SITC 2016

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Society for Immunotherapy of Cancer

AURIGENE
Accelerating Discovery

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CA170
Oral Small Molecule Immune Checkpoint Inhibitor (PD-L1/VISTA)

David Tuck, M.D.

Presenter Disclosure Information

David Tuck

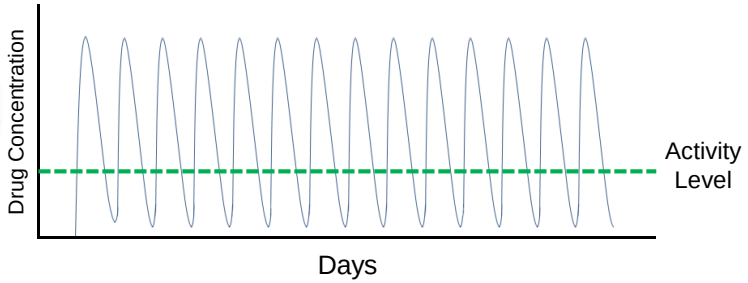
The following relationships exist related to this presentation:

David Tuck is a full-time employee and Chief Medical Officer of CURIS

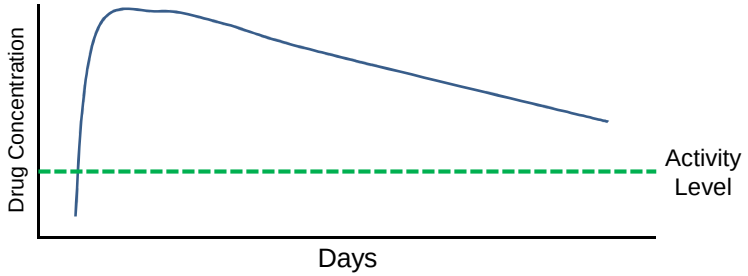
Why Oral Immune Checkpoint Blockade?

- **Small molecule PK profile allows optimization of dose and administration schedule**
  - Usually less than 24 hour half-life ($T_{1/2}$) permits flexibility with dosing schedule – daily or intermittent dosing
  - Permits flexible adjustment of exposure as measured by C_{max} and AUC – both parameters can be adjusted to match mechanism-of-action
  - Flexibility to adjust dose and schedule to address emergent adverse events
- **Oral dosing**
  - Untether patient from infusion chair

Typical Small Molecule Drug PK Profile



Typical Antibody Drug PK Profile

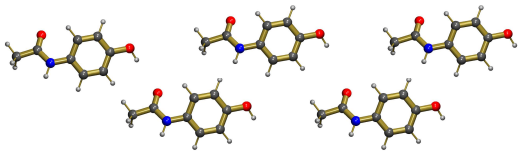


Can small molecule immune checkpoint blockade work?

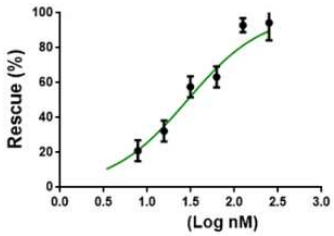
PD-1 PD-L1

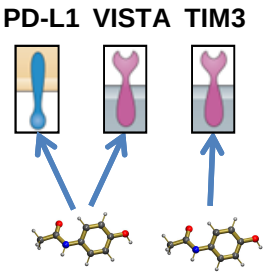
<u>Aurigene discovery platform</u>
Small molecule design based on structure of interaction hotspots

Small molecule library



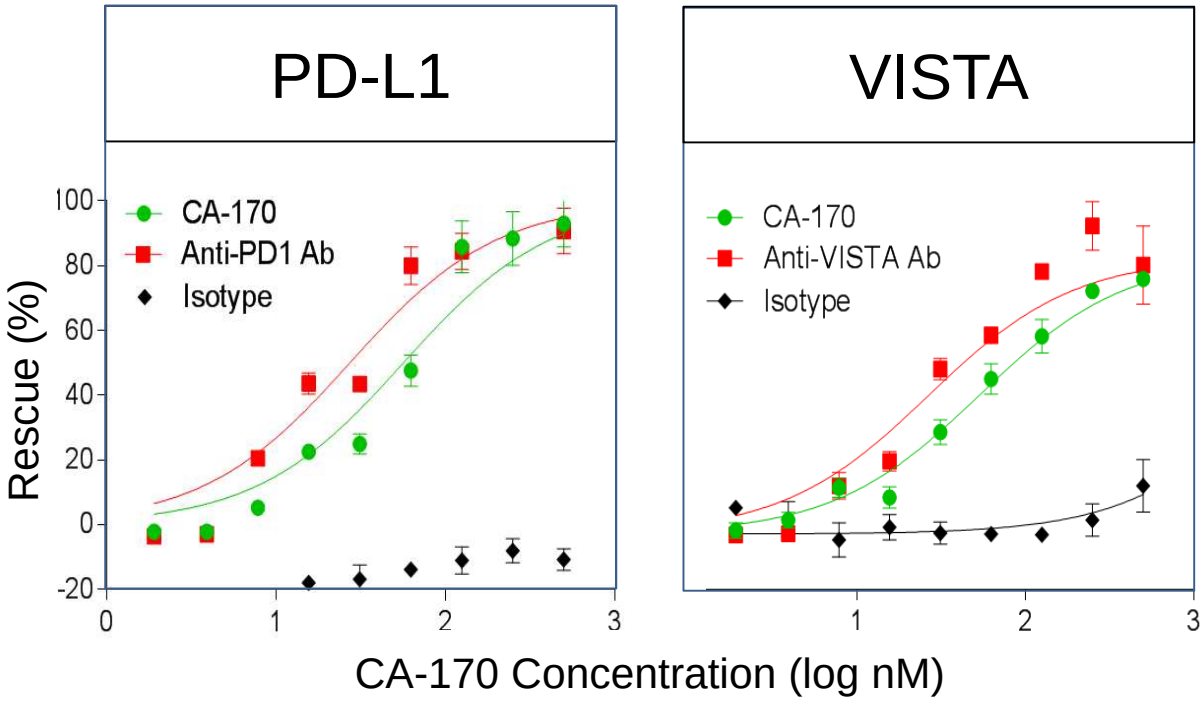
Functional screening to identify compounds capable of selectively rescuing T cell proliferation and activation in the presence of inhibitory checkpoints





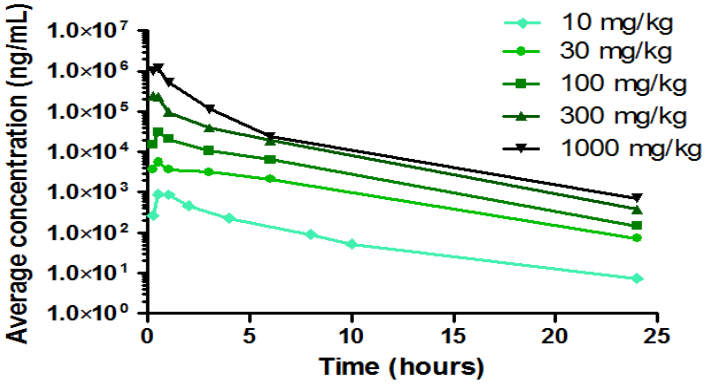
CA-170 rescues human T cell proliferation and IFN-γ production inhibited by recombinant PD-L1 or VISTA

- Potent, dose-dependent and checkpoint specific rescue of human T cell activation
- Similar to that observed with anti-PD1 or anti-VISTA antibodies

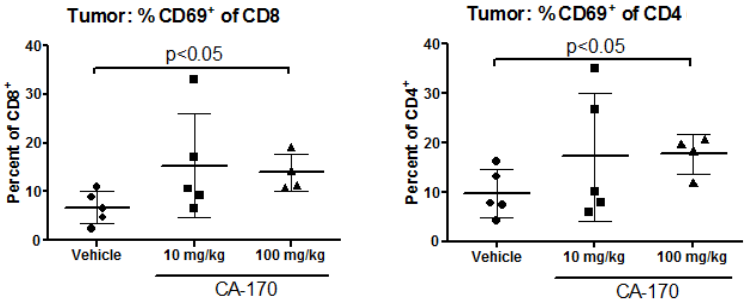


Predictable Dose Exposure, T cell Activation and Efficacy in anti-PD-1 Non-responsive Mouse Models with CA-170

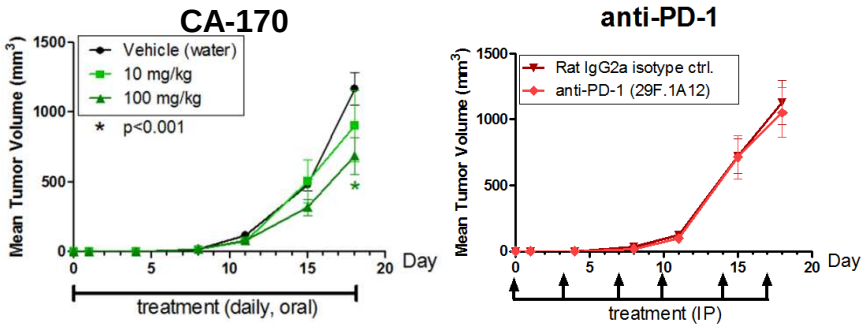
Mouse single dose exposure



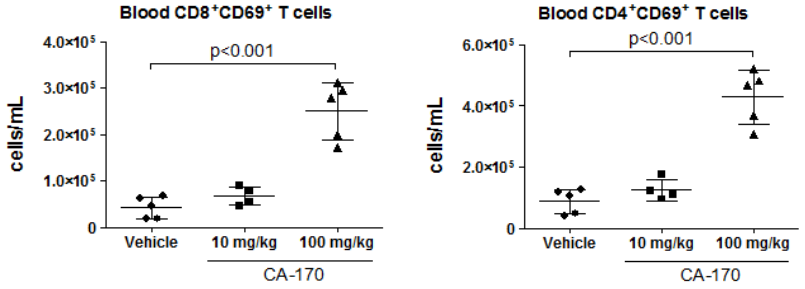
T Cell Activation – In Tumor



Efficacy in the B16/F1 Model

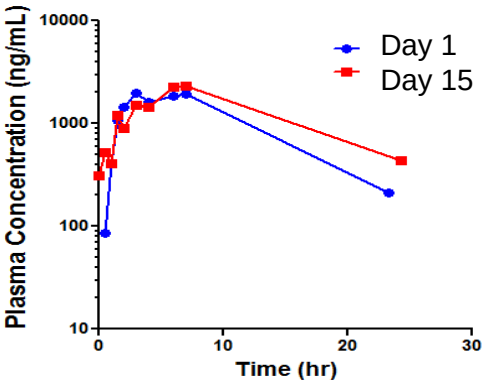


T Cell Activation – In Blood

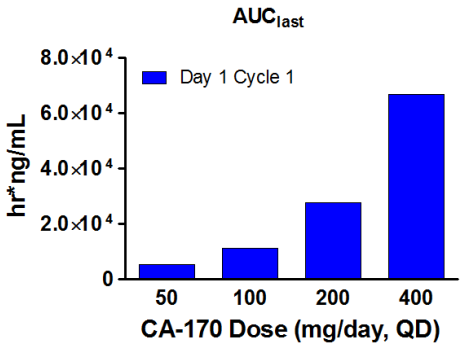


First dose levels in patients are consistent with Preclinical Predictable Dose Exposure and T Cell Activation (NCT02812875)

Human PK (200 mg/day)

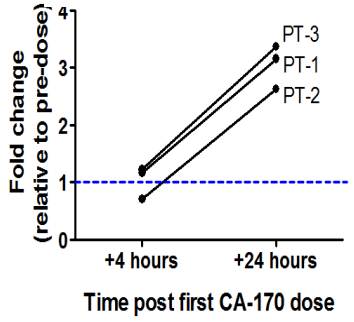


CA-170 exposure in humans

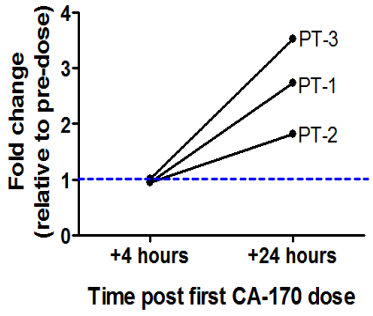


Change in the percentage of circulating CD8+ T cells expressing:

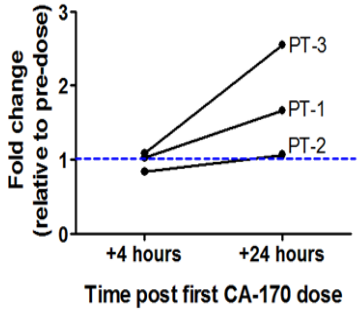
CD69+



CD134+



Granzyme B+



Summary

- CA170 is a potent and selective, oral small molecule checkpoint inhibitor, and the first to enter the clinic
- Preclinical data demonstrate dose-dependent oral exposure, immune modulation and anti-tumor activity
- Clinical PK profile is similar to non-clinical and human exposure appears predictable on oral dosing
- CA-170 appears to be biologically active in patients, supporting continued clinical development

Acknowledgements

Curis

A. Lazorchak …. T. Wyant

CA-170 (PD-L1/VISTA)
CA-170, an Oral Small Molecule Immune Checkpoint Antagonist, Promotes T Cell Immune Activation and Inhibits Tumor Growth in Pre-clinical Models of Cancer

FRIDAY POSTER SESSION #P219

Generation of a second clinical candidate CA-327, targeting PD-L1/TIM-3

Aurigene

P. Sasikumar ….. M. Ramachandra

CA-327 (PD-L1/TIM-3)
First-in-class orally bioavailable checkpoint inhibitors targeting single and multiple immune inhibitory pathways

SATURDAY POSTER SESSION #P185

Carolina BioOncology

Participating Patients

John Powderly, M.D.

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THANK YOU