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Society for Immunotherapy of Cancer

Immunobiology and Clinical Activity of CPI-006, an Anti-CD73 Antibody with Immunomodulating Properties in a Phase 1/1b Trial in Advanced Cancers

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Disclosures

Jason J. Luke: University of Pittsburgh Medical Center, Pittsburgh

The following relationships exist related to this presentation:

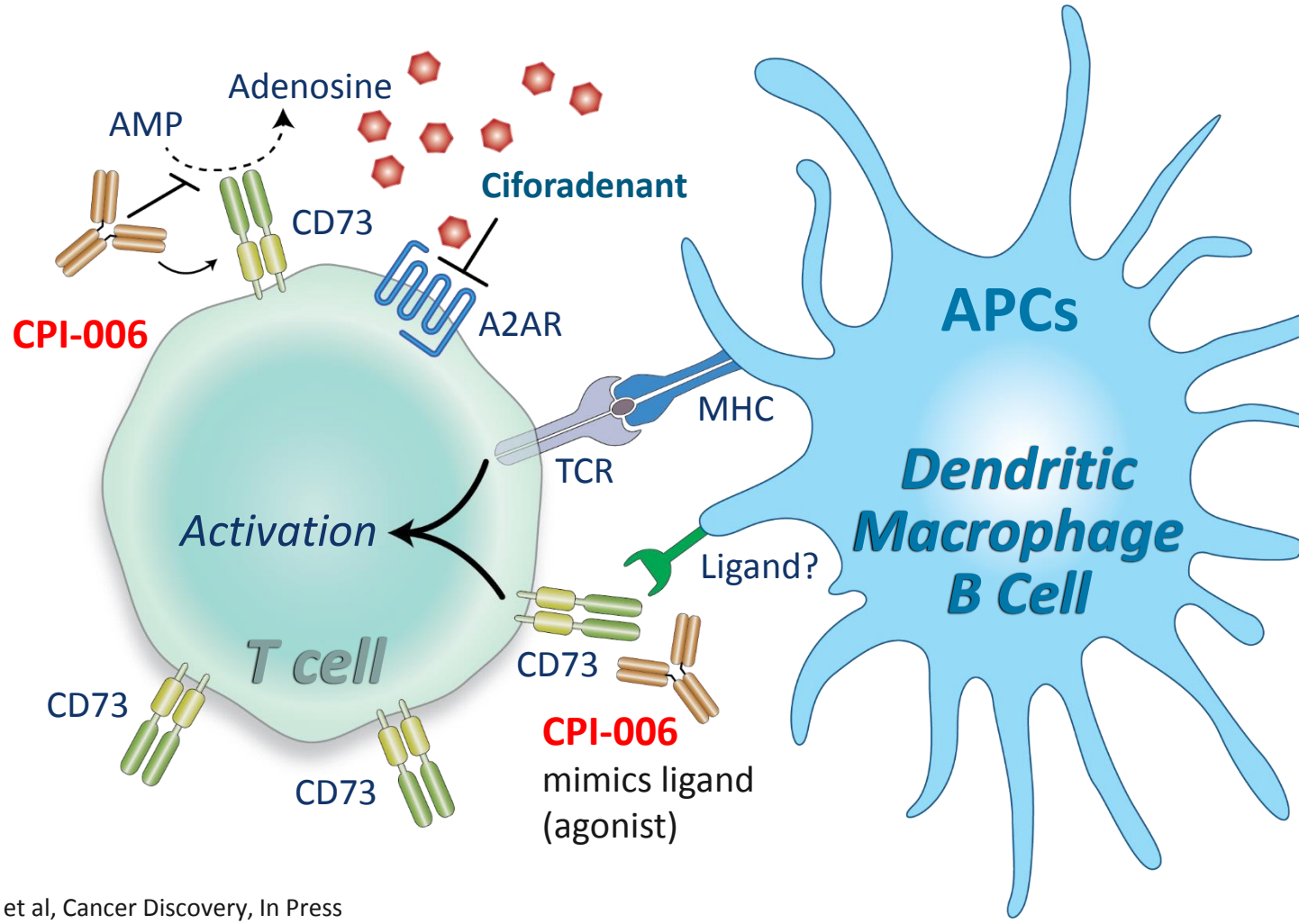
- **Data and Safety Monitoring Board:** TTC Oncology
- **Scientific Advisory Board:** 7 Hills, Actym, Alphamab Oncology, Mavu, Pyxis, Springbank, Tempest
- **Consultancy**: Abbvie, Akrevia, Array, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Compugen, EMD Serono, Ideaya, Immunocore, Incyte, Janssen, Leap, Merck, Mersana, Novartis, RefleXion, Silicon, Vividion
- **Research Support:** (all to institution for clinical trials unless noted) AbbVie, Agios (IIT), Array (IIT), Astellas, Boston Biomedical, Bristol-Myers Squibb, CheckMate (SRA), Compugen, Corvus, EMD Serono, Evelo (SRA), Five Prime, FLX Bio, Genentech, Immatics, Immunocore, Incyte, Leap, MedImmune, Macrogenics, Necktar, Novartis, Palleon (SRA), Merck, Springbank, Tesaro, Tizona, Xencor
- **Travel**: Akrevia, AstraZeneca, Bayer, Bristol-Myers Squibb, EMD Serono, Immunocore, Incyte, Janssen, Merck, Mersana, Novartis, RefleXion
- **Patents**: (both provisional) Serial #15/612,657 (Cancer Immunotherapy), PCT/US18/36052 (Microbiome Biomarkers for Anti-PD-1/PD-L1 Responsiveness: Diagnostic, Prognostic and Therapeutic Uses Thereof)

Corvus Pharmaceutical Inc. is the sponsor of this study.

Background

CPI-006 is an Anti-CD73 with Adenosine Independent Immunomodulatory Properties

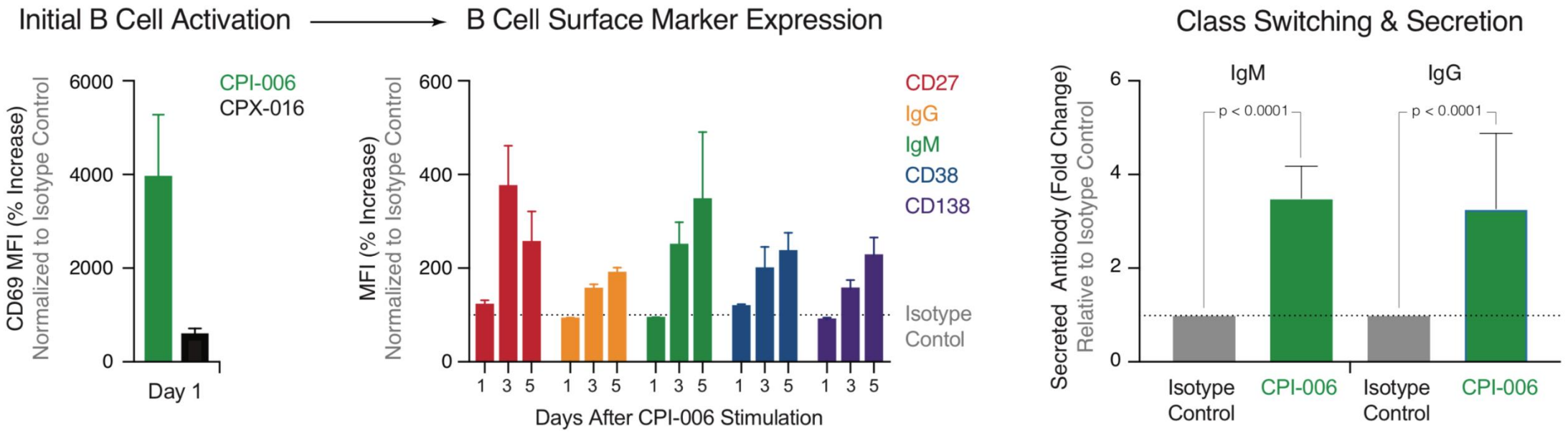
- CD73 is an ectoenzyme present on many tissues including subsets of T and B cells
  - Converts AMP to adenosine
  - Functions in lymphocyte adhesion, migration and activation[1]
- CPI-006 is a humanized IgG1 Fcγ receptor deficient anti-CD73 with unique properties[2]
  - Blocks catalytic activity
  - Has agonistic immunomodulatory activity on CD73 positive cells that are **adenosine independent**
  - Increases expression of CD69, HLA-DR, etc. on APC
- Early results from Ph1 dose escalation trial demonstrate lymphocyte activation and effects on trafficking[2]
- Ciforadenant (CPI-444) is an adenosine 2A receptor (A2AR) antagonist with reported anti-tumor activity in mCRPC, RCC and NSCLC[3]
  - Adenosine gene signature in tumor correlates with response in RCC

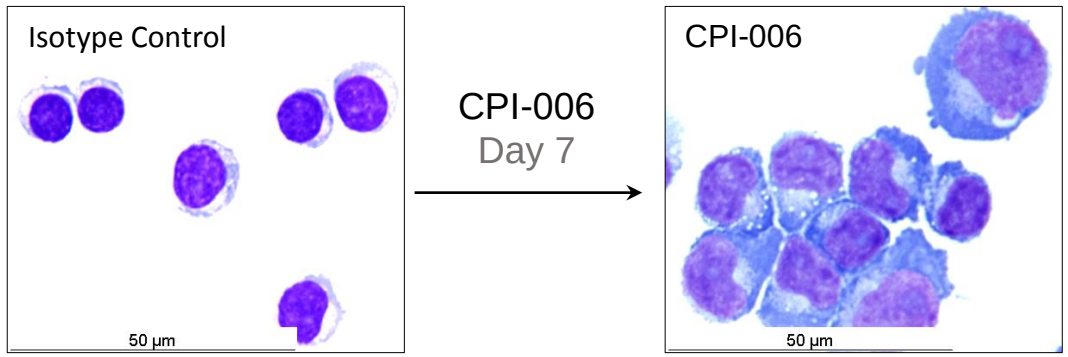


[1]Resta & Thompson, Cell Signaling, 1997 [2]Luke, ASCO Annual Meeting, 2019 [3]Fong et al, Cancer Discovery, In Press

CPI-006 is an Anti-CD73 with Unique Properties

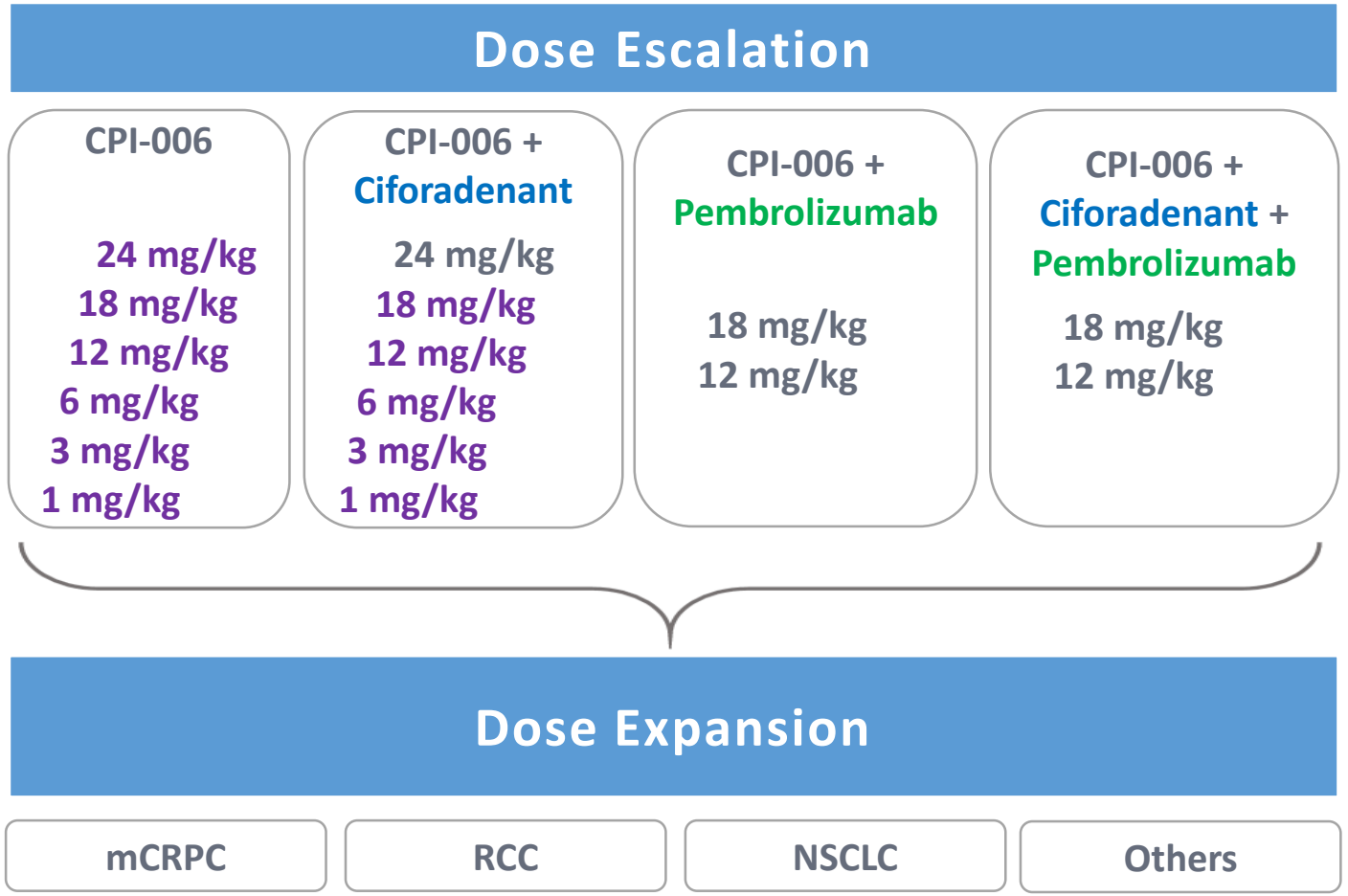
CPI-006 induces B cell differentiation: isotype switching and immunoglobulin secretion in vitro





- CPI-006 activates B cells, resulting in morphological and surface marker changes consistent with B cell differentiation and isotype class switching
- Comparison to adenosine blocking anti-CD73 antibody (CPX-016) demonstrates unique CPI-006 property

CPI-006-001 Clinical Trial Design



Doses explored to date & planned doses

Design
- Phase 1/1b dose escalation/dose expansion in disease specific cohorts
- CPI-006 every 3 weeks; fixed dose of ciforadenant

Eligibility
- Cancers progressed on 1-5 prior therapies
- CD73 expression: required in expansion, not in dose escalation
- Adenosine gene signature not used to select patients

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

Biomarker Assessments
- Tumor markers, cytokines, etc.

See Poster P434, Saturday Nov 9th

Patient Characteristics

Total Patients N=40	CPI-006 (N = 24)	CPI-006 + Ciforadenant (N=16)
Age (yrs), median (range)	62 (46, 78)	67 (36, 86)
Gender, male N (%)	18 (75)	12 (75)
No. of prior therapies, median (range)	4 (1, 6)	4 (2, 7)
Histologies	**N**	**N**
Renal Cell Cancer	2	4
Non-small cell lung cancer	2	1
Prostate Cancer	5	1
Colorectal Cancer	7	5
Head and Neck Cancer	3	2
Pancreatic Cancer	3	3
Sarcoma	1	0
Bladder Cancer	1	0

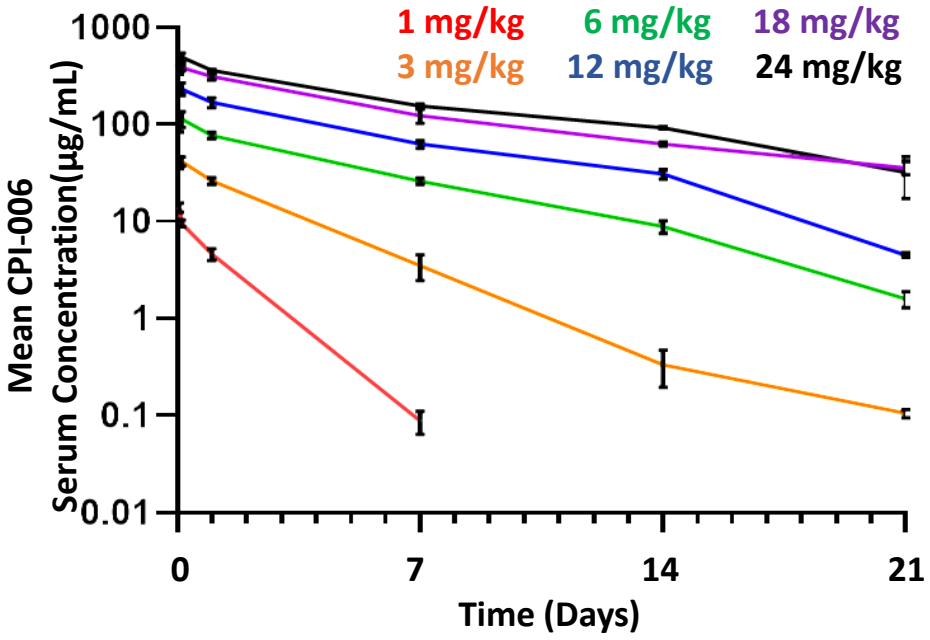
Adverse Events

Adverse Events N (%)	CPI-006 Monotherapy (N=24)		CPI-006 + Ciforadenant (N= 16)	
	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4
Patients with any TEAE	18 (75.0)	4 (16.7)	12 (75.0)	2 (12.5)
Anemia	1 (4.2)	1 (4.2)	2 (12.5)	1 (6.3)
Lymphopenia	2 (8.3)	1 (4.2)	0 (0.0)	0 (0.0)
Colitis	0 (0.0)	0 (0.0)	1 (6.3)	1 (6.3)
Diarrhea	1 (4.2)	0 (0.0)	3 (18.8)	1 (6.3)
Nausea	4 (16.7)	0 (0.0)	2 (12.5)	0 (0.0)
Vomiting	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	11 (45.8)	0 (0.0)	3 (18.8)	0 (0.0)
Fatigue	3 (12.5)	0 (0.0)	3 (18.8)	0 (0.0)
Pyrexia	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Infusion related reaction	3 (12.5)	0 (0.0)	0 (0.0)	0 (0.0)
Liver enzymes increased (AST & ALP)	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
Blood creatinine increased	0 (0.0)	0 (0.0)	2 (12.5)	0 (0.0)
WBC decreased	1 (4.2)	0 (0.0)	3 (18.8)	0 (0.0)
Decreased appetite	1 (4.2)	0 (0.0)	1 (6.3)	0 (0.0)
Hyponatremia	1 (4.2)	1 (4.2)	0 (0.0)	0 (0.0)
Tumor pain	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Headache	2 (8.3)	0 (0.0)	1 (6.3)	0 (0.0)
Pruritus	2 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	1 (4.2)	0 (0.0)	2 (12.5)	0 (0.0)

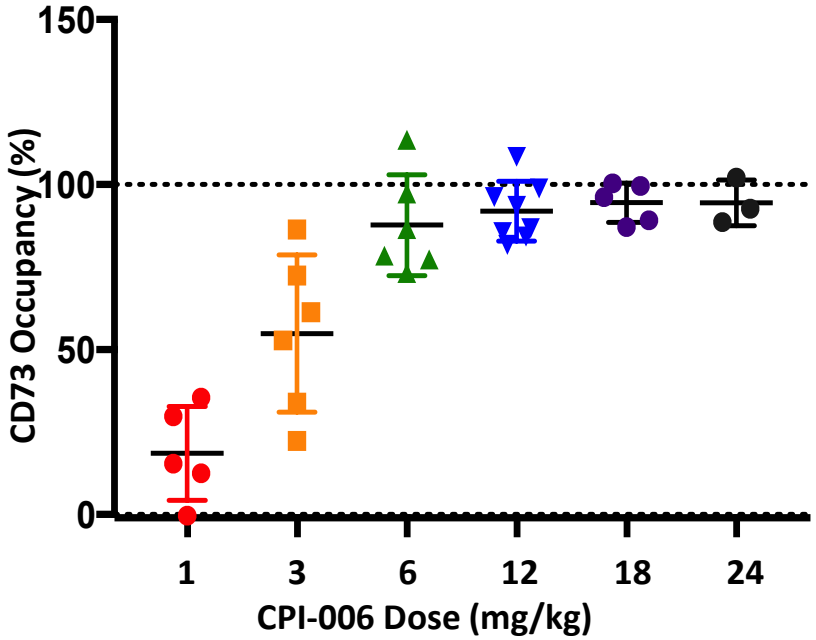
Treatment related adverse events: Any grade 3 or 4 events, or 2 or more all grades

Pharmacokinetics and Receptor Occupancy

Serum Pharmacokinetics



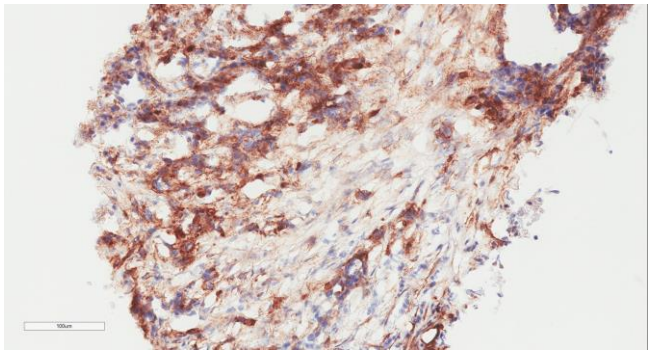
Target Occupancy on Peripheral B Cells



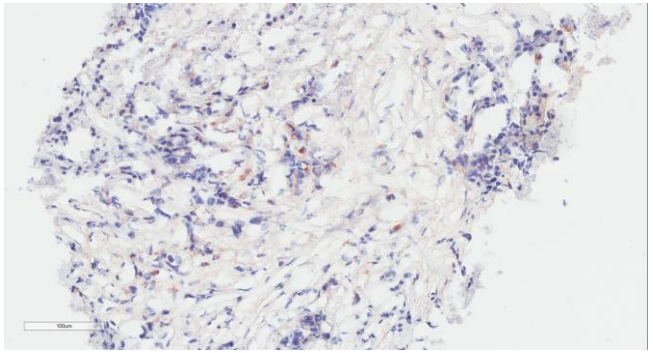
Tissue Occupancy

(18 mg/kg CPI-006)

CD73 with non-cross blocking antibody (total CD73)

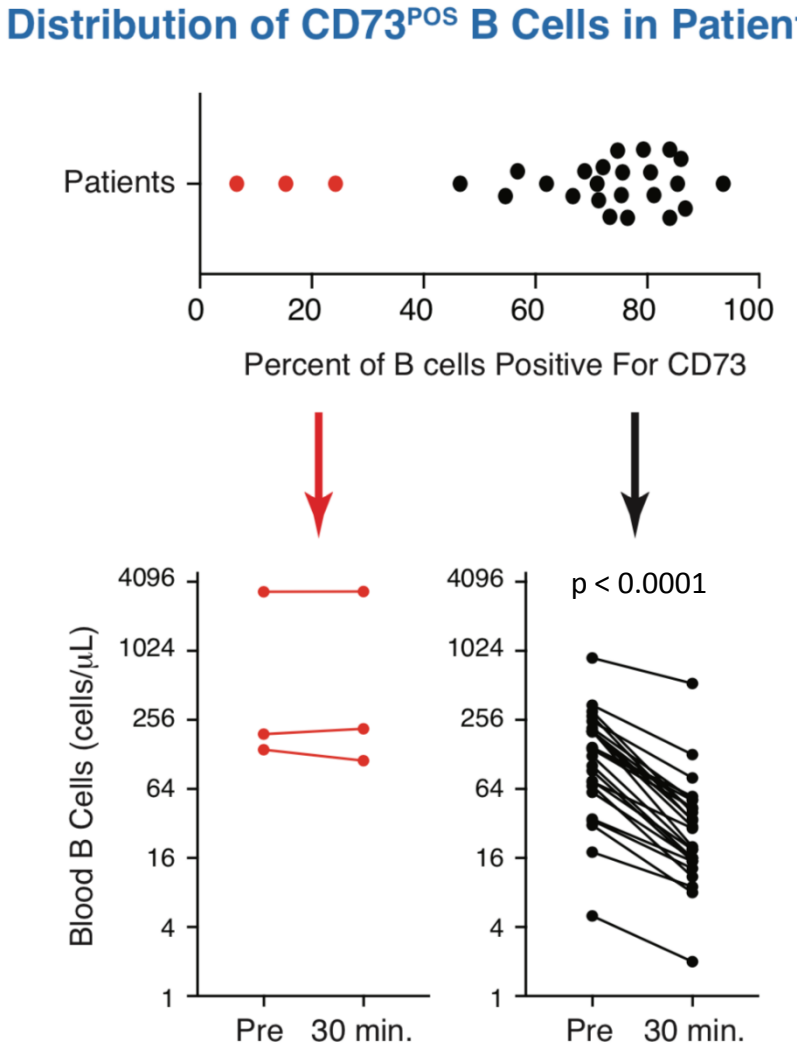


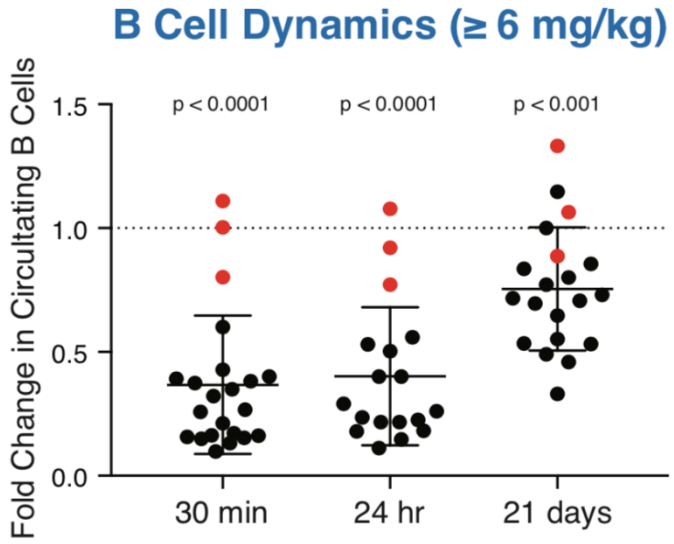
CD73 with CPI-006 demonstrates sites occupied

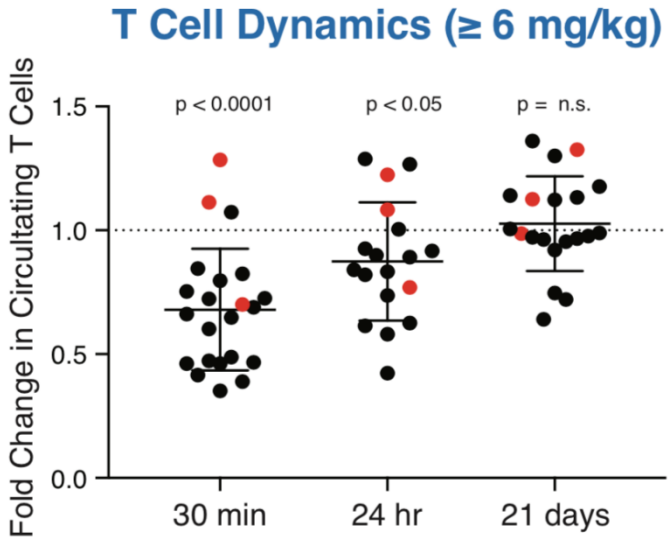


- Sustained CD73 occupancy of peripheral blood at ≥ 6 mg/kg
- Full tumor occupancy observed at ≥ 18 mg/kg

Treatment Induces Rapid Changes in Blood B and T Cells



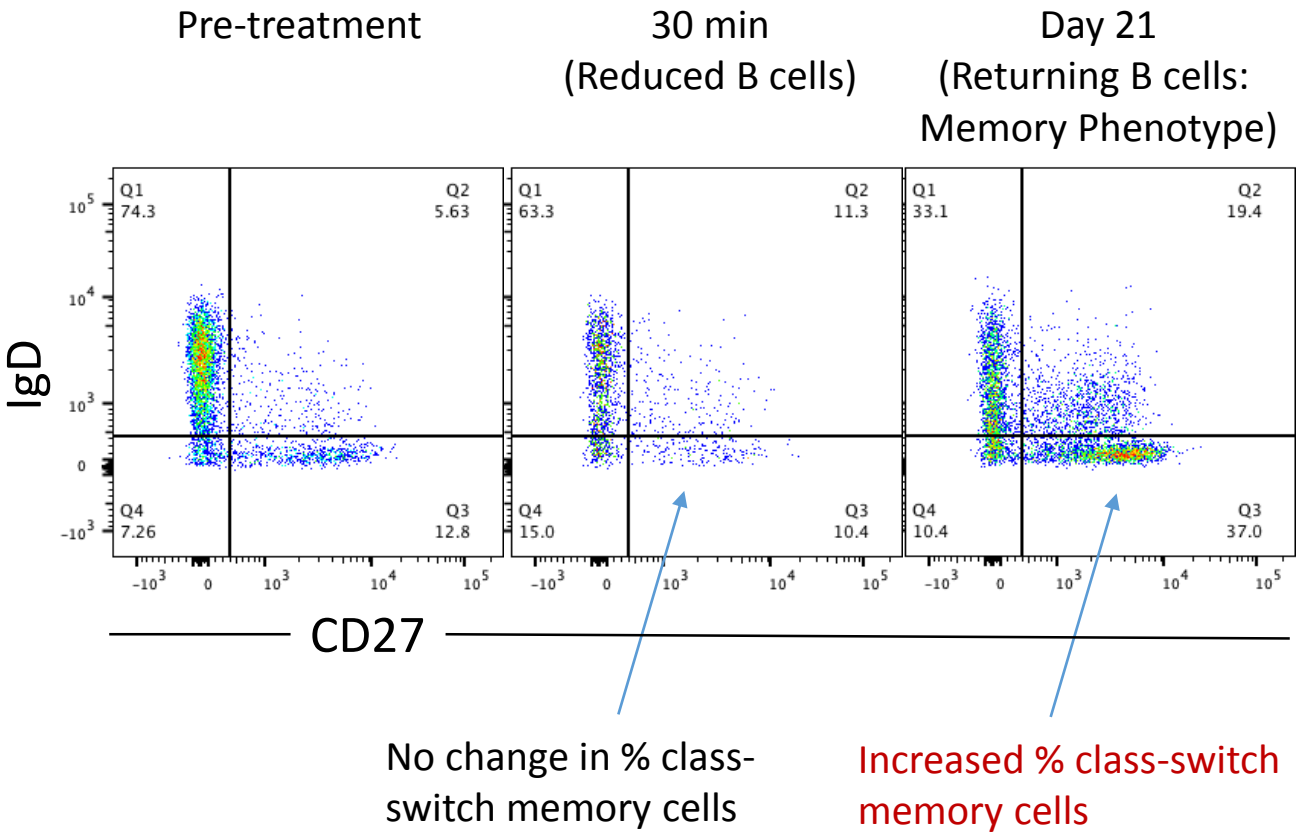




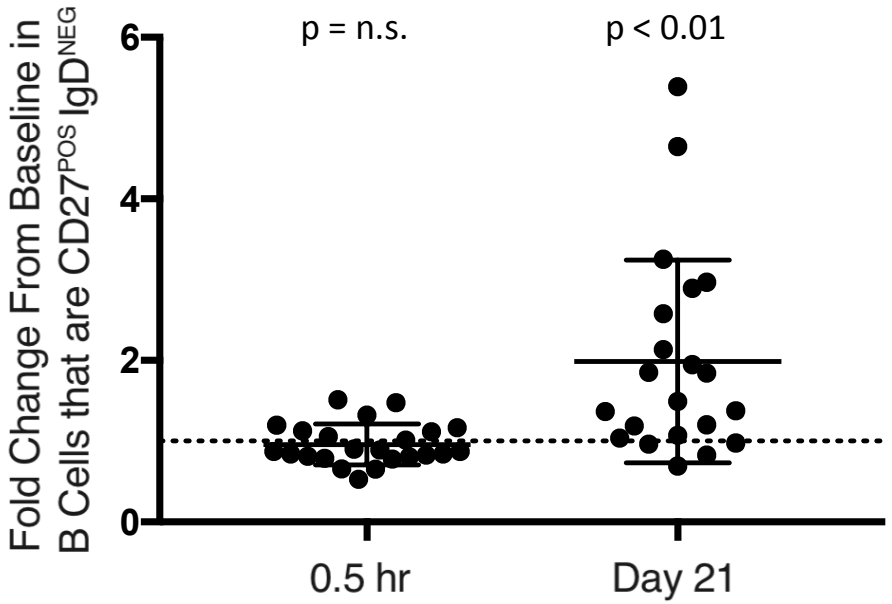
- Changes in B cells (but not T cells) appear to be CD73 expression dependent
- B cell numbers partially return by 21 days; T cells fully return

Increase in Memory B Cells in Returning Lymphocytes

Peripheral Blood Gated on CD19+ and CD20+ B Cells



Increased Memory B Cells at Day 21

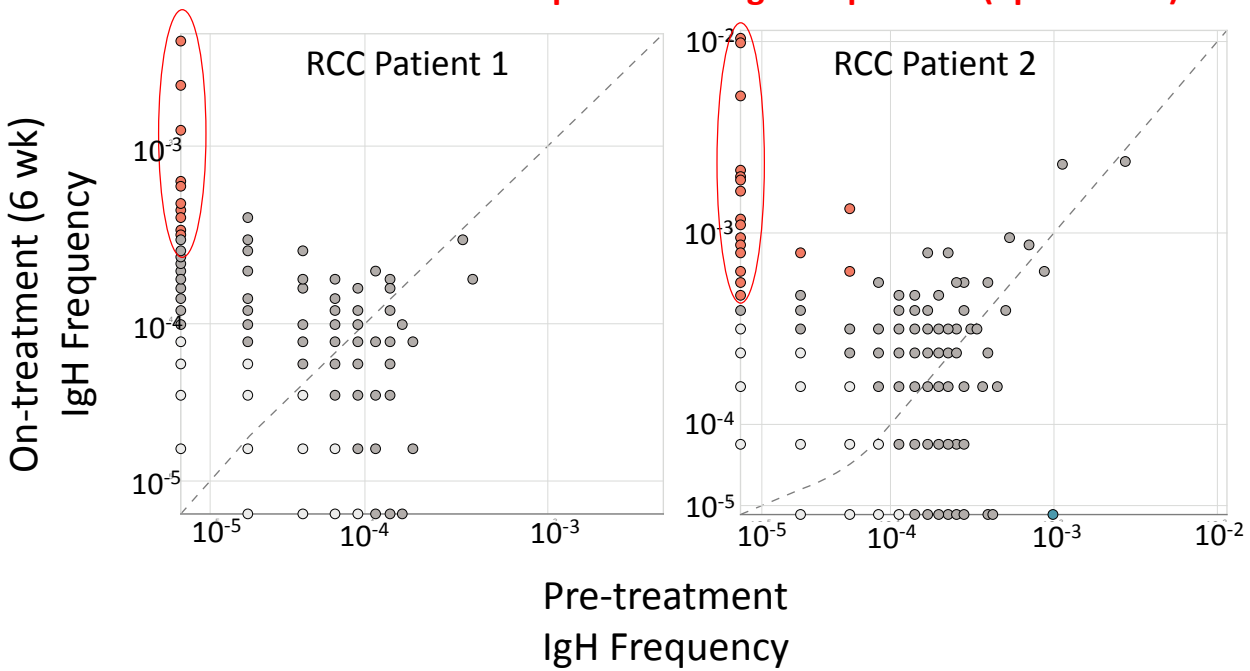


- At 0.5 hours no change in proportion of naïve and memory B cells; returning cells have a greater proportion of memory B cells
- These findings are consistent with a humoral adaptive response

Significant Expansion of New B and T cell Clones

Differential Abundance Plots of B cell Clonal Expansion

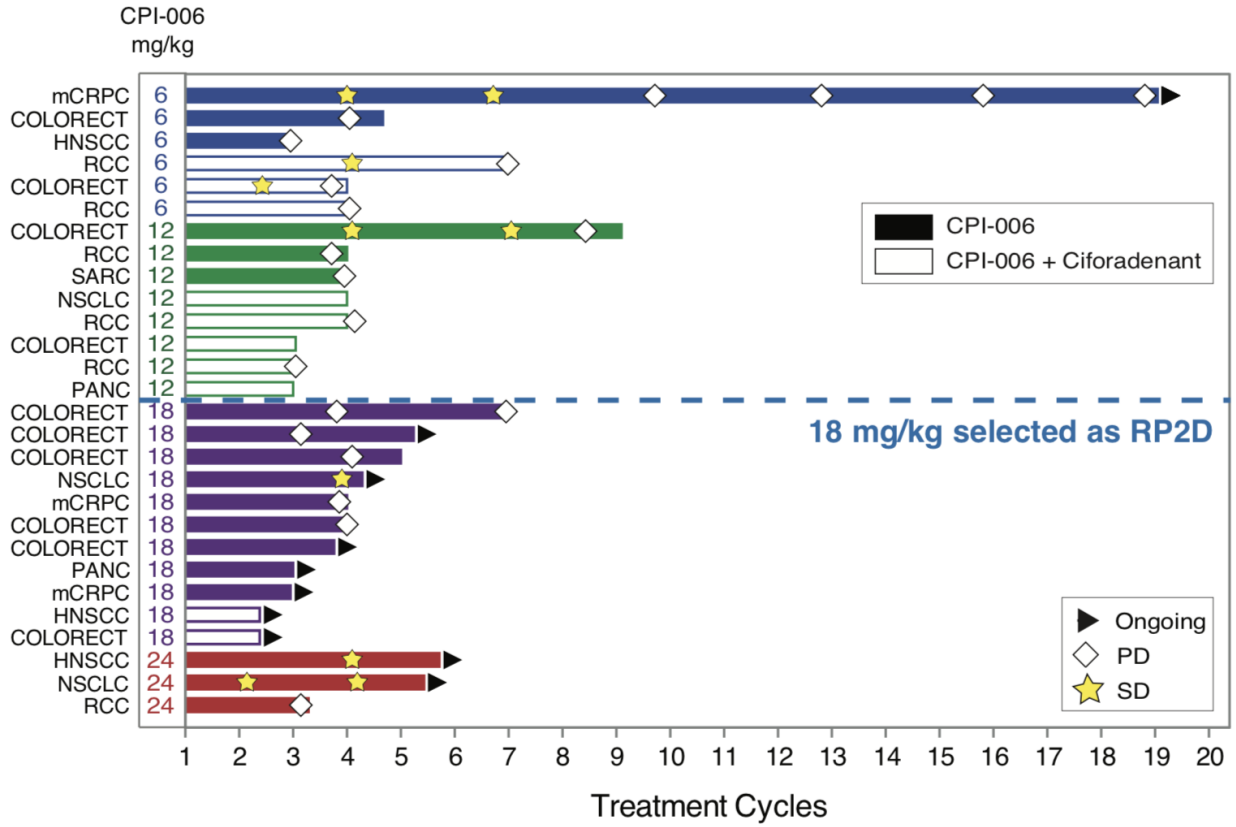
New B cell clones on treatment present at high frequencies (up to 1:100)

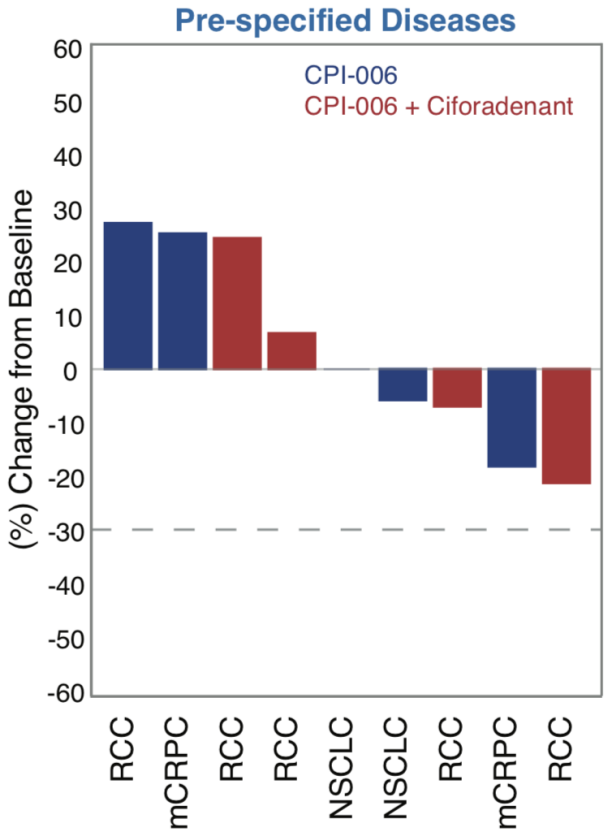


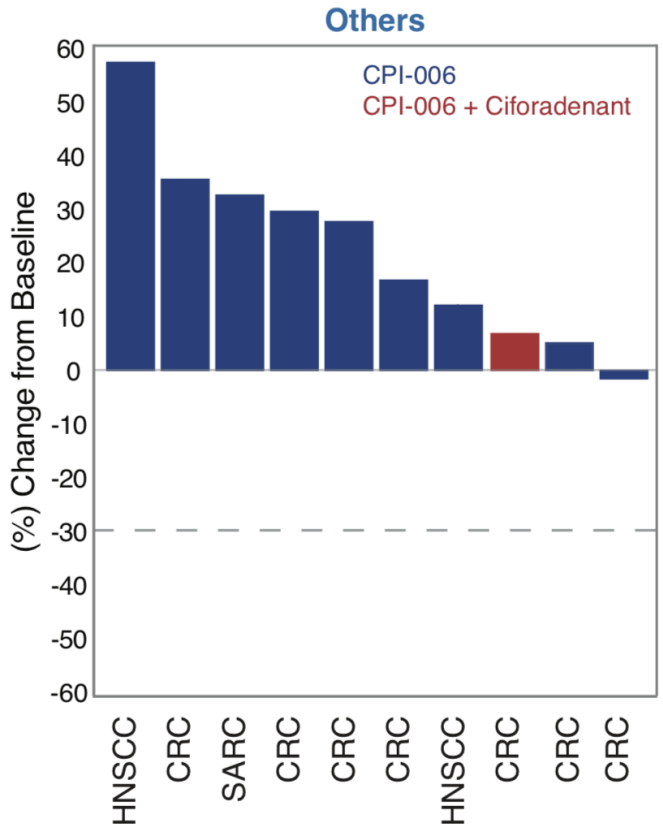
Cohort	Number of Patients with B Cell Expansion	Number of Patients with T Cell Expansion
CPI-006 monotherapy	5 of 7	2 of 4
CPI-006 + ciforadenant	2 of 4	1 of 4
Total	7 of 11	3 of 8

- Generation of prevalent B and T cell clones on therapy
- Consistent with antigen-driven clonal selection
- No change in serum immunoglobulins observed

Response Assessments



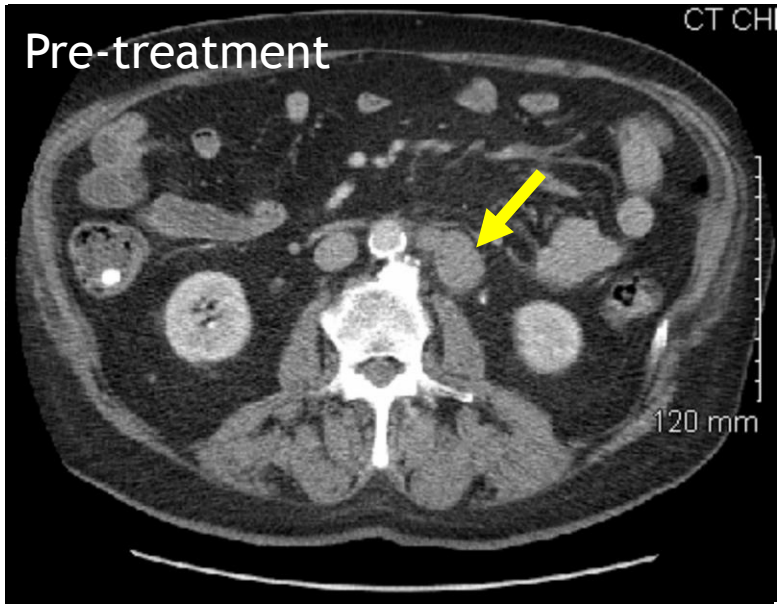


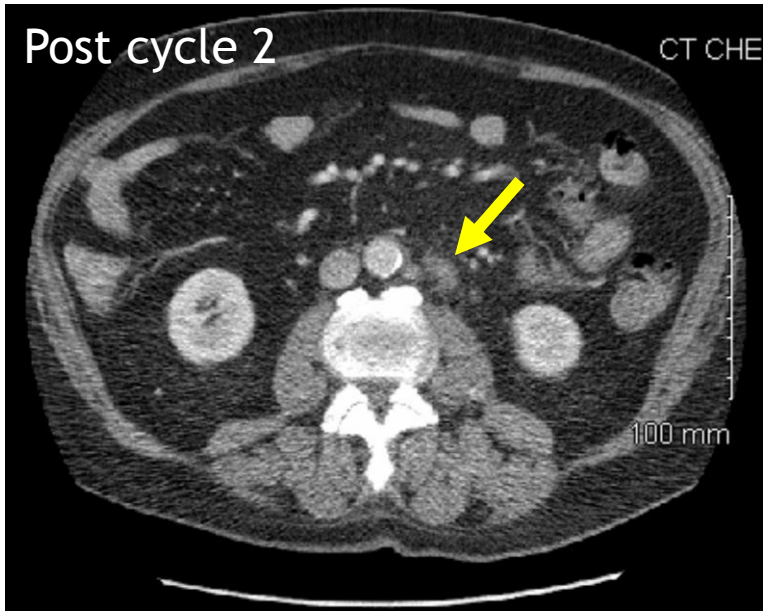


- Response assessments in patients receiving ≥ 6 mg/kg dose

Tumor Reduction in a Prostate Cancer Patient

CPI-006 monotherapy





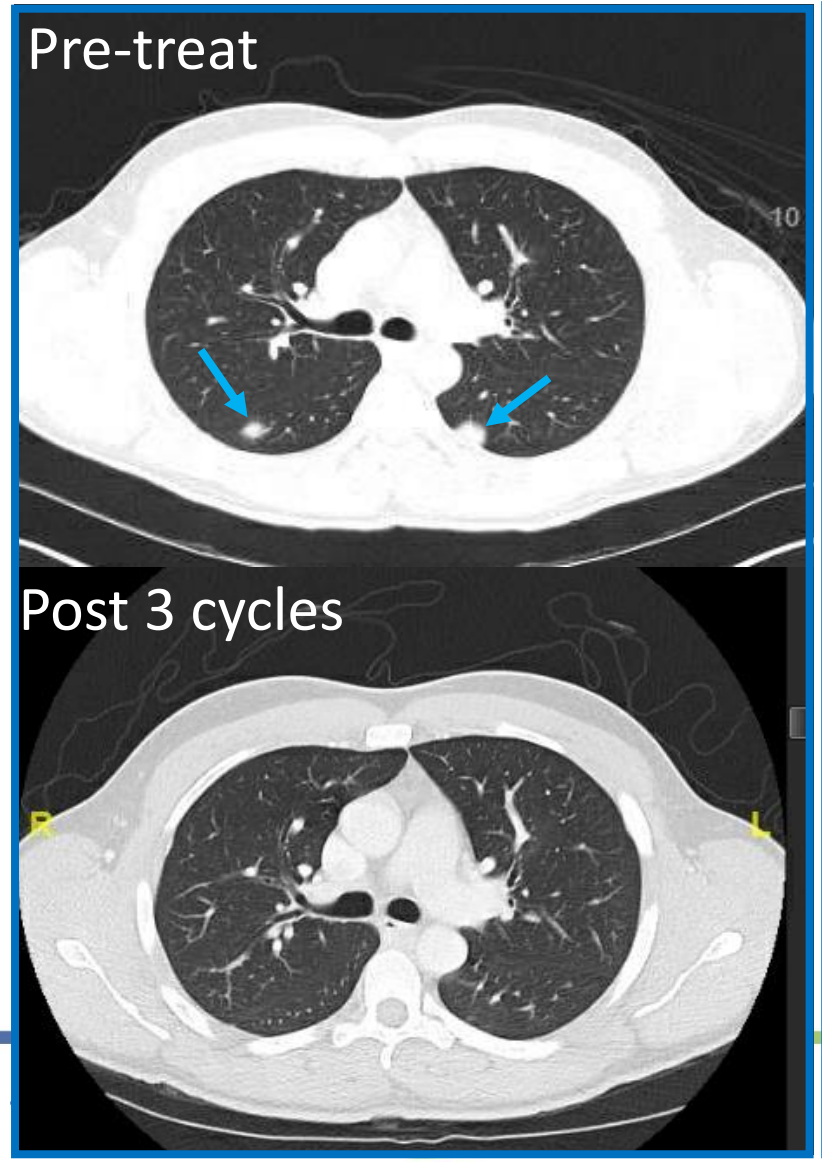
- 72 year old man with widely metastatic prostate cancer; previous therapies include leuprolide/bicalutamide, abiraterone, enzalutamide and docetaxel

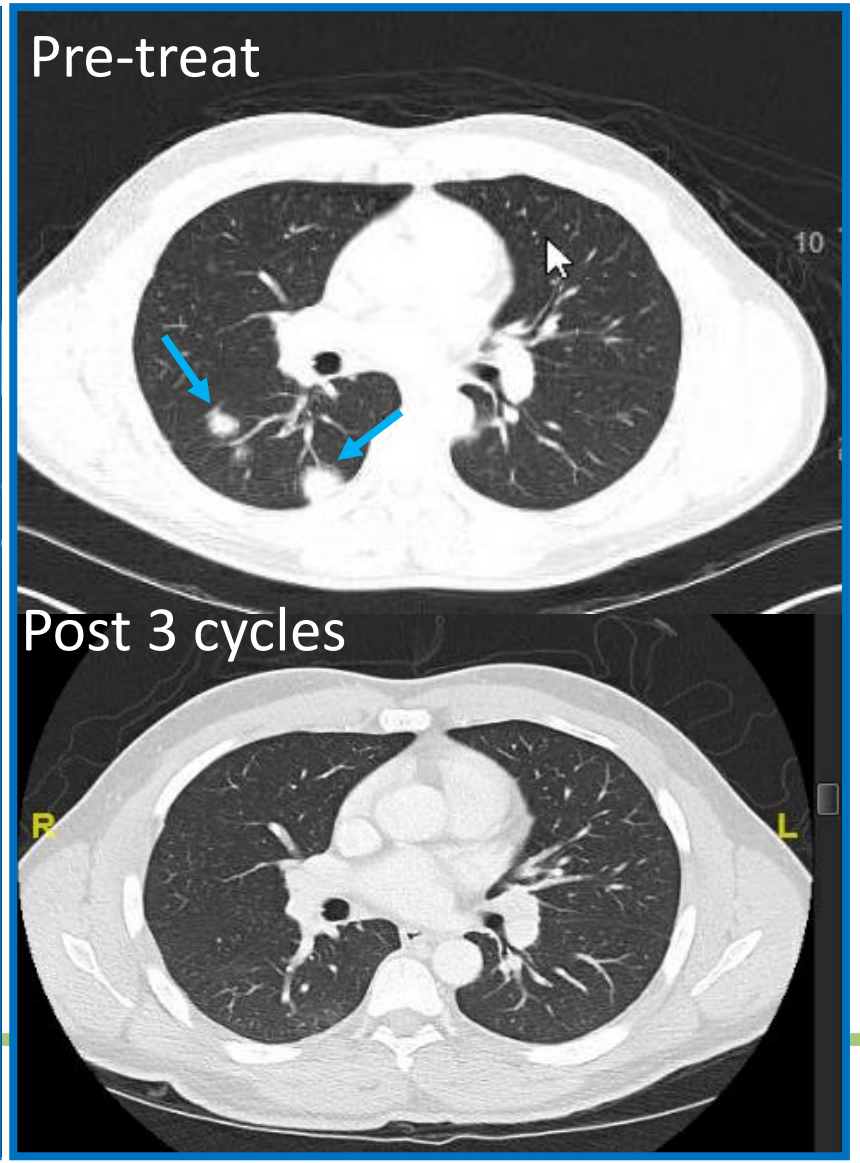
- Decrease in target lesion in patient receiving 6 mg/kg monotherapy, treatment ongoing through 19 cycles

Responding Pulmonary Metastases in RCC Patient

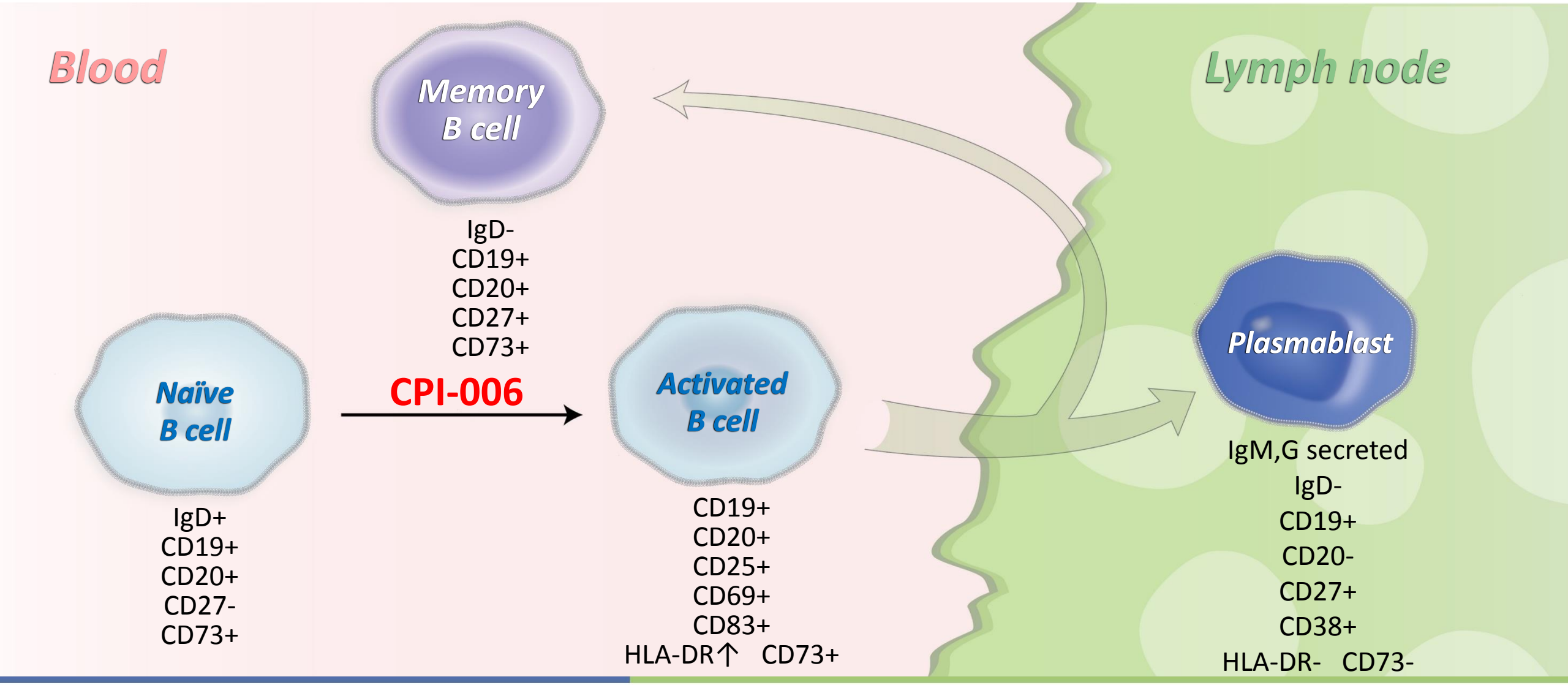
CPI-006 6 mg/kg plus ciforadenant combination

- 36 year old male presented in 2015 with renal mass and bone metastases
- Failed TKI, nivo and nivo/ipi with increase pulmonary mets
- Regression of multiple biopsy proven pulmonary metastases on CPI-006 + ciforadenant





Model for CPI-006 Effects on Cells



Conclusions

- CPI-006 has novel immunomodulatory activities:
  - Induces differentiation of B cells, class switching, secretion of immunoglobulin (in vitro), and generation of memory B cells
  - Increases expression of CD69 and other markers consistent with increased antigen presentation by APCs
- The optimum and well tolerated dose of CPI-006 is 18 mg/kg
- Treatment with CPI-006 induces redistribution of T and B cells with an increase in returning memory B cells and expansion of new B cell clones
- Changes in lymphocytes are consistent with induction of adaptive humoral immunity
- Tumor regression observed in RCC and prostate
- *Treatment with CPI-006 may represent an opportunity to identify novel anti-tumor antibodies*

Acknowledgements

- **The patients and their families**
- **Participating Centers and Investigators**: *Dana Farber Cancer Institute, Medical College of Wisconsin, Monash Health, Mount Sinai Icahn School of Medicine, University of California San Francisco Medical Center, University of Chicago, University of Miami, University of Oklahoma, Yale University, Carolina BioOncology Institute, City of Hope, Mary Crowley Cancer Research, Roswell Park Cancer Institute, Sarah Cannon Research Institute*
- **Colleagues at Corvus**