



SITC 2018

NOVEMBER 7-11
WASHINGTON, D.C.

Walter E. Washington
Convention Center



Society for Immunotherapy of Cancer



Refractory Renal Cell Cancer (RCC) Exhibits High Adenosine A2A Receptor (A2AR) Expression and Prolonged Survival Following Treatment With the A2AR Antagonist CPI-444

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Presenter Disclosure Information

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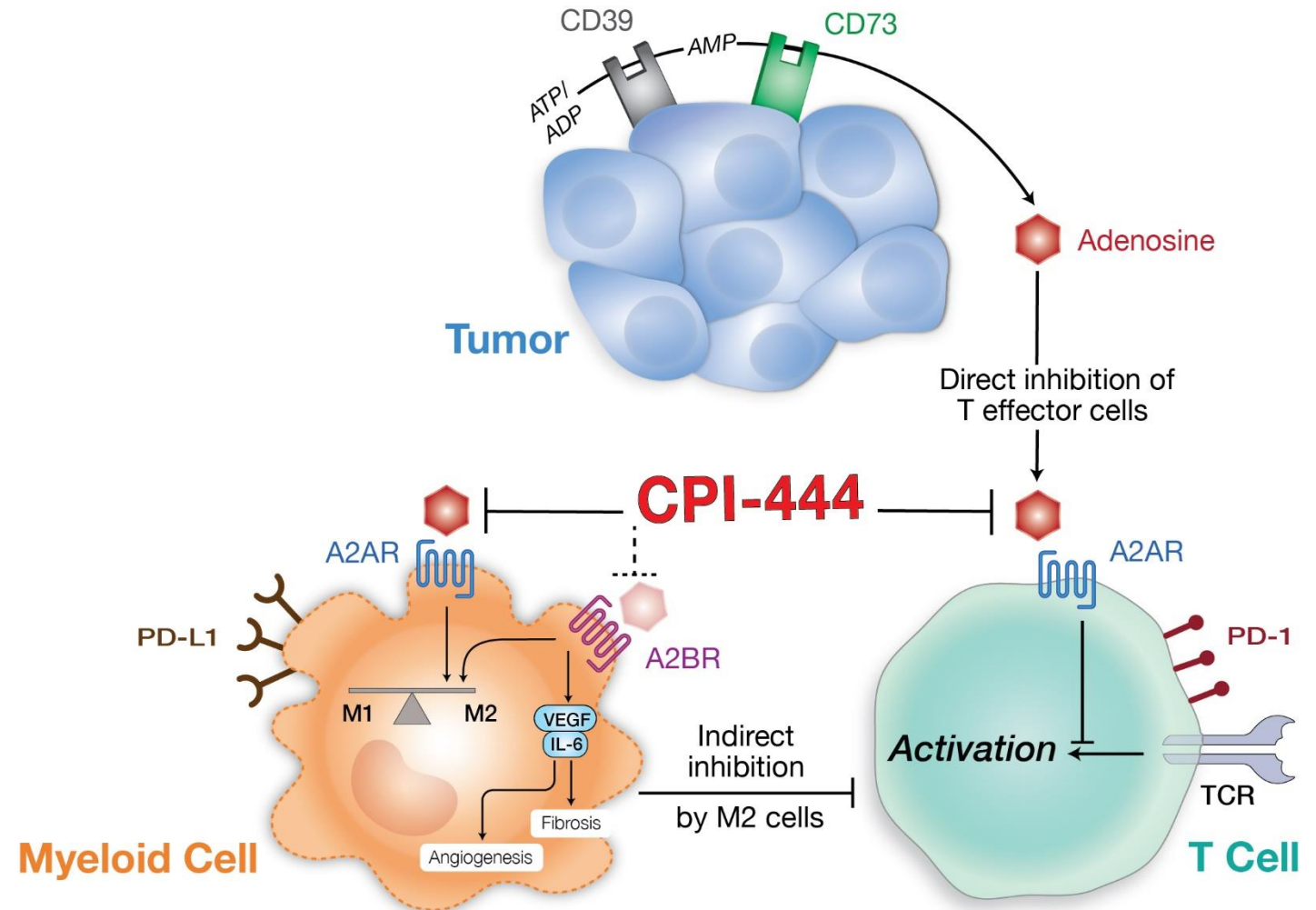
The following relationships exist related to this presentation:

Research support from Roche Genentech, Merck, Bristol-Myers Squibb, Abbvie, and Janssen Pharmaceuticals.

Corvus Pharmaceuticals Inc. is the sponsor of this study.

ROLE OF ADENOSINE IN THE TUMOR MICRO-ENVIRONMENT

- Anti-PD-(L)1 antibodies are approved for treatment of RCC but most patients progress.
- Adenosine blocks T-cell activation and promotes myeloid suppression.^{a,b,c}
- Resistance to PD-1 blockade is associated with an immunosuppressive myeloid signature.^{c,d}
- CPI-444 is a oral small molecule antagonist of the adenosine 2A receptor (A2AR) that has shown efficacy in animal models and is associated with T cell activation.^{c,e}

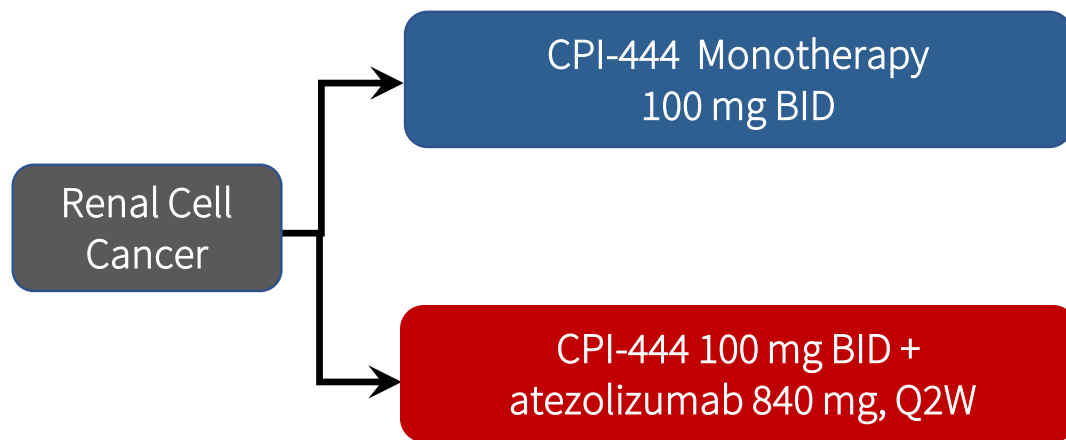


- a) Vijayan et al, Nature Reviews, 2017
 b) Ohta and Sitkovsky et al, PNAS, 2006
 c) Willingham et al, Cancer Immunology Research, 2018
 d) McDermott et al, Nature Medicine, 2018
 e) Leone et al, Cancer Immunology Immunotherapy, 2018

M2 polarization
 ↑ Adenosine Signature

↑ PD-1 expression
 ↓ IL-2 & IFN γ production
 ↓ Proliferation

TRIAL DESIGN & PATIENT CHARACTERISTICS



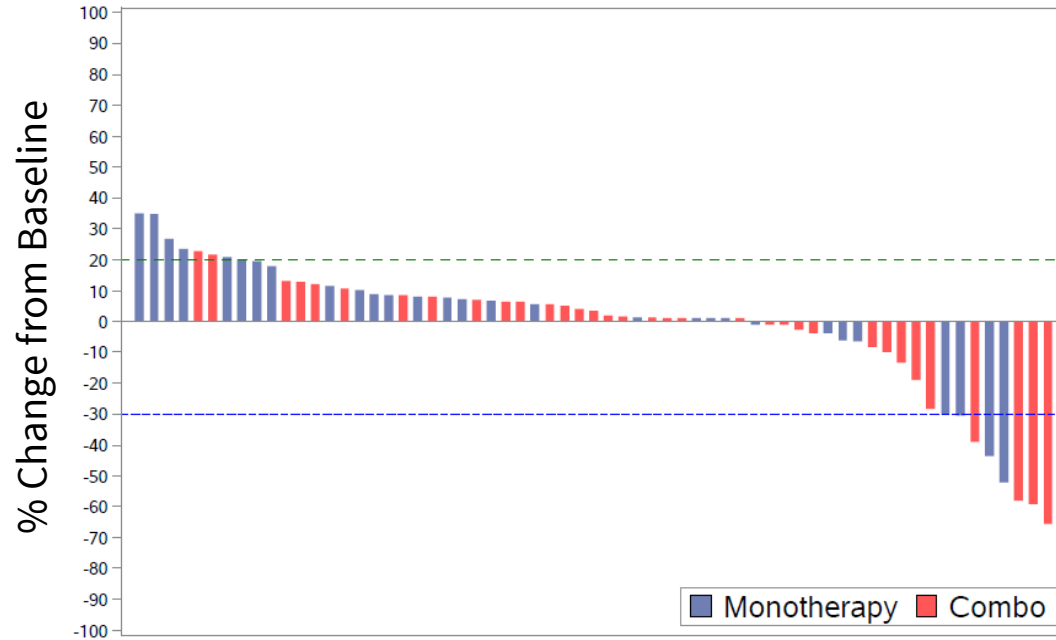
Eligibility

- Prior anti PD-(L)1 allowed
- Progressive disease at time of entry
- No selection for PD-L1 expression

Baseline Demographics	CPI-444 (n=33)	CPI-444 + atezolizumab (n=35)
Age (years), median (range)	60 (47, 76)	65 (44, 77)
Gender, male n (%)	25 (75.8)	28 (80.0)
Number of prior therapies median (range)	3 (1, 5)	3 (1, 5)
Prior IO, number of subjects n (%)	24 (72.7)	25 (71.4)
Months since prior IO therapy, median (range)	3.1 (1.2, 70.4)	1.7 (0.9, 23.6)
Prior Anti-Cancer Therapy n (%)		
TKI	27 (81.8)	30 (85.7)
mTor	9 (27.3)	11 (31.4)
anti-PD-1	23 (69.7)	25 (71.4)
anti-VEGF, Bevacizumab	6 (18.2)	4 (11.4)
IL-2	7 (21.2)	9 (25.7)

TUMOR RESPONSE TO TREATMENT

Best Response of All Patients

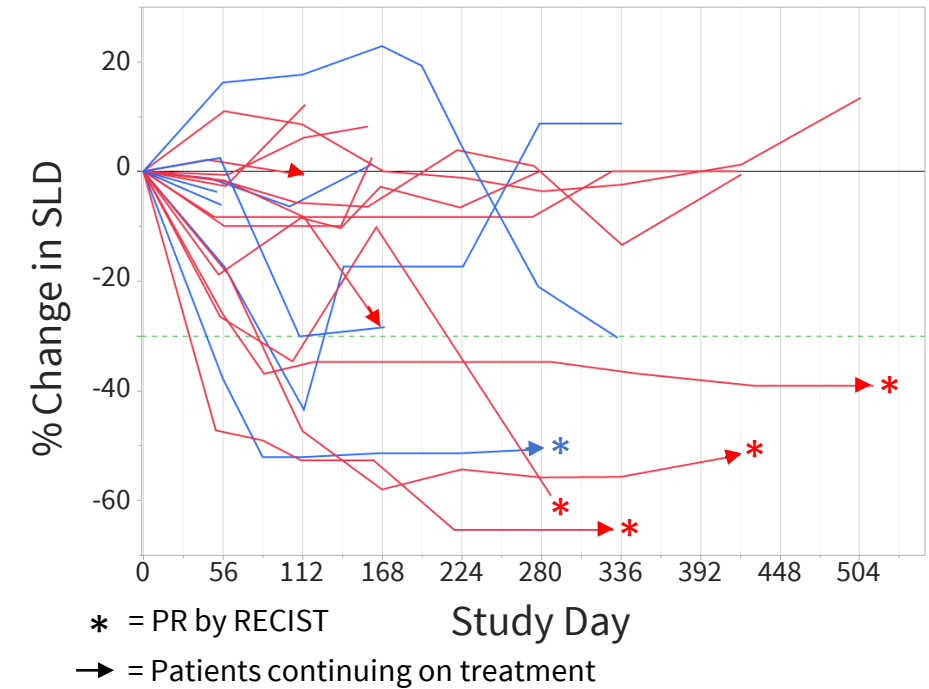


6 Month Disease Control Rate

	Mono*	Combo*
Prior PD(L)-1	25% (5/20)	32% (7/22)
Naive	0% (0/9)	44% (4/9)
Total	17% (5/29)	35% (11/31)

* Disease control % (# Disease control patients/total)

Spider Plot of Patients with Tumor Regression

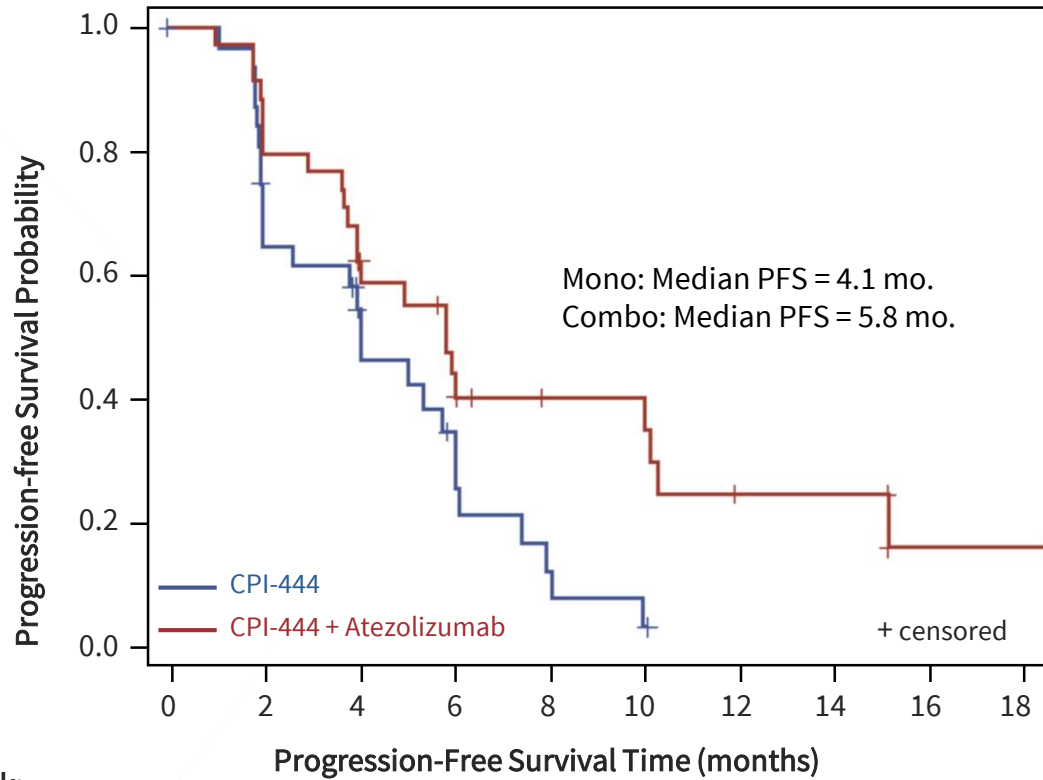


Median time to best tumor response:

- Monotherapy 3.4 months
- Combination 5.5 months

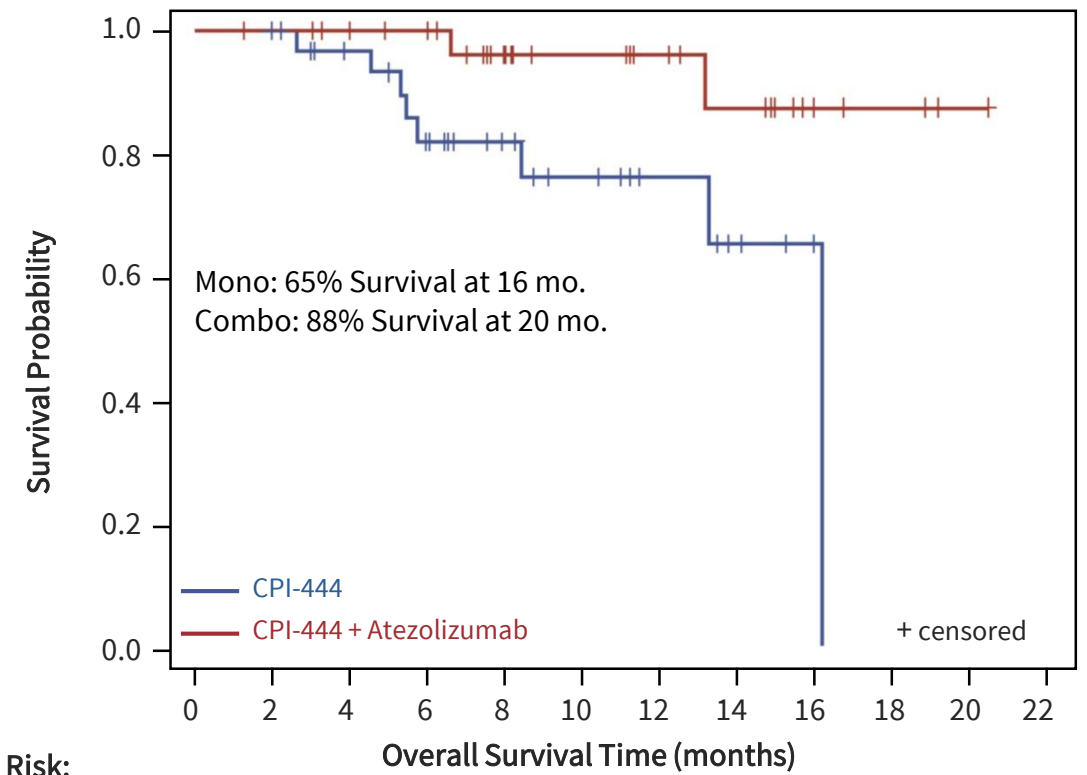
PROGRESSION FREE AND OVERALL SURVIVAL

Median follow-up 8.7 months



N. At Risk:

CPI-444	33	23	15	8	3	1						
CPI-444 + Atezolizumab	35	31	23	12	8	7	4	4	1	1		



N. At Risk:

CPI-444	33	33	27	22	15	11	7	4	2	0		
CPI-444 + Atezolizumab	35	34	32	30	22	16	13	10	5	3	1	0

TREATMENT-RELATED ADVERSE EVENTS

- CPI-444 is well tolerated as monotherapy and in combination

Adverse Event	Number (%) of Patients			
	Monotherapy (N=33)		Combination Therapy (N=35)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Nausea	3(9.1)	0(0.0)	7(20.0)	1(2.9)
Arthralgia	2(6.1)	1(3.0)	4(11.4)	1(2.9)
Hypophosphataemia	2(6.1)	0(0.0)	3(8.6)	1(2.9)
Abdominal pain	1(3.0)	0(0.0)	3(8.6)	1(2.9)
Aspartate aminotransferase increased	1(3.0)	0(0.0)	2(5.7)	1(2.9)
Decreased appetite	4(12.1)	1(3.0)	6(17.1)	0(0.0)
Anaemia	2(6.1)	1(3.0)	4(11.4)	0(0.0)
Oedema peripheral	2(6.1)	1(3.0)	1(2.9)	0(0.0)
Fatigue	13(39.4)	0(0.0)	16(45.7)	0(0.0)
Pruritus	7(21.2)	0(0.0)	9(25.7)	0(0.0)
Diarrhoea	2(6.1)	0(0.0)	5(14.3)	0(0.0)
Vomiting	2(6.1)	0(0.0)	4(11.4)	0(0.0)
Dizziness	4(12.1)	0(0.0)	1(2.9)	0(0.0)
Cough	2(6.1)	0(0.0)	3(8.6)	0(0.0)
Rash	2(6.1)	0(0.0)	3(8.6)	0(0.0)
Influenza like illness	0(0.0)	0(0.0)	3(8.6)	0(0.0)
Pyrexia	3(9.1)	0(0.0)	1(2.9)	0(0.0)
Musculoskeletal chest pain	2(6.1)	0(0.0)	2(5.7)	0(0.0)
Myalgia	2(6.1)	0(0.0)	2(5.7)	0(0.0)
Osteoarthritis	2(6.1)	0(0.0)	2(5.7)	0(0.0)
Blood creatinine increased	1(3.0)	0(0.0)	2(5.7)	0(0.0)
Insomnia	1(3.0)	0(0.0)	2(5.7)	0(0.0)
Dysgeusia	0(0.0)	0(0.0)	2(5.7)	0(0.0)
Musculoskeletal pain	0(0.0)	0(0.0)	2(5.7)	0(0.0)
Neuropathy peripheral	0(0.0)	0(0.0)	2(5.7)	0(0.0)
Paraesthesia	0(0.0)	0(0.0)	2(5.7)	0(0.0)
Rash maculo-papular	0(0.0)	0(0.0)	2(5.7)	0(0.0)
Chills	2(6.1)	0(0.0)	1(2.9)	0(0.0)
Hyperhidrosis	2(6.1)	0(0.0)	1(2.9)	0(0.0)
Epistaxis	2(6.1)	0(0.0)	0(0.0)	0(0.0)

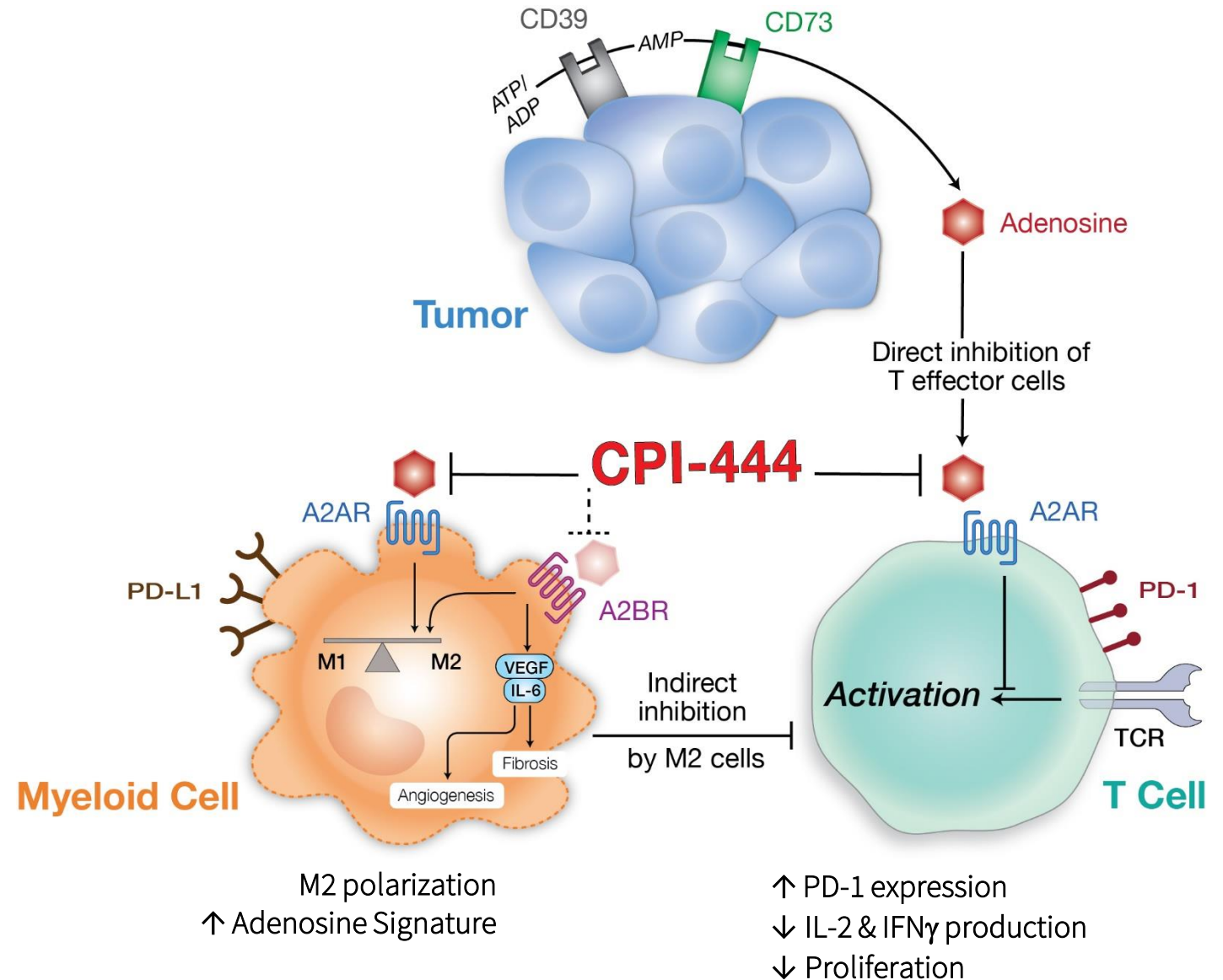
BIOMARKERS TO ASSESS IMMUNE FUNCTION AND CLINICAL ACTIVITY

Intra tumoral adenosine leads to:

- T cell suppression
- M2 polarization

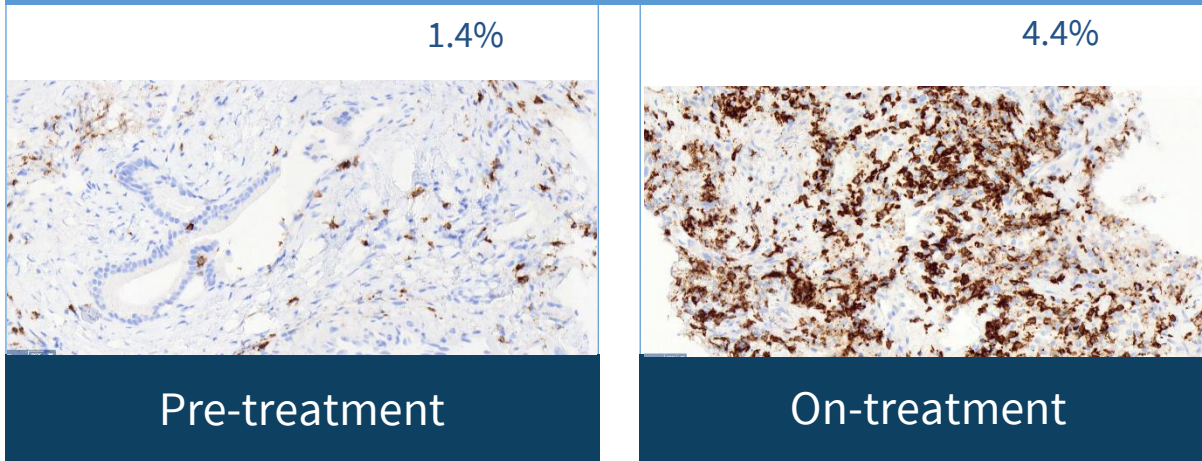
Hypothesis:

- CPI-444 treatment will enhance T cell responses
- Patients with M2 skewed tumors may be most sensitive to treatment

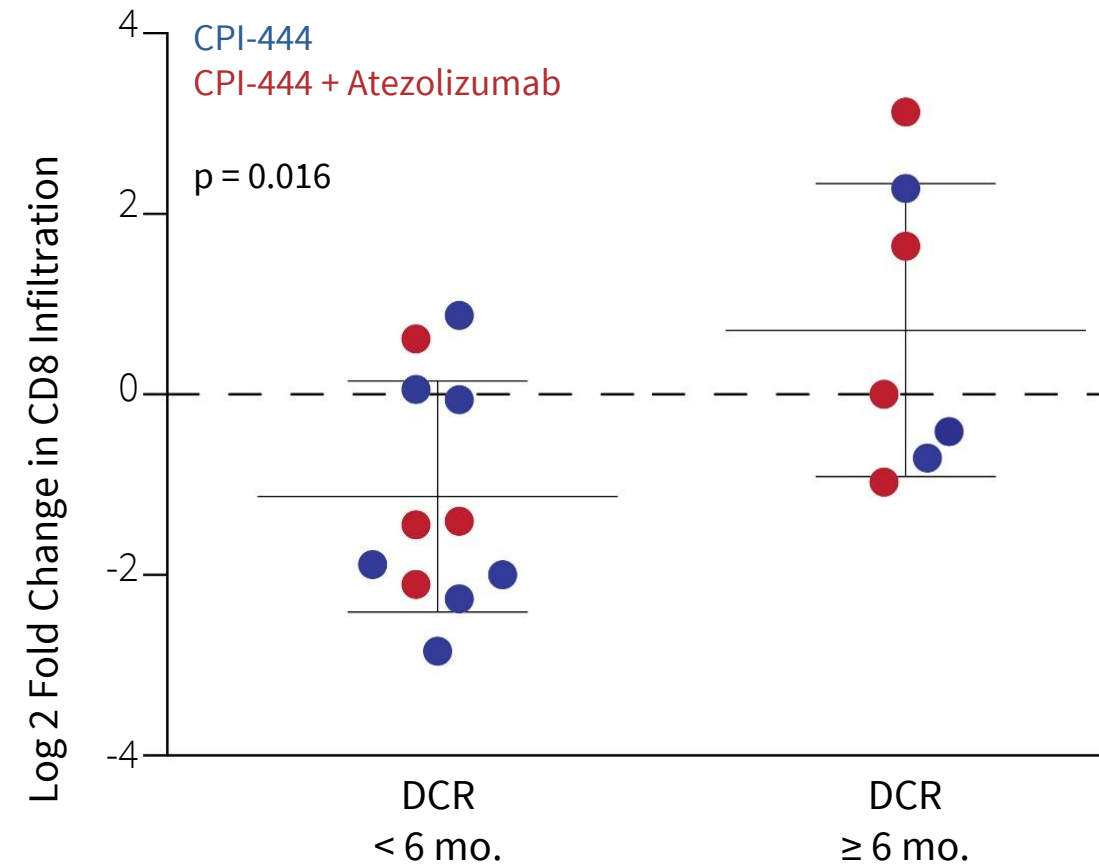
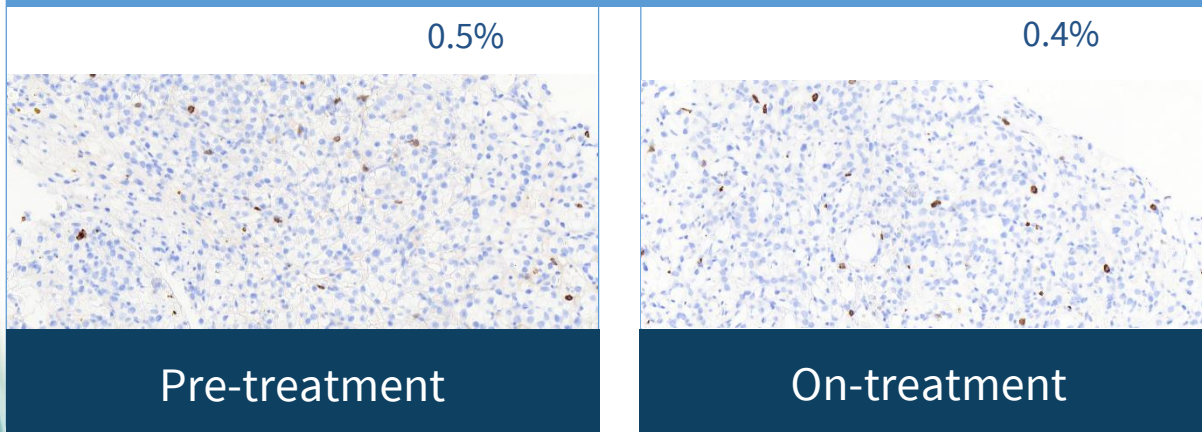


CD8⁺ T CELL INFILTRATION CORRELATES WITH DISEASE CONTROL

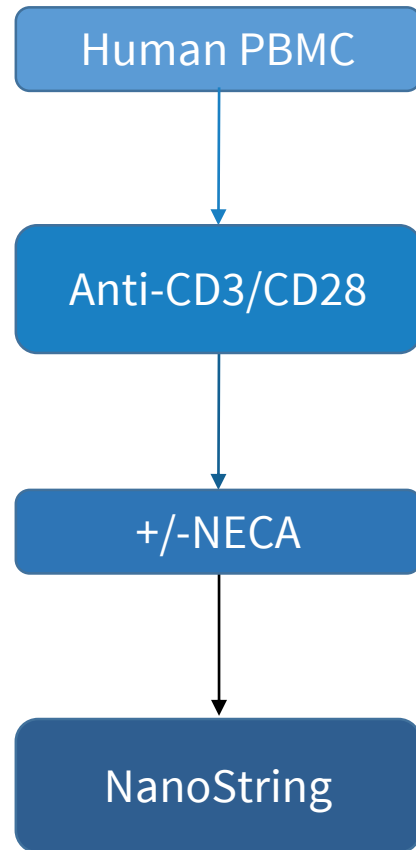
CD8 IHC in subject with disease control > 6 mo.



CD8 IHC in subject with disease control < 6 mo.



DEVELOPMENT OF AN ADENOSINE IMMUNE SIGNATURE

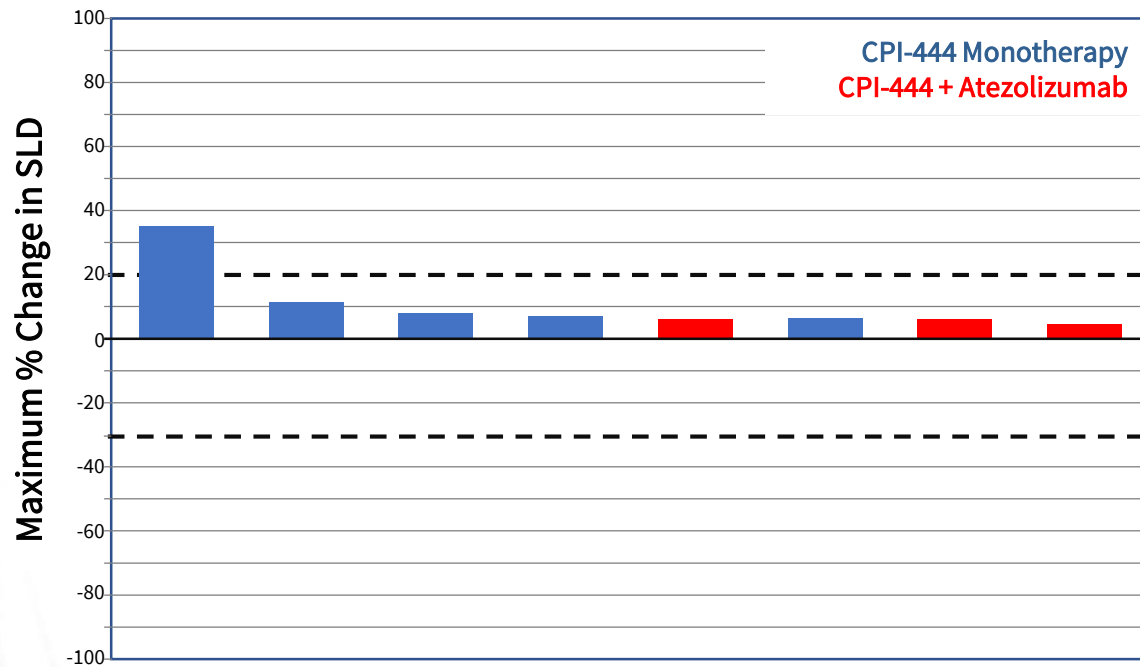


GENE AND FUNCTION	
CXCL1	Neutrophil chemo attractant
CXCL2	MIP2a: Macrophage inflammatory protein 2
CXCL3	Controls migration and adhesion of monocytes
CXCL5	Attracts and activates neutrophils
CXCL8	IL-8. Neutrophil chemotactic factor
THBS1	Multiple functions
IL-6	Multiple functions
CSF3	G-CSF. Master regulator of neutrophil development
IL-1 β	Inflammation
CCL2	MCP1: Monocyte chemoattractant protein 1
CCL3	MIP1a: Macrophage inflammatory protein 1
CCL7	MCP3: Monocyte chemotactic protein 3

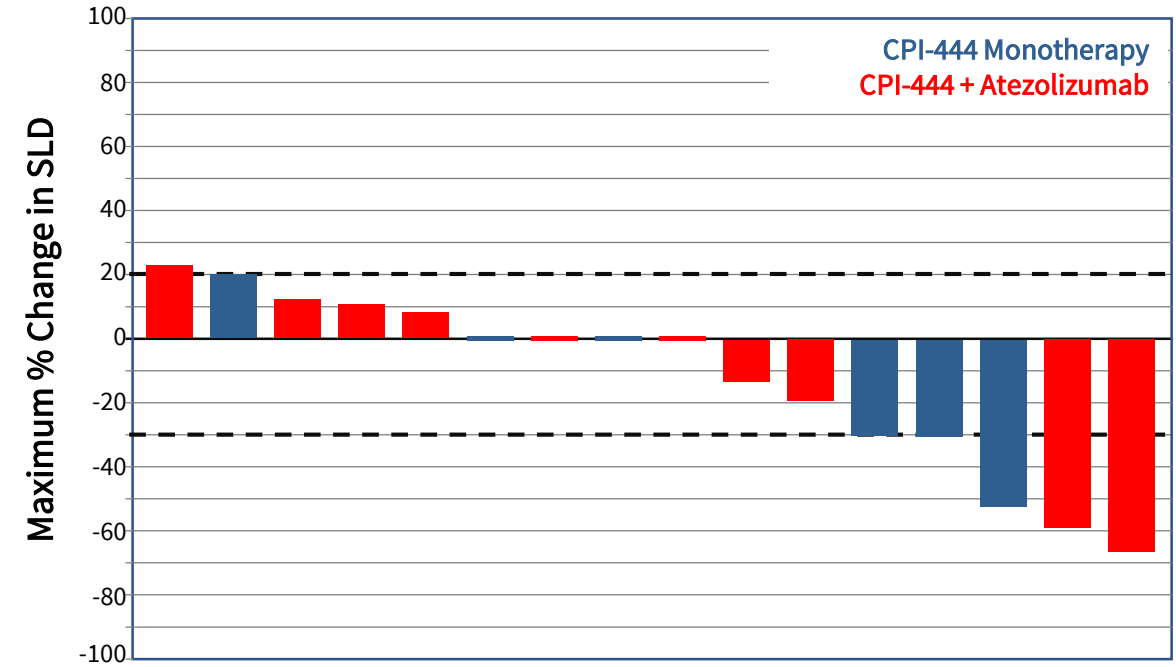
- Significant overlap with myeloid signature associated with anti-PD-L1 resistance (McDermott et al, Nature Medicine, 2018)

TUMOR EXPRESSION OF THE “ADENOSINE SIGNATURE” CORRELATES WITH RESPONSE

Adenosine Signature Low



Adenosine Signature High



Responders in Adenosine Signature High vs Low: $p < 0.008$

CONCLUSIONS

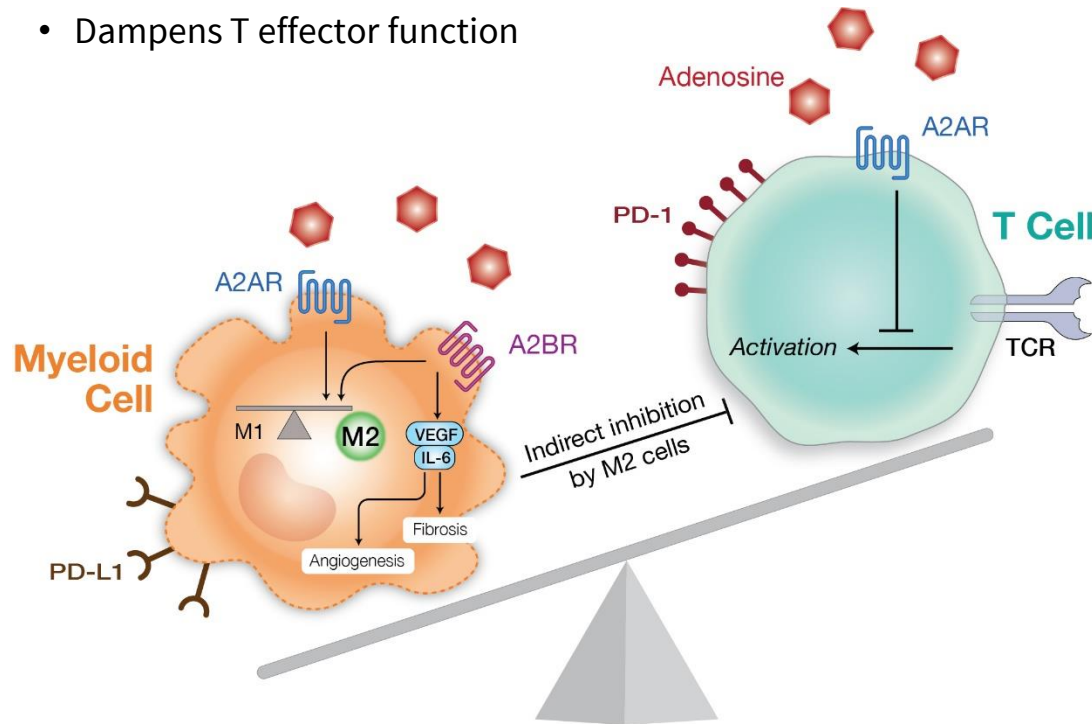
- CPI-444 is active as monotherapy and in combination with atezolizumab in
 - PD-(L)1 naive patients
 - PD-(L)1 resistant/refractory patients
- Combination therapy appears more active than monotherapy
- Combination efficacy results:
 - PR = 11%
 - DCR at 6 months = 35%
 - PFS = 5.9 months
 - OS = 88% at 20+ months
- Treatment-induced CD8+ T cell infiltration associates with an improved disease control rate
- The adenosine gene signature is associated with tumor response to therapy with CPI-444, and could be used as a biomarker for future patient selection
- CPI-444 is currently being evaluated in RCC patients in earlier lines of therapy

ROLE OF ADENOSINE IN THE TUMOR MICROENVIRONMENT

PRE-TREATMENT

Adenosine

- Promotes myeloid suppression
- Dampens T effector function



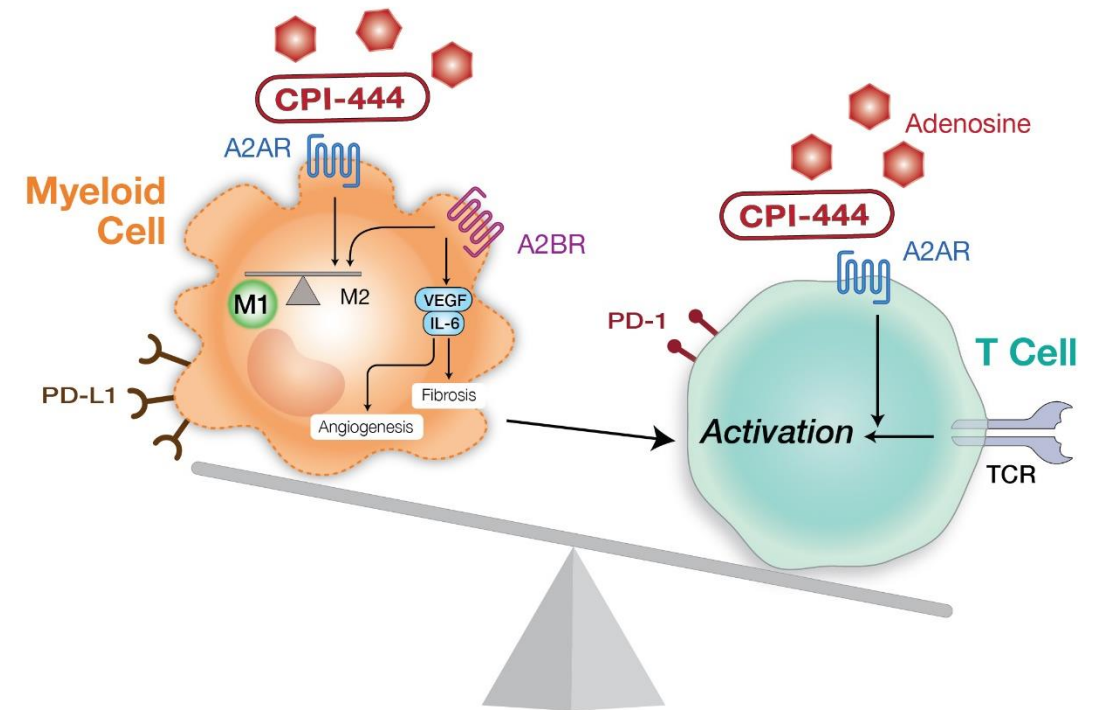
↑ Myeloid Suppression
↑ Adenosine Signature

↑ PD-1 expression
↓ IL-2 & IFN γ production
↓ Proliferation

Immunosuppressive

TREATED WITH CPI-444

- Inhibits adenosine and restores immune balance



↓ Myeloid Suppression
↓ Adenosine Signature

↓ PD-1 expression
↑ IL-2 & IFN γ production
↑ Proliferation

Immunostimulatory

ACKNOWLEDGEMENTS

Participating centers:

Beth Israel Deaconess Medical Center, British Columbia Cancer Agency, Cabrini Hospital, Carolina BioOncology Institute, Chris O'Brien Lifehouse, Cleveland Clinic, Columbia University Medical Center, Cross Cancer Institute, Dana Farber Cancer Institute, Emory University, Georgetown University, Indiana University, Johns Hopkins University, Juravinski Cancer Centre, Karmanos Cancer Center, Mary Crowley Cancer Research Centers, Massachusetts General Hospital, Medical College of Wisconsin, Memorial Sloan Kettering Cancer Center, Monash Health, Mount Sinai School of Medicine, Ohio State University, Ottawa Hospital Cancer Centre, Peter McCallum Cancer Center, Roswell Park, Royal Brisbane and Women's Hospital, Rush University, Stanford University, University of California at Los Angeles Medical Center, University of California at San Francisco Medical Center, University of Arizona Medical Center, University of Chicago Medical Center, University of Colorado Cancer Center, University of Nebraska, University of Pittsburgh, University of Washington, UT Southwestern, Washington University at Saint Louis, Yale University

Colleagues at Corvus Pharmaceuticals

The patients and their families