Corvus R&D Symposium

New York City | May 10, 2022

An immunology focused company developing drugs and antibodies that target the most critical elements of the tumor immunity axis

CORVUS PHARMACEUTICALS

Forward-Looking Statements / Safe Harbor

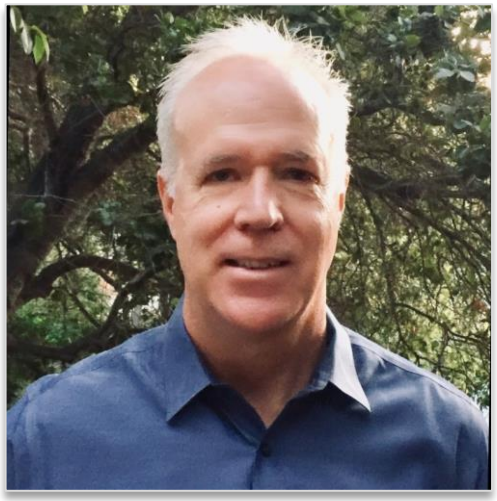
This presentation and the accompanying oral presentation contain “forward-looking” statements, including statements related to the potential safety and efficacy of mupadolimab, CPI-818 and ciforadenant; the Company’s ability and Angel Pharmaceutical’s ability to develop and advance product candidates into and successfully complete preclinical studies and clinical trials, including the Company’s planned initiation of a Phase 2 clinical trial of mupadolimab, and the Company’s plan to initiate a Phase 2 clinical trial with ciforadenant in collaboration with the Kidney Cancer Clinical Trials Consortium, the timing of the availability and announcement of clinical data and certain other product development milestones, including the timing of results in the Phase 1/1b clinical trial of CPI-818, the Phase 1b/2 clinical trial for mupadolimab, and in the phase 1b/2 clinical trial of ciforadenant. All statements other than statements of historical fact contained in this press release are forward-looking statements. These statements often include words such as “believe,” “expect,” “anticipate,” “intend,” “plan,” “estimate,” “seek,” “will,” “may” or similar expressions. Forward-looking statements are subject to a number of risks and uncertainties, many of which involve factors or circumstances that are beyond the Company’s control. The Company’s actual results could differ materially from those stated or implied in forward-looking statements due to a number of factors, including but not limited to, risks detailed in the Company’s Annual Report on Form 10-Q for the quarter ended March 31, 2022, filed with the Securities and Exchange Commission on May 5, 2022, as well as other documents that may be filed by the Company from time to time with the Securities and Exchange Commission. In particular, the following factors, among others, could cause results to differ materially from those expressed or implied by such forward-looking statements: the Company’s ability to demonstrate sufficient evidence of efficacy and safety in its clinical trials of mupadolimab, CPI-818 and ciforadenant; the accuracy of the Company’s estimates relating to its ability to initiate and/or complete preclinical studies and clinical trials; the results of preclinical studies may not be predictive of future results; the unpredictability of the regulatory process; regulatory developments in the United States, and other foreign countries; regulatory developments in the United States, and other foreign countries; the costs of clinical trials may exceed expectations; and the Company’s ability to raise additional capital. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the events and circumstances reflected in the forward-looking statements will be achieved or occur, and the timing of events and circumstances and actual results could differ materially from those projected in the forward-looking statements. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and the Company undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise. The Company’s results for the quarter ended March 31, 2022 are not necessarily indicative of its operating results for any future periods.

This presentation concerns products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. Such products are currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

Today's Speakers

Richard A. Miller, M.D.
Co-founder, President and CEO
Corvus Pharmaceuticals

Neel K. Gupta, M.D.
Clinical Assistant Professor
Stanford University
School of Medicine



Erik Verner, Ph.D.
Senior VP of Research
Angel Pharmaceuticals

Suresh Mahabhashyam, M.D., M.P.H.
VP of Clinical Development
Corvus Pharmaceuticals

Agenda

Time	Topic	Presenter
09:00 – 09:10 am	Event and Company Intro	Richard Miller, M.D. *President & CEO* *Corvus Pharmaceuticals*
09:10 – 09:25 am	Prognosis and Management of T-cell Lymphomas	Neel K. Gupta, M.D. *Clinical Assistant Professor* *Stanford University School of Medicine*
09:25 – 09:55 am	CPI-818: First-in-class ITK Inhibitor	Erik Verner, Ph.D. *Senior Vice President of Research* *Angel Pharmaceuticals*
09:55 – 10:10 am	Q&A	
10:10 – 10:35 am	Mupadolimab: B-cell Activation and Adenosine Blockade	Suresh Mahabhashyam, M.D. *Vice President Clinical Development* *Corvus Pharmaceuticals*
10:35 – 10:50 am	Ciforadenant: Adenosine Receptor Inhibitor	Richard Miller *President & CEO* *Corvus Pharmaceuticals*
10:50 – 11:15 am	Q&A and Closing	

Corvus Development Strategy

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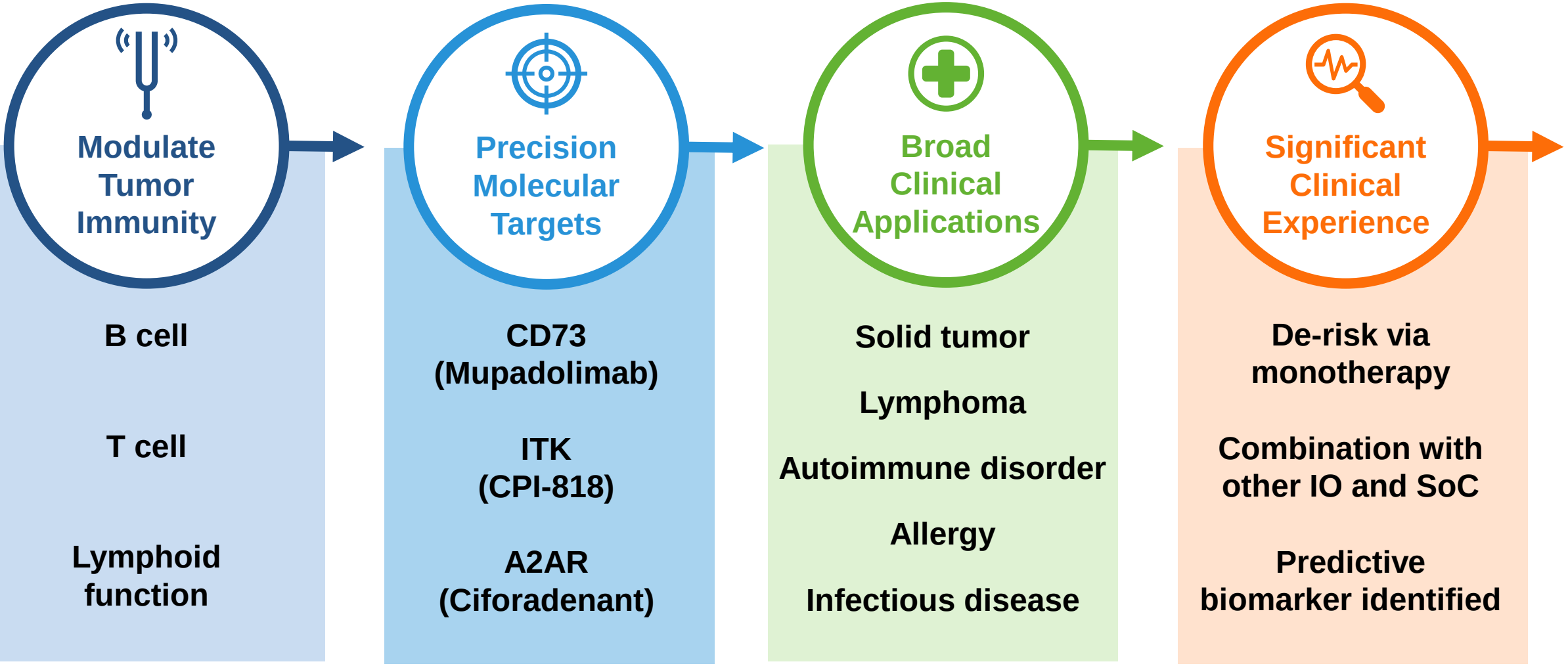
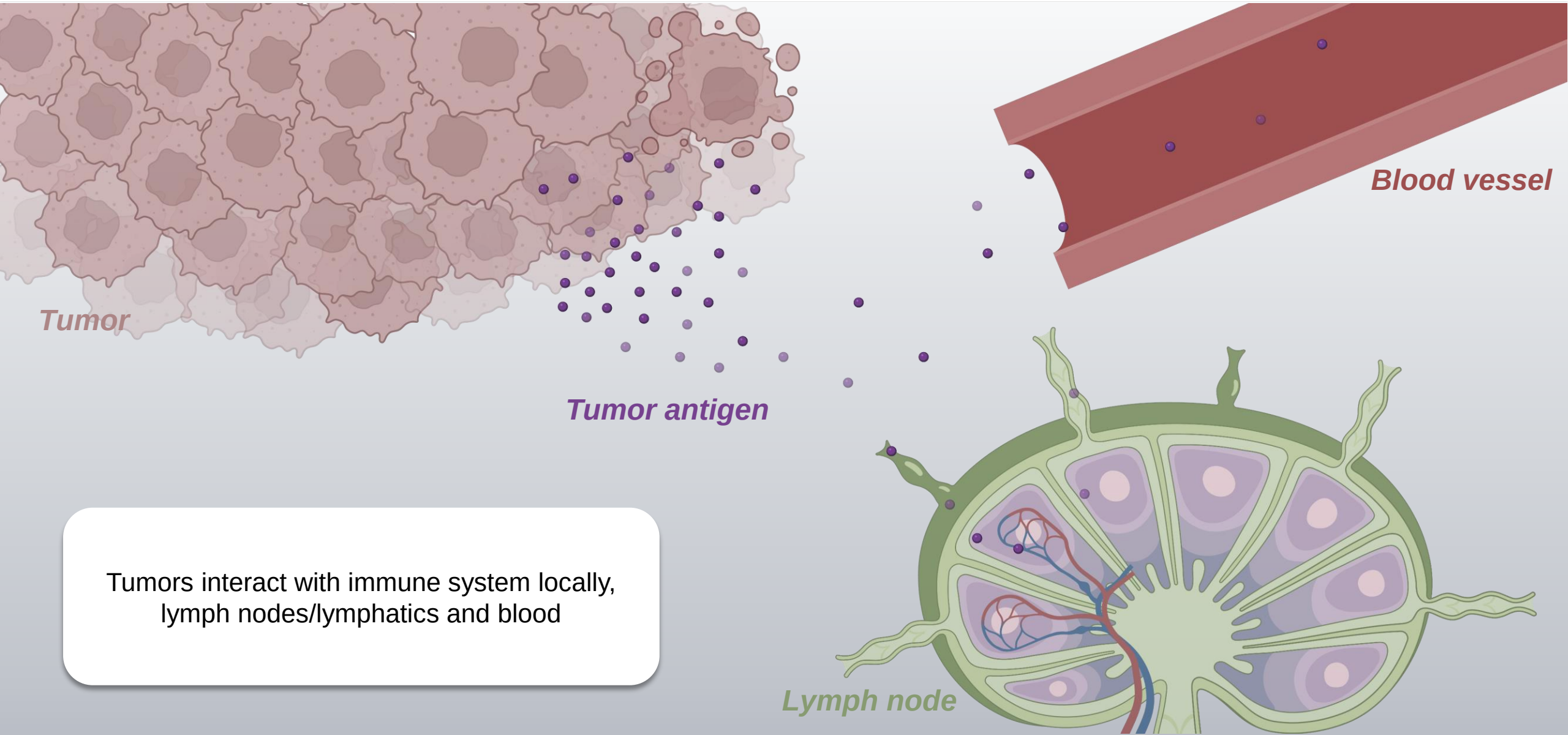


Corvus Precision Immunotherapy

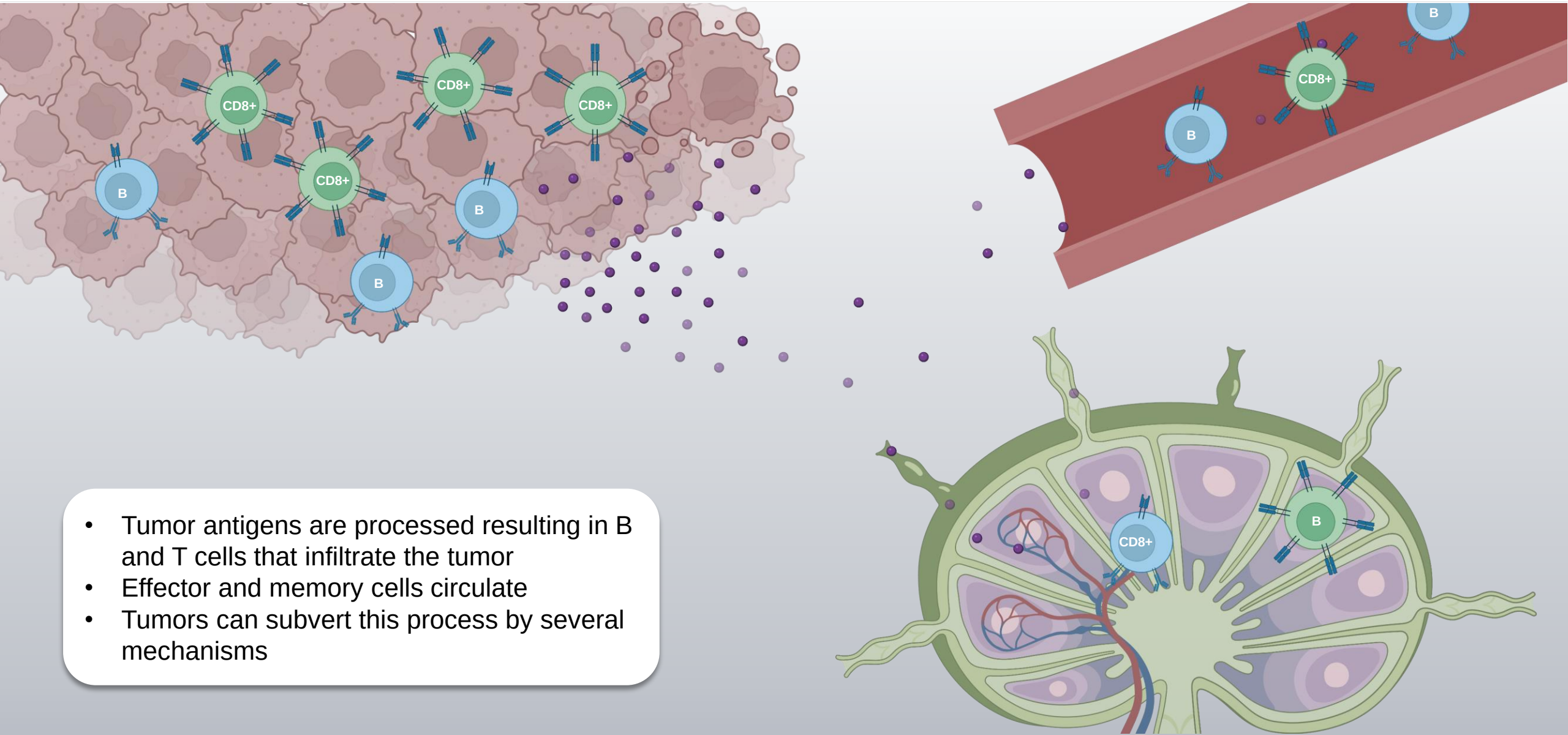
Controlling multiple steps in the tumor immunity axis



Tumors interact with immune system locally, lymph nodes/lymphatics and blood

Corvus Precision Immunotherapy

Controlling multiple steps in the tumor immunity axis

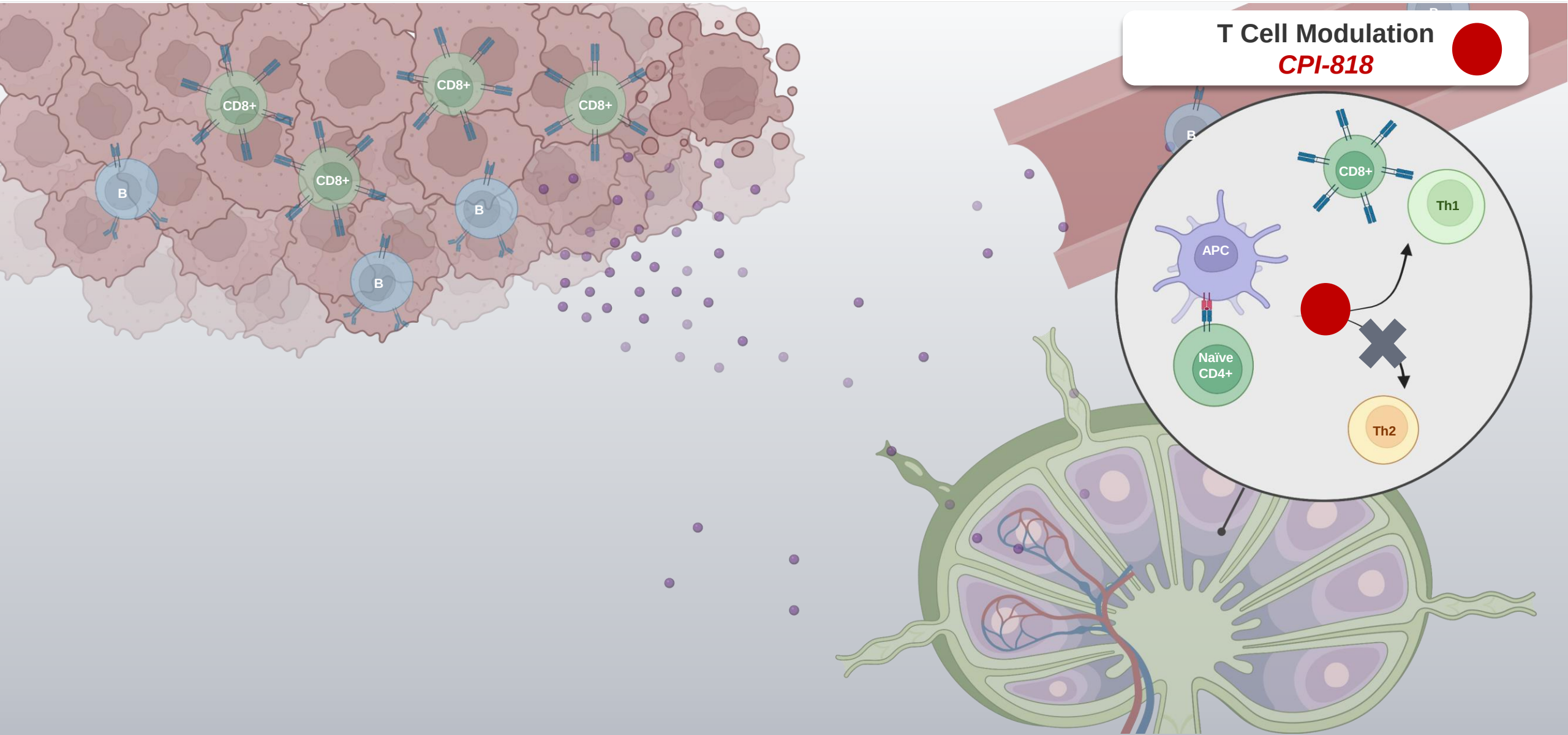


- Tumor antigens are processed resulting in B and T cells that infiltrate the tumor
- Effector and memory cells circulate
- Tumors can subvert this process by several mechanisms

Corvus Precision Immunotherapy

Controlling multiple steps in the tumor immunity axis

CORVUS PHARMACEUTICALS



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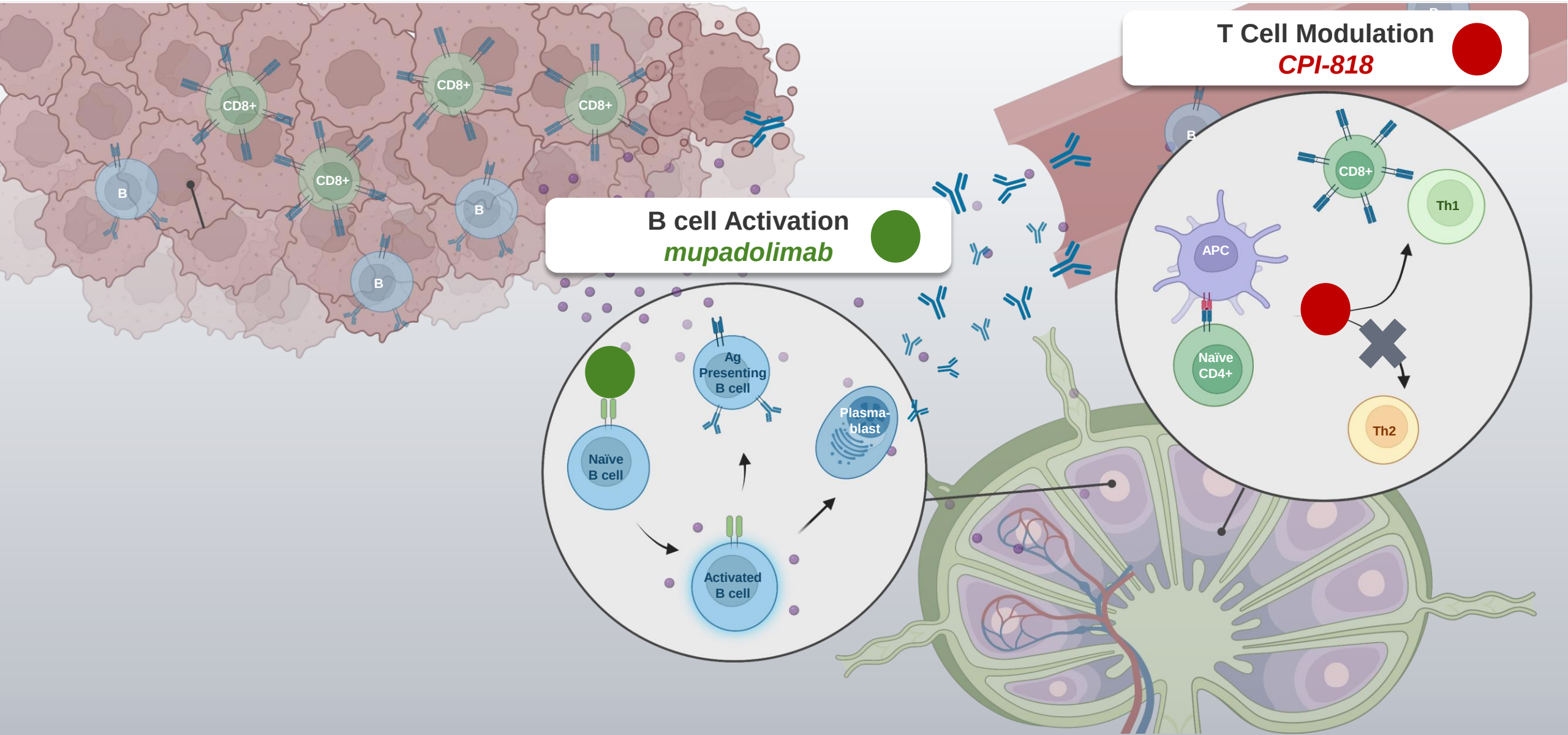

Corvus Precision Immunotherapy

Controlling multiple steps in the tumor immunity axis

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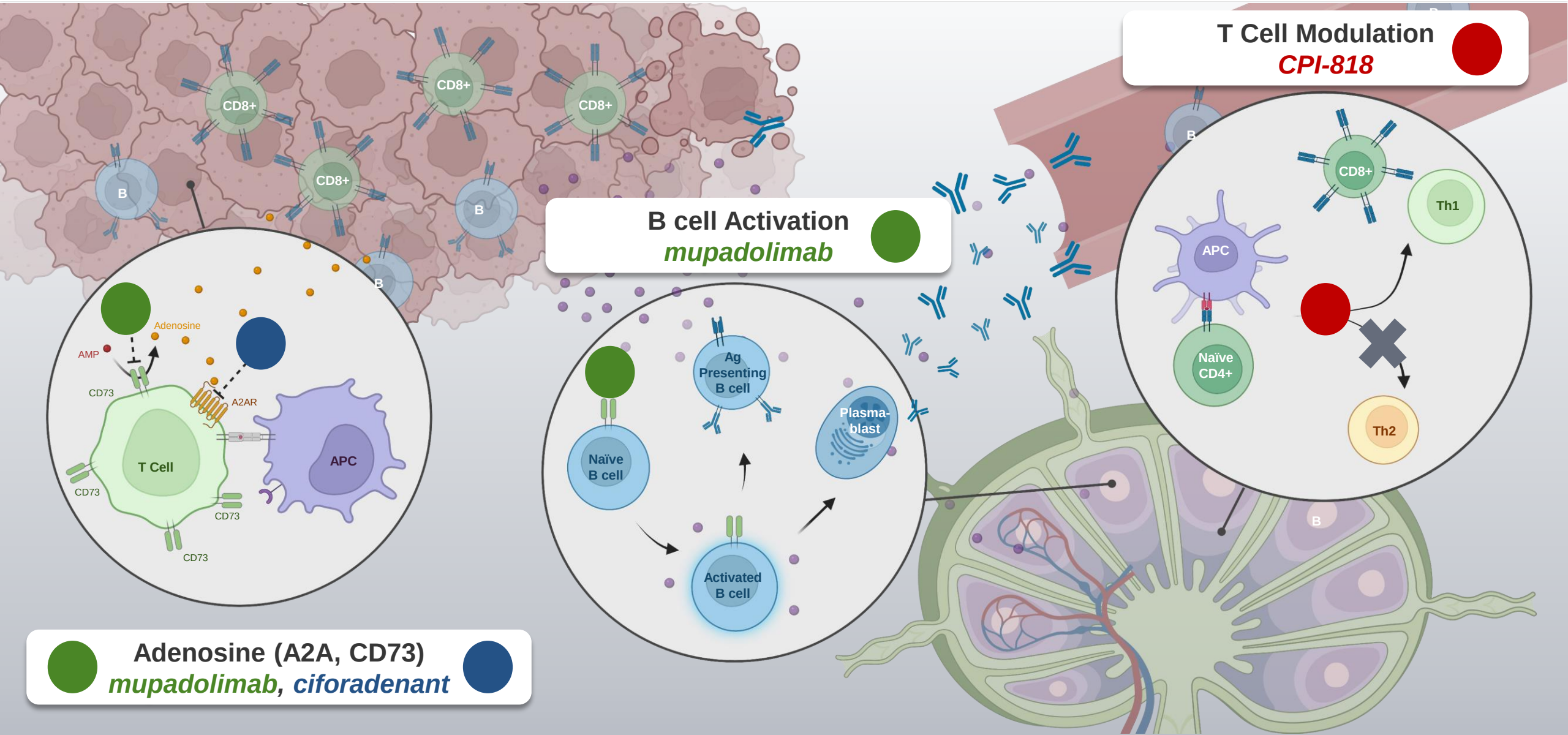


Corvus Pharmaceutical Overview

Advancing Pipeline

Target	Program	Indication	IND enabling	Phase 1a	Phase 1b	Phase 2
Anti-CD73	Mupadolimab	r/r Advanced Tumors *Mono or in combo with anti-PD-1*				
		r/r NSCLC and HNSCC *Mono or in combo with anti-PD-1*				
		Frontline Stage IV NSCLC *In combo with Pembro + Chemo*			Plan to Initiate Randomized Trial in 2H22	
A2A Inhibitor	Ciforadenant	r/r RCC *Mono or in combo with Atezolizumab*				
		Frontline RCC *In combo with Nivo and Ipi*			Plan to Initiate Trial in 2H22	Kidney Cancer RESEARCH CONSORTIUM
ITK Inhibitor	CPI-818	T-cell Lymphoma			Data anticipated in 2H22	和记药业 ANGEL PHARMACEUTICALS
Anti-CXCR2	CPI-182	Multiple Cancers				
		Inflammation				
A2B Inhibitor	CPI-935	Fibrosis				

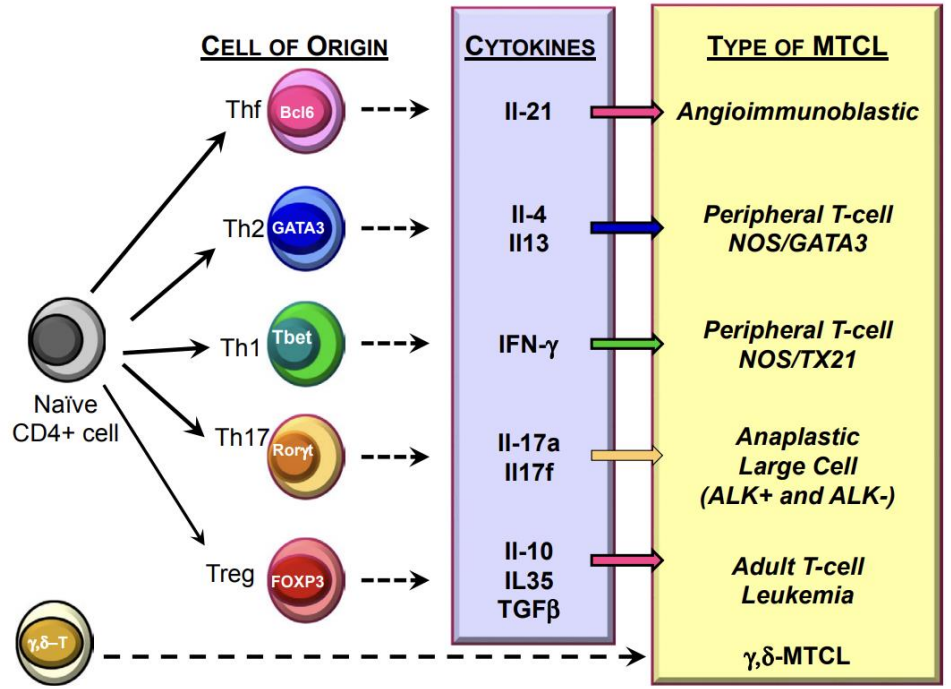
Prognosis and Management of T-cell Lymphomas

Neel K. Gupta, MD
Clinical Assistant Professor
Divisions of Hematology and Oncology
Stanford University School of Medicine

T-cell Lymphoma Classification

Mature T-Cell Lymphomas – WHO 2016 Classification

Nodal	Extranodal	Cutaneous	Leukemic
PTCL-NOS	ENKTL, nasal	MF	HTLV-1 Adult T-cell Leukemia/Lymphoma
AITL	EATL	Sezary Syndrome	T-Prolymphocytic LeukemiaL
Systemic ALCL. ALK+ and ALK-	MEITL	Subcutaneous panniculitis-like TCL	T-Cell Large Granular Lymphocytes (LGL)
Follicular TCL	Indolent T-cell LPD of GI tract	Primary cutaneous CD30+ LPD	Aggressive NK cell Leukemia
Nodal PTCL with TFH phenotype	Hepatosplenic TCL	Lymphomatoid papulosis	
Systemic EBV TCL, childhood	Breast-implant ALCL	Primary cutaneous ALCL	
Hydroa-vaccinform like LPD	Chronic LPD of NK cells	Primary cutaneous γ,δ TCL	
		Primary cutaneous CD8+ aggressive epidermotropic cytotoxic TCL	
		Primary cutaneous CD4+ TCL	



Marchi and O'Conner, CA Cancer J Clin 2020

T-cell Lymphoma Subtypes

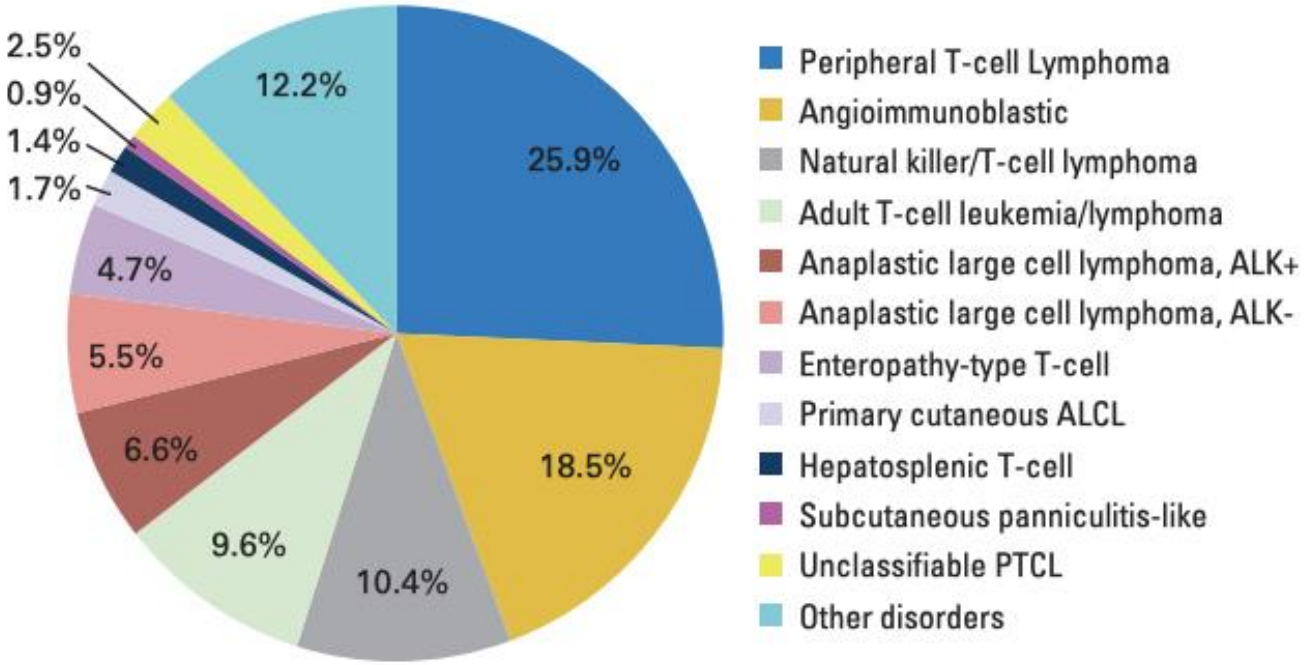


Table 1. Major Lymphoma Subtypes by Geographic Region

Subtype	%		
	North America	Europe	Asia
PTCL-NOS	34.4	34.3	22.4
Angioimmunoblastic	16.0	28.7	17.9
ALCL, ALK positive	16.0	6.4	3.2
ALCL, ALK negative	7.8	9.4	2.6
NKTCL	5.1	4.3	22.4
ATLL	2.0	1.0	25.0
Enteropathy-type	5.8	9.1	1.9
Hepatosplenic	3.0	2.3	0.2
Primary cutaneous ALCL	5.4	0.8	0.7
Subcutaneous panniculitis-like	1.3	0.5	1.3
Unclassifiable T-cell	2.3	3.3	2.4

Abbreviations: PTCL, peripheral T-cell lymphoma; NOS, not otherwise specified; ALCL, anaplastic large-cell lymphoma; NKTCL, natural killer/T-cell lymphoma.

Vose et al, JCO 2008; Al-Naeeb et al, BMJ 2018

T-cell Lymphoma – Prognosis

Inferior Prognosis Compared to B-cell NHL

Diagnosis	%	5-Year OS	
		IPI 0/1	IPI 4/5
PTCL-NOS	32	50	11
Angioimmunoblastic	32	56	25
Nasal NKTCL	42	57	0
Extranasal NKTCL	9	17	20
ATLL	14	28	7
ALCL, ALK+	70	90	33
ALCL, ALK−	49	74	13
Enteropathy-type	20	29	14

Revised IPI DLBCL

Risk Factors	4-yr OS (yrs)
0	**92%**
1 - 2	**82%**
3 - 5	**58%**

IPI = age > 60, ECOG > 1, extra-nodal sites > 1, stage III/IV, elevated LDH

Sehn et al, Blood 2007; Vose et al, JCO 2008

T-cell Lymphoma – SOC for Frontline Therapy?

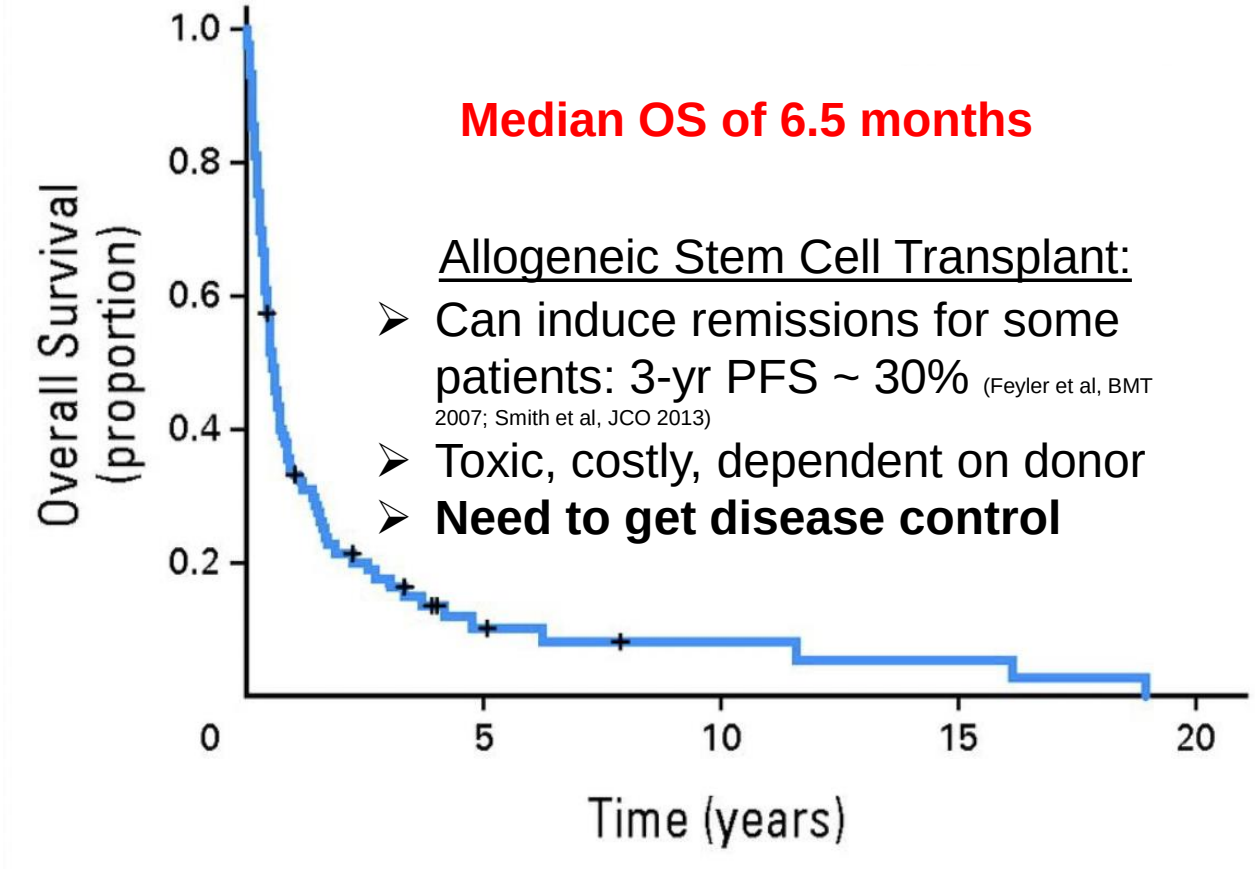
- **CHOEP** (Schmitz et al, Blood 2010)
  - German High-Grade Non-Hodgkin Lymphoma Study Group (343 patients)
  - 3-yr OS ~ 68% (AITL); ~ 62% (ALK-negative ALCL); 54%(PTCL NOS)
  - *Toxic, difficult for patients > 60 years of age, retrospective*
- **BV-CHP** (Horwitz et al, The Lancet 2019)
  - ECHELON2 (452 patients): RCT of BV-CHP vs CHOP
  - 3-year PFS: ~ 57% for BV-CHP vs ~ 44% for CHOP
  - *Largely a regimen for ALCL (70% of trial patients), data has been extrapolated to other TCLs, no one uses CHOP alone any more*
- **Autologous transplant (autoSCT) in first remission**
  - 5-year OS ~ 50% (D'amore et al, JCO 2012)
  - No randomized studies compared to chemotherapy alone
  - *Middling results, toxic, unclear which subtypes benefit*

T-cell Lymphoma – Rel/Ref Disease

Retrospective analysis of 153 patients with rel/ref PTCL NOS, AITL, ALCL

No stem cell transplant

89 patients received 'salvage' chemotherapy (eg ICE, DHAP, GemOx)



Median OS of 6.5 months

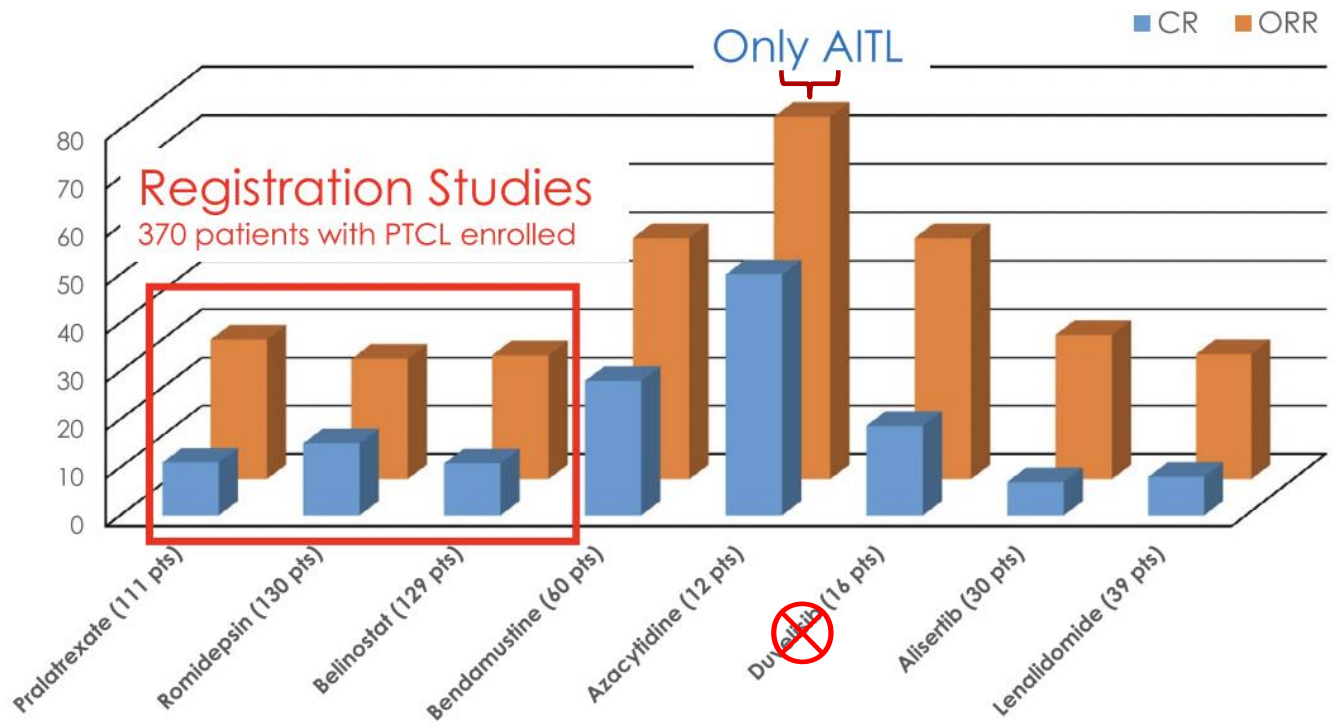
<u>Allogeneic Stem Cell Transplant:</u>

- Can induce remissions for some patients: 3-yr PFS ~ 30% (Feyler et al, BMT 2007; Smith et al, JCO 2013)
- Toxic, costly, dependent on donor
- **Need to get disease control**

Mak et al, JCO 2012

T-cell Lymphoma – Treatment of Rel/Ref Disease

SINGLE-AGENT ACTIVITY OF NEW DRUGS IN R/R MATURE T-CELL LYMPHOMA



	ORR (%)	CR (%)
Pralatrexate	29	11
Romidepsin	25	15
Belinostat	25.8	10.8
Bendamustine	50	28
Azacytidine	75	50
Duvelisib	50	18.7
Alisertib	30	7
Lenalidomide	26	8

FDA-approved

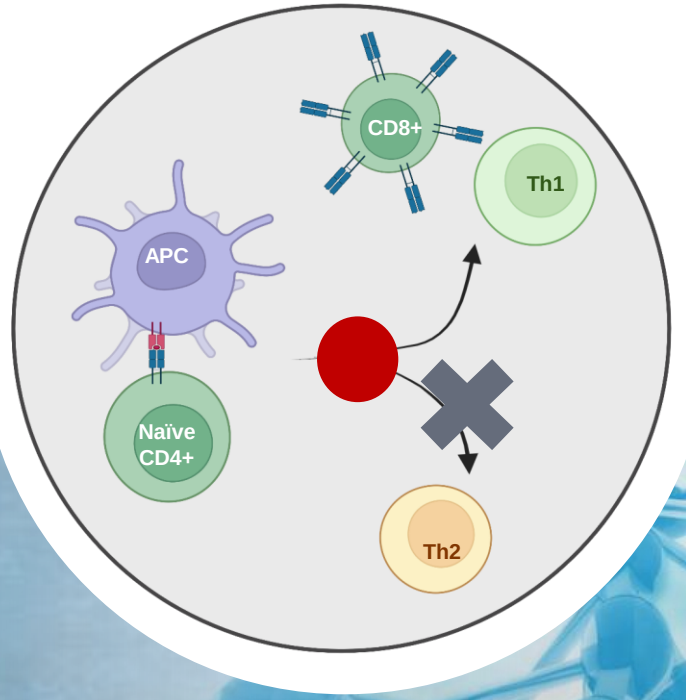
Marchi and O'Conner, CA Cancer J Clin 2020

T-cell Lymphoma Therapeutics – What's Needed?

- Therapy with a novel mechanism of action that improves patient outcomes in a clinically meaningful way
- Single agent activity while able to combine with cytotoxic and/or other therapies
- Safety, especially with respect to blood counts
- Active against range of T-cell lymphomas
- Less burdensome than current options (eg pill vs frequent infusion) for this sick and heavily treated patient population

CPI-818

Novel ITK Inhibitor



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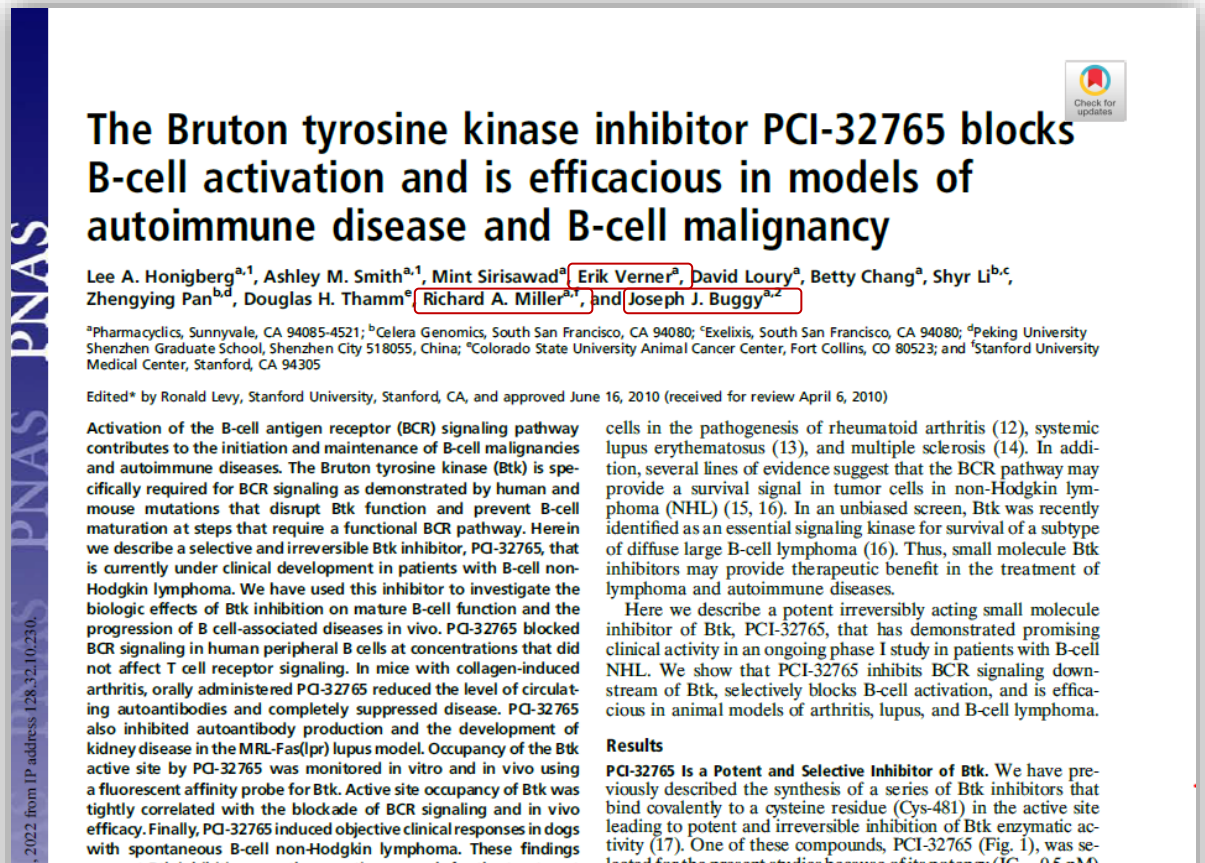
Ibrutinib – Novel BTK Inhibitor

- Founders of Corvus developed ibrutinib
- Among the top 4 oncology drugs by worldwide sales in 2021



PNAS

The Bruton tyrosine kinase inhibitor PCI-32765 blocks B-cell activation and is efficacious in models of autoimmune disease and B-cell malignancy

Lee A. Honigberg[a,1], Ashley M. Smith[a,1], Mint Sirisawad[a], Erik Verner[a], David Loury[a], Betty Chang[a], Shyr Li[b,c], Zhengying Pan[b,d], Douglas H. Thamm[e], Richard A. Miller[a,f], and Joseph J. Buggy[a,2]

[a]Pharmacyclics, Sunnyvale, CA 94085-4521; [b]Celera Genomics, South San Francisco, CA 94080; [c]Exelixis, South San Francisco, CA 94080; [d]Peking University Shenzhen Graduate School, Shenzhen City 518055, China; [e]Colorado State University Animal Cancer Center, Fort Collins, CO 80523; and [f]Stanford University Medical Center, Stanford, CA 94305

Edited* by Ronald Levy, Stanford University, Stanford, CA, and approved June 16, 2010 (received for review April 6, 2010)

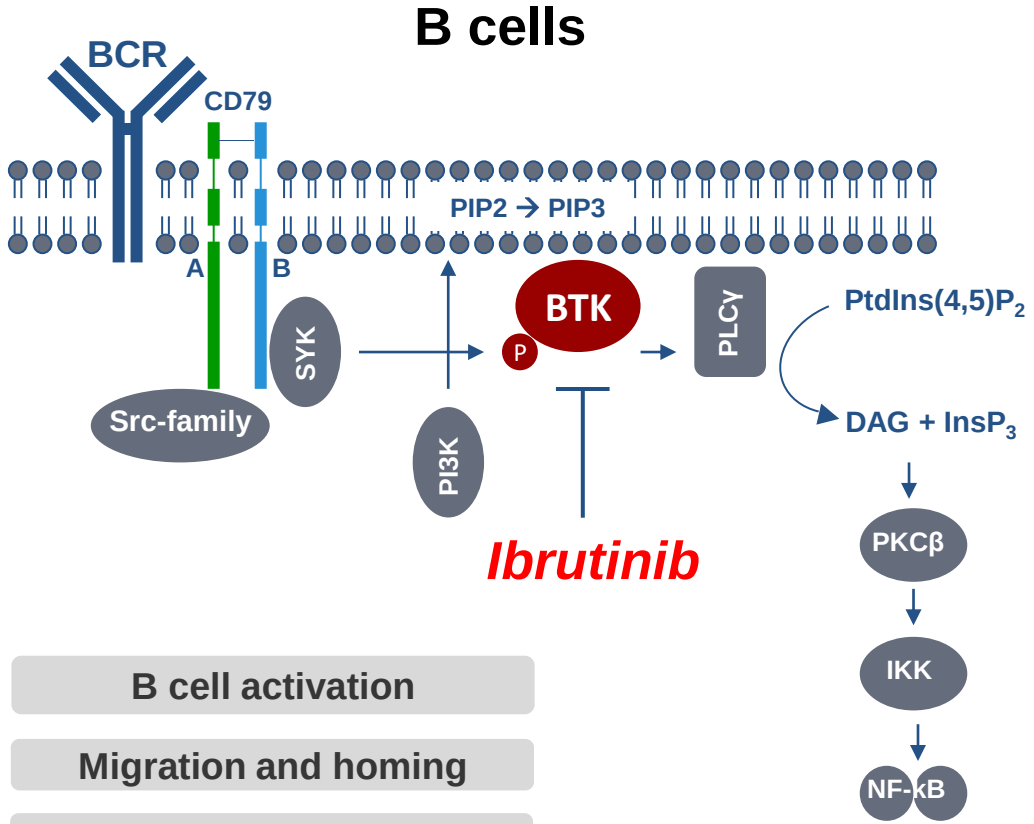
Activation of the B-cell antigen receptor (BCR) signaling pathway contributes to the initiation and maintenance of B-cell malignancies and autoimmune diseases. The Bruton tyrosine kinase (Btk) is specifically required for BCR signaling as demonstrated by human and mouse mutations that disrupt Btk function and prevent B-cell maturation at steps that require a functional BCR pathway. Herein we describe a selective and irreversible Btk inhibitor, PCI-32765, that is currently under clinical development in patients with B-cell non-Hodgkin lymphoma. We have used this inhibitor to investigate the biologic effects of Btk inhibition on mature B-cell function and the progression of B cell-associated diseases in vivo. PCI-32765 blocked BCR signaling in human peripheral B cells at concentrations that did not affect T cell receptor signaling. In mice with collagen-induced arthritis, orally administered PCI-32765 reduced the level of circulating autoantibodies and completely suppressed disease. PCI-32765 also inhibited autoantibody production and the development of kidney disease in the MRL-Fas(lpr) lupus model. Occupancy of the Btk active site by PCI-32765 was monitored in vitro and in vivo using a fluorescent affinity probe for Btk. Active site occupancy of Btk was tightly correlated with the blockade of BCR signaling and in vivo efficacy. Finally, PCI-32765 induced objective clinical responses in dogs with spontaneous B-cell non-Hodgkin lymphoma. These findings

cells in the pathogenesis of rheumatoid arthritis (12), systemic lupus erythematosus (13), and multiple sclerosis (14). In addition, several lines of evidence suggest that the BCR pathway may provide a survival signal in tumor cells in non-Hodgkin lymphoma (NHL) (15, 16). In an unbiased screen, Btk was recently identified as an essential signaling kinase for survival of a subtype of diffuse large B-cell lymphoma (16). Thus, small molecule Btk inhibitors may provide therapeutic benefit in the treatment of lymphoma and autoimmune diseases.

Here we describe a potent irreversibly acting small molecule inhibitor of Btk, PCI-32765, that has demonstrated promising clinical activity in an ongoing phase I study in patients with B-cell NHL. We show that PCI-32765 inhibits BCR signaling downstream of Btk, selectively blocks B-cell activation, and is efficacious in animal models of arthritis, lupus, and B-cell lymphoma.

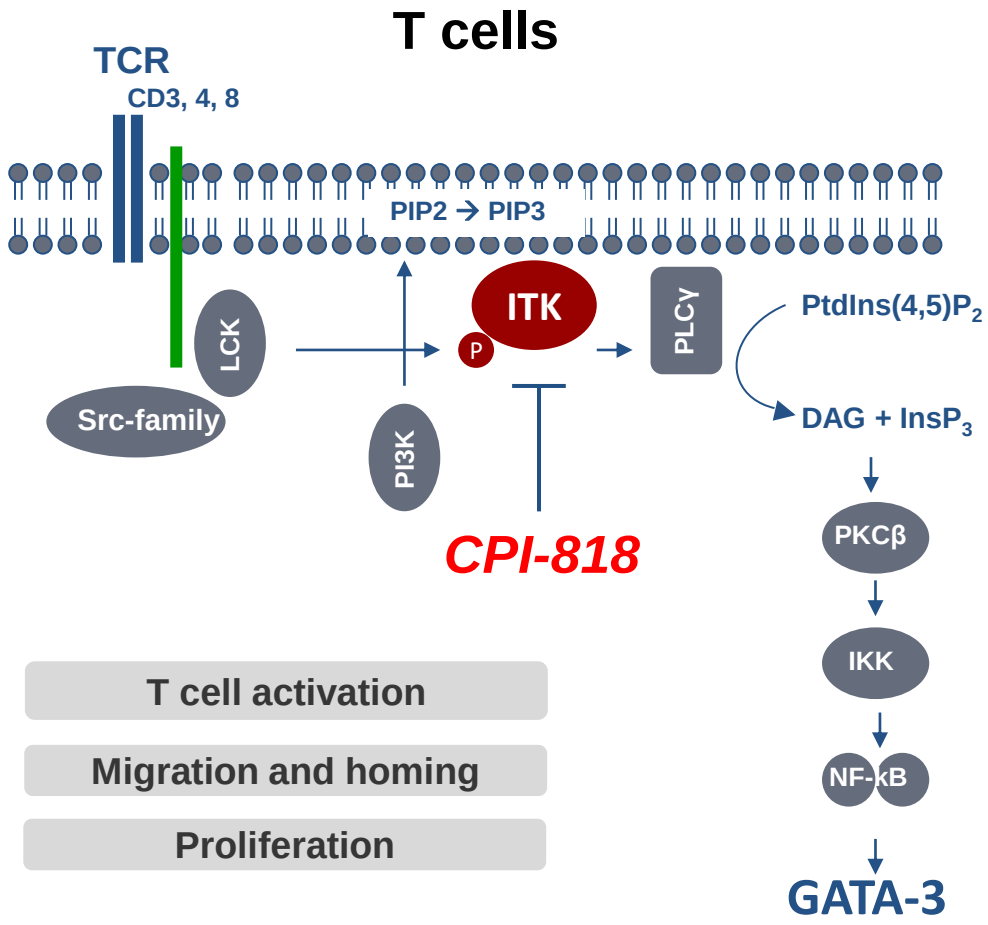
Results

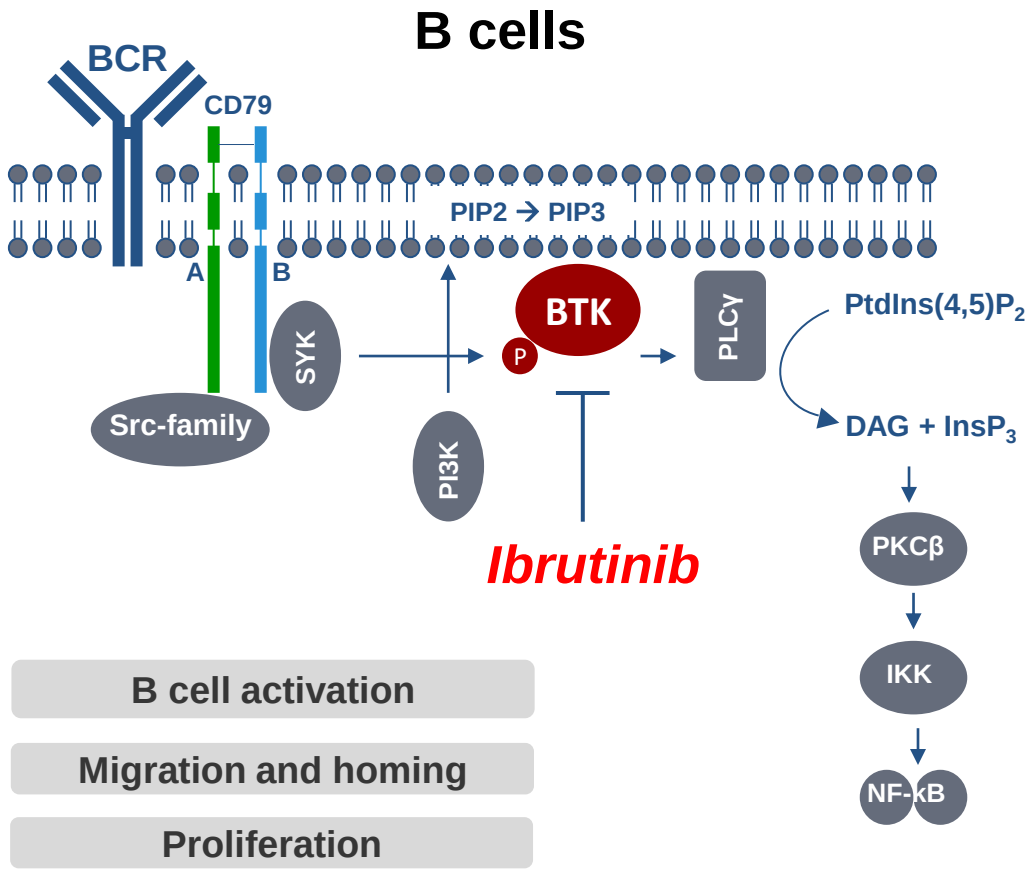
PCI-32765 Is a Potent and Selective Inhibitor of Btk. We have previously described the synthesis of a series of Btk inhibitors that bind covalently to a cysteine residue (Cys-481) in the active site leading to potent and irreversible inhibition of Btk enzymatic activity (17). One of these compounds, PCI-32765 (Fig. 1), was se-



- B cell activation
- Migration and homing
- Proliferation

CPI-818: Novel ITK Inhibitor





ITK Plays Critical Roles in T Cell Mediated Diseases

Selectivity is crucial for immune modulation

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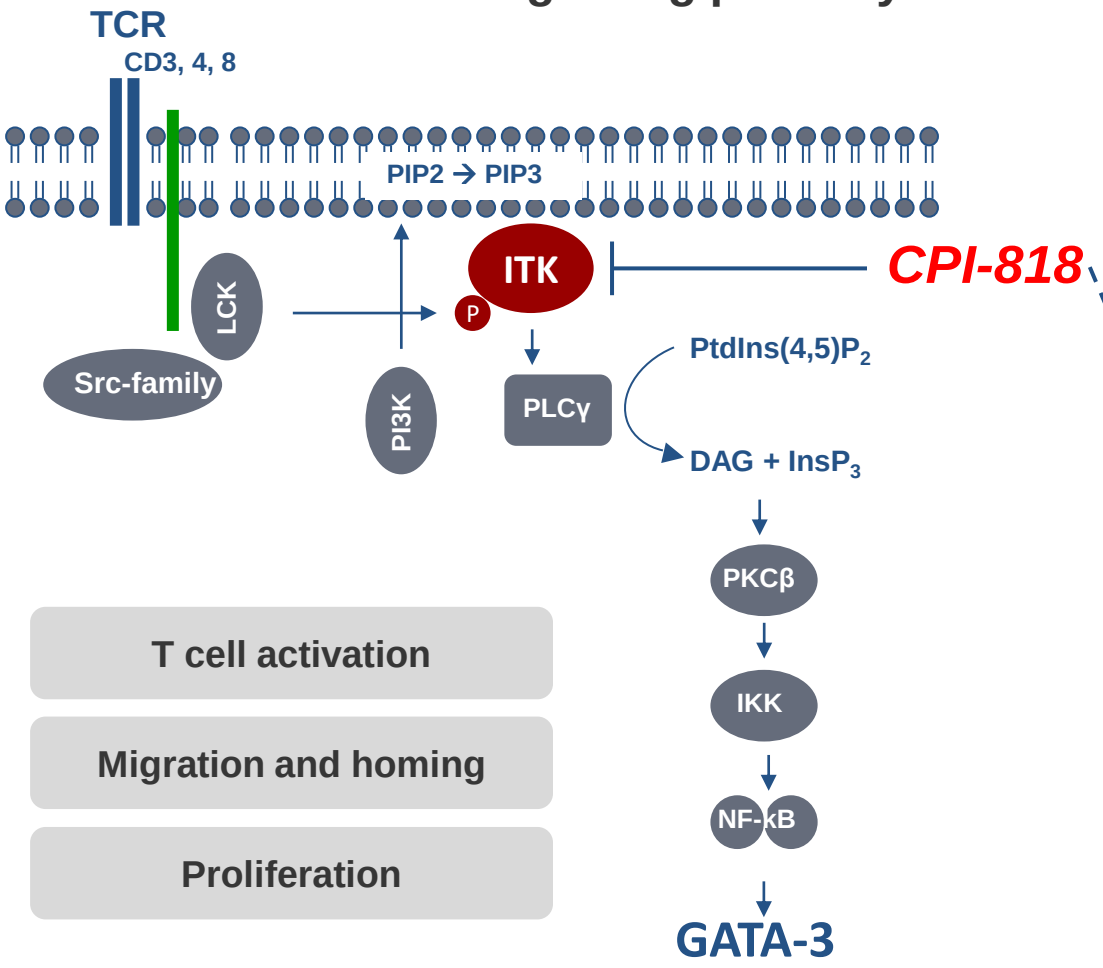
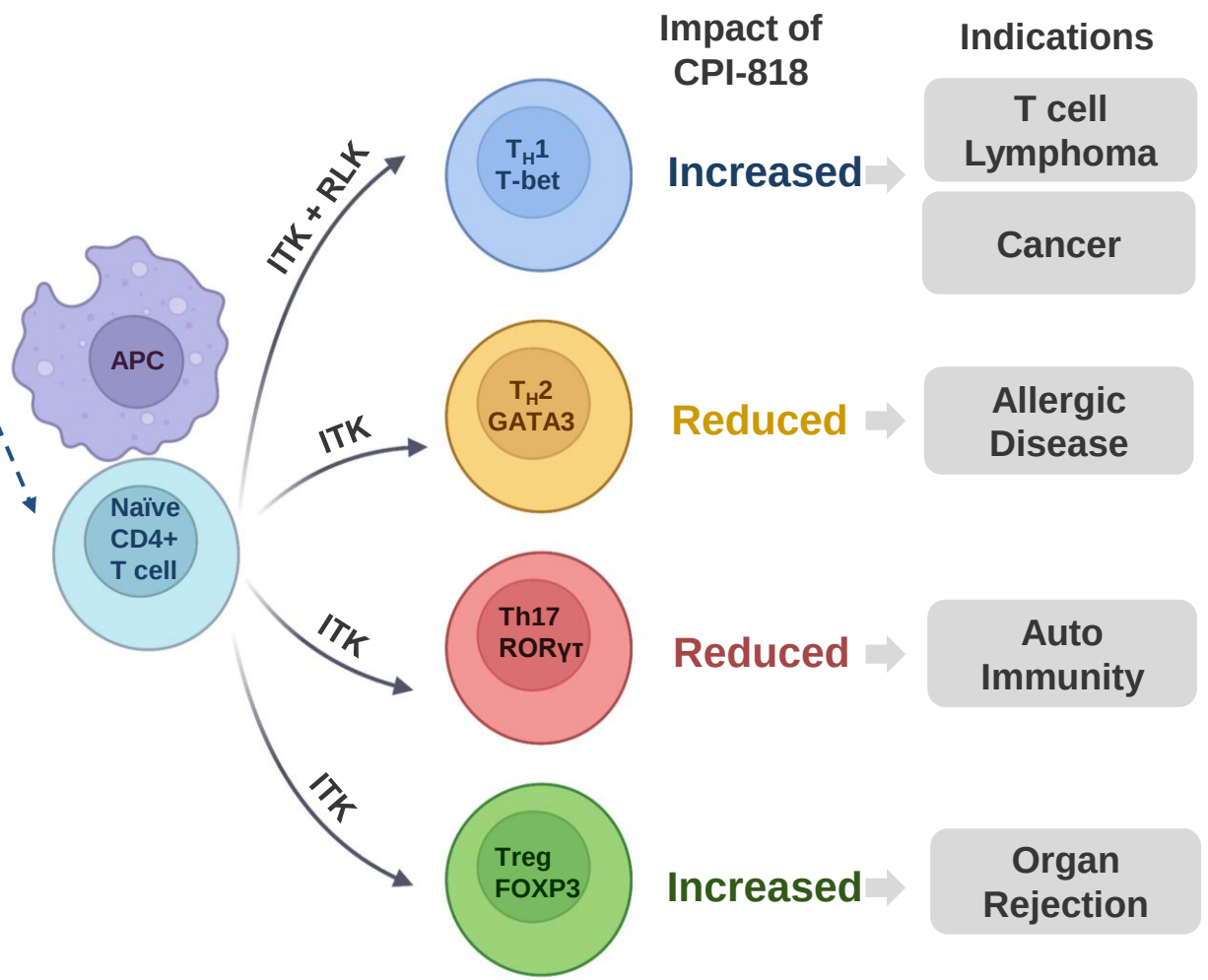
Blocks TCR signaling pathway



- T cell activation
- Migration and homing
- Proliferation

Modulates T helper cell differentiation

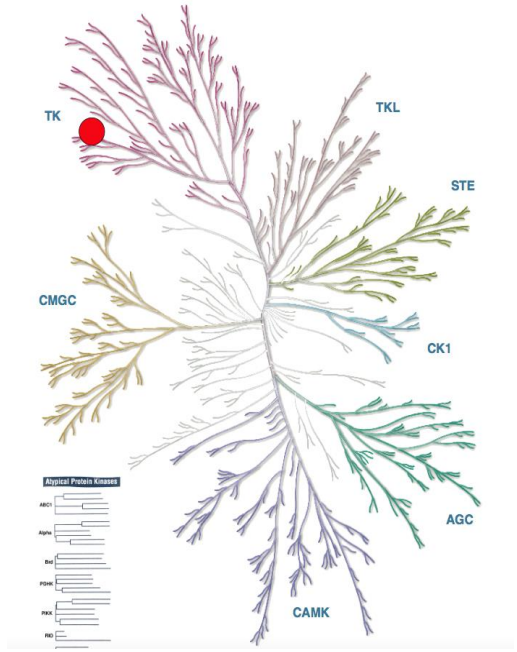


Kinome-Wide Selectivity of CPI-818 for ITK

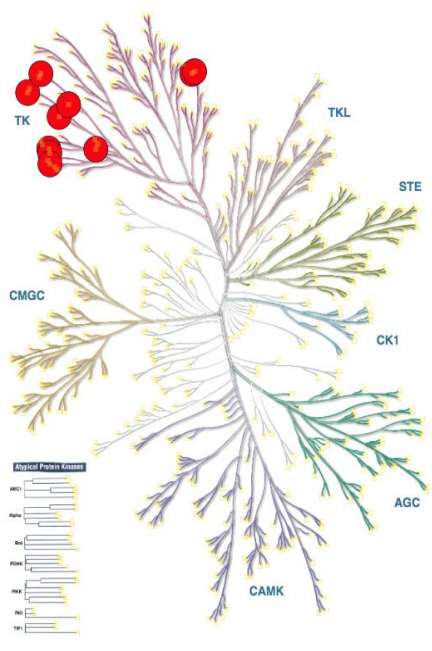
CPI-818 is highly selective for ITK

	Ibrutinib Kd (nM)	CPI-818 Kd (nM)
ITK	29.2	2.5
BLK	0.19	4700
BMX	0.72	9100
BTK	0.42	1200
EGFR	2.5	>10000
ERBB2	ND	>10000
ERBB4	ND	>10000
JAK3	13	2800
MKK7	ND	>10000
TEC	0.45	540
RLK	0.52	2700

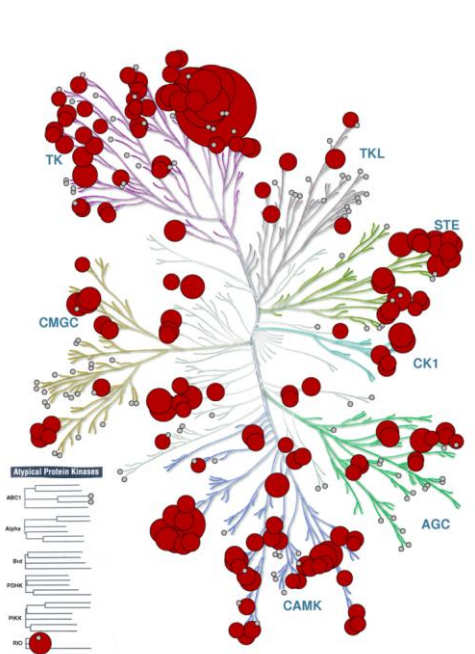
CPI-818



Ibrutinib

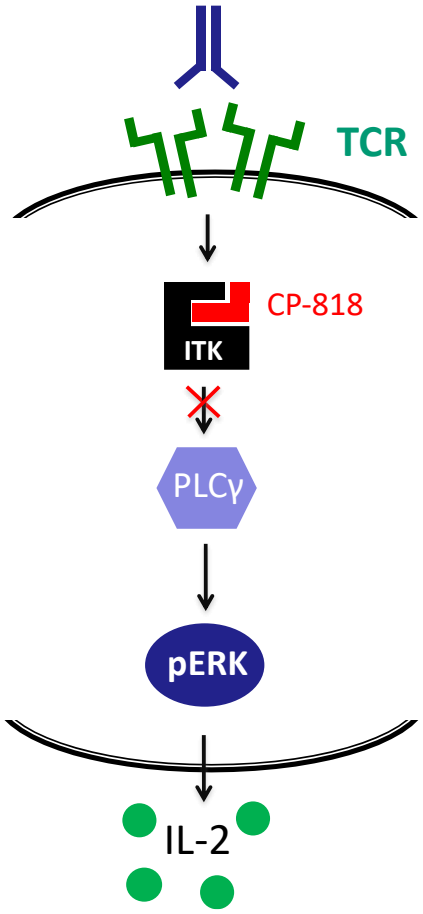


Sunitinib

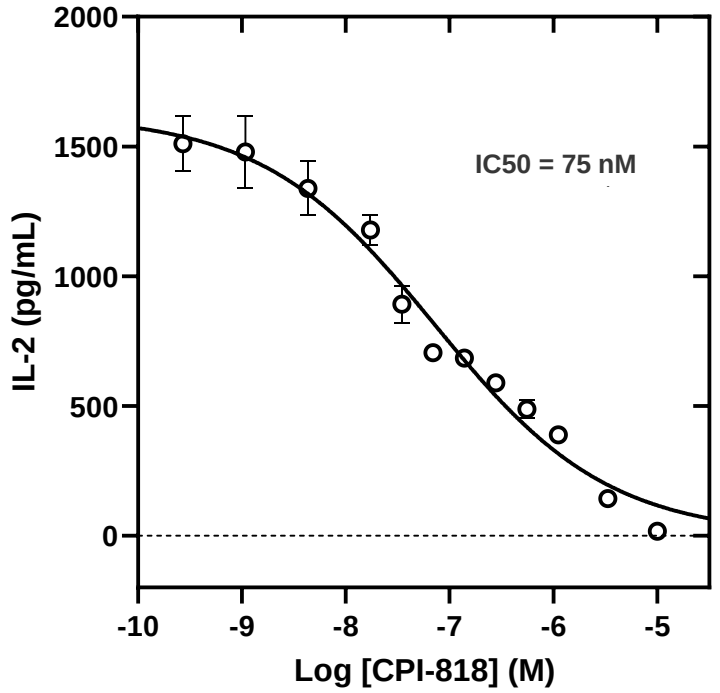


Cellular Potency and Signal Transduction Blockade

CPI-818 blocks T cell receptor signaling pathway



CPI-818 inhibits IL-2 production



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Selectivity is crucial for immune modulation

CORVUS PHARMACEUTICALS

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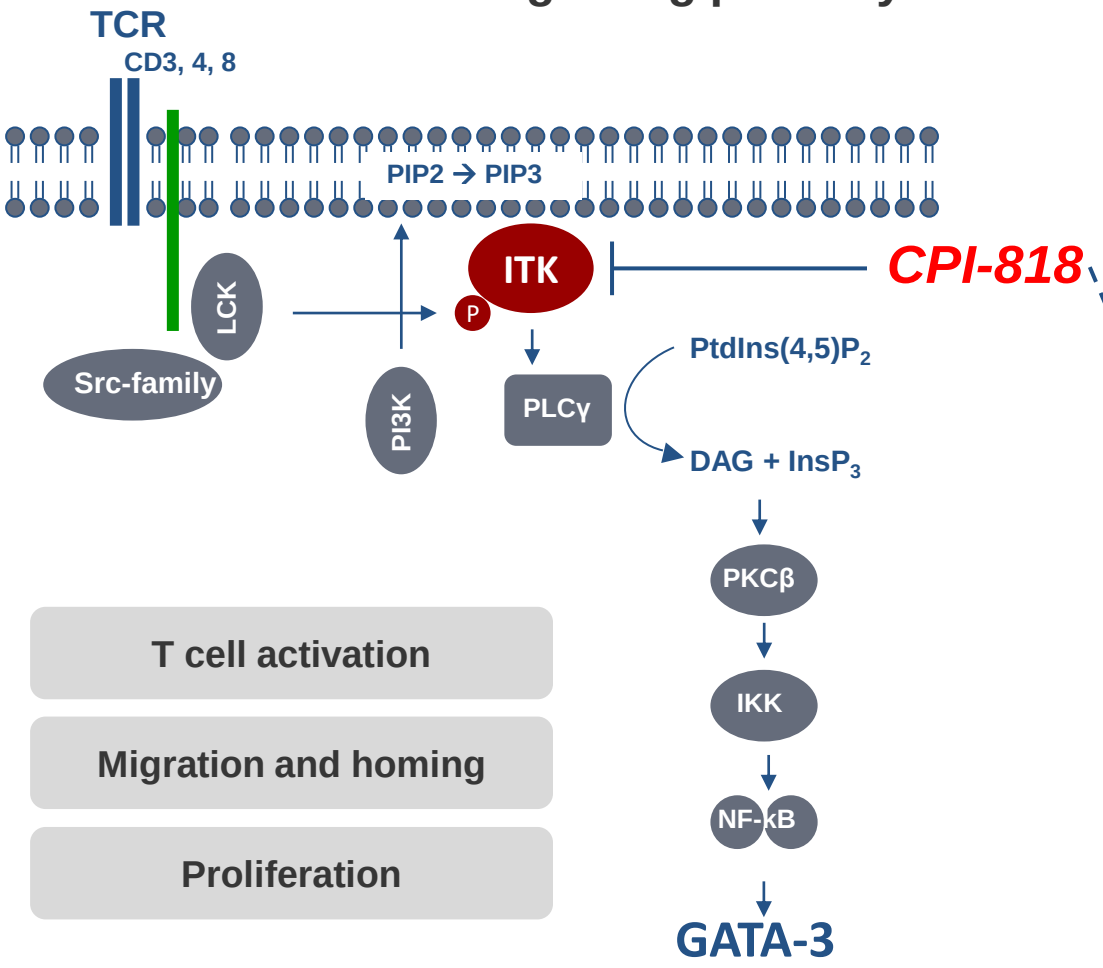
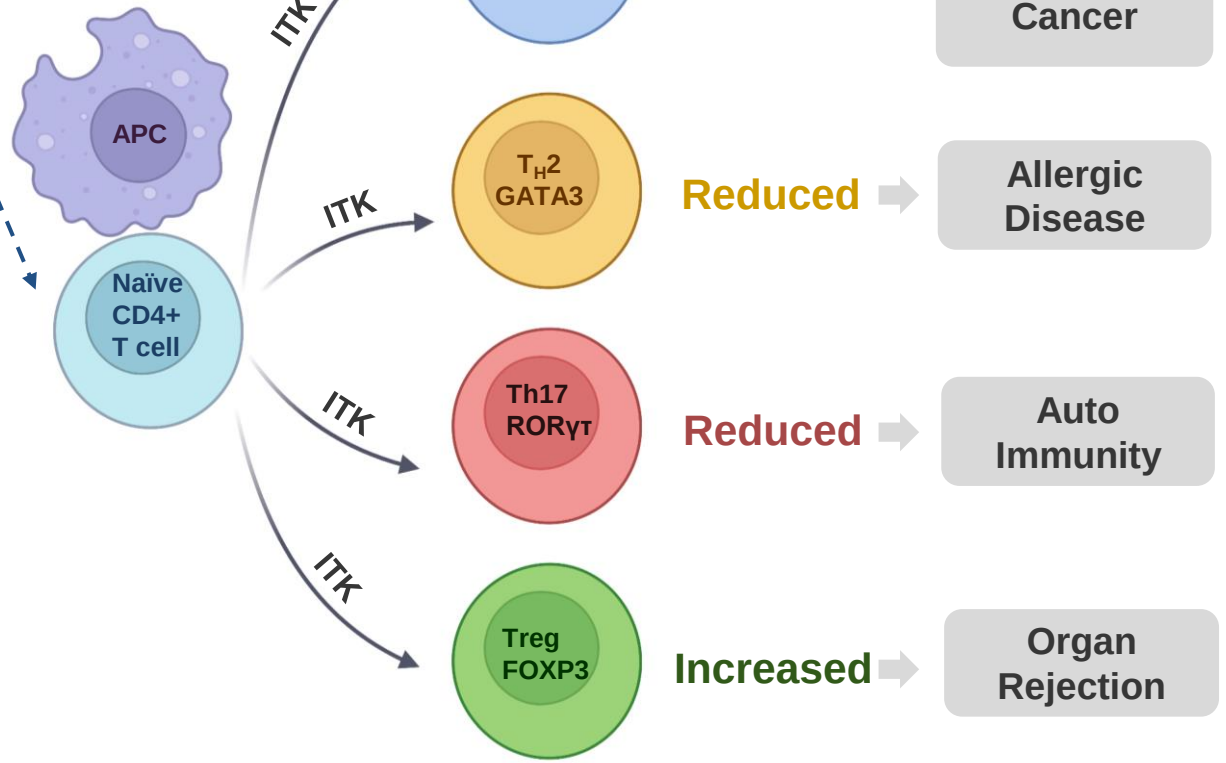


CPI-818

- T cell activation
- Migration and homing
- Proliferation

Modulates T helper cell differentiation



T Cells Have Different Sensitivity to ITK Blockade

Sezary cells (Th2+) are blocked by CPI-818

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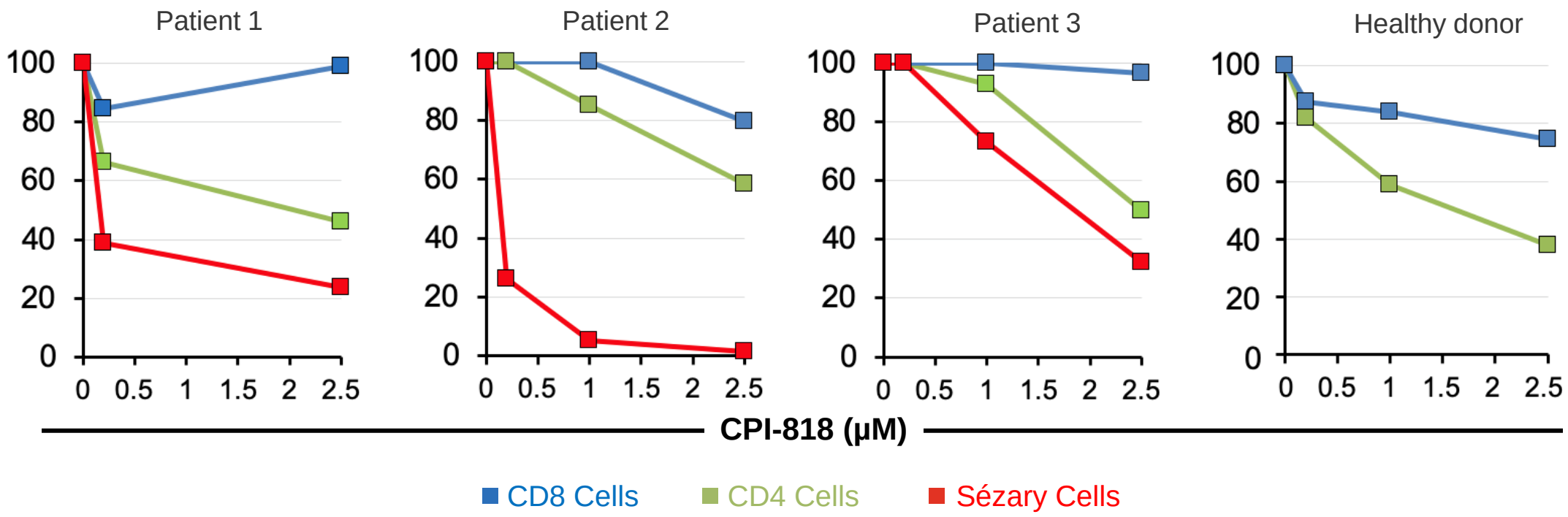
In vitro Anti-Proliferative Effect

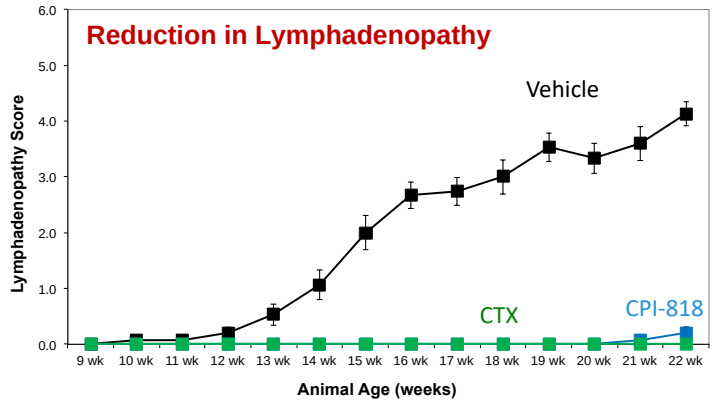


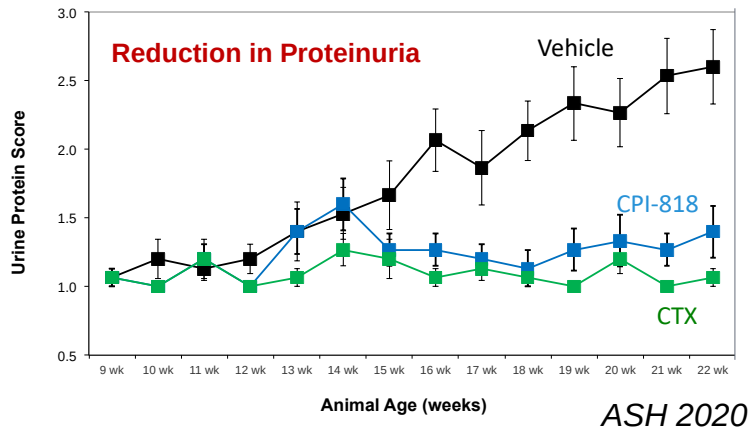
- Sensitivity of Sézary cells > normal CD4 > normal CD8+ T cells
- CPI-818 concentrations have selective effects on T cell subsets

CPI-818 Activity in Autoimmunity

Lupus, Psoriasis and GVHD model

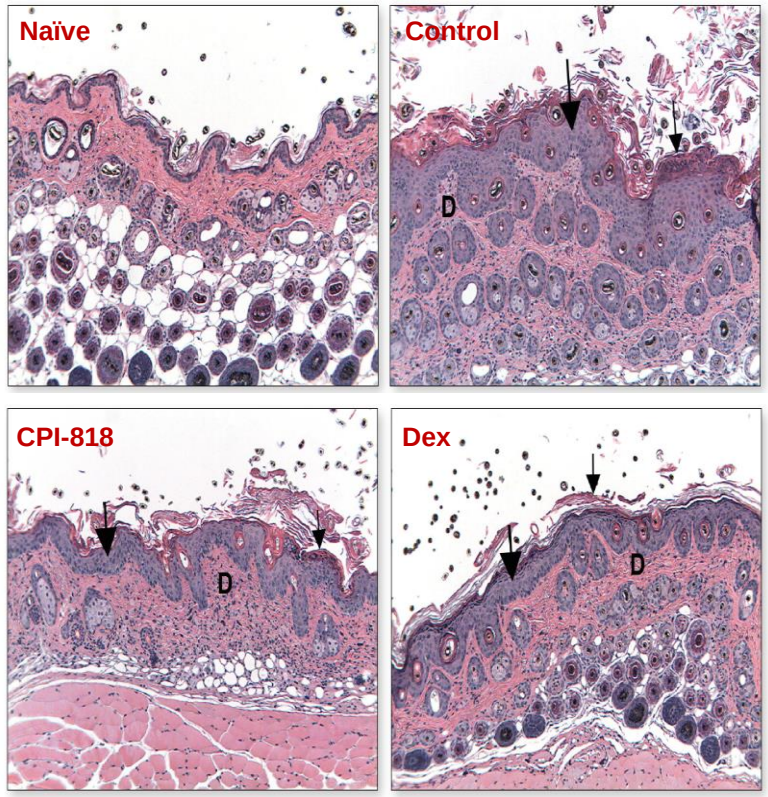
CPI-818 inhibits proteinuria and lymphadenopathy in MRL/lpr$^{-/-}$ Lupus Model



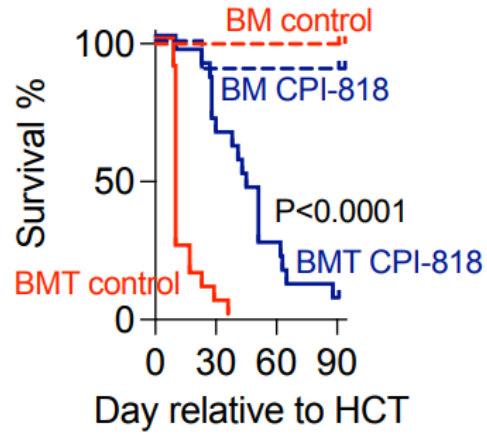


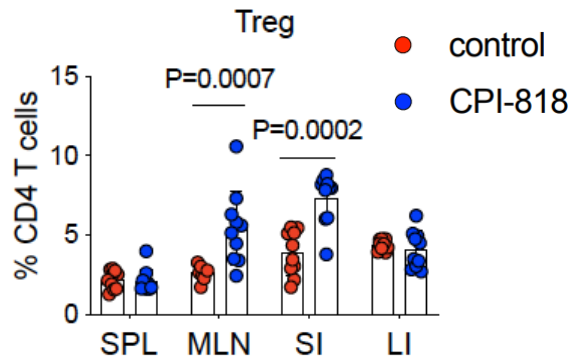
ASH 2020

CPI-818 significantly reduced skin thickening and dermal inflammation in imiquimod-induced psoriasis



CPI-818 reduces GVHD, improves survival and increases Treg



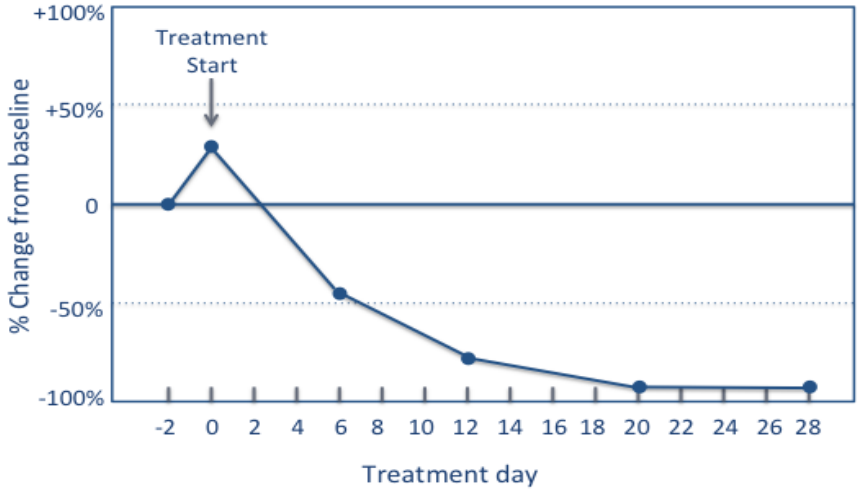


ASH 2021

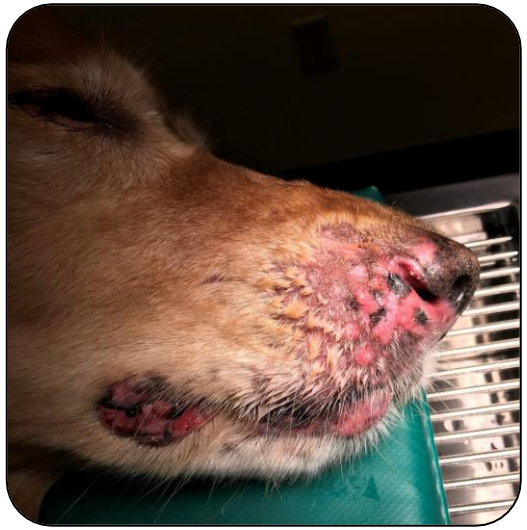
Tumor Responses with CPI-818 in Canine T Cell Lymphoma

Naturally occurring disease in companion dogs

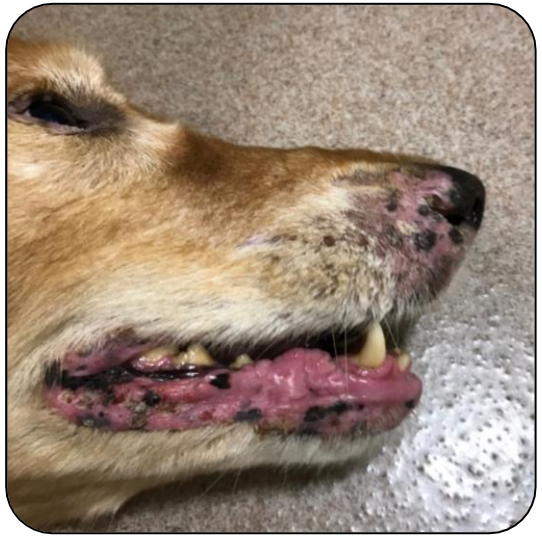
Chloe
7 yo
Boxer
Aggressive PTCL



Rudy
11 yo
Golden Retriever
CTCL

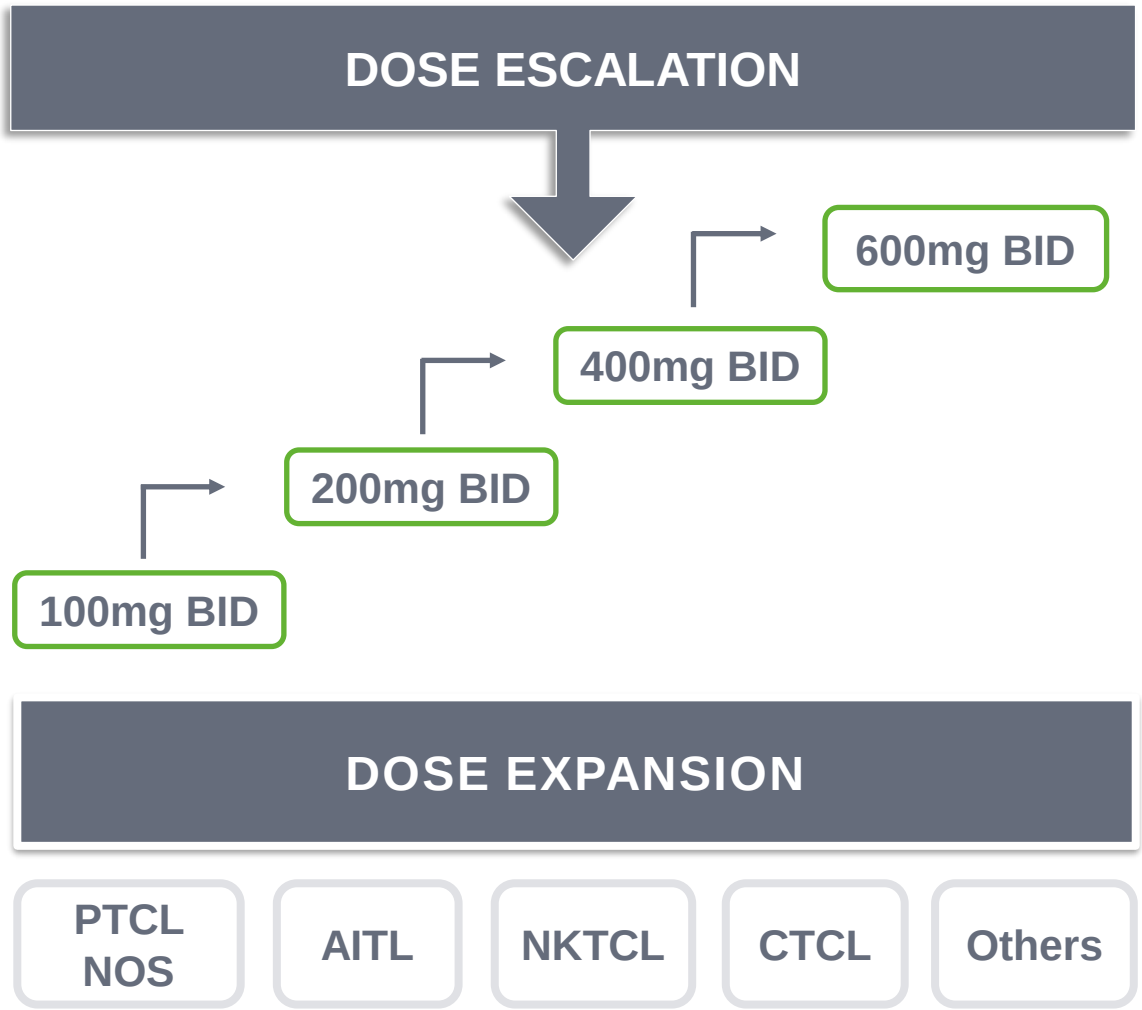


14 days



CPI-818 in T cell Lymphomas

Phase 1/1b clinical trial design



Design

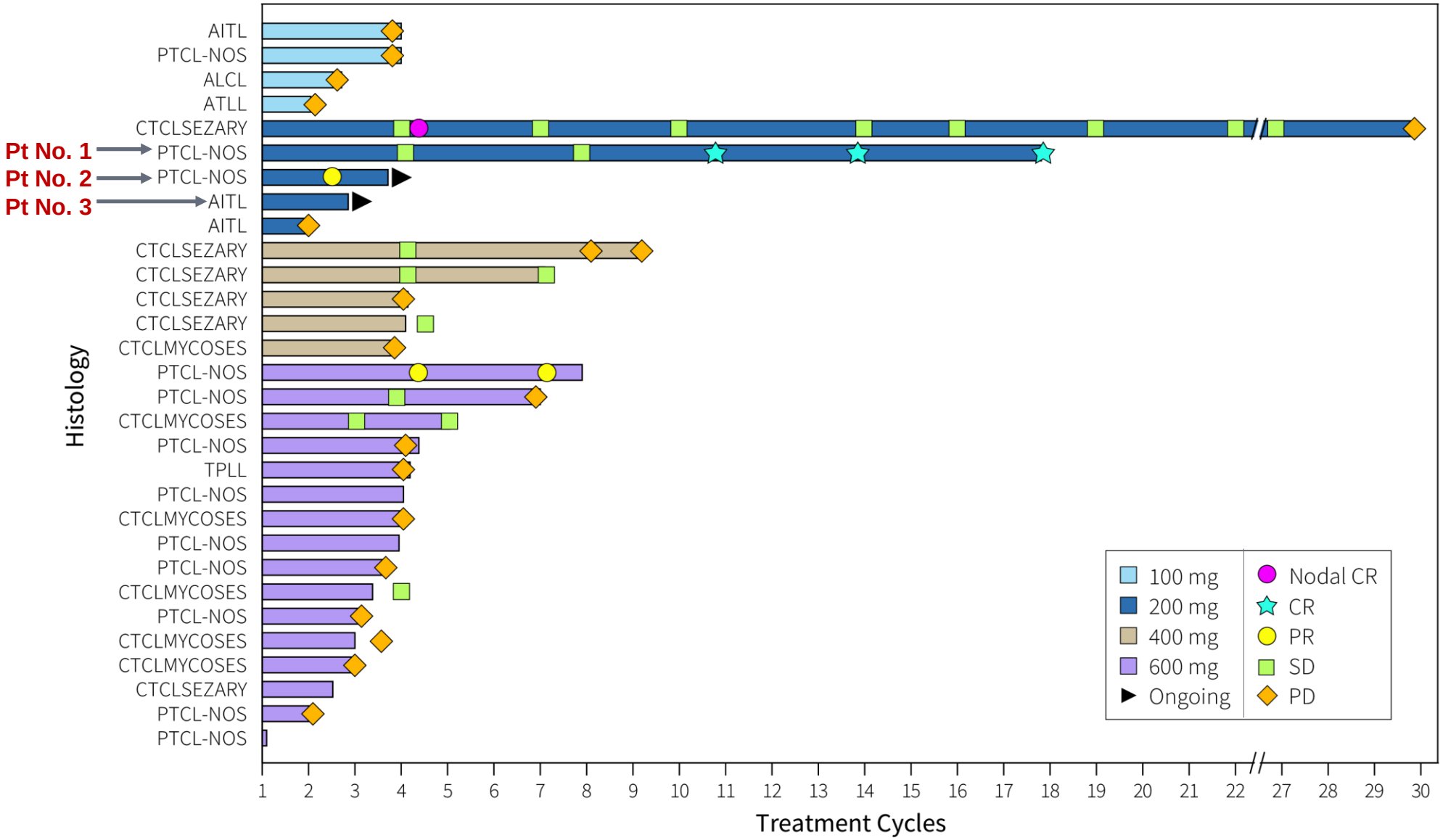
- Dose escalation 3+3 design
- Patients with T cell lymphoma (PTCL and CTCL) who have progressed on, refractory to, relapsed, to standard therapies
- CPI-818 orally BID continuously up to sixteen 21-day cycles, until progression or unacceptable toxicity

Objectives

- Primary: To establish safety / tolerability and determine MTD or MAD, as well as expansion cohort dose
- Secondary: PK/PD, biomarkers and efficacy

Interim Results of Anti-tumor Activity in PTCL & CTCL

Optimum dose identified

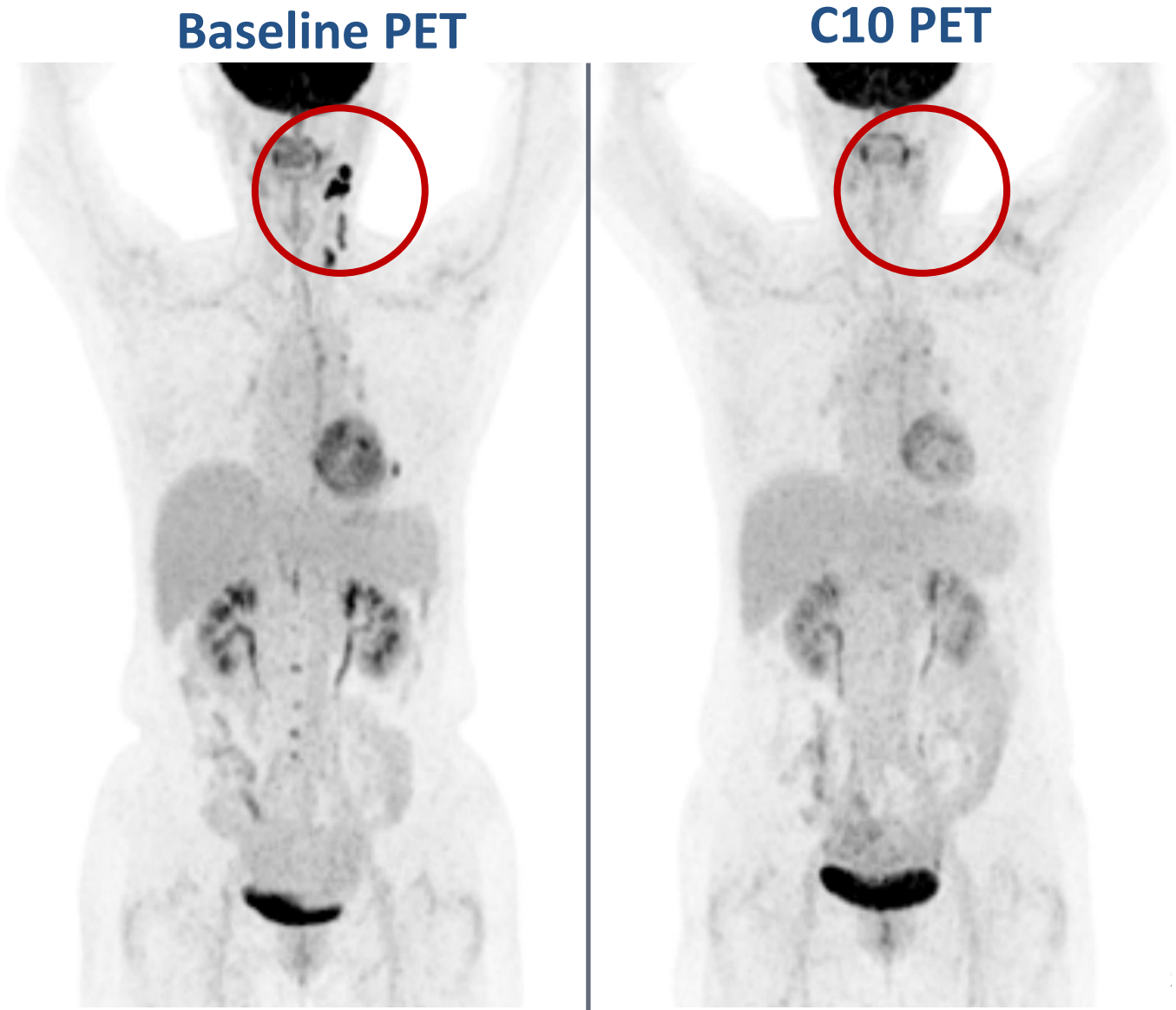


PTCL Patient No. 1 with Complete Response

Durable response lasting 19 months

CORVUS PHARMACEUTICALS

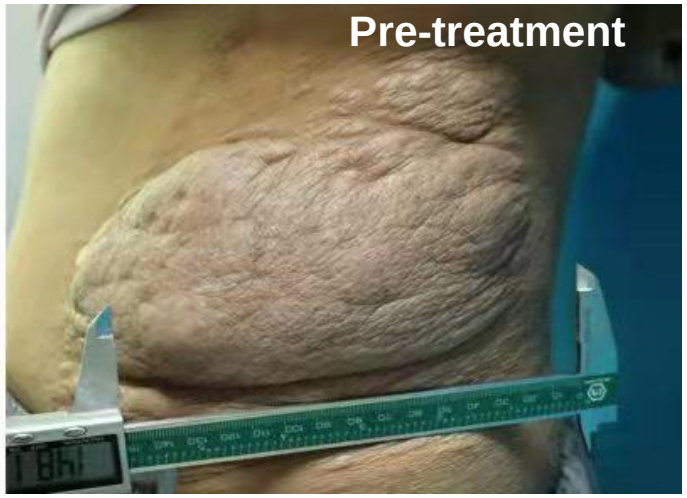
- 57 y/o female with PTCL-NOS
  - Multiple nodes in neck, mediastinum abdomen, pelvis, groin
- CHOP with PR for 5 months
- ASCT for progressive disease
  - Relapse 1 yr
- Started on CPI-818 with disease involving multiple nodal sites
  - CR lasting 19 months

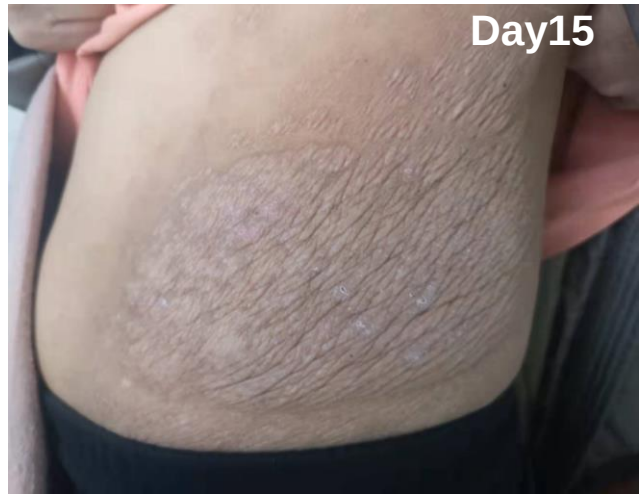


PTCL Patient No. 2 with Prompt Response

Marked tumor reduction in subcutaneous mass and lymph nodes

- Patient with PTCL NOS
  - CD3-,CD4+, CD20-, TCR clonal, EBV+
- Involvement of LN, skin, blood
- Prior therapies
  - CHOEP x 4, PR;
  - GDP x 2 SD;
  - anti-PD1/HDACi/azacytidine x 4 PD
- CPI-818 monotherapy
  - Dramatic reduction of SQ tumor and improvement in Eos, platelets and LDH
  - Transient lymphocytosis





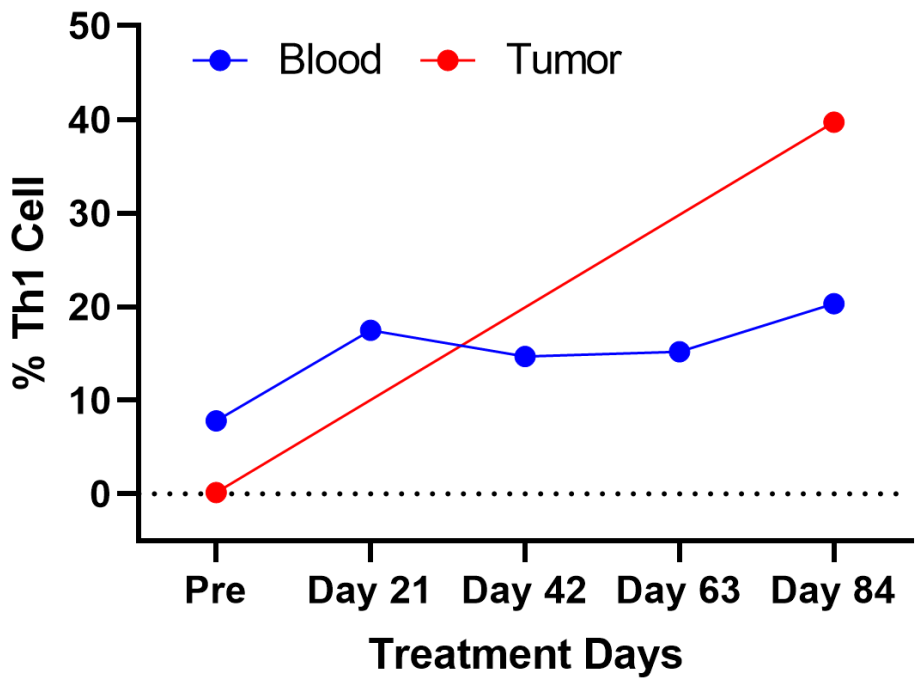
Lab	Pre-treatment	Day 8	Day 15	Day 21	Day 42	Day 63
White Blood Cells ($x10^9$/L)	27.13	21.92	18.50	16.87	17.87	17.24
Lymphocyte ($x10^9$/L)	6.62	16.17	13.52	13.11	10.22	10.57
Eosinophil count ($x10^9$/L)	17.18	1.6	0.93	1.34	4.21	4.42
Platelets ($x10^9$/L)	105	104	141	145	153	159
LDH (IU/L)	651	378	299	262	286	253

PTCL Patient No. 2 with Prompt Response

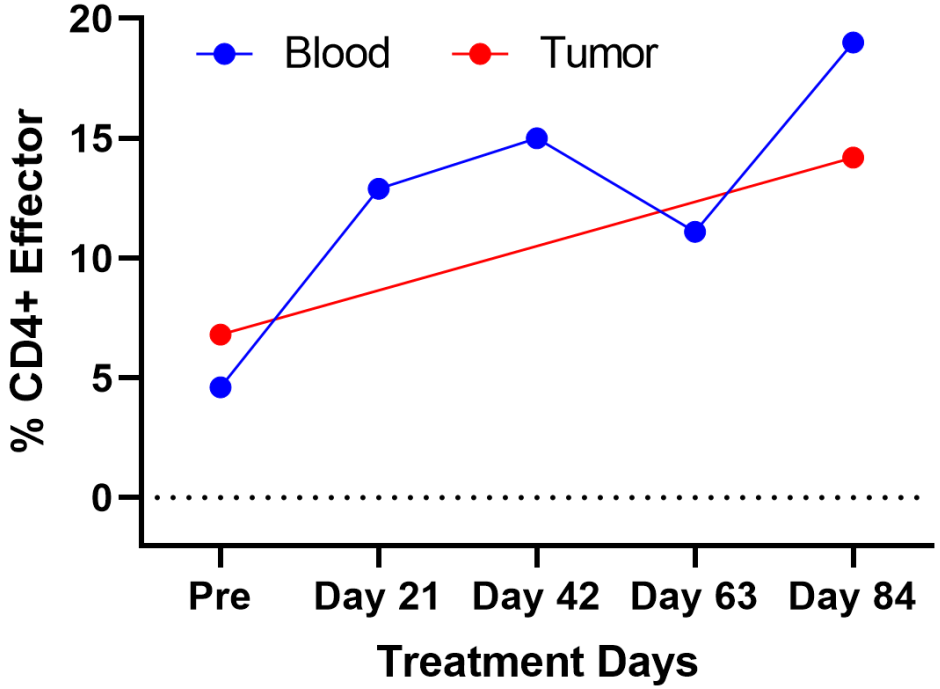
Th1 and T effector cells increase on treatment

CORVUS PHARMACEUTICALS

Th1 cells increase in blood and tumor during CPI-818 treatment



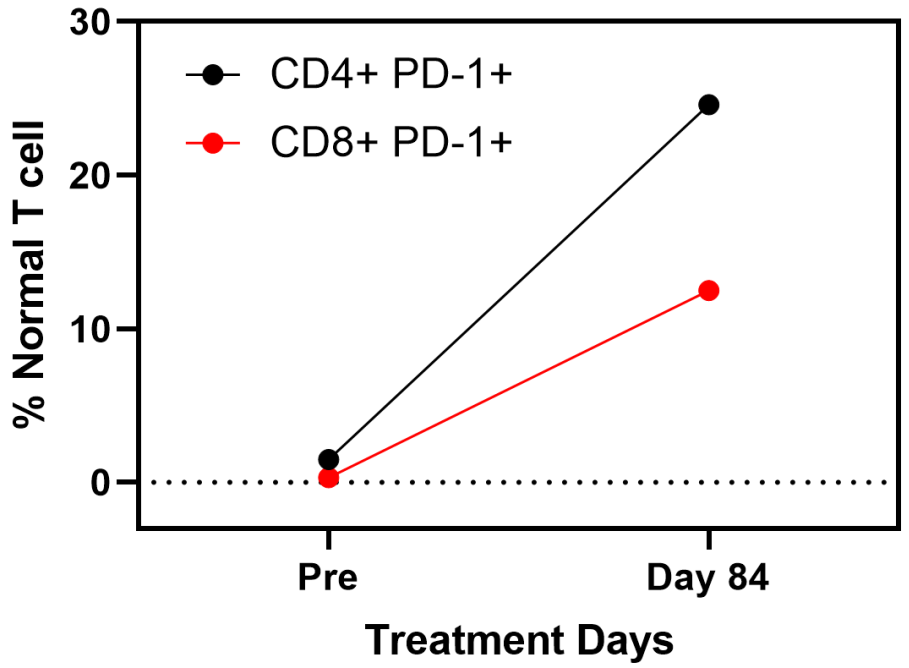
CD4+ effector cells increase in blood and tumor during CPI-818 treatment



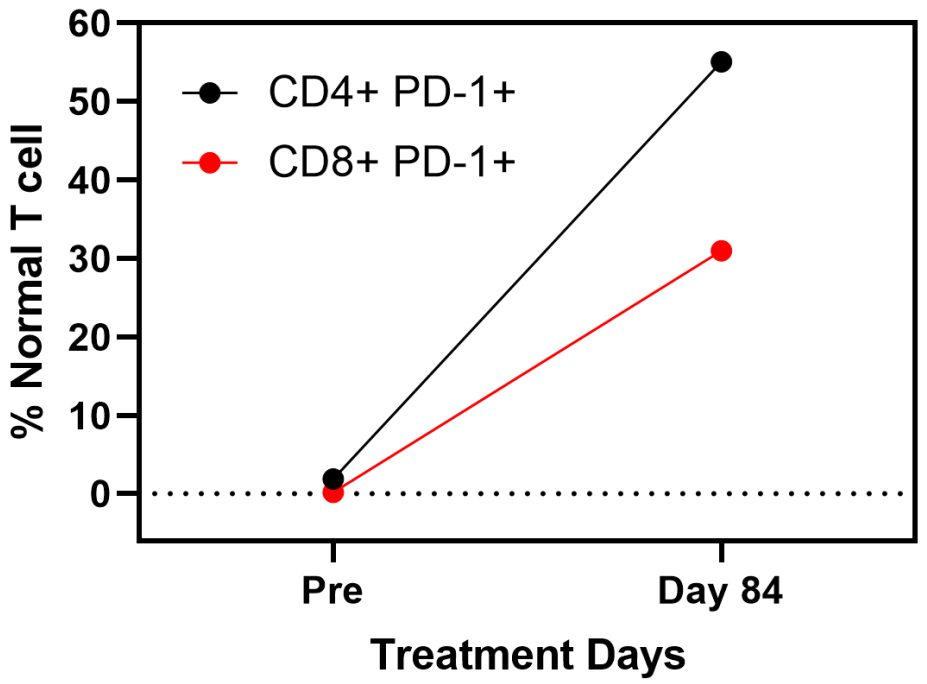
PTCL Patient No. 2 with Prompt Response

Activated T cells increase on treatment

CD4+PD-1+ and CD8+PD-1+ normal T cells increase in *blood* during CPI-818 treatment



CD4+PD-1+ and CD8+PD-1+ normal T cells increase in *tumor* during CPI-818 treatment

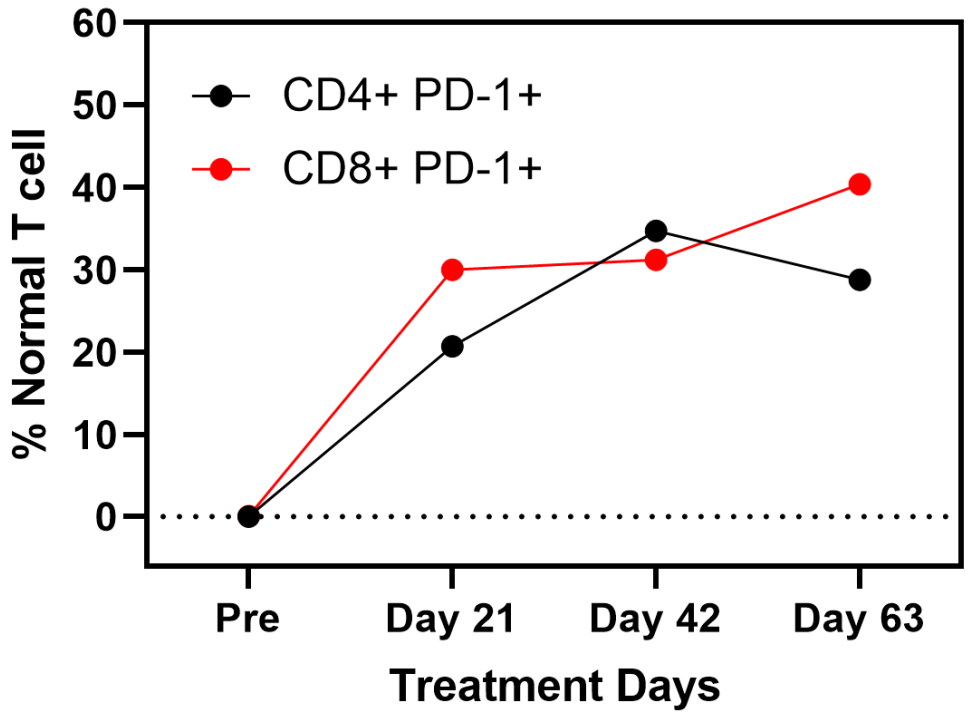


Responding PTCL Patient No. 3

Activated T cells increase in blood on treatment

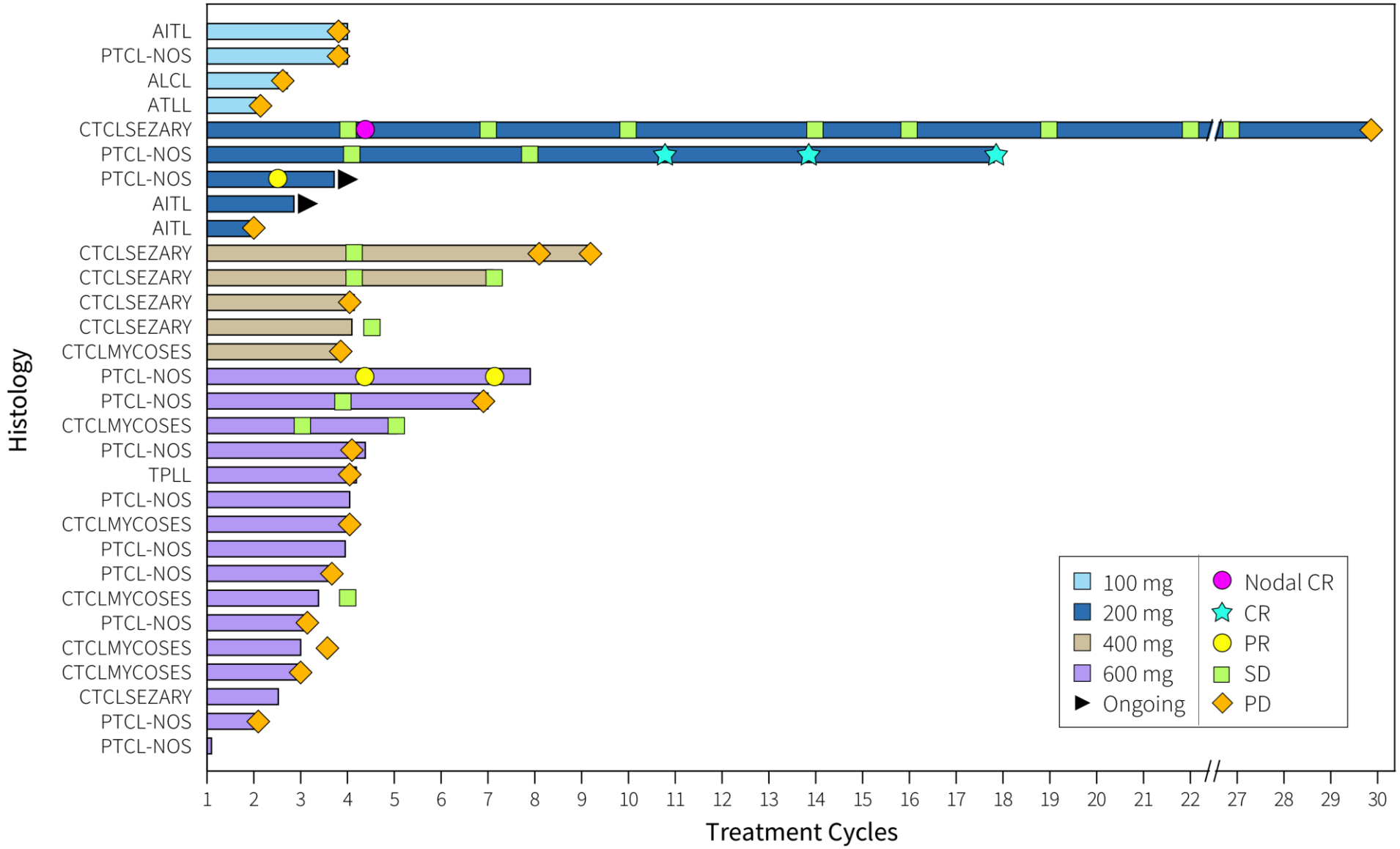
- Patient with AITL
  - CD3+, CD4+, EBV-
- Involvement of LNs, blood, spleen
- Prior therapies
  - CHOEP x 8 CR
  - GDP x 2 PD
  - anti-PD1/HDACi/azacytidine x 4 PD
- CPI-818 monotherapy
  - Ongoing treatment with CPI-818
- Increase in activated T cells in blood consistent with stimulation of immune response

CD4+PD-1+ and CD8+PD-1+ normal T cells Increase in blood during CPI-818 treatment



CPI-818 Anti-tumor Activity in PTCL & CTCL

Optimum dose drives Th1 skewing and T effector expansion

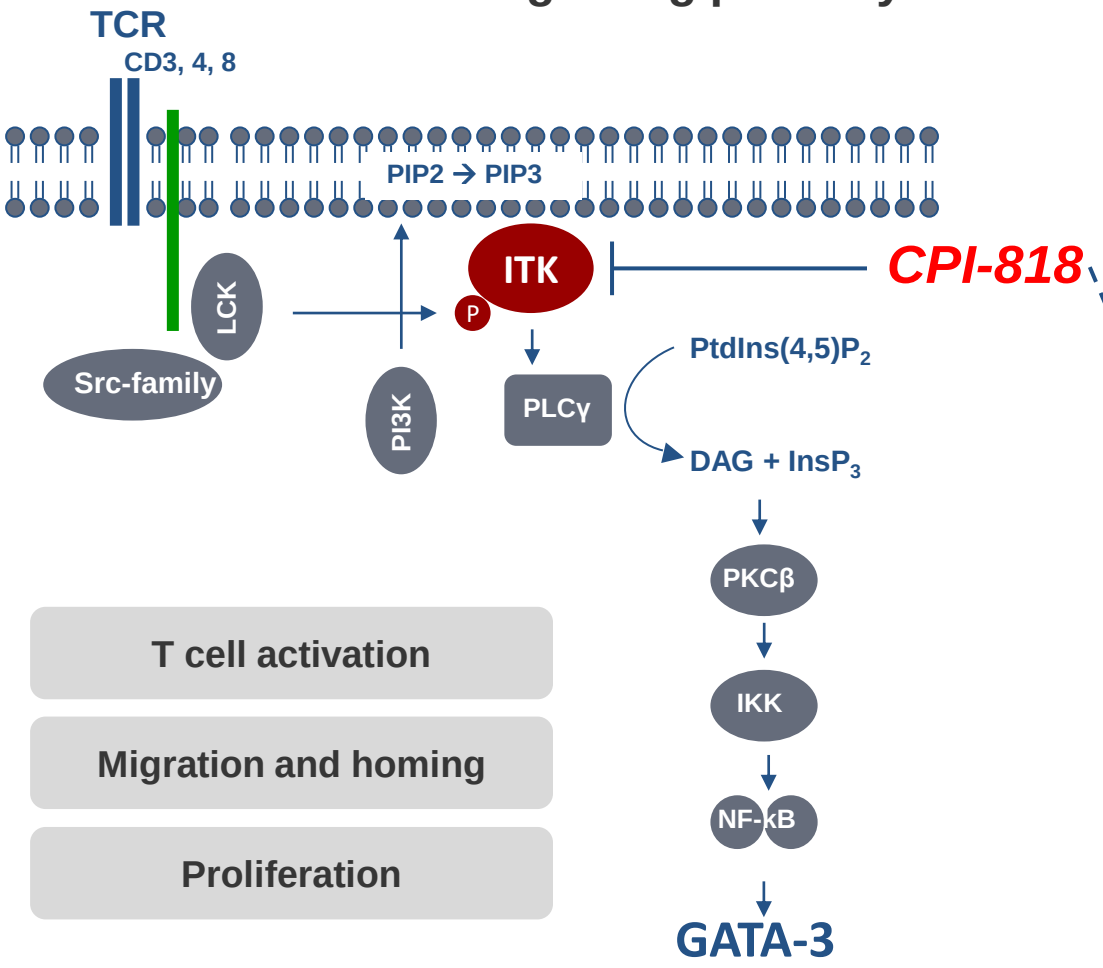


ITK Plays Critical Roles in T Cell Mediated Diseases

Selectivity is crucial for immune modulation

CORVUS PHARMACEUTICALS

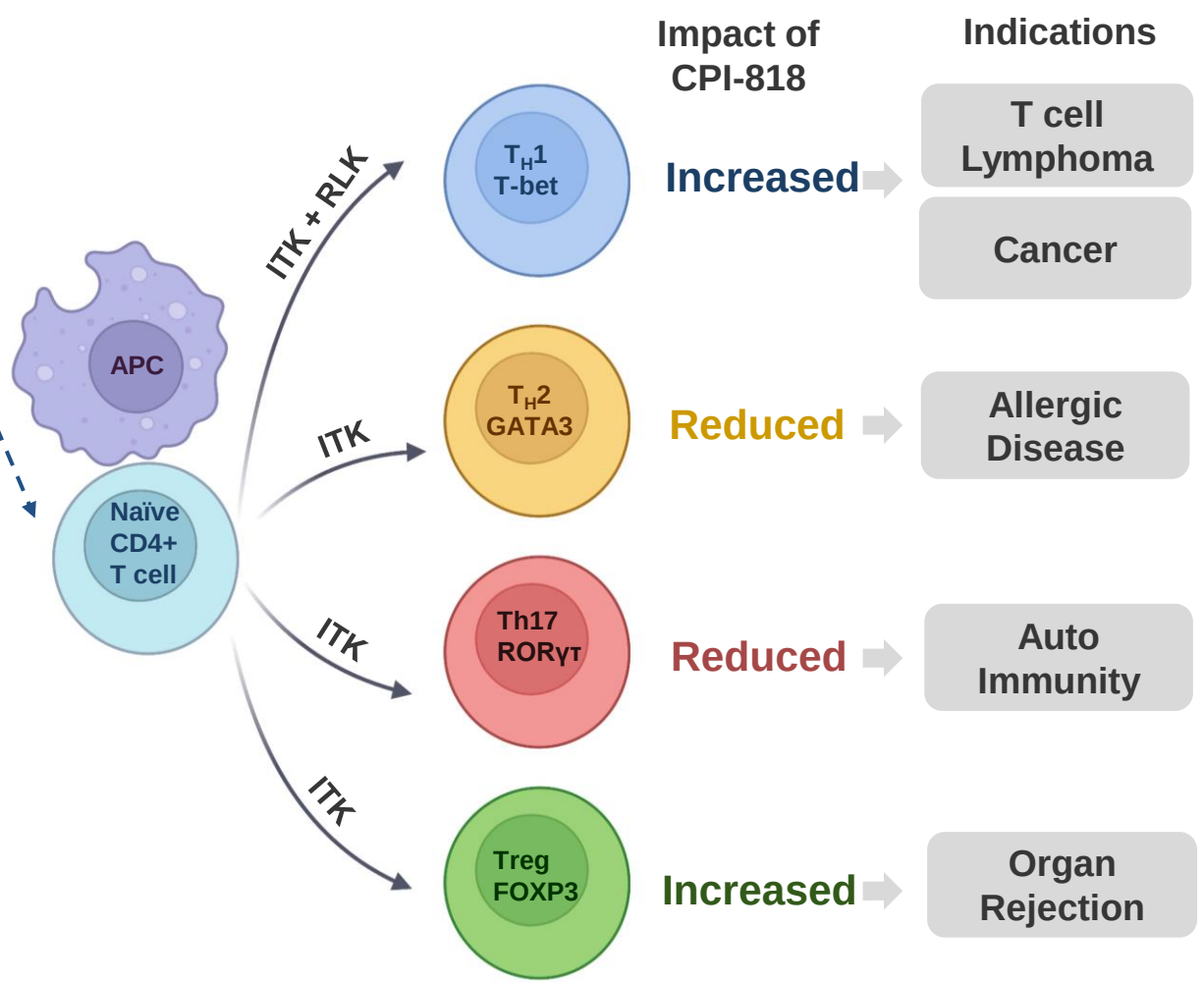
Blocks TCR signaling pathway



CPI-818

- T cell activation
- Migration and homing
- Proliferation

Modulates T helper cell differentiation



CPI-818 Summary

Modulate Tumor Immunity

Induces Th1 skewing

Increases effector cells in the tumor

Evidence of T cell activation in the tumor

Precision Molecular Targets

Oral, selective, covalent inhibitor

Occupancy of ITK

Well-tolerated

Broad Clinical Applications

Activity seen in PTCL, CTCL and AITL

Preclinical activity in autoimmunity model

Next Steps

Corvus enrolling patients at optimal dose

Angel enrolling in China

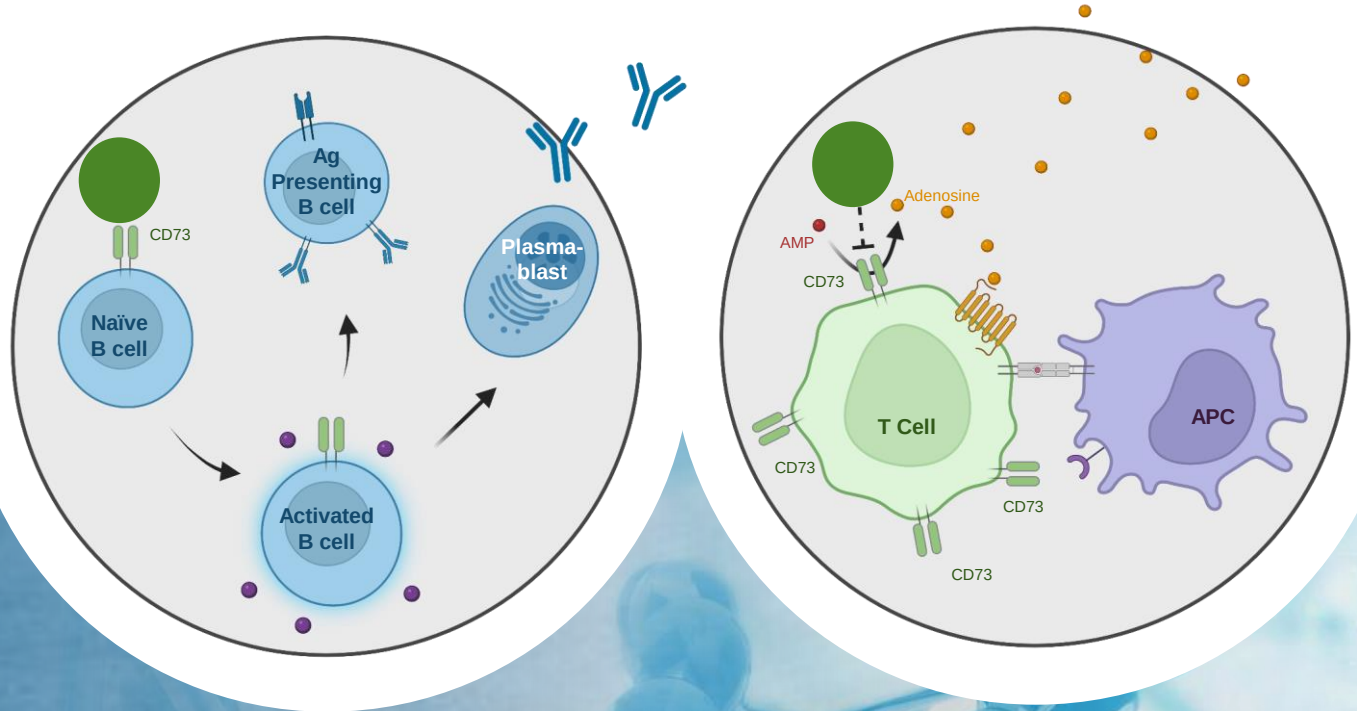
Data expected 2H 2022

Q&A

CORVUS PHARMACEUTICALS

Mupadolimab

B cell Activation
And Adenosine Blockade

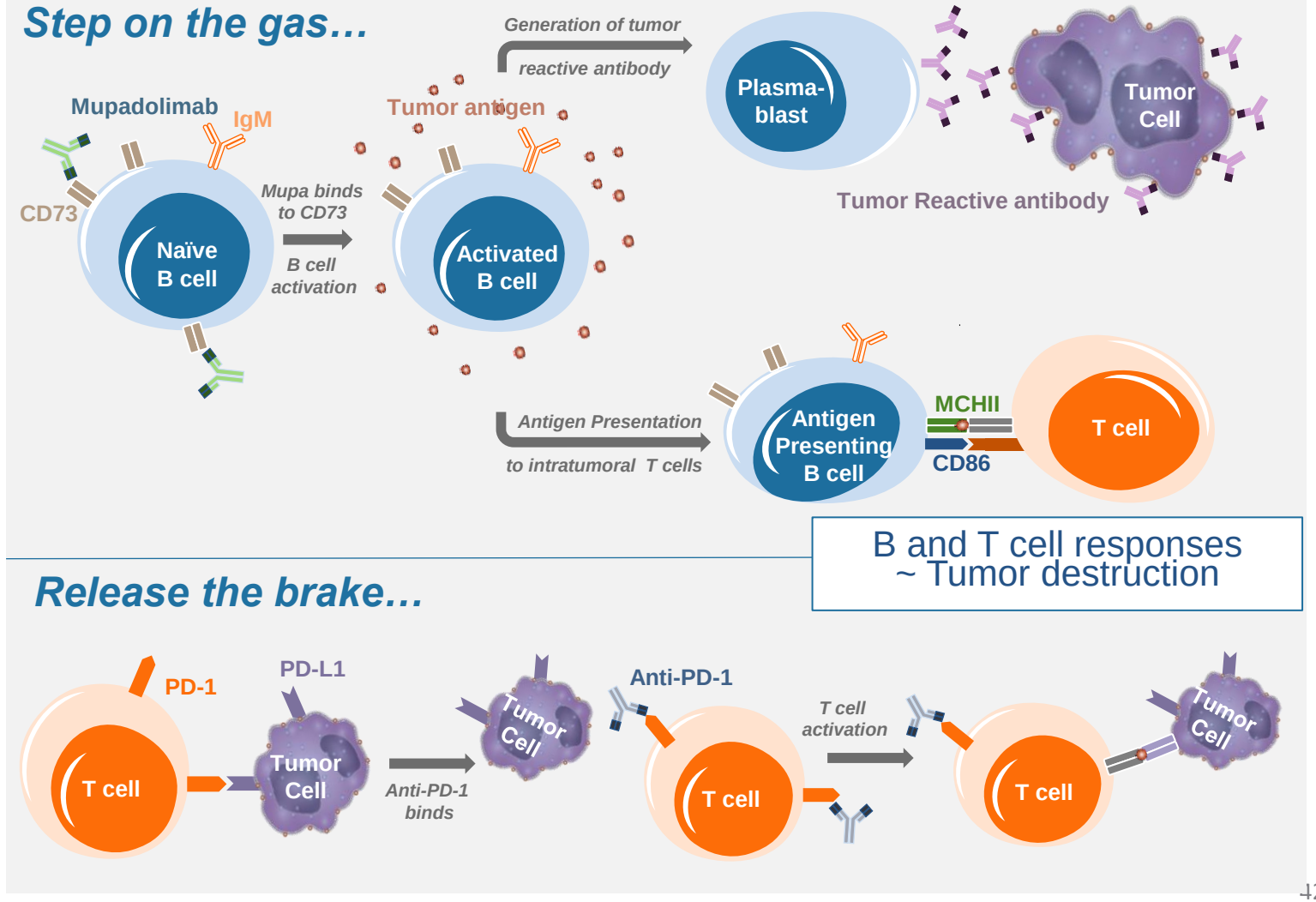


CORVUS PHARMACEUTICALS

Mupadolimab Background and Strategy

- CD73 is an ectoenzyme present on many tissues including subsets of T (CD4 10%, CD8 50%) and B cells (70%)
  - Catalyzes conversion of AMP into immunosuppressive adenosine
  - Functions in lymphocyte adhesion, migration and activation
- Mupadolimab is a humanized IgG1 Fcγ receptor binding deficient anti-CD73 with unique properties
  - Blocks CD73's catalytic activity
  - Agonistic immunomodulatory activity on CD73 positive B cells and T cells

Targeting B Cells and T Cells: Mupa, anti-PD-1 Combo



Corvus is a Leader with a Differentiated Antibody

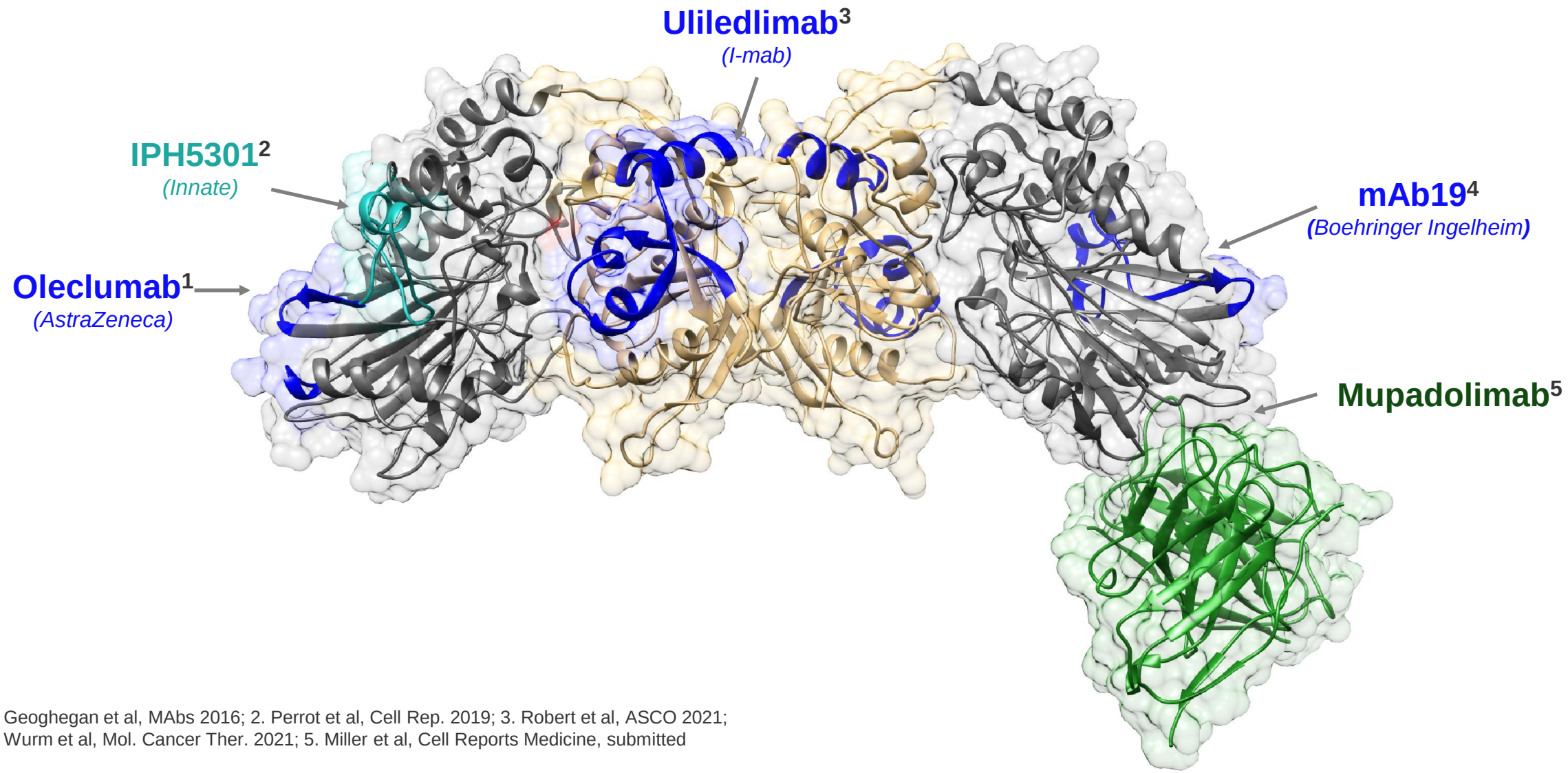
Anti-CD73 competitive landscape

Company	Program	Adenosine Blockade	B Cell Activation	Status
CORVUS PHARMACEUTICALS	Mupadolimab	Full	Strong*	Phase 2
AstraZeneca	Oleclumab	Partial	Weak	Phase 3
I-MAB BIOPHARMA / TRACON PHARMA	Uliledlimab	Full	No Data	Phase 2
Bristol Myers Squibb	BMS-986179	Partial	Not reported	Phase 1
NOVARTIS / SURFACE ONCOLOGY	NZV930	Partial	Not reported	Phase 1
Incyte	INCA00186	Partial	Not reported	Phase 1

* Also shown to activate T cells and antigen presenting cells

Unique Binding Epitope Confirmed by Cryo-EM

Comparison with other CD73 antibodies



1. Geoghegan et al, MAbs 2016; 2. Perrot et al, Cell Rep. 2019; 3. Robert et al, ASCO 2021;
4. Wurm et al, Mol. Cancer Ther. 2021; 5. Miller et al, Cell Reports Medicine, submitted

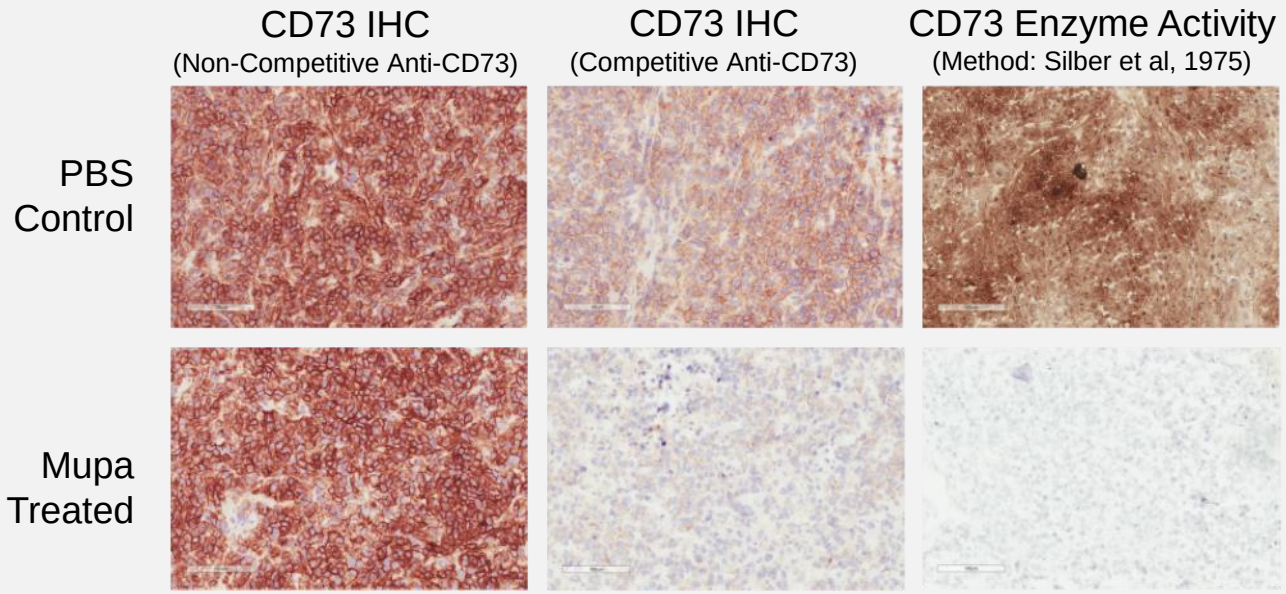
Comparison Between Mupadolimab and Oleclumab

Parameters	Mupadolimab	Oleclumab
Isotype	human IgG1κ	human IgG1λ
Fc engineering	Deficient FcγR-binding	Deficient FcγR-binding
Affinity (K_D)[1]	~100-200 picomolar	~100-200 picomolar
Internalization	No	Yes
Hook Effect	No, fully blocking adenosine	Yes, partially blocking adenosine
B cell activation	Strong	Weak
T cell restoration	Effective	Less Effective
Stage of Development	Phase 2	Phase 3
RP2D	1200 mg Q3W	3000 mg Q2W (first 2 cycles, then Q4W)

1. Binding of CD73 antibody to recombinant human CD73-His was measured by Octet

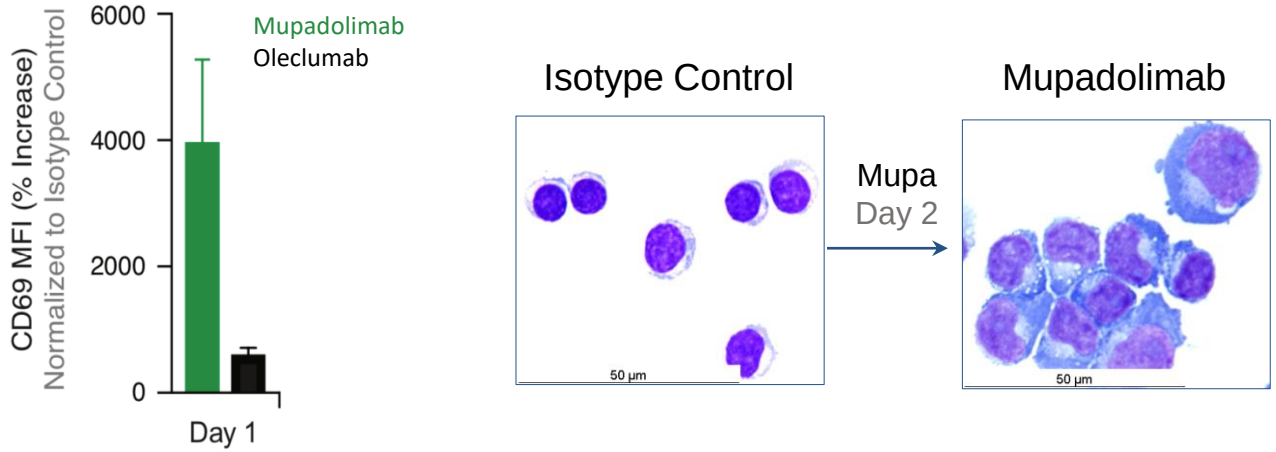
Mupadolimab: Anti-CD73 Antibody with Dual Functions

B cell activation and adenosine blockade



CD73 Enzymatic Activity Blockade

- Mupadolimab binds to tumor cells and blocks the production of adenosine as demonstrated by immunohistochemistry (IHC)
- Mupadolimab treatment does not cause loss of CD73 by internalization



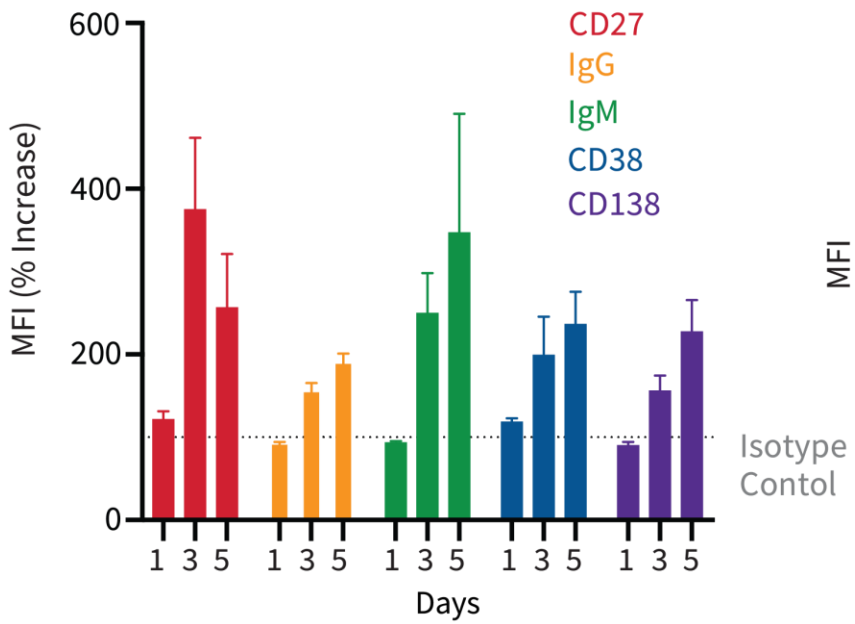
B Cell Activation & Differentiation

- Mupadolimab demonstrates a potent B cell stimulation compared to oleclumab, an adenosine blocking anti-CD73 antibody
- Mupadolimab activates B cells, resulting in morphological and surface marker changes consistent with B cell differentiation

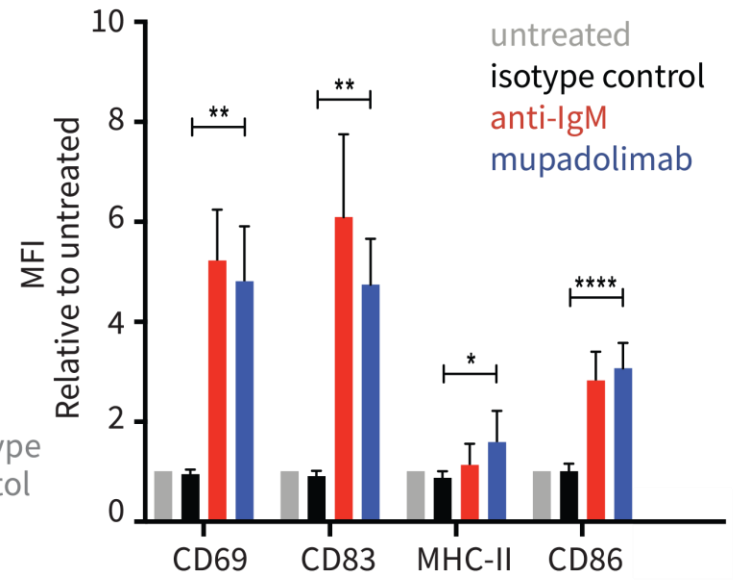
Activates B cell and Promotes Differentiation

Unique to mupadolimab

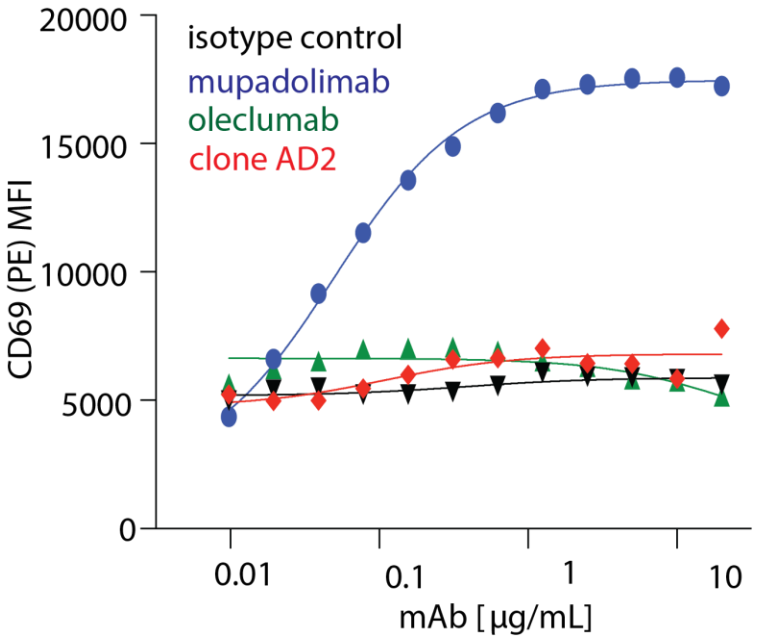
B cell Differentiation Markers



Antigen Presentation Markers



CD69 Upregulation



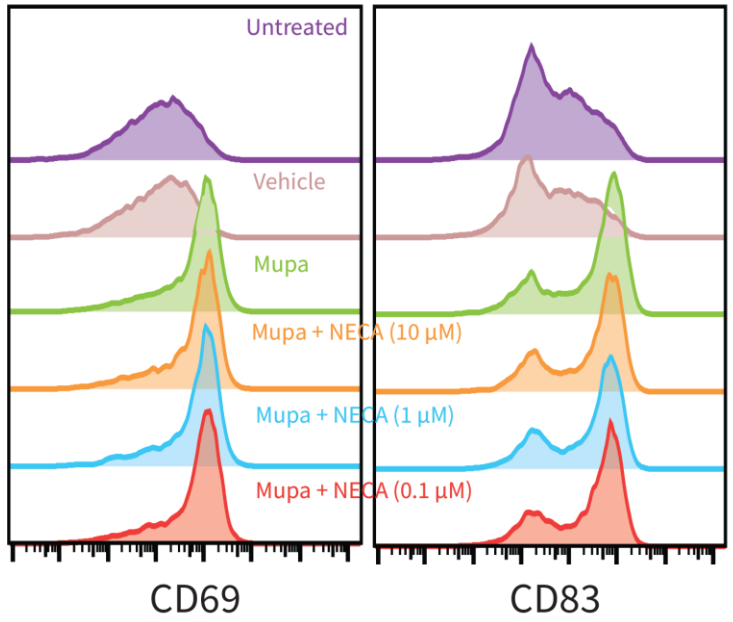
- Mupadolimab activates B cells, resulting in the upregulation of activation and antigen presentation markers
- Increased cell surface expression markers consistent with B cell maturation
- B cell activation is unique to mupadolimab as other anti-CD73 antibodies do not induce CD69 upregulation

Mupa-induced B cell Activation Mechanism

Independent of adenosine and through BCR signaling pathway

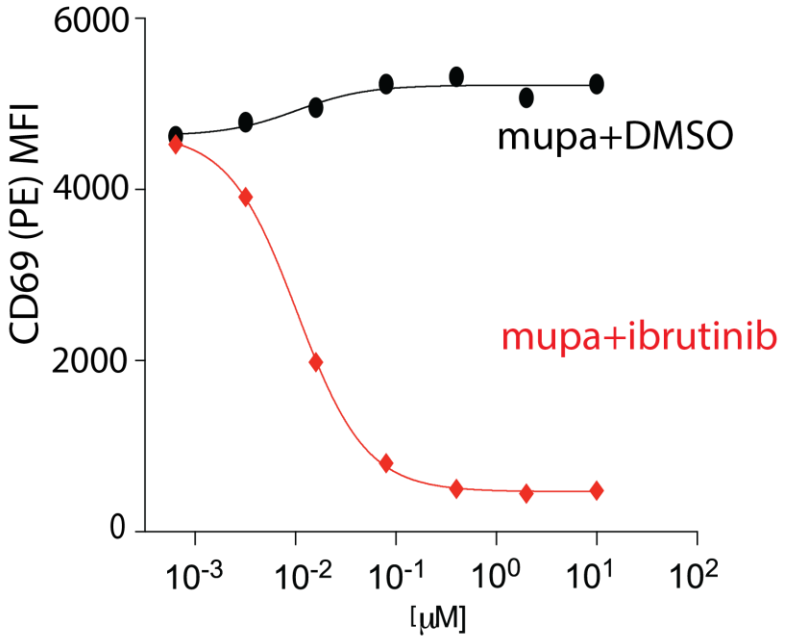
CORVUS PHARMACEUTICALS

An adenosine agonist does not interfere with mupadolimab-induced B cell activation and differentiation

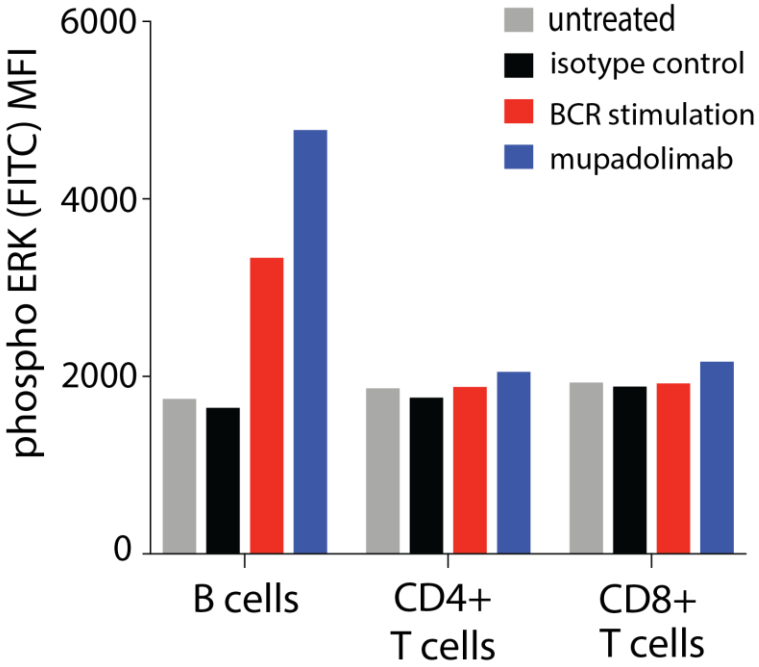


NECA: 5′-(N-Ethylcarboxamido)adenosine, an adenosine agonist

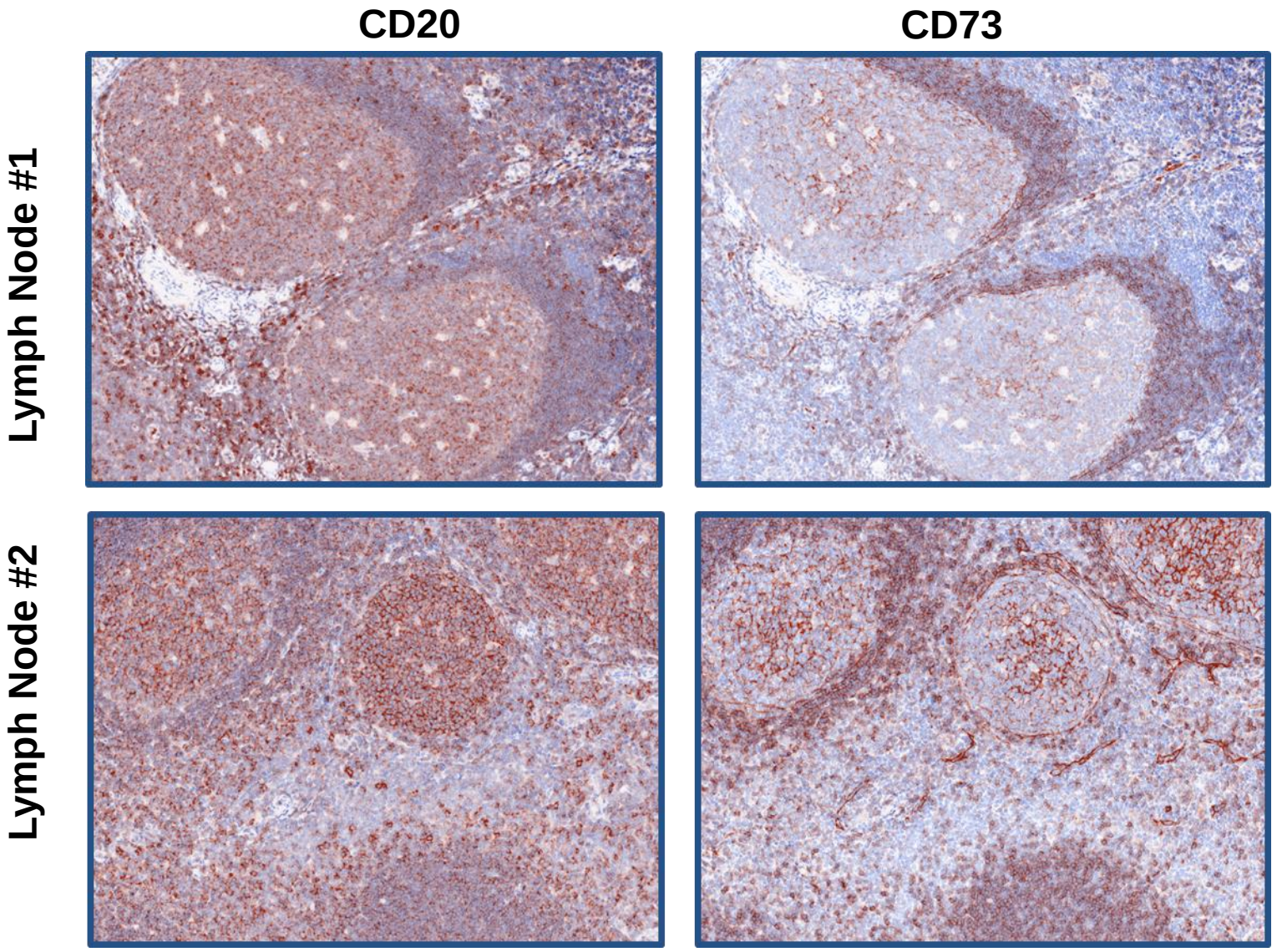
Ibrutinib inhibition of mupadolimab induced B Cell



Phosphorylation of ERK induced by mupadolimab selectively in B cell



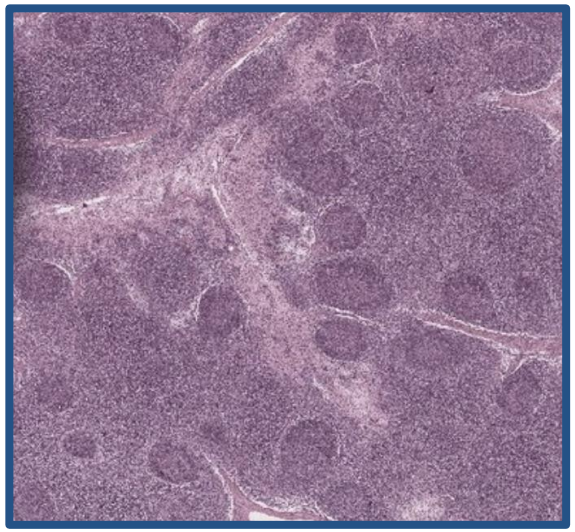
CD73 Expression in Lymph Nodes



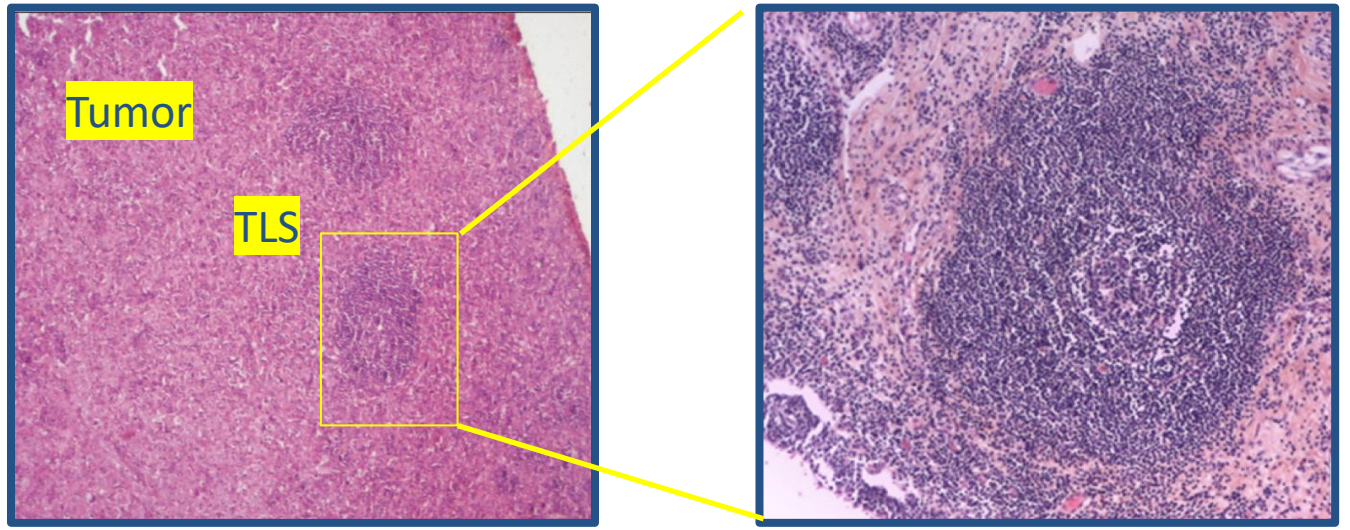
- CD73 expression in lymph nodes is localized in the germinal center and mantle zone
- CD73 is involved in B cell differentiation and maturation
- Germinal centers and mantle zones are areas where B cell maturation into plasma cells and memory B cells occur

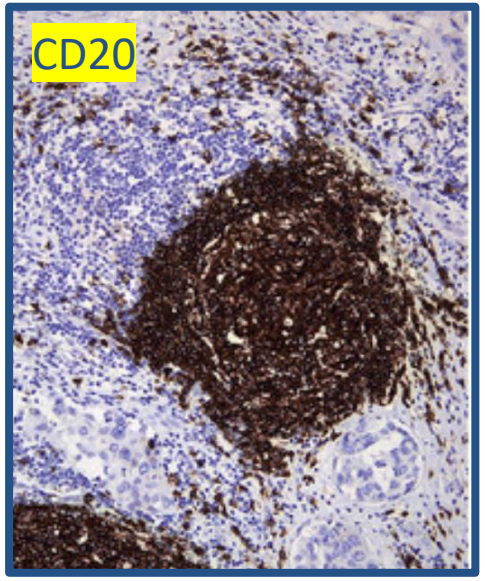
Tertiary Lymphoid Structures

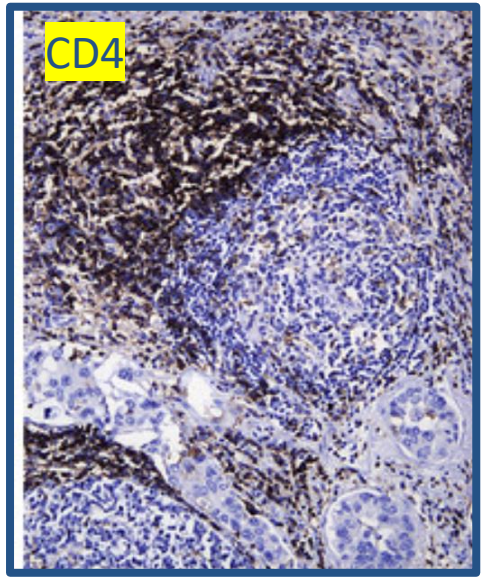
Seen in cancers and responsible for local immunity

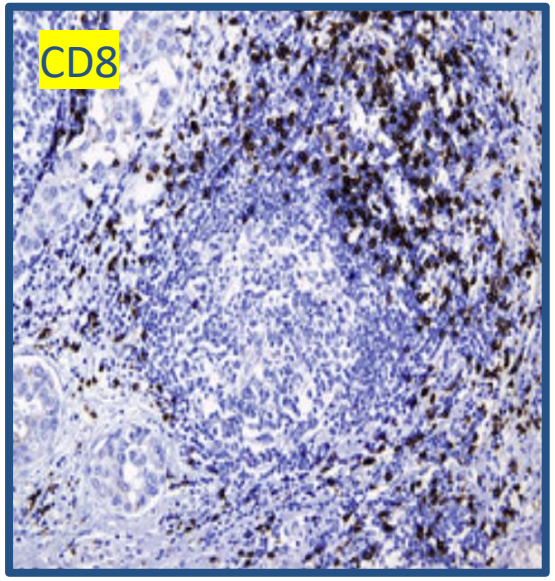


Normal Lymph Node (low magnification)

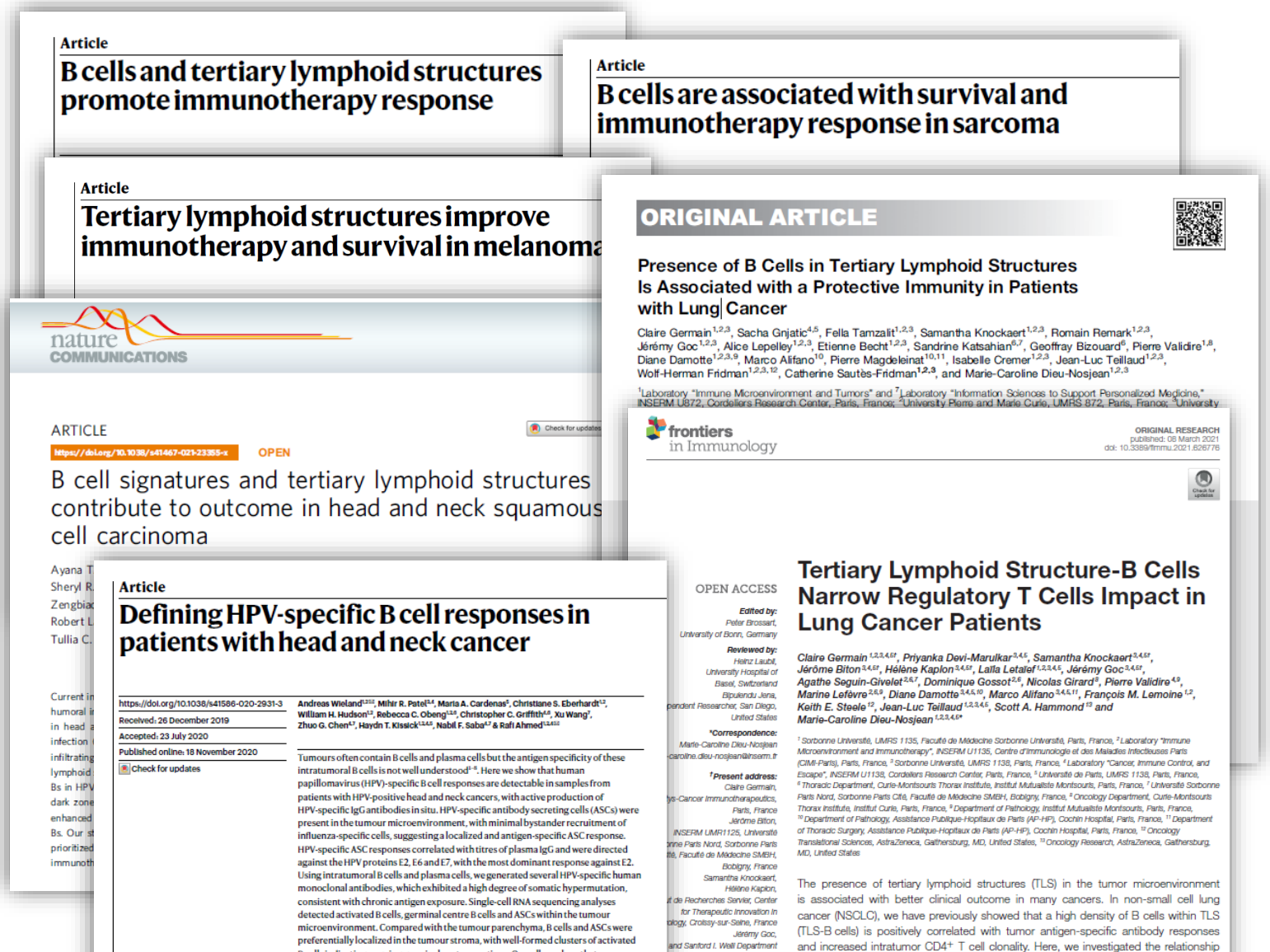








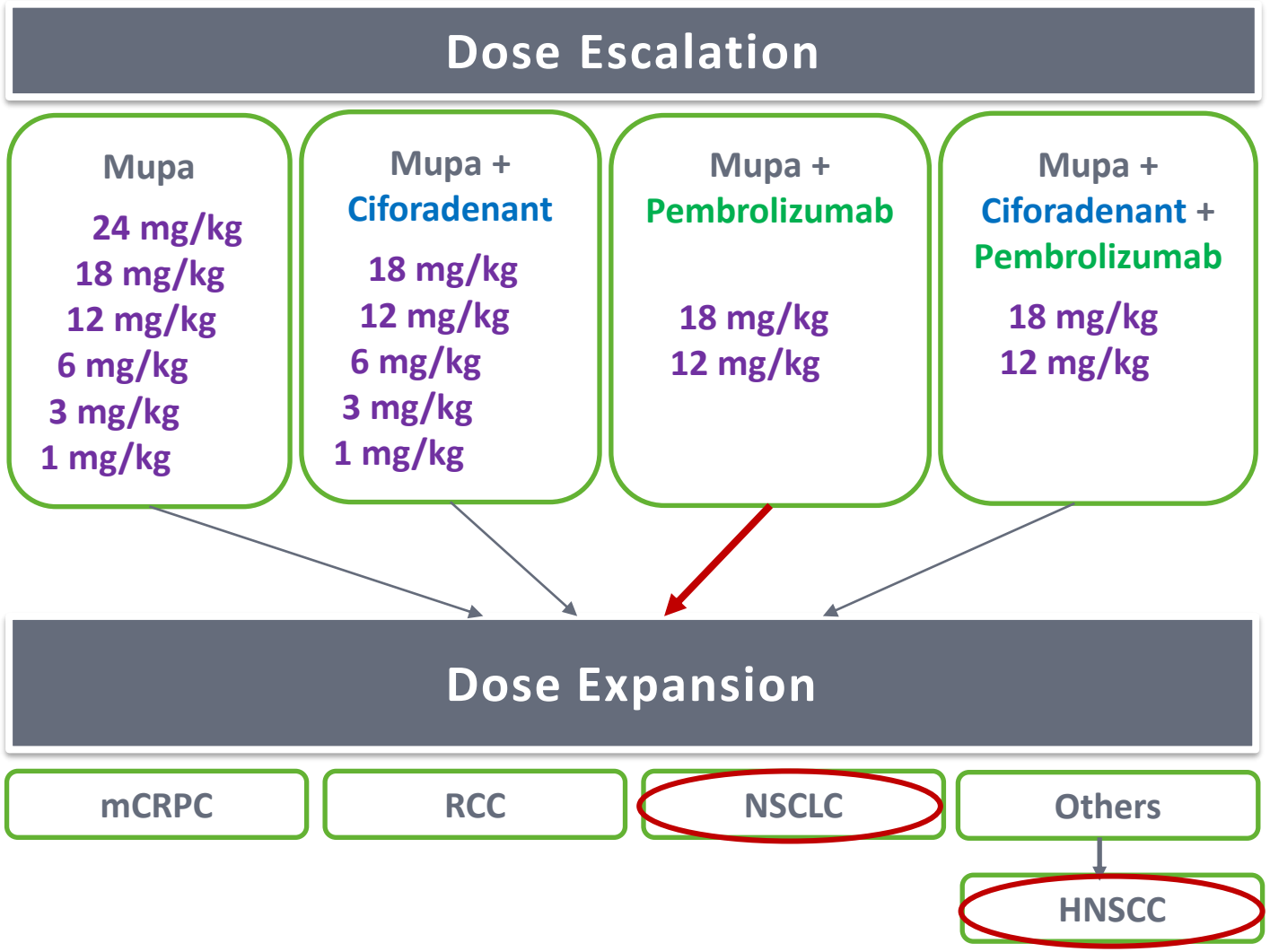
B cells - Important Predictors of IO Response and Prognosis



- B cells are found in tumors of responders[1,2,3]
- The B lineage signature in tumors was the dominant parameter for overall survival[2]
- Activated B cells and antibody secreting cells specific for tumor-specific antigens found in the tumor microenvironment in HPV$^+$ head and neck patient samples[4,5]
- High density B cells within tertiary lymphoid structure promote CD4+ T cell response and are associated with superior clinical outcomes in NSCLC patients[6,7]

1. Helmink et al, Nature, 2020; 2. Petitprez et al, Nature 2020; 3. Cabrita et al, Nature 2020; 4. Weiland et al, Nature 2020; 5. Ruffin et al, Nat. Commun. 2021; 6. Germain et al, Am. J. Respir. Crit. Care. Med. 2014; 7. Germain et al, Front Immunol. 2021

Mupadolimab Phase 1/1b Study



Design

- Phase 1/1b dose escalation/dose expansion in disease specific cohorts
- 3+3 design for dose escalation

Eligibility

- Cancers progressed on 1-5 prior therapies

Objectives

- Primary: Safety and tolerability
- Secondary: PK/PD, efficacy, biomarkers

Currently enrolling HNSCC & NSCLC in mupa + pembro

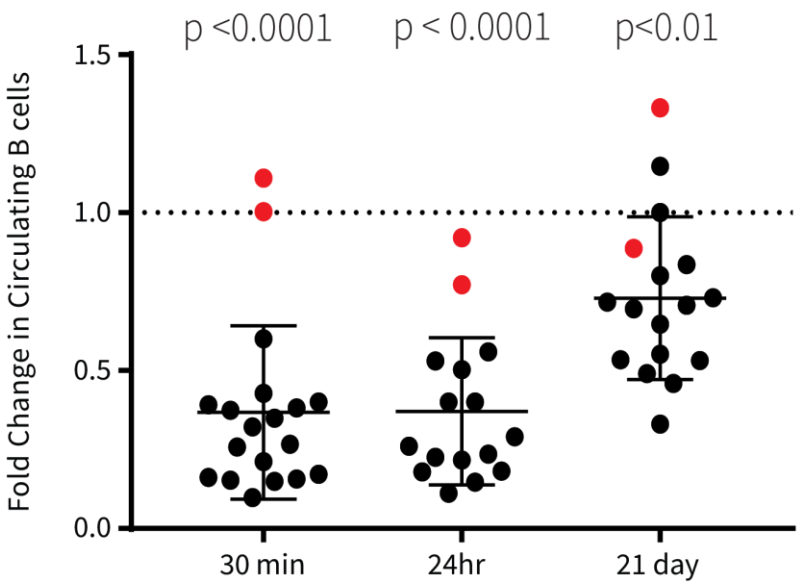
Phase 1/1b Trial Patient Characteristics

- 104 patients with advanced cancers enrolled
- Dose escalation in all arms (monotherapy and combination) completed
- Mupa doses up to 24 mg/kg in monotherapy and 18 mg/kg in combination arms
- MTD not reached for monotherapy and combination

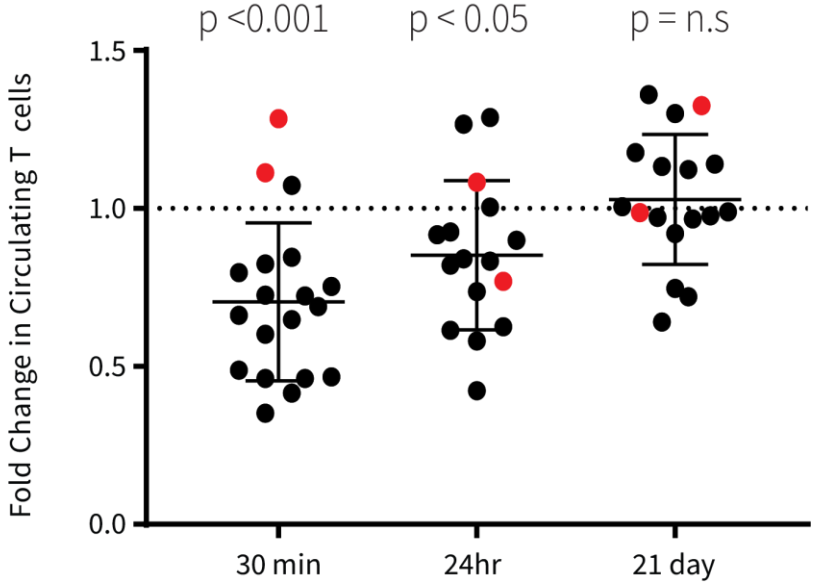
Patient Characteristics	Mupa Monotherapy (N=35)	Mupa + cifo (N=48)	Mupa + pembro +/- cifo (N=21)
Age (yrs.), median (range)	64 (46, 79)	62.5 (36, 89)	64.5 (40, 80)
Gender, male N (%)	27 (77)	27 (56)	16 (76)
No. of prior therapies, median (range)	4 (1, 6)	3 (1, 9)	3 (1, 7)
Histologies			
Colorectal	8	18	2
Renal Cell	5	8	6
Prostate	5	2	3
Head & Neck	3	5	5
Non-Small Cell Lung	3	7	5
Pancreatic	4	4	0
Other	7	4	0

Treatment Induces Rapid Changes in Blood B and T Cells

B cell dynamics*
(≥ 12 mg/kg)



T cell dynamics*
(≥ 12 mg/kg)



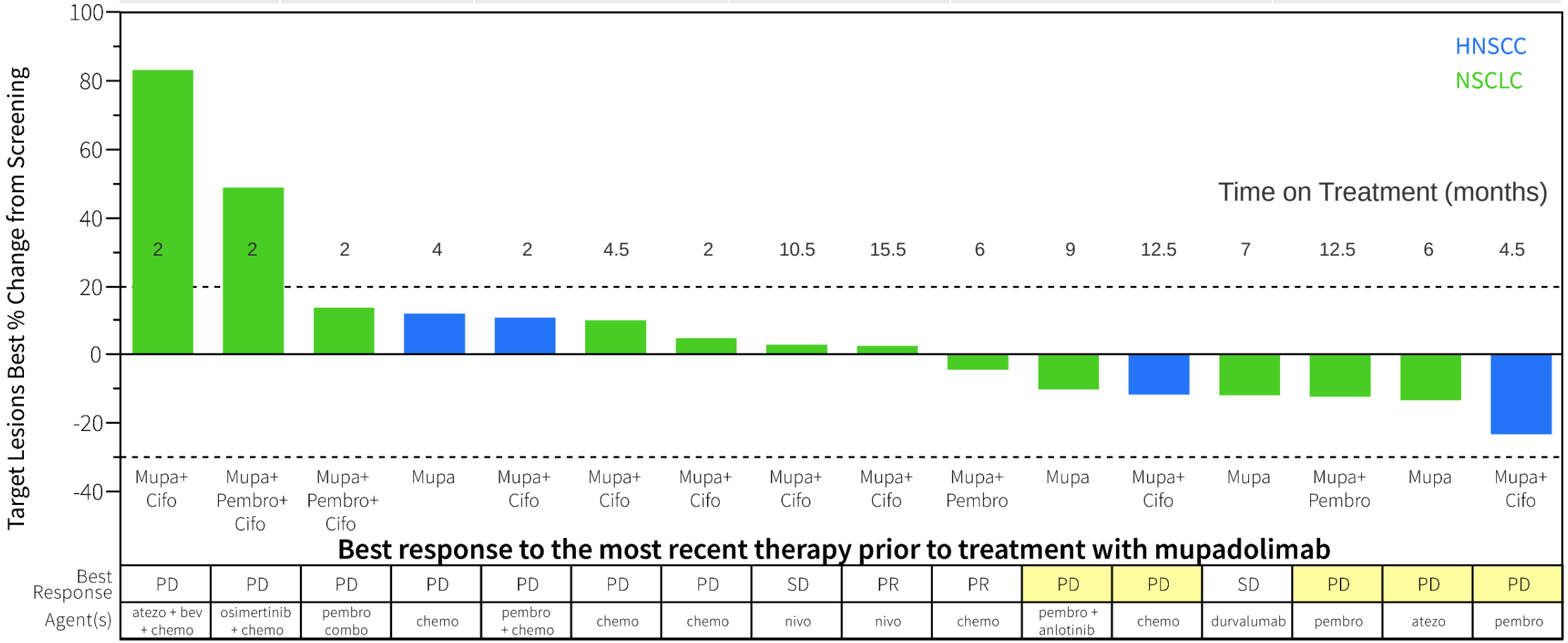
- The B cell reduction is correlated with CD73 expression on B cell
- B cell numbers partially return by 21 days; T cells fully return
- >60% of B cells are CD73+ positive in most patients at baseline

* Red dot = low baseline CD73 expression

Anti-tumor Activity in HNSCC and NSCLC with ≥12 mg/kg

Tumor regression seen in pts with PD as best response to prior Rx

	Subject Counts	Age (yrs) Median (range)	Gender, male N (%)	No. of Prior Therapy Median (range)	Prior PD-(L)1 Therapy N (%)
HNSCC	10	65 (43, 87)	9 (90)	3 (1,5)	10 (100)
NSCLC	15	64 (53, 80)	6 (40)	3 (2,4)	14 (93)



- Cifo = ciforadenent (A2AR antagonist), pembro = pembrolizumab (anti-PD-1), atezo = atezolizumab (anti-PD-L1), bev = bevacizumab (anti-VEGF), chemo = chemotherapy, nivo = nivolumab (anti-PD-1)
- PD = progressive disease; SD = stable disease; PR = partial response

CD73 Target Validation

COAST and NeoCOAST Phase 2 trial results from AstraZeneca

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COAST Phase 2 Trial

- Randomized (N= 189) in Stage III frontline NSCLC
- Oleclumab (anti-CD73) + durvalumab (anti-PD-L1) improved clinical outcome vs. durvalumab
- Phase 3 trial initiated

	Durvalumab	Durvalumab + oleclumab
N	67	60
ORR (95% CI), %	25.4 (15.5, 37.5)	38.3 (26.1, 51.8)
Median PFS (95% CI), %	6.3 (3.7, 11.2)	NR (10.4, NE)
PFS HR (95% CI)	--	0.44 (0.26, 0.75)

AstraZeneca, ESMO 2021

NeoCOAST Phase 2 Trial

- Randomized study of durvalumab +/- oleclumab as neoadjuvant therapy in patients with resectable, NSCLC
- Durvalumab + oleclumab showed improved pathological responses
- Upregulation of genes involved in B cell activation
- Phase 2 (NeoCOAST-2) initiated

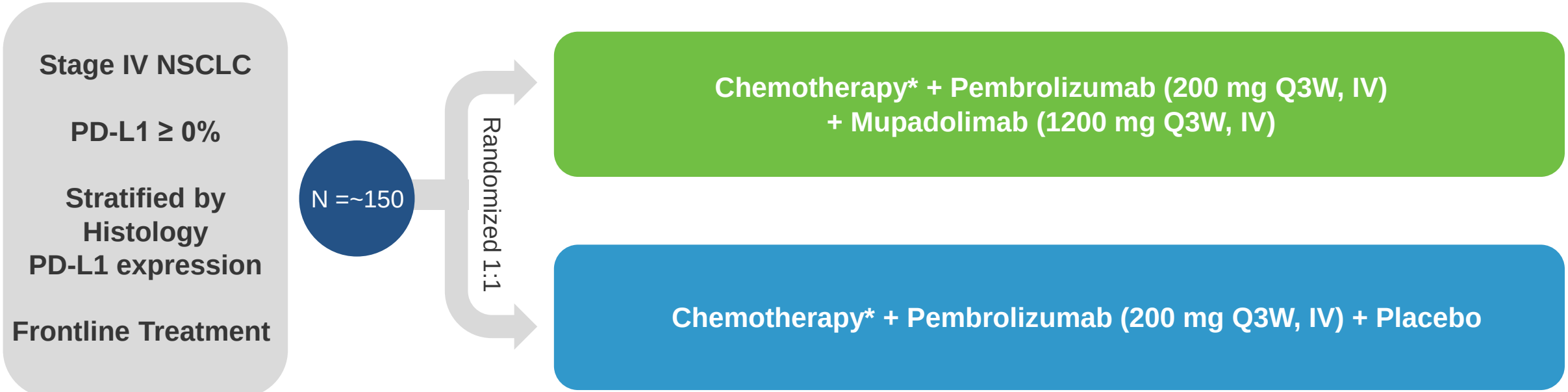
	Durvalumab	Durvalumab + oleclumab
N	27	21
MPR*, n (%)	3 (11.1)	4 (19.0)
pCR*, n (%)	1 (3.7)	2 (9.5)

* MCR, major pathological response; pCR, pathological complete response

AstraZeneca, AACR 2022

Randomized Placebo Controlled Phase 2 Trial Design

Plan to start in 2H 2022



* Non squamous: carboplatin + pemetrexed; Squamous: carboplatin + paclitaxel

Primary Endpoint	• Progression free survival (PFS) Interim analyses (Corvus unblinded)
Secondary Endpoints	• Objective response rate (ORR) • Duration of Objective Response (DOR) • Overall survival (OS) • Safety and tolerability

Mupadolimab Summary

Modulate Tumor Immunity

Evidence of B cell activation

B cell redistribution to lymphoid tissues

Evidence of anti-tumor antibodies

Precision Molecular Targets

CD73 novel epitope defined by Cryo-EM

Complete adenosine blockade

Favorable safety in mono and combo therapy

Broad Clinical Applications

Anti-tumor activity seen in advanced cancers

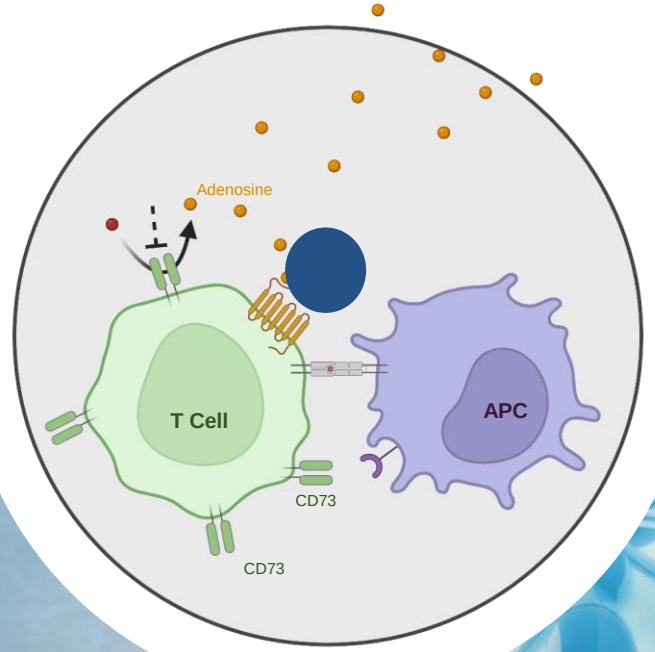
Potential application in infectious disease

Next Steps

Initiate randomized, placebo-controlled Phase 2 trial in frontline NSCLC in 2H 2022

Ciforadenant

Adenosine Receptor Inhibition



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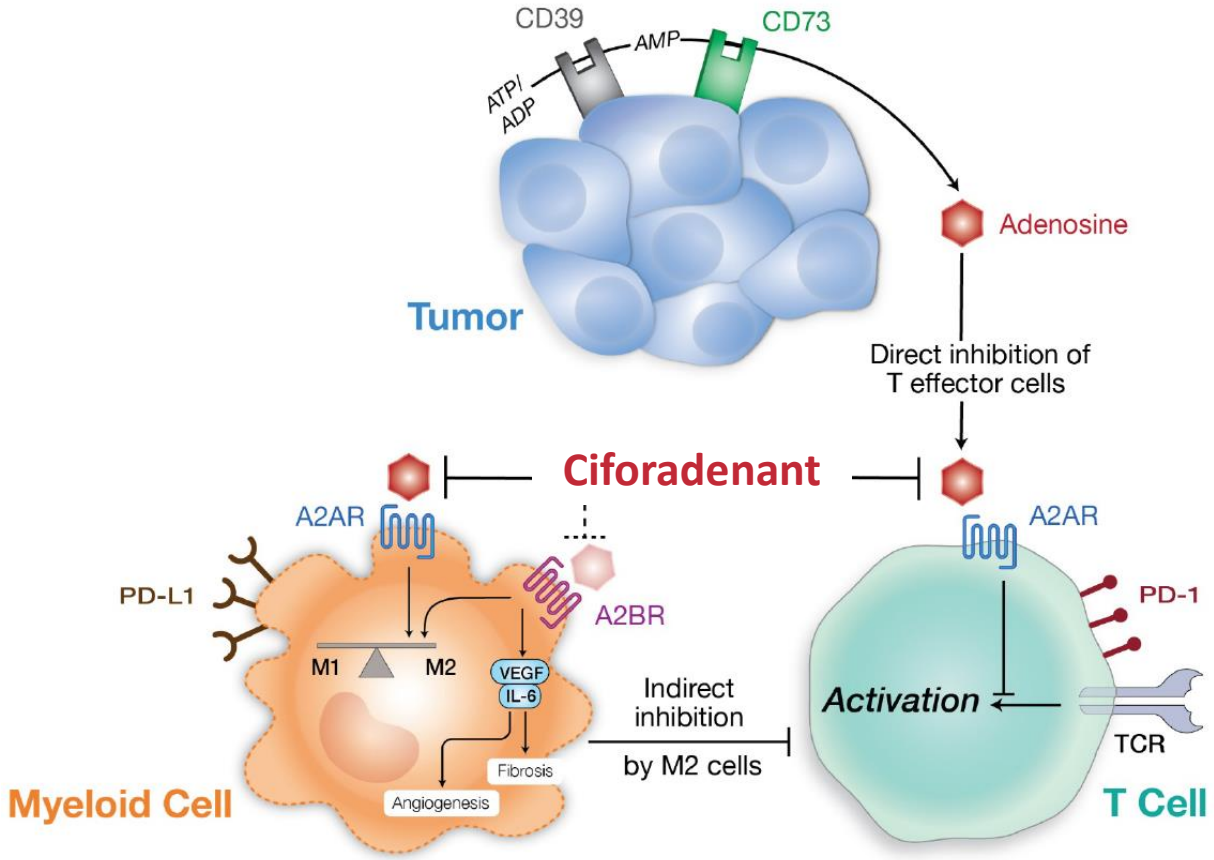
Adenosine in the Tumor Microenvironment

- Extracellular adenosine blocks T-cell activation and promotes myeloid suppression[1,2,3]
- Adenosine 2A receptor (A2AR) is the high affinity adenosine receptor on immune cells
- Ciforadenant is an oral small molecule antagonist of the A2AR that has shown efficacy in animal tumor models and early-stage cancer clinical trials[3,4]



M2 polarization
Corvus Adenosine gene signature

PD-1 expression
IL-2 & IFNγ production
Proliferation

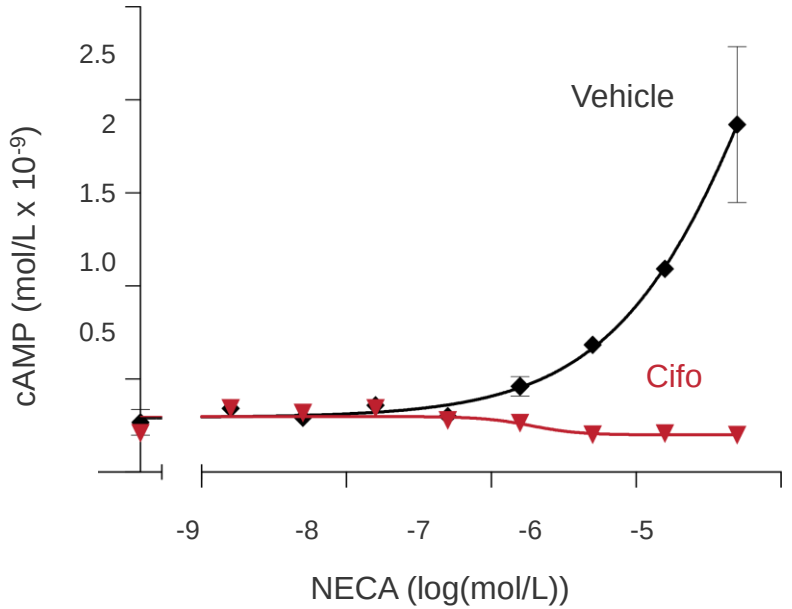
1. Vijayan et al, Nature Review, 2017; 2. Ohta and Sitkovsky et al, PNAS 2006; 3. Willingham et al, Cancer Immunology Research 2018; 4. Leone et al, Cancer Immunology Immunotherapy, 2018

Ciforadenant – a Selective A2AR Inhibitor

Inhibits Signaling and Restores T Cell Function

Receptor	Ki (nM)	Selectivity Versus A2A
A2A	3.5	-
A1	192	X 54
A2B	1528	X 431
A3	2455	X 693

Blocks A2AR signaling in T cells

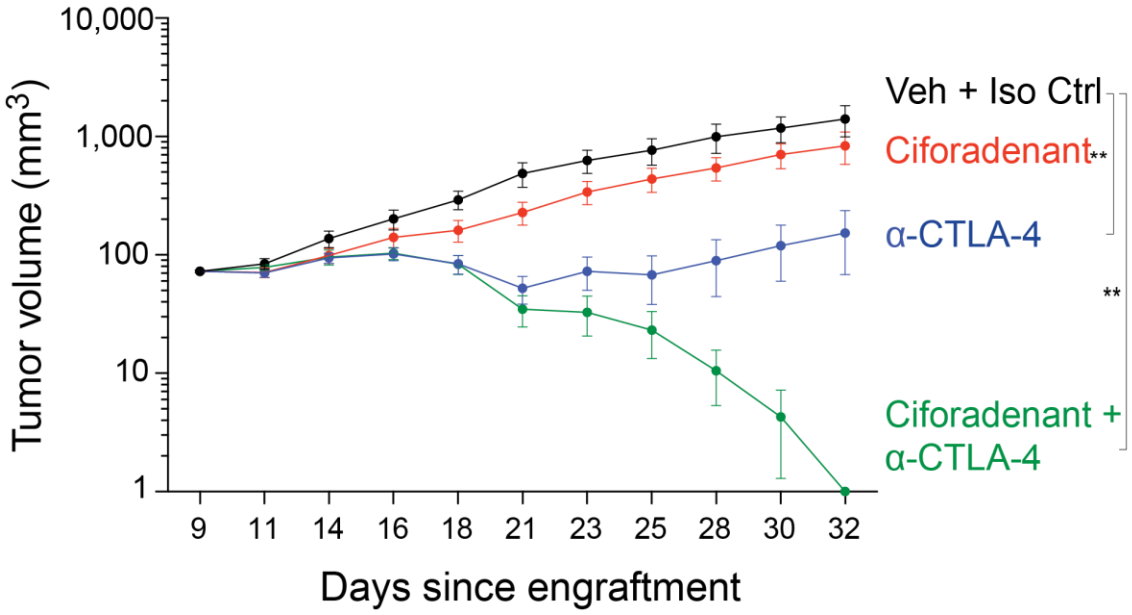


NECA - an adenosine agonist

Ciforadenant Combination with Anti-CTLA-4

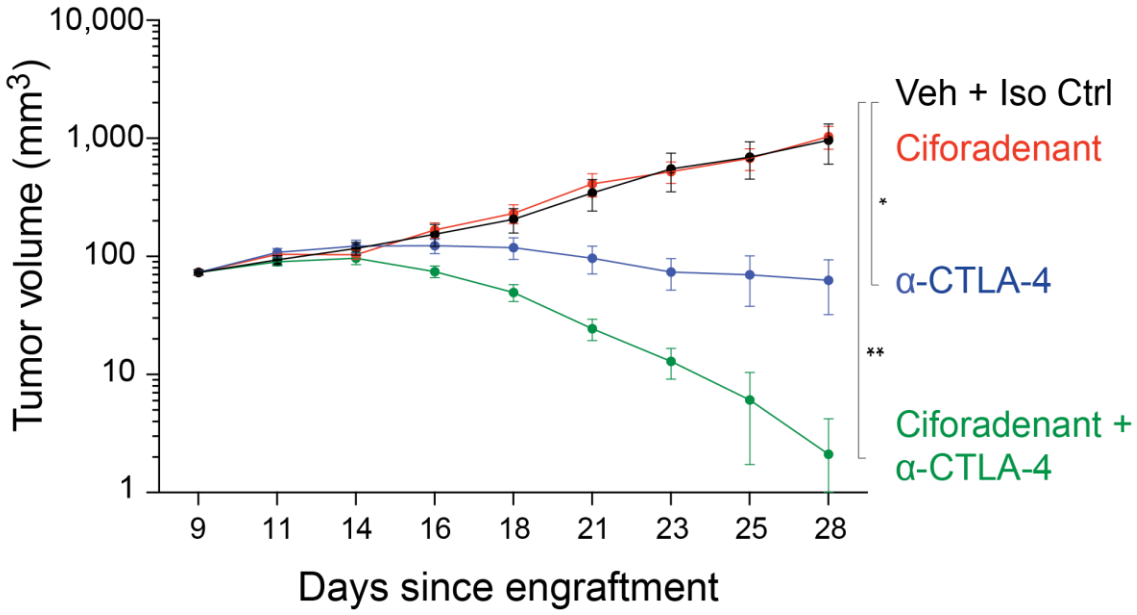
*Published Corvus data**

MC38: Combo leads to complete tumor elimination in 100% of treated mice



Ciforadenant:100 mg/kg, PO, Day 9-23;
anti-CTLA-4: 100 μg, IP, Day 9, 12, 15, 18

CT26: Combo is more effective than either monotherapy

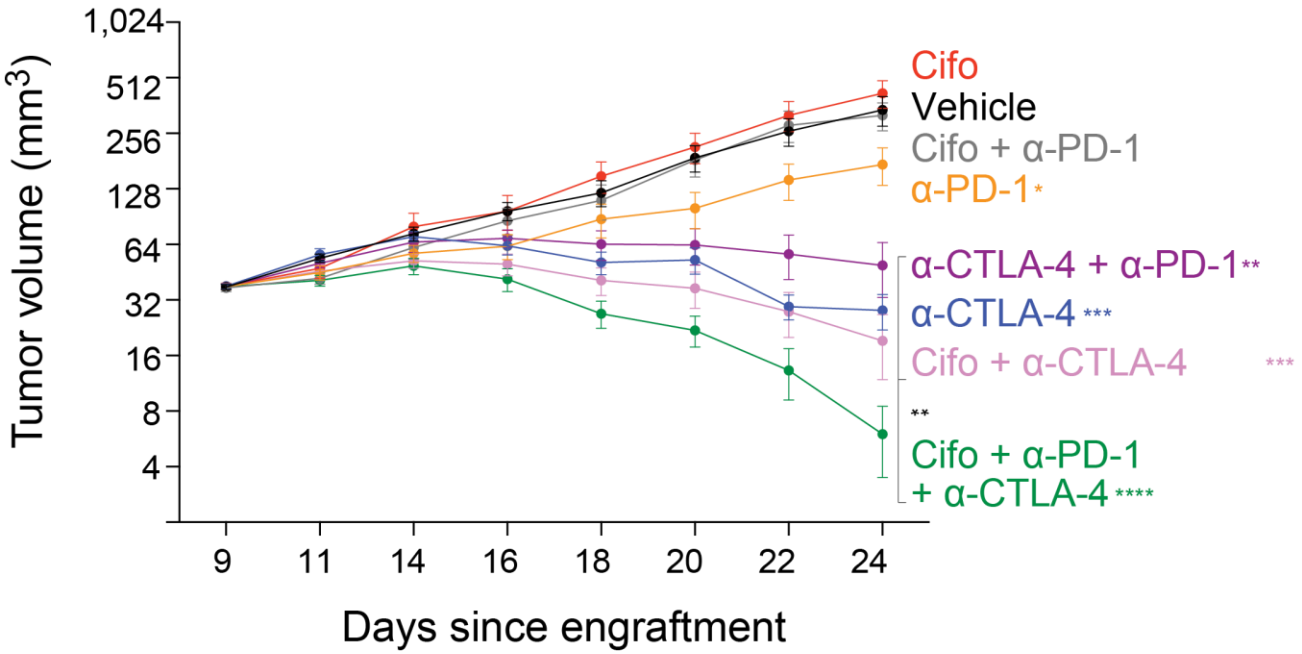


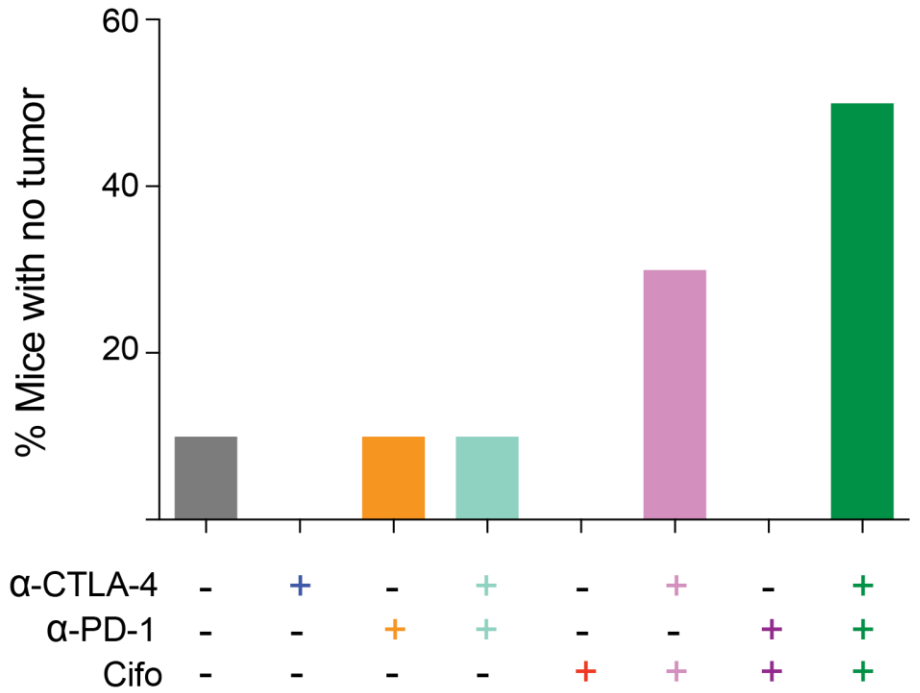
Ciforadenant: 10 mg/kg, PO, Day 10-16;
anti-CTLA-4: 100 μg, IP, Day 9, 12, 15

*Willingham et al, Cancer Immunol. 2018

Ciforadenant Triplet with Anti-PD-1 and Anti-CTLA-4

Highly effective and allows lower doses





- Ciforadenant (10 mg/kg, PO, Day 10-16) enables lower doses of anti-PD-1 (**25 µg/dose**, IP, Day 10, 13, 16) and anti-CTLA-4 (**25 µg/dose**, IP, day 10, 13, 16) combination while preserving the enhanced efficacy in CT26 model

Willingham et al, Cancer Immunol. 2018

Cancer Discovery January 2020

Publication of clinical results in RCC

Published OnlineFirst November 15, 2019; DOI: 10.1158/2159-8290.CD-19-0980

RESEARCH ARTICLE

Adenosine 2A Receptor Blockade as an Immunotherapy for Treatment-Refractory Re

Lawr
Saby
Shiva
Daru
Philip
Brian
Richa

VIEWS

IN THE SPOTLIGHT

Lessons from the A2A Adenosine Receptor Antagonist–Enabled Tumor Regression and Survival in Patients with Treatment-Refractory Renal Cell Cancer

Michail V. Sitkovsky

Summary: In this issue of *Cancer Discovery*, Fong and colleagues describe the encouraging observations of tumor regression, disease control, and survival of patients with otherwise refractory renal cell cancer with progressive disease after treatment with the conceptually novel oral antagonist of the A2A adenosine receptor (A2AR), ciforadenant. A2AR antagonists may represent the until now missing but critically important part of more effective immunotherapies of cancer, because they prevent the inhibition of tumor-reactive T and natural killer cells by blocking the immunosuppressive hypoxia–A2A-adenosinergic signaling, which represents an emerging immunosuppressive hallmark of tumors that are the most resistant to therapies.

See related article by Fong et al., p. 40 (1).

Currently, the majority of patients with cancer are still eventually refractory to any cancer therapy despite a massive and decades-long effort. The hope for the solution to this acute medical problem may come from taking a different and novel therapeutic path, as did Fong and colleagues (1), who, in an "out-of-the-box" approach, treated patients with refractory renal cell cancer (RCC) with a drug that inactivates the biochemical, hypoxia-A2-adenosinergic, immunosuppressive tumor protection (2–8). This powerful mechanism of tumor protection inhibits the antitumor T and natural killer (NK) cells near and within tumors, thereby making them the most resistant to cancer therapies (3, 4, 7), even after the blockade of immunologic negative regulators (4, 6).

misguidedly protects the hypoxic and extracellular adenosine-rich cancerous tissues (3, 4, 7). This is why A2AR blockade with synthetic A2AR antagonists has been proposed for a long time (2, 3) as a therapeutic tool to unleash tumor-reactive T and NK cells to enable immunotherapy-mediated tumor regression (3–7). The synthetic A2AR antagonists can also be termed "super-caffeine," because the research and development of these highly selective for A2AR and long-lived *in vivo* drugs was in part prompted by observations of favorable effects of caffeine consumption in patients with Parkinson disease.

Originally, not only the A2AR but also the low-affinity A2B adenosine receptor (A2BR) were considered to be targets to antagonize to improve immunotherapies of cancer (3). However, the subsequent biochemical considerations of the differences between the Gs-coupled A2AR and Gs/Gq-coupled A2BR, as well as the more detailed preclinical tumor

THE A2A ADENOSINE RECEPTOR IS A

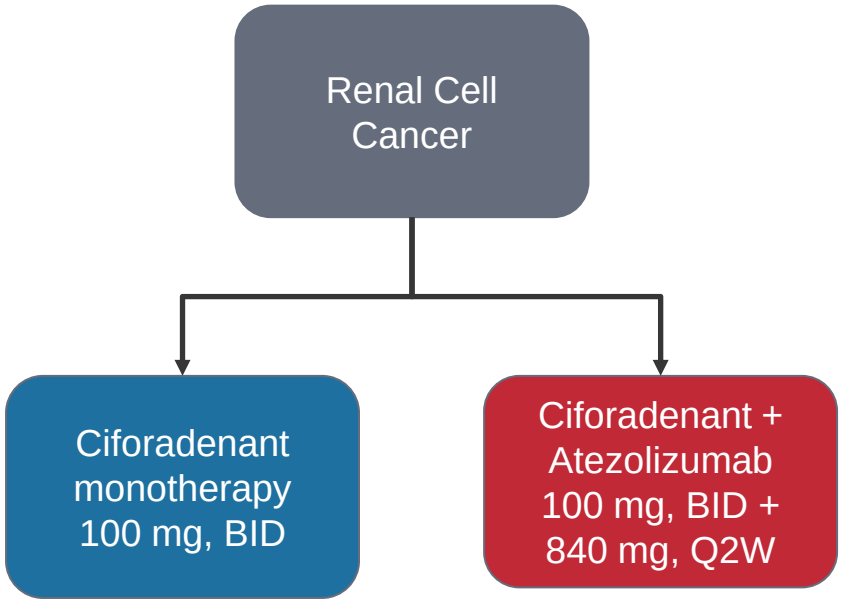
"Fong and colleagues describe… tumor regression, disease control, and survival of patients with otherwise refractory renal cell cancer with progressive disease after treatment with the conceptually novel…. ciforadenant."

"Fong and colleagues are among the first clinical development teams that aimed to block not only the immunologic negative regulators, but also the powerful A2A-adenosinergic negative regulators of antitumor immunity."

Renal Cell Cancer Clinical Results

Patient characteristics

- 68 patients with RCC enrolled
- Median on-treatment time was 5 (1-21.7) months

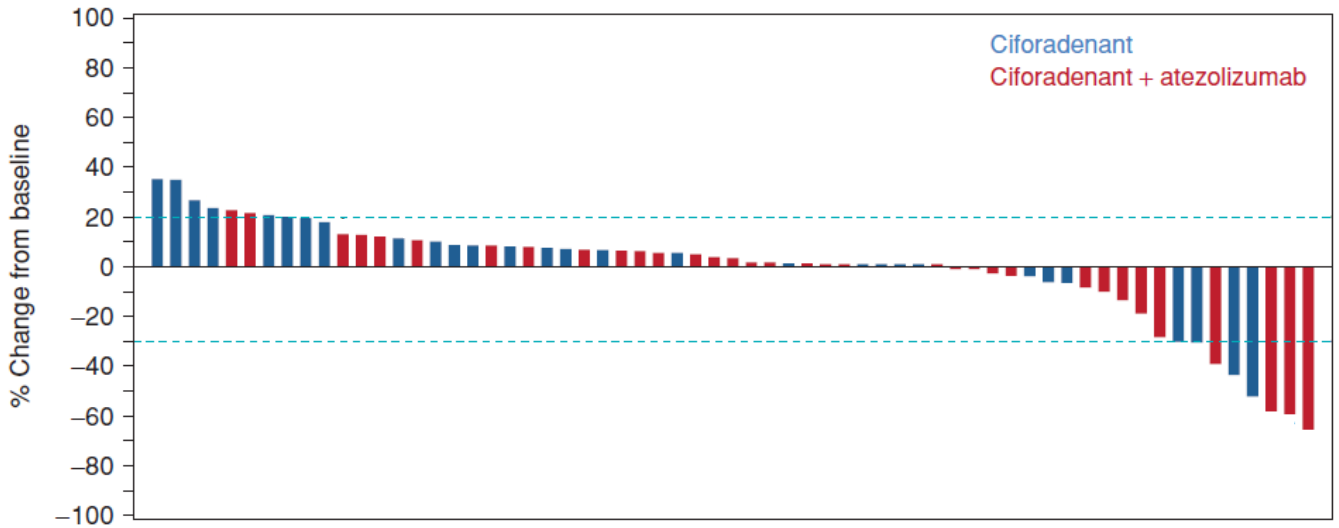


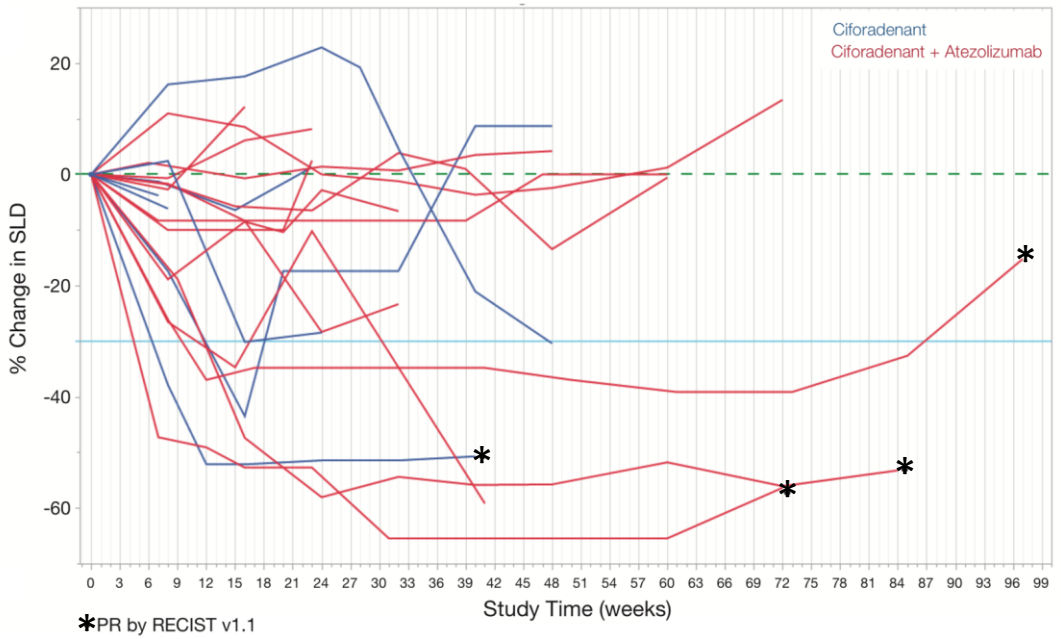
Characteristic	Ciforadenant (n=33)	Ciforadenant + Atezolizumab (n=35)
Median Age (range), years	60 (47, 76)	65 (44, 77)
Gender, male, n (%)	25 (75.8)	28 (80)
No. of prior therapies, median (range)	3 (1, 5)	3 (1,5)
Prior IO, number of subject, n (%)	24 (72.7)	25 (71.4)
Months since prior IO Median (Range)	3.1 (1,2, 70.4)	1.7 (0.9, 23.6)
PD-L1 Negative, n(%)*	25/27 (92.6)	28/31 (90.3)
Prior PD-1 therapy, n (%)	23 (69.7)	25 (71.4)

* PD-L1 status determined using FDA-approved assay (SP142, cutoff = 5%)

Fong et al, Cancer Discovery, 2020

Renal Cell Cancer Response to Treatment



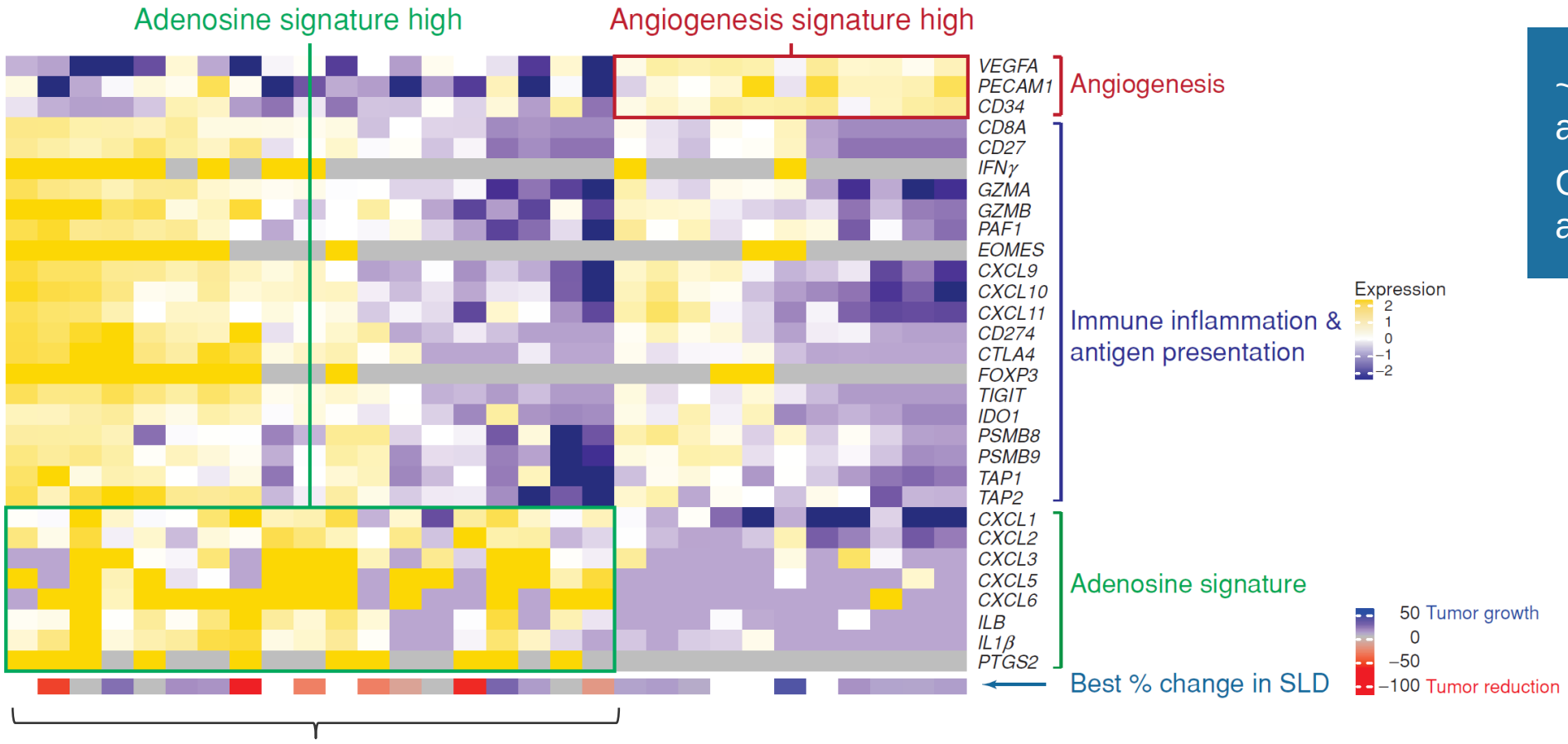


	Ciforadenant (n=29)	Ciforadenant + Atezolizumab (n=33)
6-month Disease Control rate		
Prior anti-PD-(L)1	25% (5/20)	35% (8/23)
Naïve	0% (0/9)	50% (5/10)
Total	17% (5/29)	39% (13/33)
Median time to best tumor response	3.4 months	5.5 months

Fong et al, Cancer Discovery, 2020

Adenosine Signature Correlates with Anti-Tumor Activity

Potential predictive biomarker



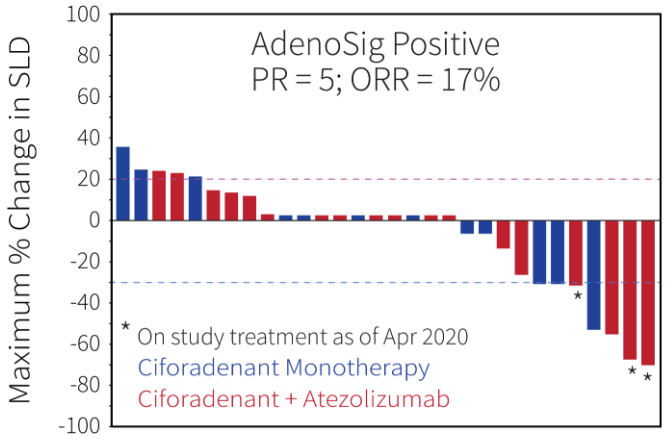
~50 – 60% of RCC pts are positive

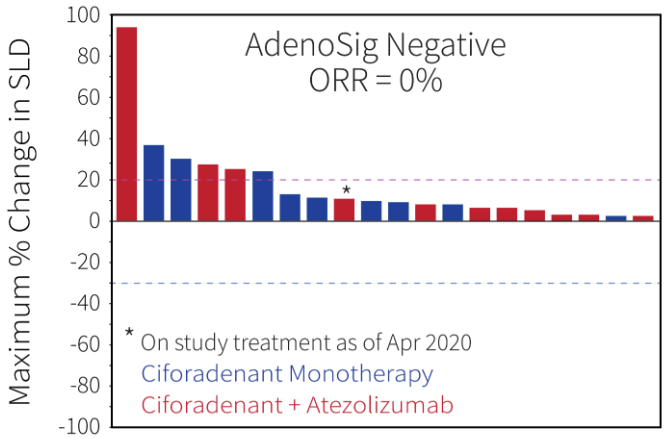
Confirmed by outside academic groups

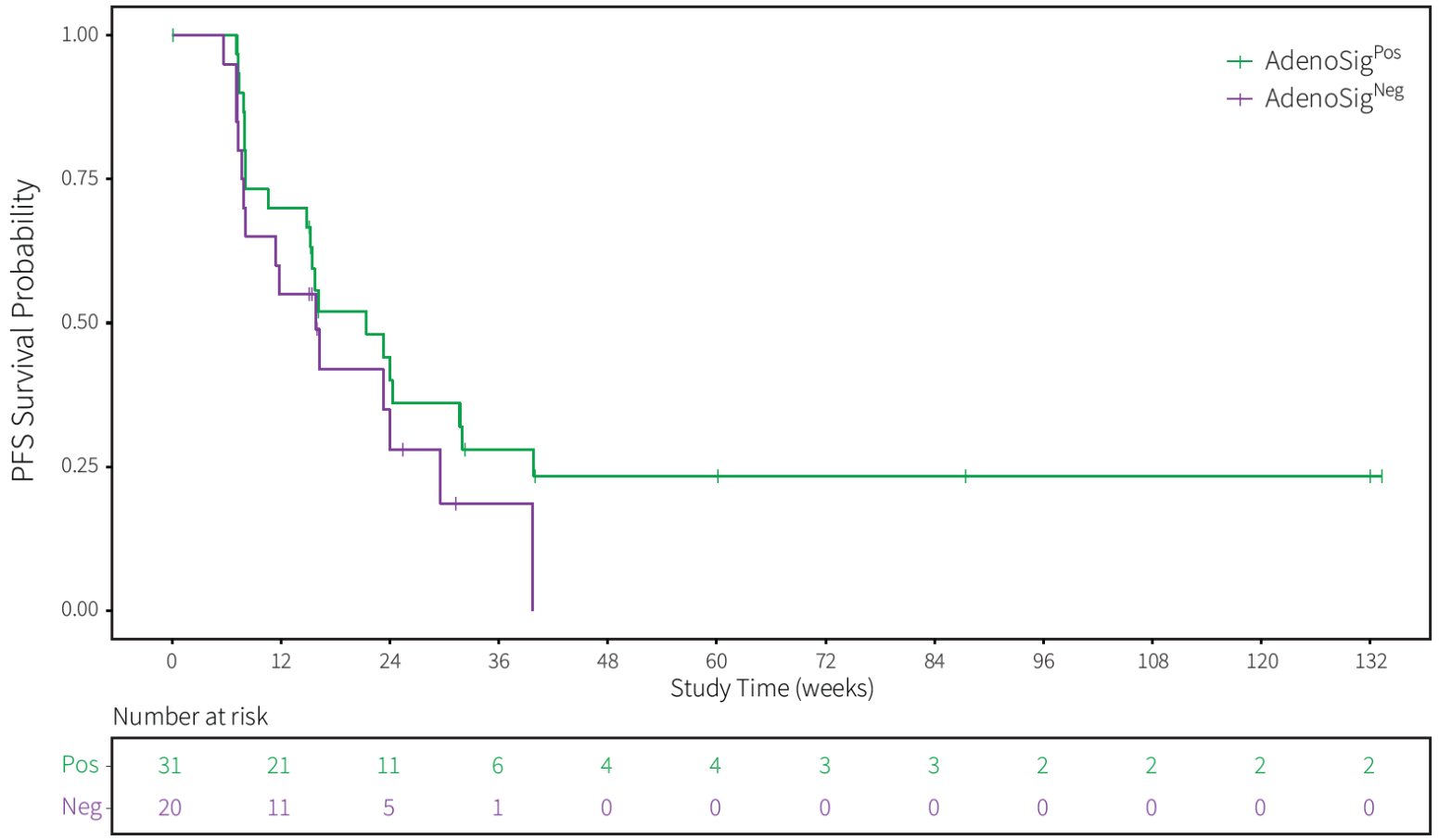
- **Enriched for ciforadenant response**
- Angio^{Low}: Poor PFS with TKI[1,2]
- Myeloid^{High} : Poor PFS with single agent atezolizumab[1]

1. McDermott et al, Nature Medicine, 2018; 2. Fong et al, Cancer Discovery, 2020

Adenosine Signature Correlates with Anti-Tumor Activity







Fong et al, Cancer Discovery, 2020

Anti-tumor Activity in RCC and NSCLC Patients

Tumor regression seen in pts failed prior anti-PD(L)-1

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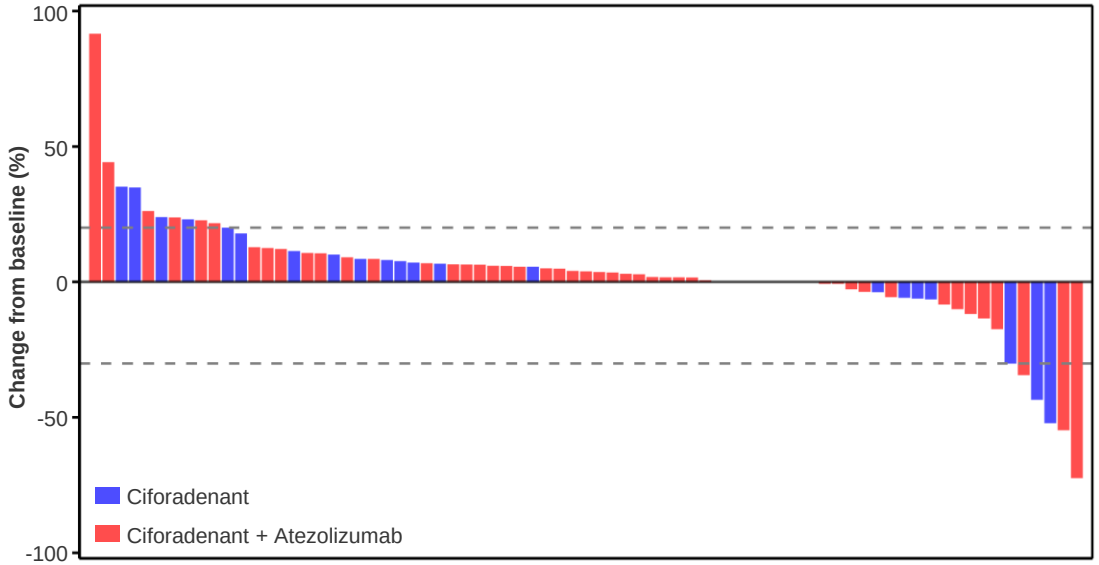
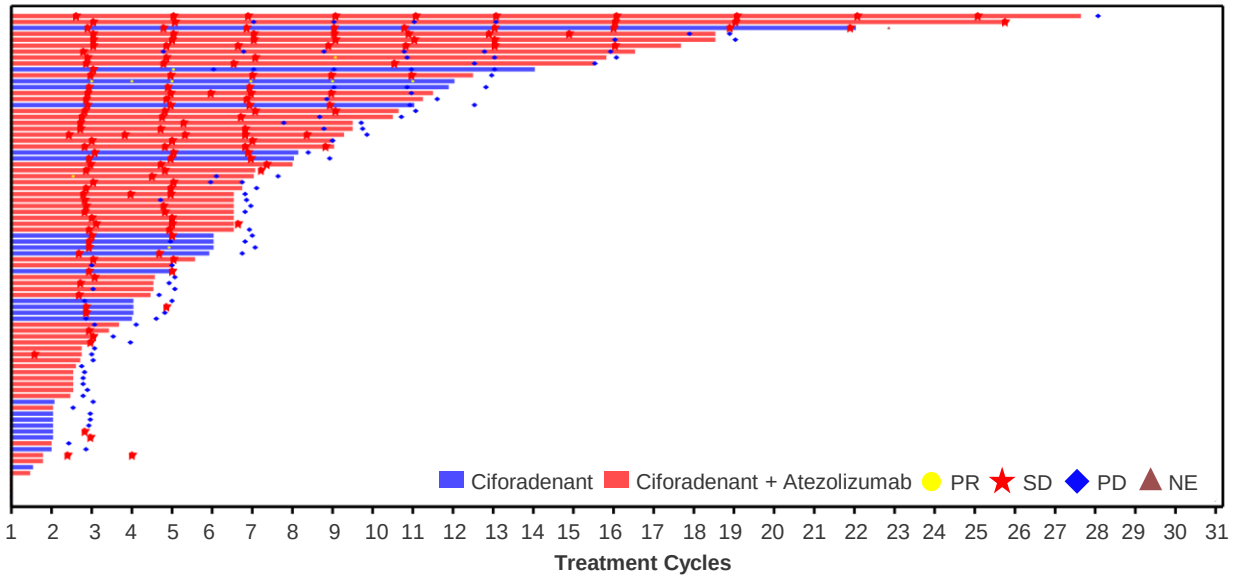
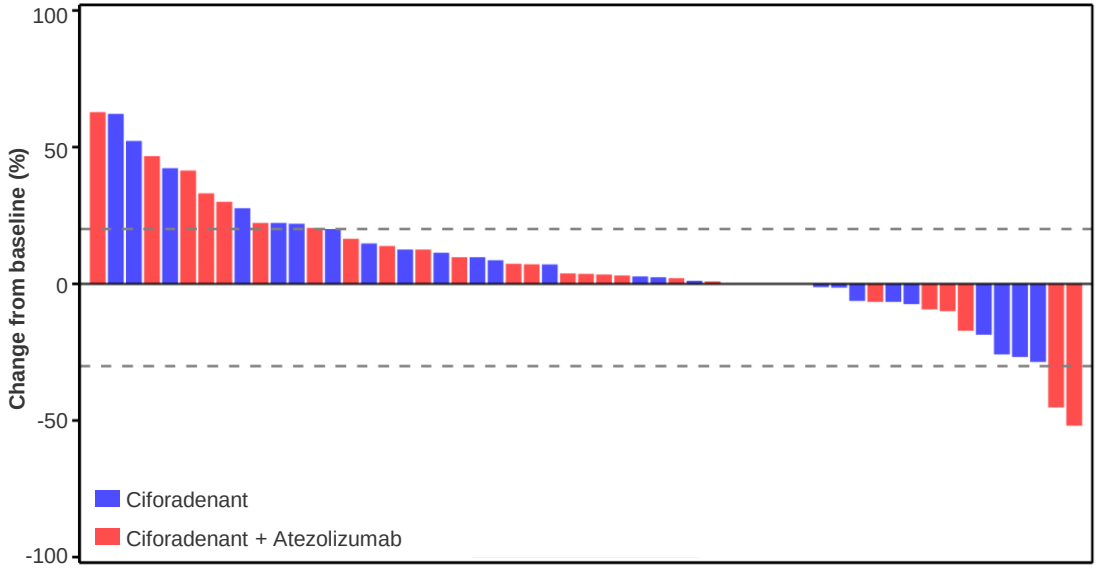
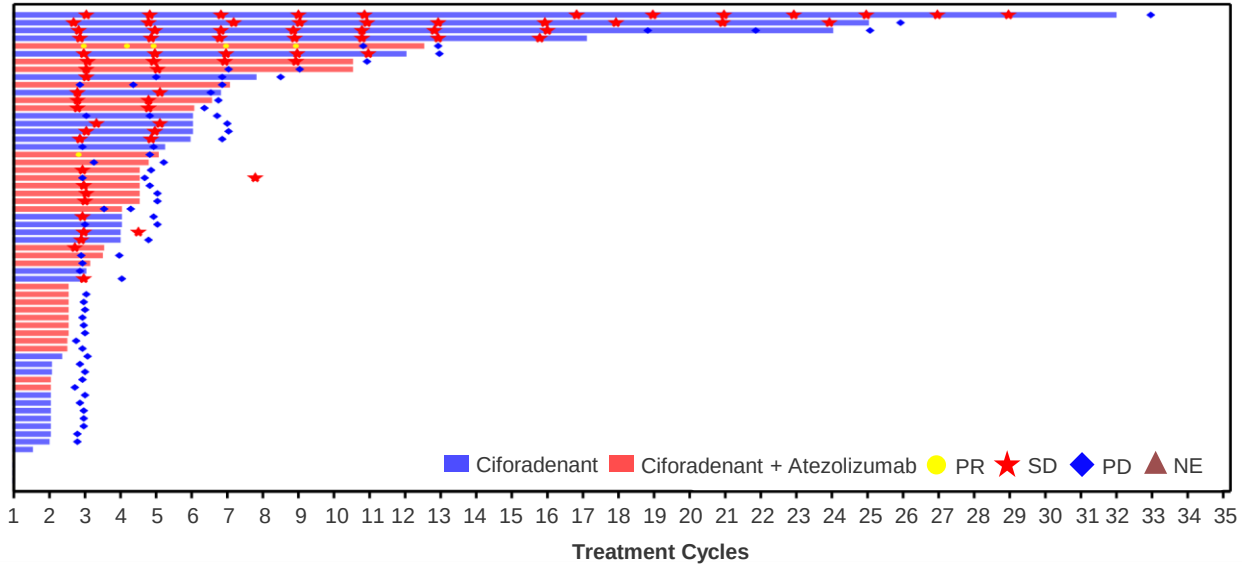
Renal Cell Cancer Pts





NSCLC Pts

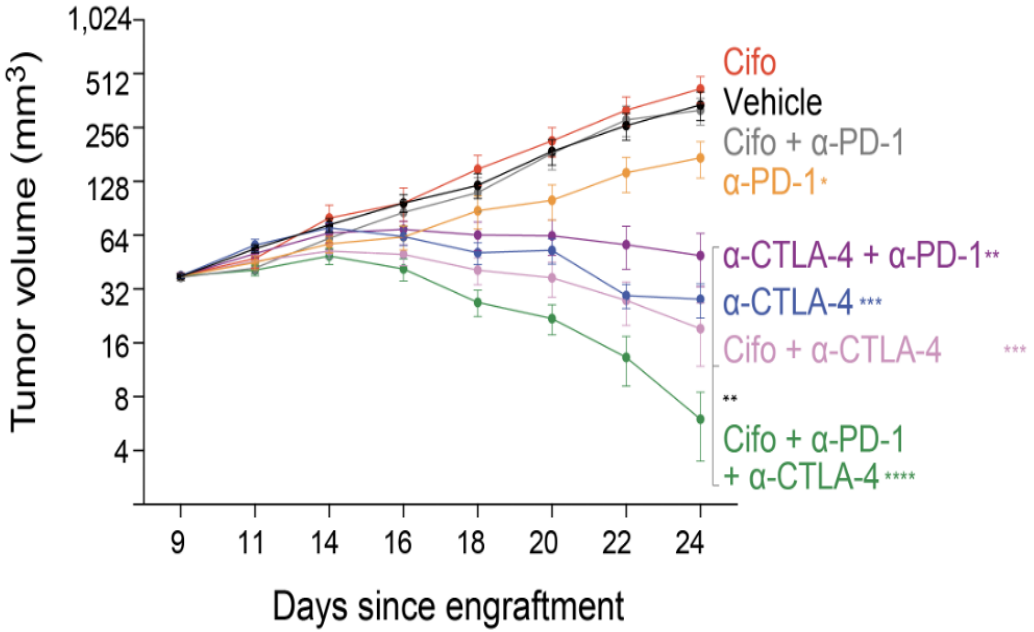




Strong Rationale for Frontline Triplet Combination

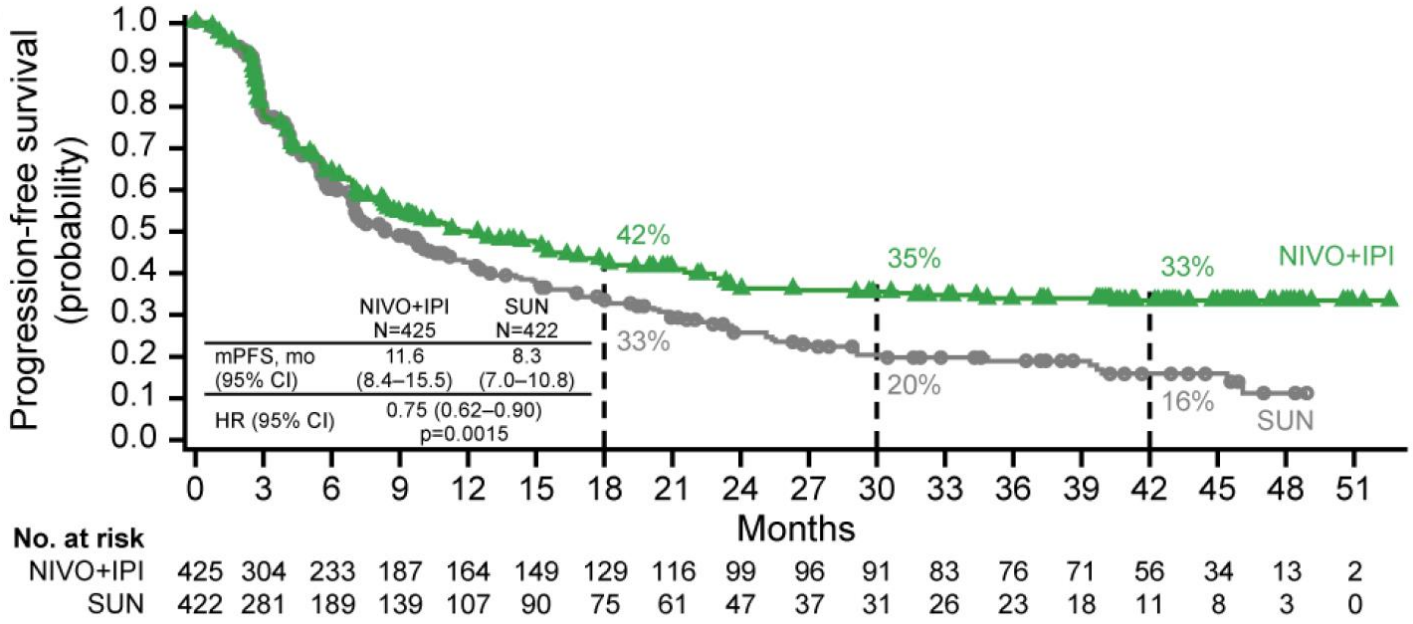
Supports triplet aimed at increasing durable remissions

CT26 Preclinical Model Established Tumor
(*Willingham et al, Cancer Imm Res. 2018*)



Triplet Cifo, anti-PD1, anti-CTLA4 cures most animals

CheckMate 214 Trial
(*Motzer et al, J. Immunother. Cancer, 2020*)



4-year follow-up from CheckMate 214 study of IPI/NIVO showing a tail on the curve suggesting potential cures

Phase 1b/2 Trial Design in Frontline RCC

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Eligibility

- Newly diagnosed or recurrent stage IV clear cell RCC
- No prior systemic therapy
- Tumor sample for histologic confirmation & biomarker assessment

N = 8

Phase 1b

Ipilimumab 1 mg/kg
IV q3w x 4
+
Nivolumab 3 mg/kg
IV q3w
+
Ciforadenant 100 mg
PO BID

- Primary endpoint: Safety, tolerability and anti-tumor

N = 51

(Minmax two stage <7/28 stop for futility)

Phase 2

Ipilimumab 1 mg/kg
IV q3w x 4
+
Nivolumab 3 mg/kg
IV q3w
+
Ciforadenant 100 mg
PO BID

- Primary endpoint: percentage who achieve depth of response of >50% tumor reduction from historical control of 34% to 50%
- Secondary endpoint: ORR, PFS, irAE
- Exploratory: gene expression

VANDERBILT UNIVERSITY MEDICAL CENTER

Kidney Cancer RESEARCH CONSORTIUM

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Ciforadenant Summary

Modulate Tumor Immunity

Enhances T cell infiltration in tumor

New T cell clones detected in blood

Augments efficacy to anti-PD-(L)1 / CTLA-4

Precision Molecular Targets

Oral, selective

Block A2AR signaling

Treatment response correlates with adenosine signature

Broad Clinical Applications

Well tolerated and shows activity in mono and combination therapy of advanced cancer

Next Steps

Kidney Cancer Consortium to conduct Phase 2 trial in frontline RCC patients with a triplet

Corvus R&D Symposium Key Takeaways

3 Clinical programs with significant anticipated near-term milestones

- CPI-818 Phase 1/1b data in T-cell lymphoma in 2H 2022
- Ciforadenant Phase 1b/2 data in front-line RCC in 2H 2022
- Mupadolimab Phase 2 in front-line NSCLC initiated in 2H 2022

Unique pipeline focused on the tumor immunity axis

- Precisely defined targets present in the tumor and lymph nodes
- First anti-CD73 to demonstrate B cell modulation
- Novel ITK inhibitor control T cell differentiation
- Selective A2AR inhibitor augments efficacy to anti-PD-1 and anti-CTLA-4

Robust pre-clinical and clinical data

- Experience in a large number of cancer patients with ciforadenant or mupadolimab
- Pioneer in adenosine pathway and kinase inhibitor R&D
- First to show clinical activity of ITK inhibitor in lymphomas and immune diseases
- Identified predictive Adenosine Gene Signature biomarker in RCC

Q&A

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