patients with Newly Diagnosed Acute Myeloid Leukemia (AML)

IND #: 127155
Clinicaltrials.gov #: NCT02835729

Version 1.2 Dated: 05/04/2016
Replaces Version 1.1: 02/23/2016

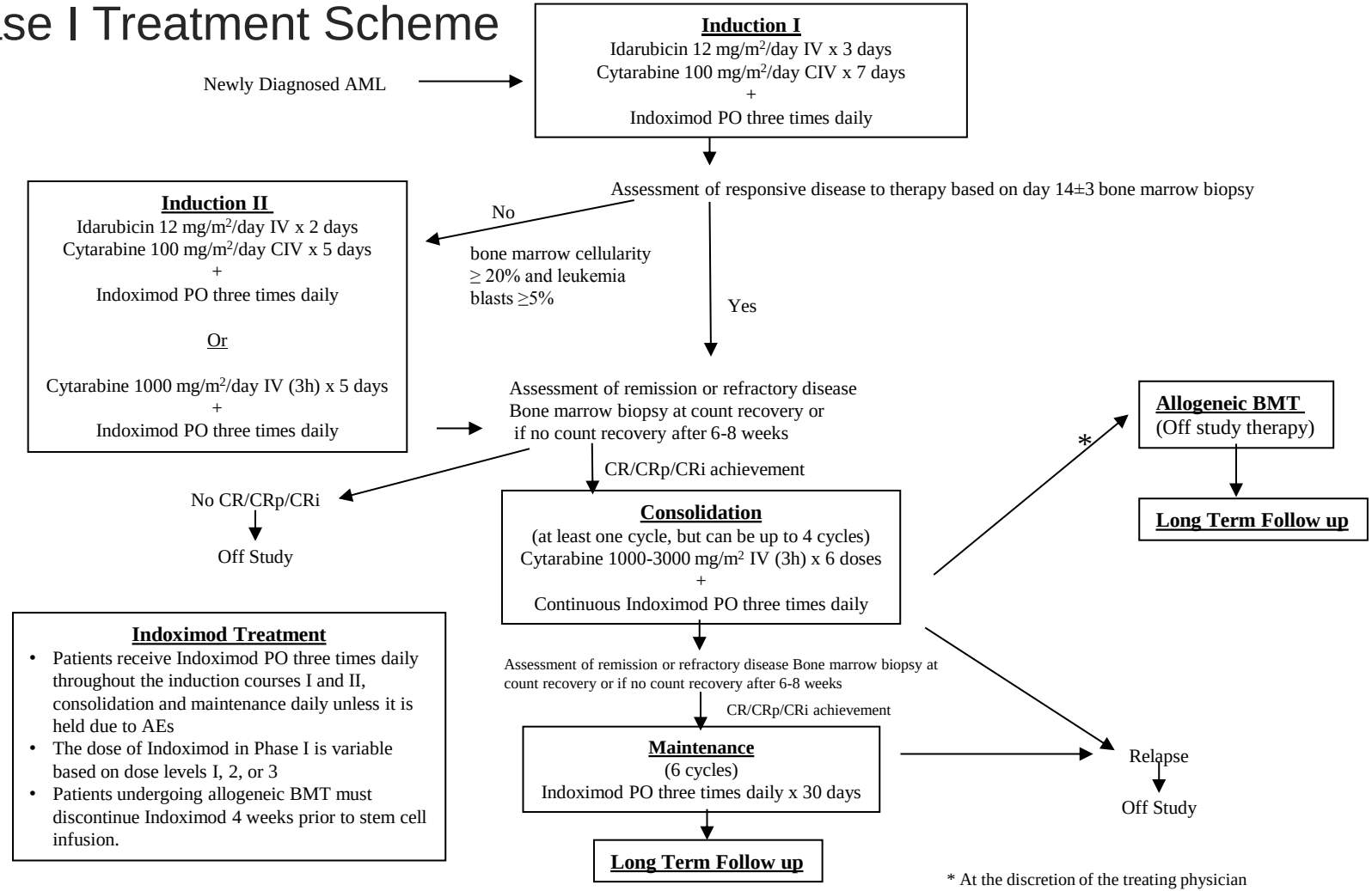
Study Sponsor:
NewLink Genetics Corporation
Iowa State University Research Park
2503 South Loop Drive, Suite 5100
Ames, Iowa, USA 50010

Investigational Agent:
Indoximod (1-methyl-D-tryptophan, D-1MT)

Trial Design: Endpoints and Sample Size

- Phase 1: 12-18 patients
- Phase 2a: 120 patients
  - 2:1 randomization, 80 in indoximod arm and 40 in placebo
- **Endpoints:**
  - Safety
  - To determine the minimal (or measurable) residual disease (MRD) in patients with AML who receive indoximod in combination with SOC chemotherapy as compared with patients receiving SOC alone at
    - The end of induction
    - After completion of the first cycle of consolidation therapy
    - Two-three weeks before maintenance therapy or two-three weeks

Phase I Treatment Scheme



Targeting IDO with Indoximod in AML

Summary

- Hematologic malignancies also overexpress IDO
- Approximately half of AML patients overexpress IDO
- Studies suggest IDO overexpression portends poor prognosis
- This novel study has been designed to add indoximod to the standard frontline chemotherapy backbone
- The trial is open and began enrollment in August 2016

Q & A

Indoximod In the Clinic

- Nicholas N. Vahanian, MD
- Montaser Shaheen, MD
- Eugene Kennedy, MD
- Ashkan Emadi, MD, PhD

NewLink GENETICS

NewLink GENETICS

Discovering New Immuno-Oncology Products

Mario Mautino, PhD, Senior Vice President, Drug Discovery, Intellectual Property Officer

Modulating the Function of Tregs

Tregs Can Be Reprogrammed Into Helper-Like T Cells

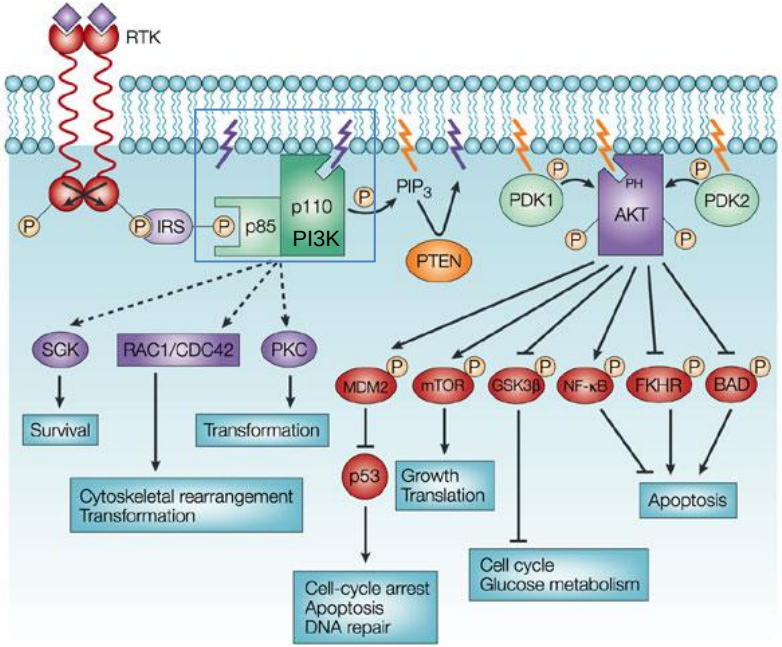
- Tumors are constantly eliciting an immune response, which is being suppressed by Tregs
- Conditions that are generally non-favorable for cell proliferation (lack of nutrients, growth factors, increased activity of tumor suppressor genes, lack of oxygen or glucose) lead to a program that results in very potent suppressive Tregs
- Identification and modulations of tumor microenvironment conditions and pathways that control the immunosuppressive phenotype of Tregs is an important goal of tumor immunotherapy
- Among several of the critical molecules regulating the function of Tregs are IDO, PD-1 and PTEN

Sharma et al, Science Adv 2015

Foe becomes Friend

PI3K/Akt/PTEN Pathway

PTEN Inhibits the PI3K/Akt Pathway



PTEN prevents cell growth

PTEN Regulates Treg Function

Proliferation and Suppressive Capacity of Tregs Is Regulated by PTEN

RESEARCH ARTICLE

CANCER IMMUNOTHERAPY

The PTEN pathway in T_{regs} is a critical driver of the suppressive tumor microenvironment

Madhav D. Sharma,[1,2] Rahul Shinde,[1]* Tracy L. McGaha,[1,3]* Lei Huang,[1,4] Rikke B. Hol
Mario R. Mautino,[6] Esteban Celis,[1,7] Arlene H. Sharpe,[8] Loise M. Francisco,[8] Jonathan
Andrew L. Mellor,[1,3] Bruce R. Blazar,[11] David H. Munn[1,2†]

ARTICLES

nature immunology

T_{reg} cells require the phosphatase PTEN to restrain T_H1 and T_{FH} cell responses

Sharad Shrestha[1,2,5], Kai Yang[1,5], Cliff Guy[1], Peter Vogel[3], Geoffrey Neale[4] & Hongbo Chi[1,2]

PTENtiating autoimmunity through T_{reg} cell deregulation

John P Ray & Joe Craft

Regulatory T cells require the phosphatase PTEN to maintain suppressive function in homeostatic conditions through preserved expression of CD25 and the transcription factor Foxp3.

Control of PI(3) kinase in T_{reg} cells maintains homeostasis and lineage stability

Alexandria Huynh[1,2], Michel DuPage[3], Bhavana Priyadharshini[2], Peter T Sage[4], Jason Quiros[3], Christopher M Borges[1,2], Natavudh Townamchai[5], Valerie A Gerriets[6], Jeffrey C Rathmell[6], Arlene H Sharpe[4], Jeffrey A Bluestone[3] & Laurence A Turka[1,2]

www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN

PTEN ameliorates autoimmune arthritis through down-regulating STAT3 activation with reciprocal balance of Th17 and Tregs

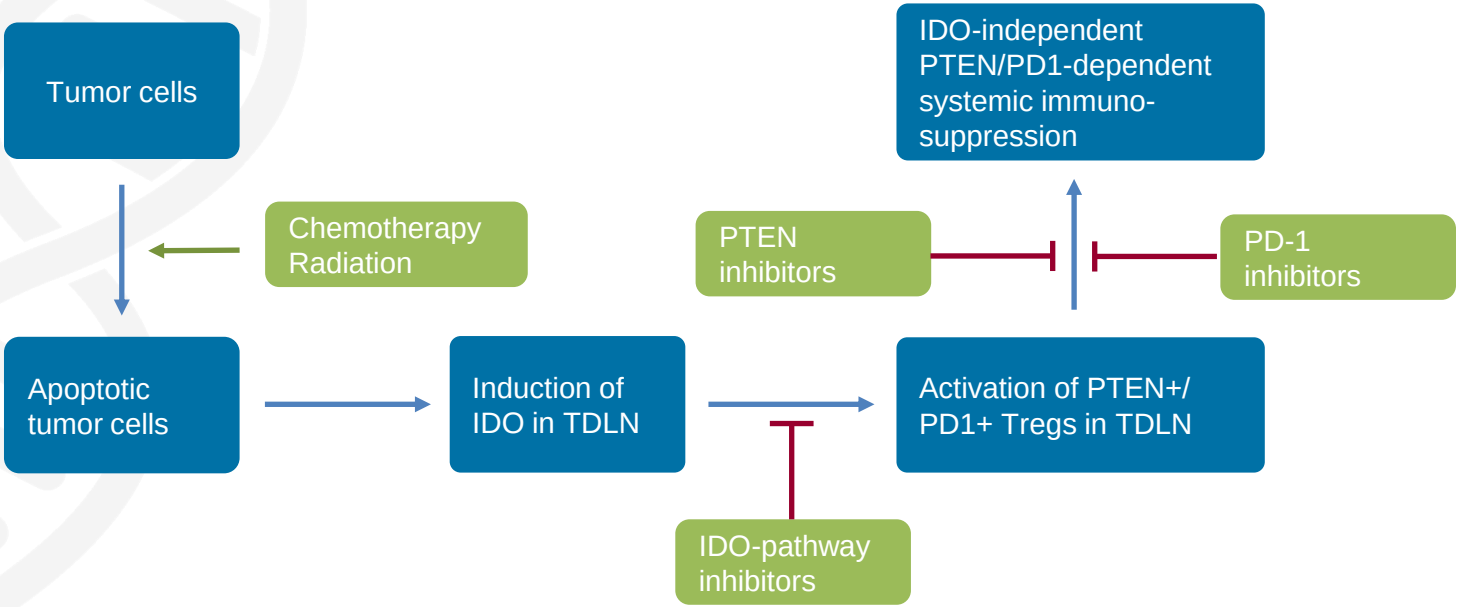
Received: 22 April 2016
Accepted: 08 September 2016
Published: 06 October 2016

Seung Hoon Lee[1,*], Jin-Sil Park[1,*], Jae-Kyung Byun[1], JooYeon Jhun[1], KyungAh Jung[2], Hyeon-Beom Seo[3], Young-Mee Moon[3], Ho-Youn Kim[1,3], Sung-Hwan Park[1,3,*] & Mi-La Cho[1,4,*]

The role of PTEN on Treg function is being revealed by several studies

Tumor Immunosuppression

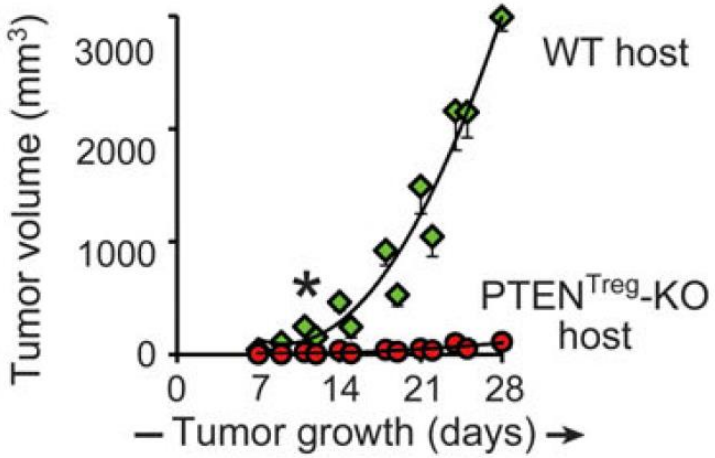
Operational Model Showing IDO, PD-1 and PTEN Roles



PTEN inhibitors could reverse IDO-mediated systemic immunosuppression

PTEN is a Key Protein Needed for Immunosuppression

PTEN Deletion Results in Tumor Regression and T_{reg} to T_{help} Conversion



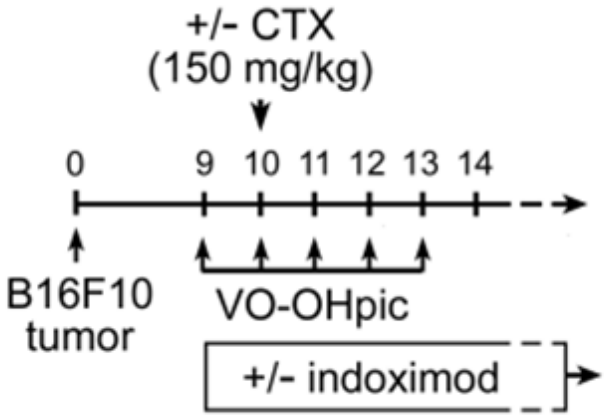
- Genetic deletion of PTEN in host Tregs results in tumor regression
- PTEN-KO Tregs do not express PD-1
- PTEN-KO Tregs acquire a T helper phenotype

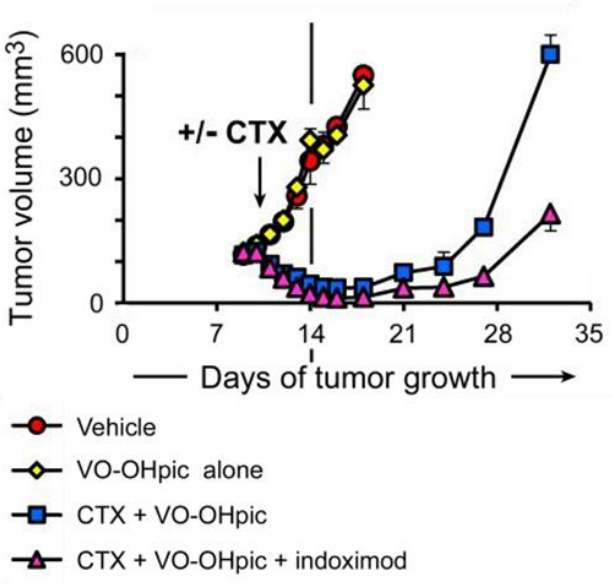
Sharma et al, Science Adv 2015

PTEN expressing Tregs are required for tumor growth

Pharmacologic Inhibition of PTEN + Chemotherapy

Transplantable Melanoma Model



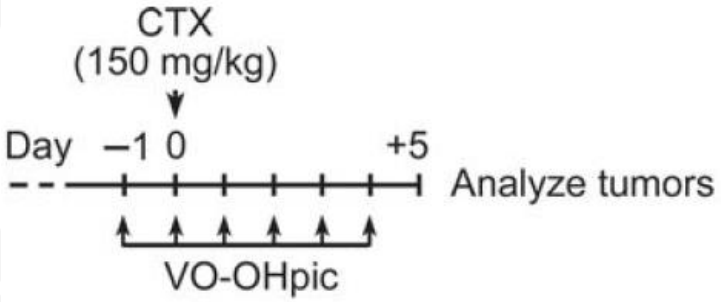


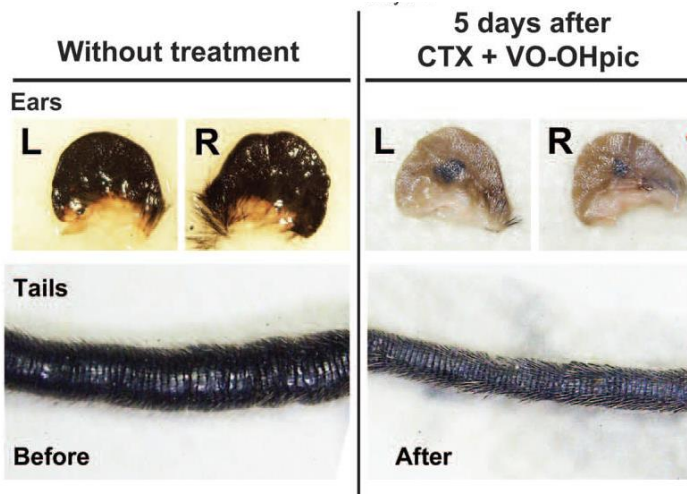
Sharma et al, Science Adv 2015

Strong antitumor effect by pharmacologic inhibition of PTEN

Pharmacologic Inhibition of PTEN + Chemotherapy

Autochthonous Melanoma Models [Tg(Grm1)Epv]





Sharma et al, Science Adv 2015

Strong antitumor effect by pharmacologic inhibition of PTEN

The PTEN Pathway in Tregs, A Critical Driver of Tumor Immunosuppression

Summary

- Exposure to apoptotic tumor cells elicits IDO-dependent activation of PTEN-expressing Tregs in TDLN
- Activation of these PTEN expressing Tregs can be prevented with IDO inhibitors
- Tregs mediate systemic immunosuppression in a PTEN and PD1-dependent and IDO-independent manner
- PTEN inhibition results in reprogramming of highly suppressive Tregs into pro-inflammatory helper-like effector cells (ex-Tregs)
- PTEN deletion or inhibition in Tregs in murine tumor models results in a potent antitumor effect

Sharma et al, Science Adv 2015

Tumors become susceptible to immune attack if PTEN is disrupted in Tregs

PTEN as a Pharmacological Target

Why PTEN Inhibitors?

- PTEN is an attractive target for pharmacological inhibition in immuno-oncology
- PTEN inhibition could also find applications in other fields such as diabetes, nerve regeneration, prevention of ischemia damages
- Licensing and research collaboration between AURI and NewLink
- We are working to identify lead PTEN inhibitor compounds
- Multiple assays to test PTEN inhibitors potency, activity and specificity

PTEN inhibitors are a very attractive opportunity in immuno-oncology

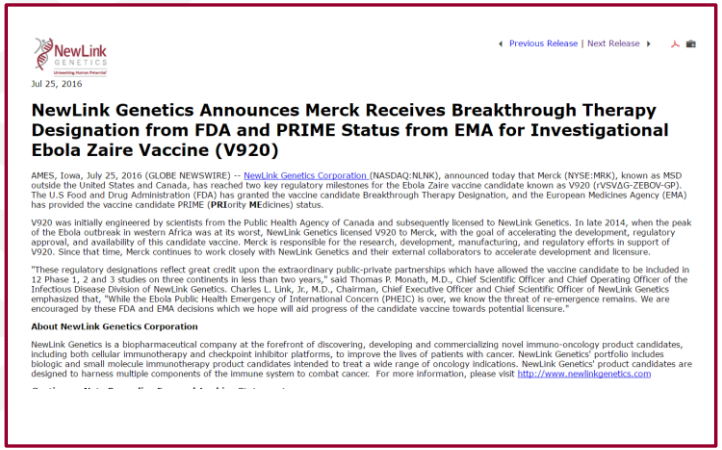
Financial Update

John B. Henneman, III, Executive Vice President, Chief Financial Officer

Infectious Disease Programs

Ebola and Zika Virus Vaccines

- Ebola vaccine candidate receives breakthrough therapy designation from FDA and PRIME status from EMA
- Project underway to develop new treatment options for the Zika virus



Previous Release | Next Release

Jul 25, 2016

NewLink Genetics Announces Merck Receives Breakthrough Therapy Designation from FDA and PRIME Status from EMA for Investigational Ebola Zaire Vaccine (V920)

AMES, Iowa, July 25, 2016 (GLOBE NEWSWIRE) -- NewLink Genetics Corporation (NASDAQ:NLNK), announced today that Merck (NYSE:MRK), known as MSD outside the United States and Canada, has reached two key regulatory milestones for the Ebola Zaire vaccine candidate known as V920 (rVSVΔG-ZEBOV-GP). The U.S Food and Drug Administration (FDA) has granted the vaccine candidate Breakthrough Therapy Designation, and the European Medicines Agency (EMA) has provided the vaccine candidate PRIME (**PRI**ority **ME**dicines) status.

V920 was initially engineered by scientists from the Public Health Agency of Canada and subsequently licensed to NewLink Genetics. In late 2014, when the peak of the Ebola outbreak in western Africa was at its worst, NewLink Genetics licensed V920 to Merck, with the goal of accelerating the development, regulatory approval, and availability of this candidate vaccine. Merck is responsible for the research, development, manufacturing, and regulatory efforts in support of V920. Since that time, Merck continues to work closely with NewLink Genetics and their external collaborators to accelerate development and licensure.

"These regulatory designations reflect great credit upon the extraordinary public-private partnerships which have allowed the vaccine candidate to be included in 12 Phase 1, 2 and 3 studies on three continents in less than two years," said Thomas P. Monath, M.D., Chief Scientific Officer and Chief Operating Officer of the Infectious Disease Division of NewLink Genetics. Charles L. Link, Jr., M.D., Chairman, Chief Executive Officer and Chief Scientific Officer of NewLink Genetics emphasized that, "While the Ebola Public Health Emergency of International Concern (PHEIC) is over, we know the threat of re-emergence remains. We are encouraged by these FDA and EMA decisions which we hope will aid progress of the candidate vaccine towards potential licensure."

About NewLink Genetics Corporation

NewLink Genetics is a biopharmaceutical company at the forefront of discovering, developing and commercializing novel immuno-oncology product candidates, including both cellular immunotherapy and checkpoint inhibitor platforms, to improve the lives of patients with cancer. NewLink Genetics' portfolio includes biologic and small molecule immunotherapy product candidates intended to treat a wide range of oncology indications. NewLink Genetics' product candidates are designed to harness multiple components of the immune system to combat cancer. For more information, please visit http://www.newlinkgenetics.com

THE WALL STREET JOURNAL.

Drug Industry Starts Race to Develop Zika Vaccine

U.S. biotech company NewLink Genetics Corp. said it too was working on developing treatment options for the disease.

At least a dozen Ebola vaccine and drug candidates were under development when the virus began to spread in West Africa.

Even so, there is still no licensed treatment or vaccine. One vaccine candidate, developed by NewLink and licensed out to Merck & Co. proved effective in a clinical trial, and the company is gathering data to apply for licensure.

Financial Position

Cash and Equivalents	$148 million (September 30, 2016)
Debt	~$0.6 million
YE 2016 Cash (Projected)	~$132 million
Quarterly Negative Cash-Flow	~$13 million
Shares Outstanding	29.1 million
Market Capitalization	$450 million*
Headcount	130

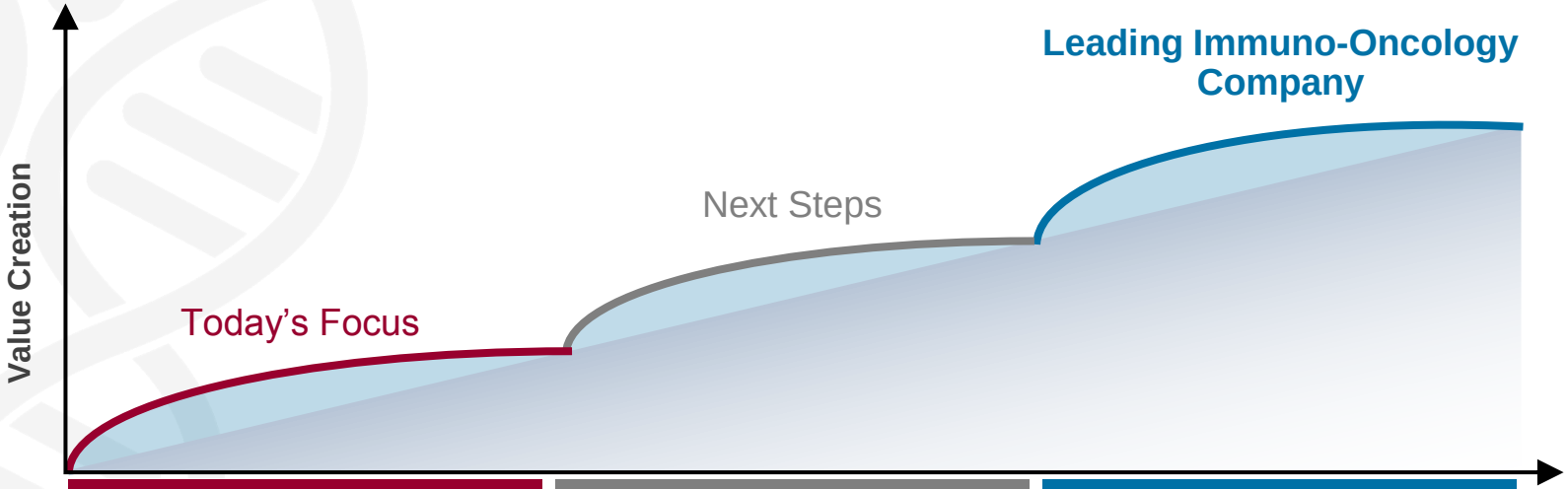
*As of October 5, 2016

NewLink Genetics

Takeaways from Today's Program

- IDO pathway is central to immune escape
- IDO pathway is becoming increasingly validated as a target for drugs
- Two promising candidates that target the IDO pathway, with distinct mechanisms of action
  - GDC-0919, which targets the enzyme directly (partnered with Genentech)
  - Indoximod, which inhibits the effects of IDO by supplying a "tryptophan-sufficiency" signal
- Scientifically visionary, with "over-the-horizon" programs, such as PTEN
- Proven track record in both in-and-out licensing
- Strong balance sheet to advance current clinical programs

Long-Term Growth Strategy



Today's Focus	Next Steps	Long-Term Potential
▪ GDC-0919 Ph 1b, solid tumors + expansion cohorts ▪ Indoximod, multiple indications	▪ GDC-0919 clinical development progressing ▪ Indoximod moving into larger trials ▪ In-licensing opportunities	▪ PTEN advancement ▪ Advanced milestones

Q & A