Abstract #: 3004

Safety and clinical activity of adenosine A2a receptor (A2aR) antagonist, CPI-444, in anti-PD1/PDL1 treatment-refractory renal cell (RCC) and non-small cell lung cancer (NSCLC) patients

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Forward Looking Statements

This presentation contains forward-looking statements, including statements related to the potential safety and efficacy of CPI-444, both as a single agent and in combination with anti-PD-1 and anti-PD-L1, and the Company's ability to develop and advance product candidates into and successfully complete clinical trials, including the Company's Phase 1/1b clinical trial of CPI-444. 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 Quarterly Report on Form 10-Q for the three months ended March 31, 2017, filed with the Securities and Exchange Commission on May 4, 2017, 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 evidence of efficacy and safety for CPI-444 during its Phase 1/1b clinical trial; the results of early clinical trials may not be predictive of future results; the unpredictability of the regulatory process; and regulatory developments in the United States and foreign countries. 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. Additional information may be available in press releases or other public announcements and public filings made after the date of this presentation.

This presentation concerns products that have not yet been approved for marketing by the U.S. Food and Drug Administration ("FDA"). No representation is made as to their safety or effectiveness for the purposes of which they are being investigated.

Safety and clinical activity of adenosine A2a receptor (A2aR) antagonist, CPI-444 in anti-PD(L)1 treatment-refractory renal cell (RCC) and non-small cell lung cancer (NSCLC) patients

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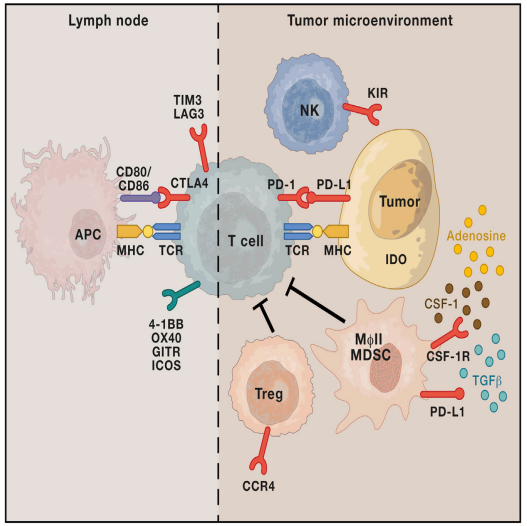
Background

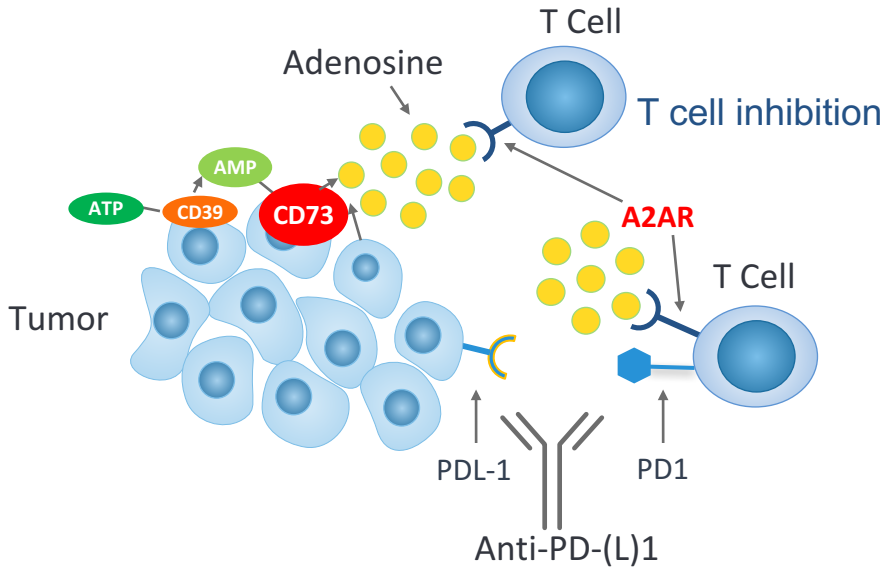
- Anti-PD-(L)1 antibodies are approved for treatment of RCC and NSCLC but a small proportion of patients benefit.
- No approved agents overcome resistance to anti-PD-(L)1 with few reporting benefit in PD-1 resistant/ refractory setting.
- Converting tumors devoid of T cell infiltration (“cold tumors”) into T cell inflamed tumors (“hot tumors”) could improve response to immunotherapies.
- Adenosine is a mediator of immunosuppression within the tumor microenvironment.
- CPI-444 is an oral small molecule antagonist of the adenosine A2A receptor (A2AR) (Emens, AACR 2017).



(Sharma et al. Cell, 2017)

Adenosine Suppresses Immunity and is a Potential Mechanism of Resistance to PD-(L)1 Therapy

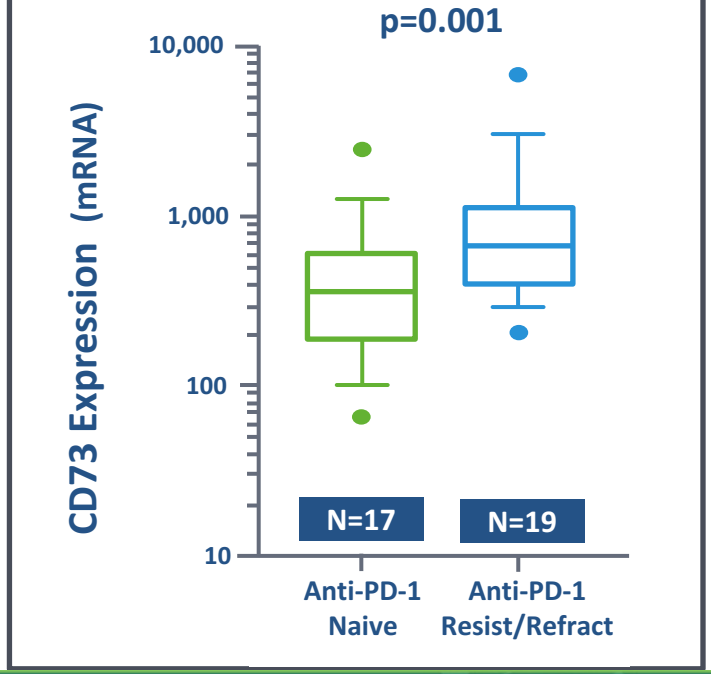
Adenosine in the tumor microenvironment



Tumors can generate adenosine in response to anti-PD-(L)1

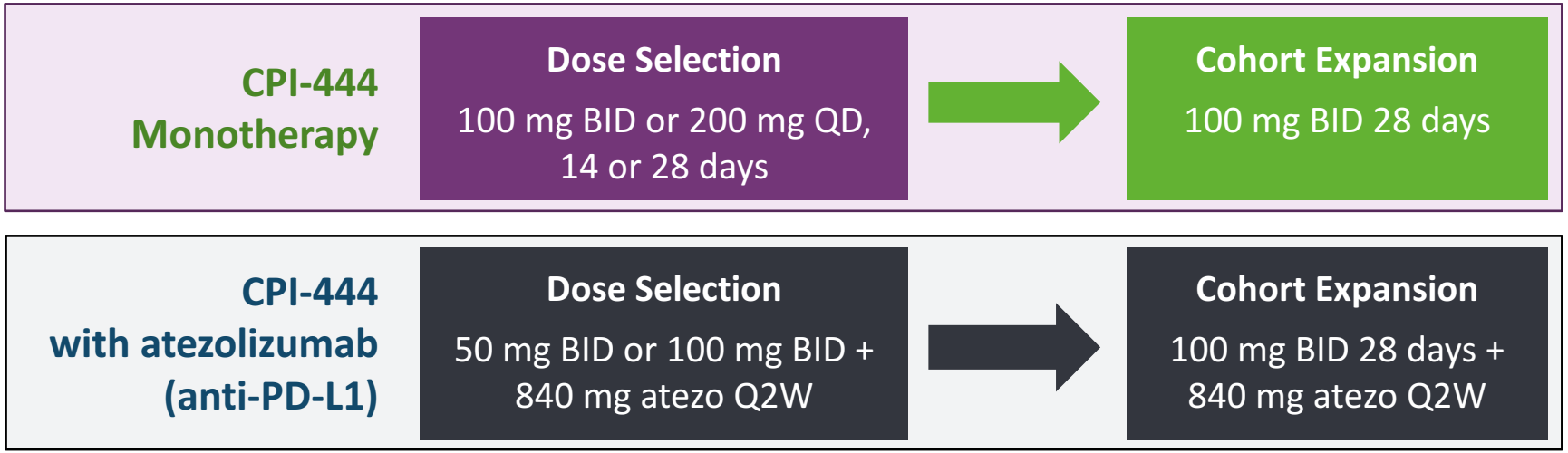
(Beavis et al, Can Immunol Res 2015)

CD73 expression in baseline tumor biopsies from the CPI-444 phase 1 trial



Phase 1/1b Clinical Study with Oral Drug CPI-444

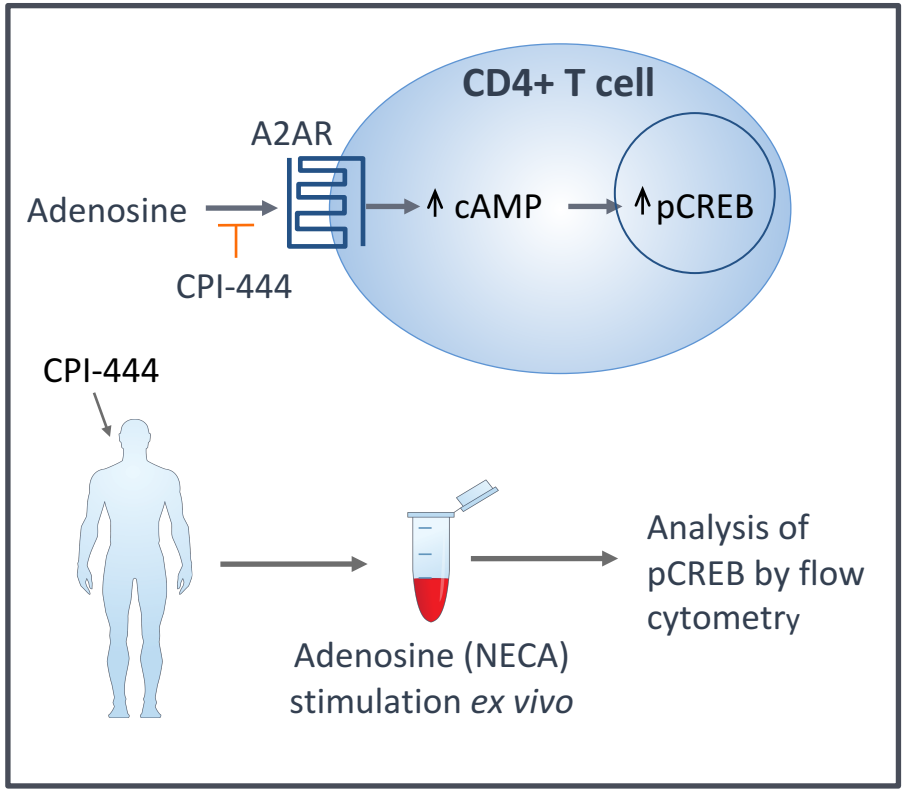
Expansion cohorts: renal cell and non-small cell lung cancer

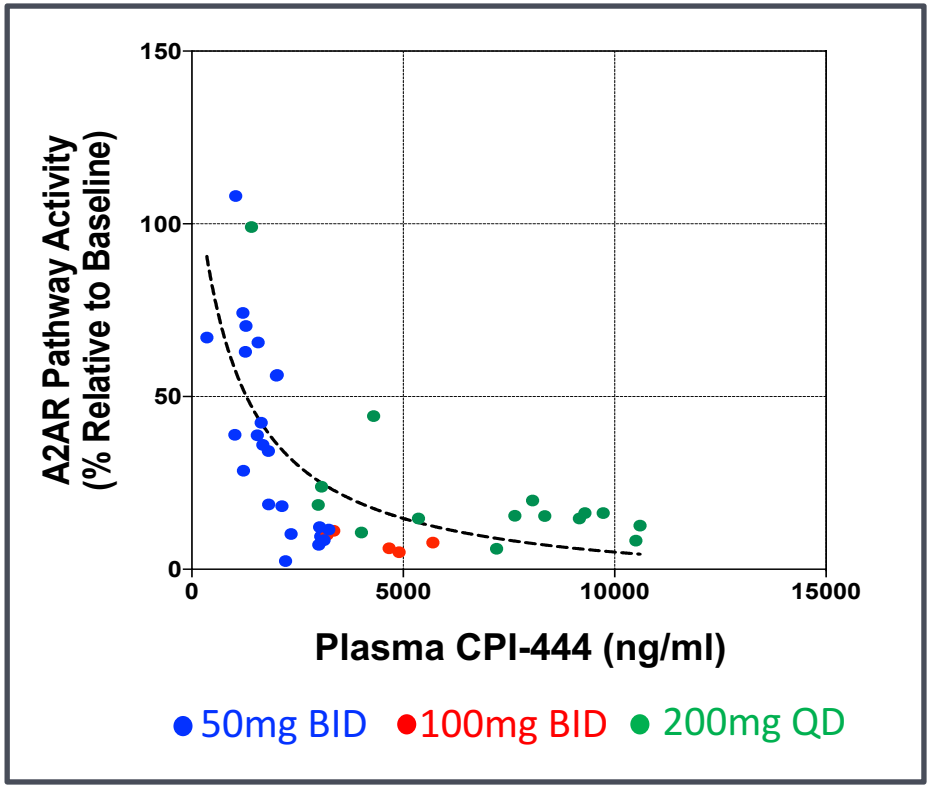


Eligibility

- Tumor types: RCC, NSCLC, Melanoma, TNBC, Others
- Prior anti PD-(L)1 allowed
  - Resistant: SD or better > 3 months of treatment
  - Refractory: progression within 3 months
- Must have progressive disease on prior therapy
- No selection for PD-L1 expression

CPI-444 Blocks A2A Receptor Signaling





Patient Characteristics

	Non-Small Cell Lung Cancer (N=45)	Renal Cell Cancer (N=30)
Prior anti-PD-(L)1 exposure Naïve Resistant/Refractory	 8 (18%) 37 (82%)	 8 (27%) 22 (73%)
PD-L1 Negative*	54%	95%
Median time since IO agent, months (range)	2.8 (0.6 – 24)	1.7 (1 – 71)
Histology	28 (62%) Non squamous 17 (38%) Squamous	28 (93%) Clear cell 2 (7%) Papillary
Median age, years (range)	70 (41-85)	65 (44-76)
No. of patients single agent / No. of patients combination	22/23	14/16
Median number prior therapies	2 (1-5)	3 (1-5)

*Archive samples data available on **19** RCC and **28** NSCLC patients based on FDA-approved test

Treatment-Related Adverse Events

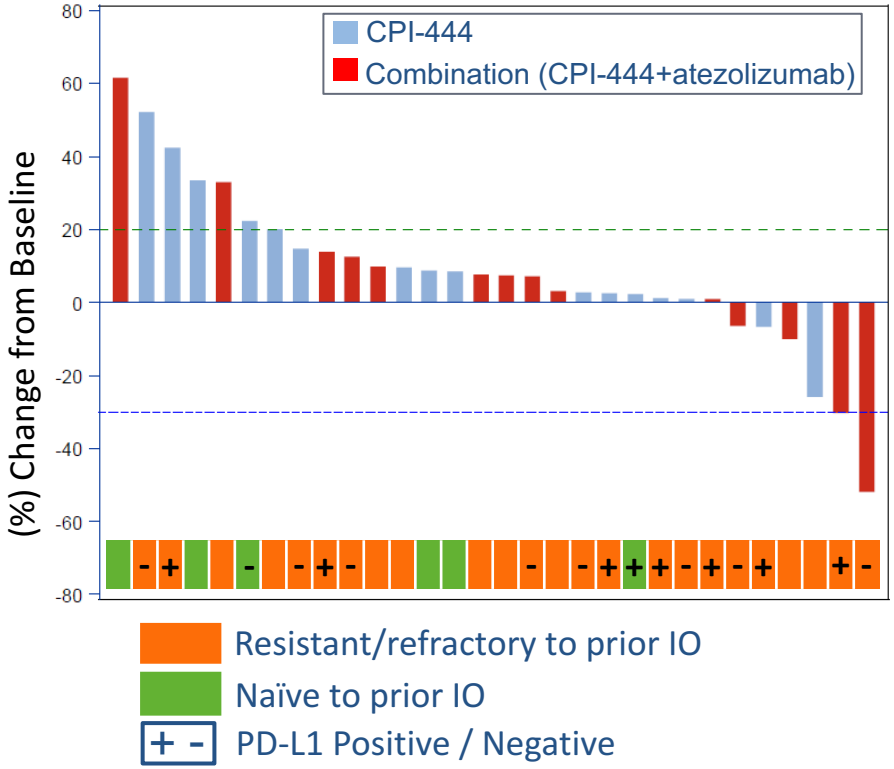
Adverse Events (Gr1/2) ≥ 5% Frequency (n=75)		
	Single Agent (%)	Combination (%)
Fatigue	11	15
Nausea	6	8
Pruritus	8	5
Constipation	6	---
Dizziness	6	---
Hypertension	6	---
Pyrexia	6	---
Rash	---	5
AST increased	---	5
ALT increased	---	5

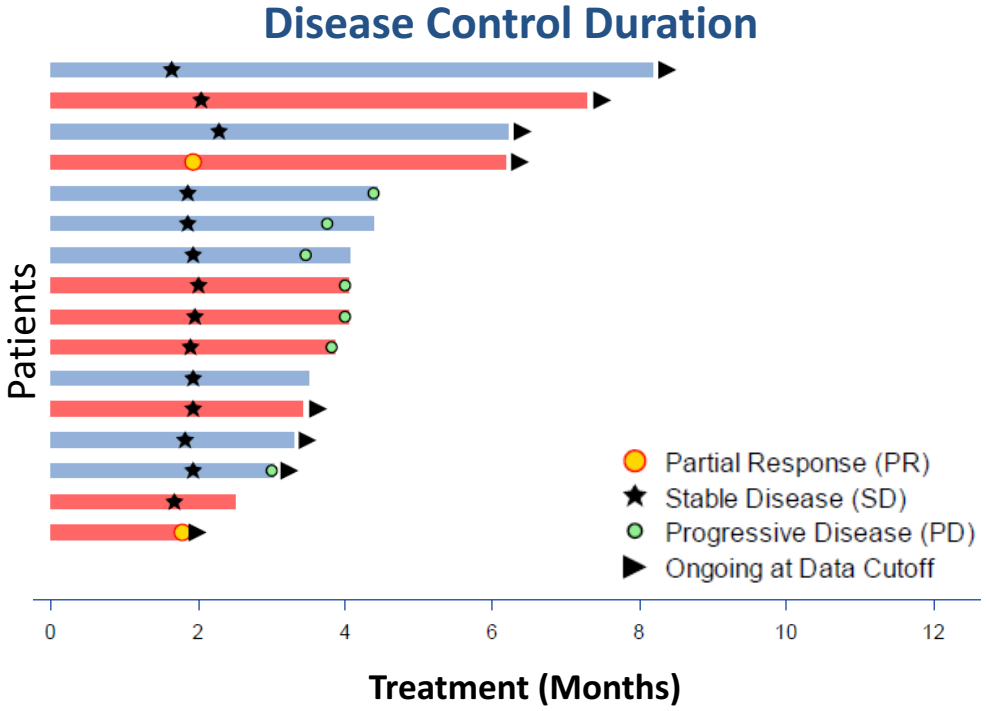
Grade ≥ 3 AEs:

- **Single agent: none**
- **Combination CPI-444 + atezolizumab**
  - One patient with Gr 3 immune related hepatitis, pneumonitis, mucositis and dermatitis

Phase 1/1b Trial with CPI-444: Disease Control in NSCLC

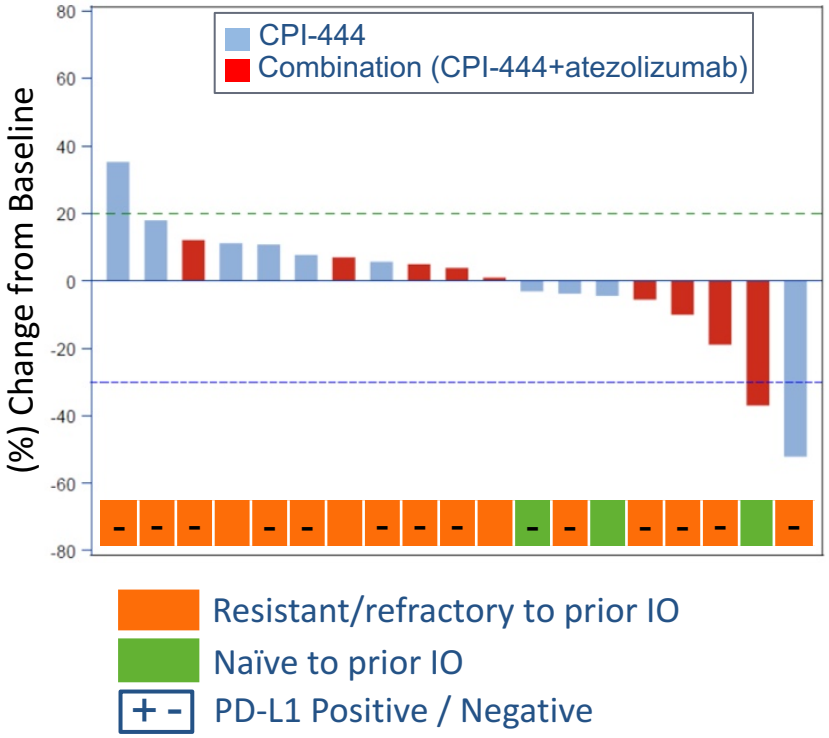
Partial responses can be seen in anti-PD-1 progressors

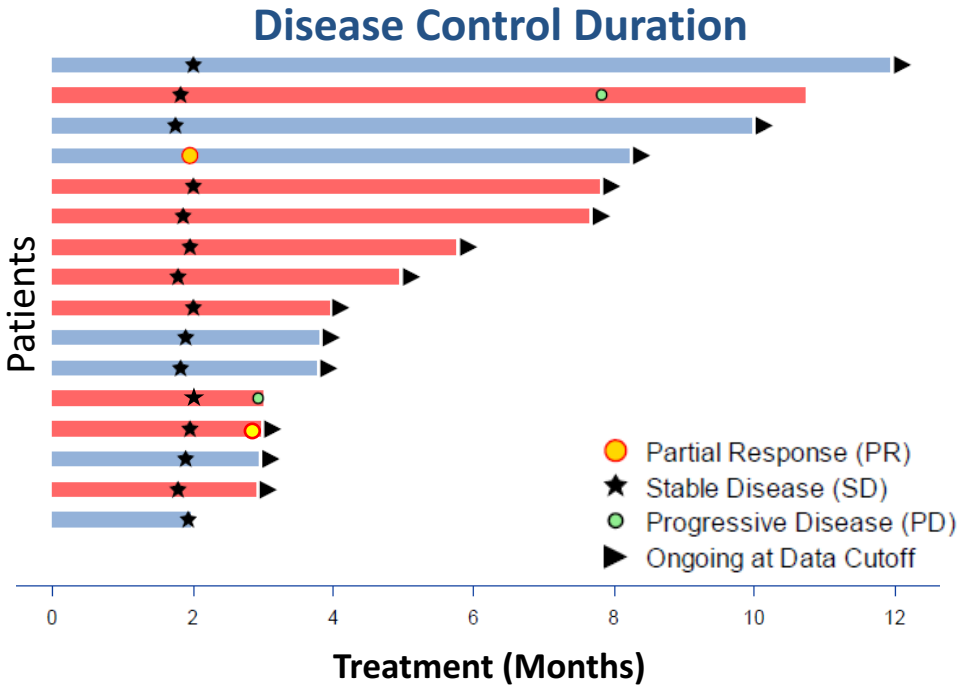




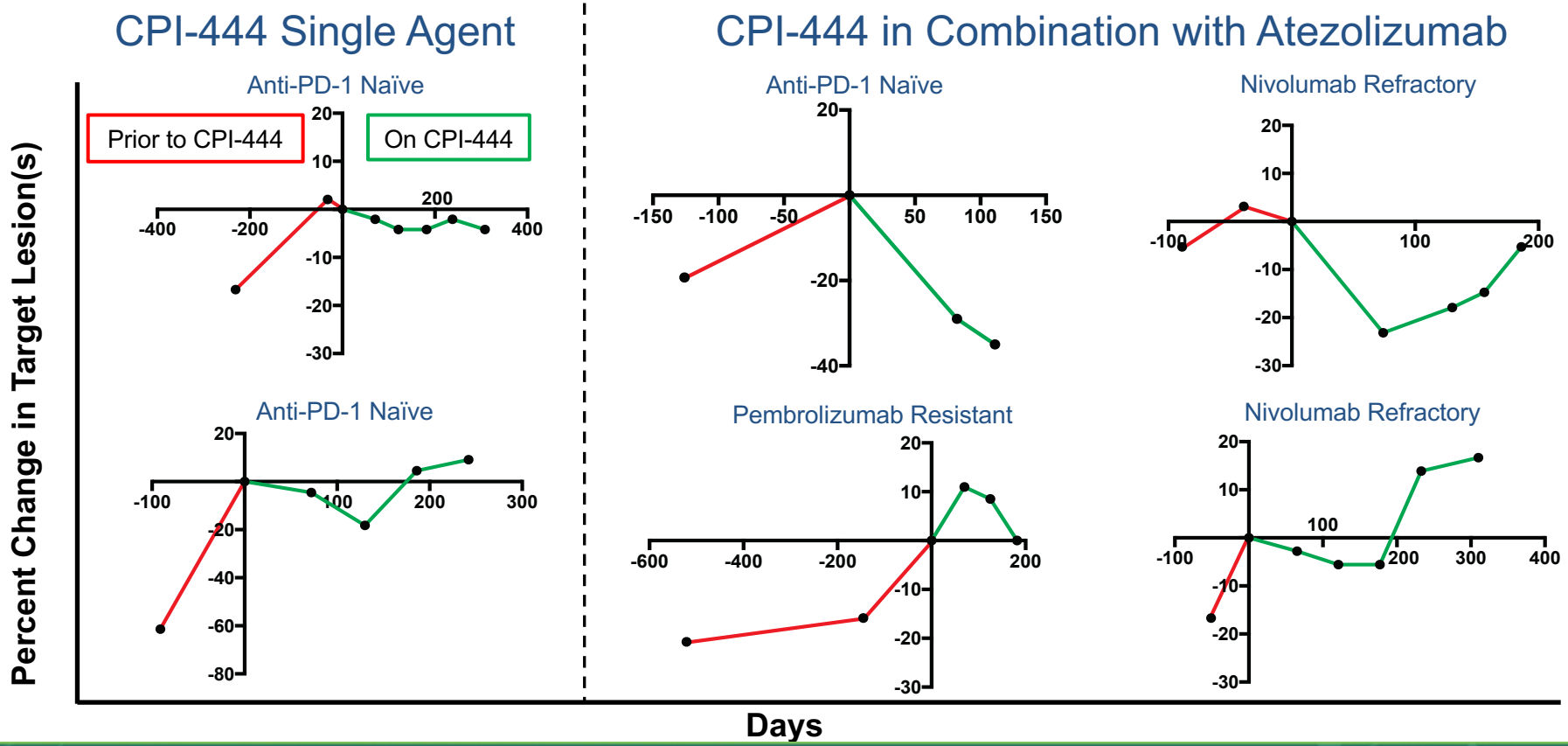
Phase 1/1b Trial with CPI-444: Disease Control in Renal Cell Cancer

Partial responses can be seen in an anti-PD-1 progressing and naïve patients





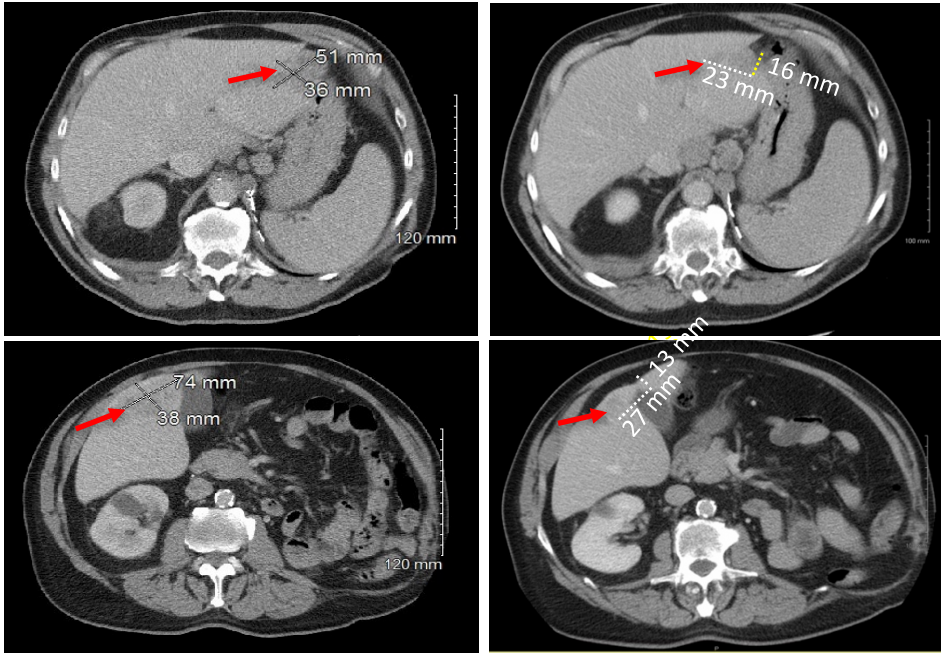
Tumor Growth Kinetics in "*Stable*" RCC Patients



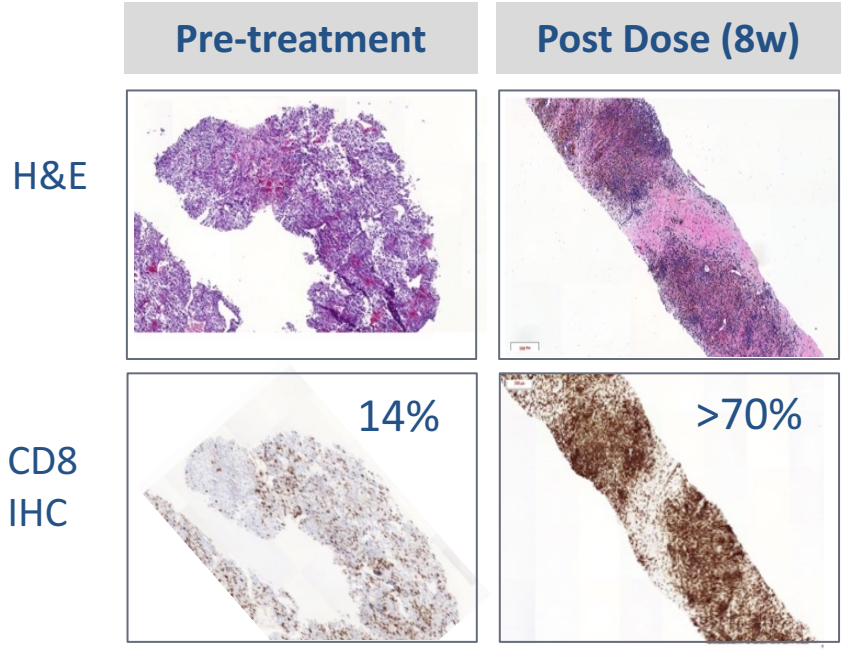
Tumor Regression in Nivolumab Refractory Renal Cancer

Single Agent CPI-444

Five prior regimens including TKIs, mTOR inhibitor, and nivolumab

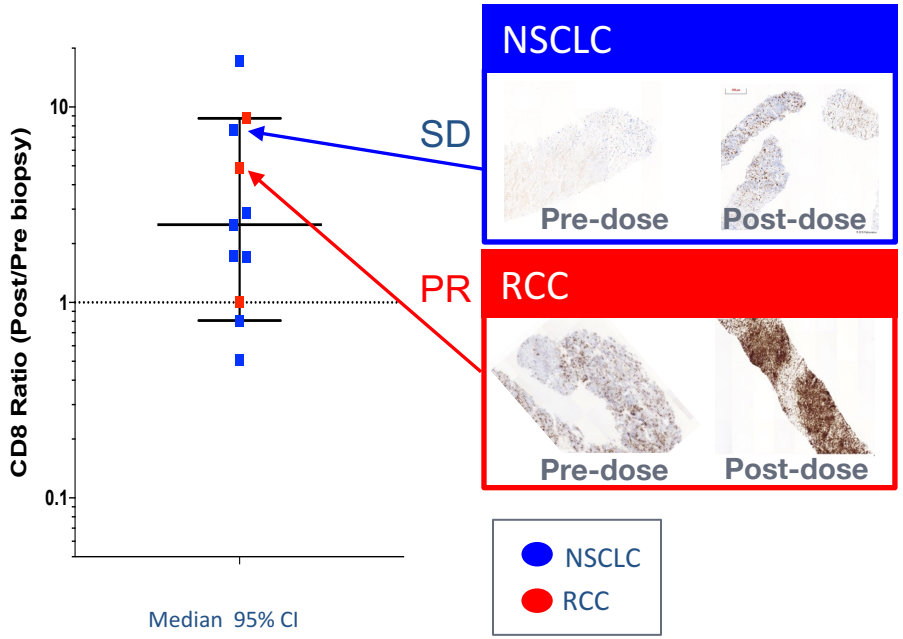


Pre-treatment **3 months of treatment**

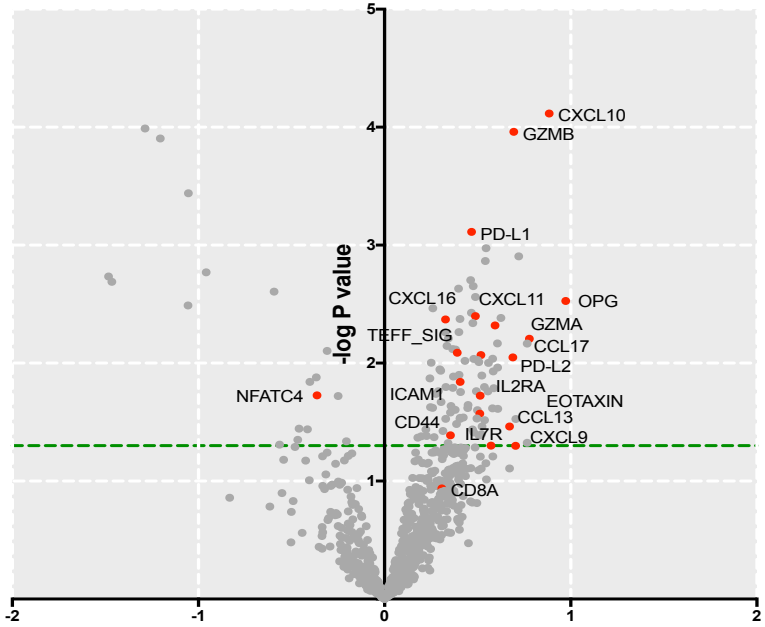


CPI-444 Induces CD8 T Cell Infiltration and Th1 Gene Expression in Tumor Tissues

CD8 T Cell Change (IHC)



Immune Gene Expression (paired biopsies)

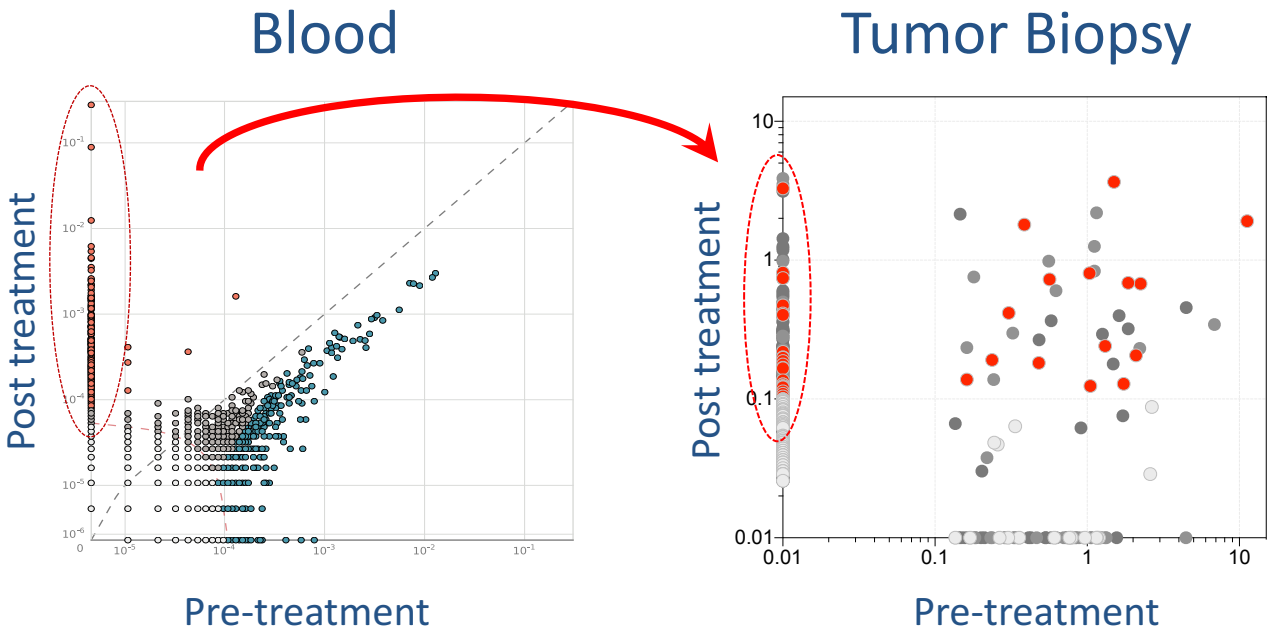


Log Fold Change Gene Expression

Post vs pre biopsies (N=14)

CPI-444 Expands New T Cell Clones in Blood and Tumor

- RCC patient with PR on single-agent CPI-444
- T cell receptor (TCR) sequencing of blood and tumor biopsies pre- and post-treatment
- T cell clonotypes can be matched between blood and tumor



Treatment induces expansion of identical T cell clones in blood and tumor

Phase 1/1b Trial with CPI-444: Summary

- CPI-444 is well-tolerated as a monotherapy and in combination with atezolizumab
- CPI-444 has clinical activity alone and in combination with atezolizumab
- Anti-tumor activity seen in:
  - Patients who have progressed on prior anti-PD-(L)1
  - Patients with PD-L1 negative tumors
- CPI-444 can induce CD 8 T cell infiltration and expression of T cell activation genes within the tumor microenvironment
- CPI-444 induces new T cell clonotypes in the blood, which are capable of migrating to tumors
- Accrual of patients into the expansion cohorts for NSCLC and RCC is ongoing

Acknowledgements

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- **Colleagues at Corvus**
- **Colleagues at Roche Genentech**