SITC 2016

NATIONAL HARBOR, MD
NOVEMBER 9-13, 2016

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Society for Immunotherapy of Cancer

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IMO-2125, an investigational intratumoral toll-like receptor 9 agonist, modulates the tumor microenvironment to enhance anti-tumor immunity

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Presenter Disclosure Information

Mark J. Cornfeld

The following relationships exist related to this presentation:

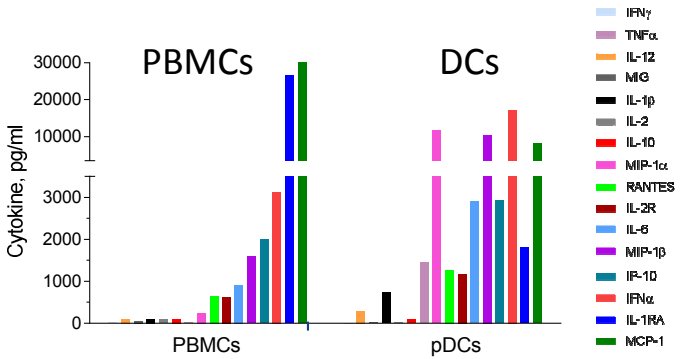
Idera Pharmaceuticals: Employee, Stock Options

IMO-2125: an optimized, novel, synthetic agonist of Toll-like receptor 9 (TLR9)

Chemistry of IMO-2125

Antimicrob. Agents Chemother., 2008, 4320-5; Nucleic Acids Research, 2002, Vol. 30 No. 20

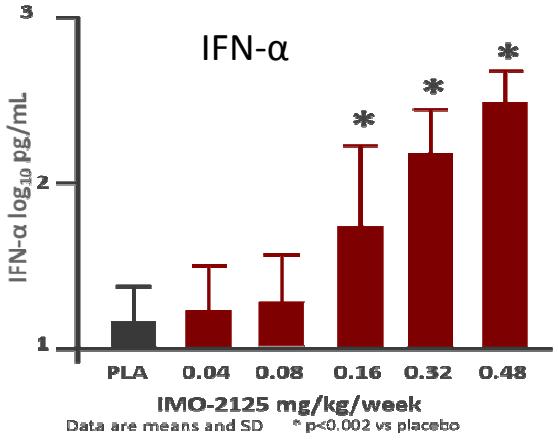
IMO-2125 induces Th-1 type cytokines through TLR9

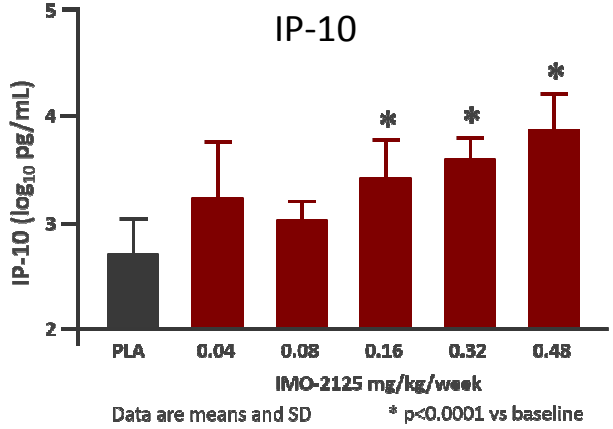


Antimicrob. Agents Chemother., 2008, p. 4320–4325

IMO-2125 induces IFN-α and other cytokines in human trial

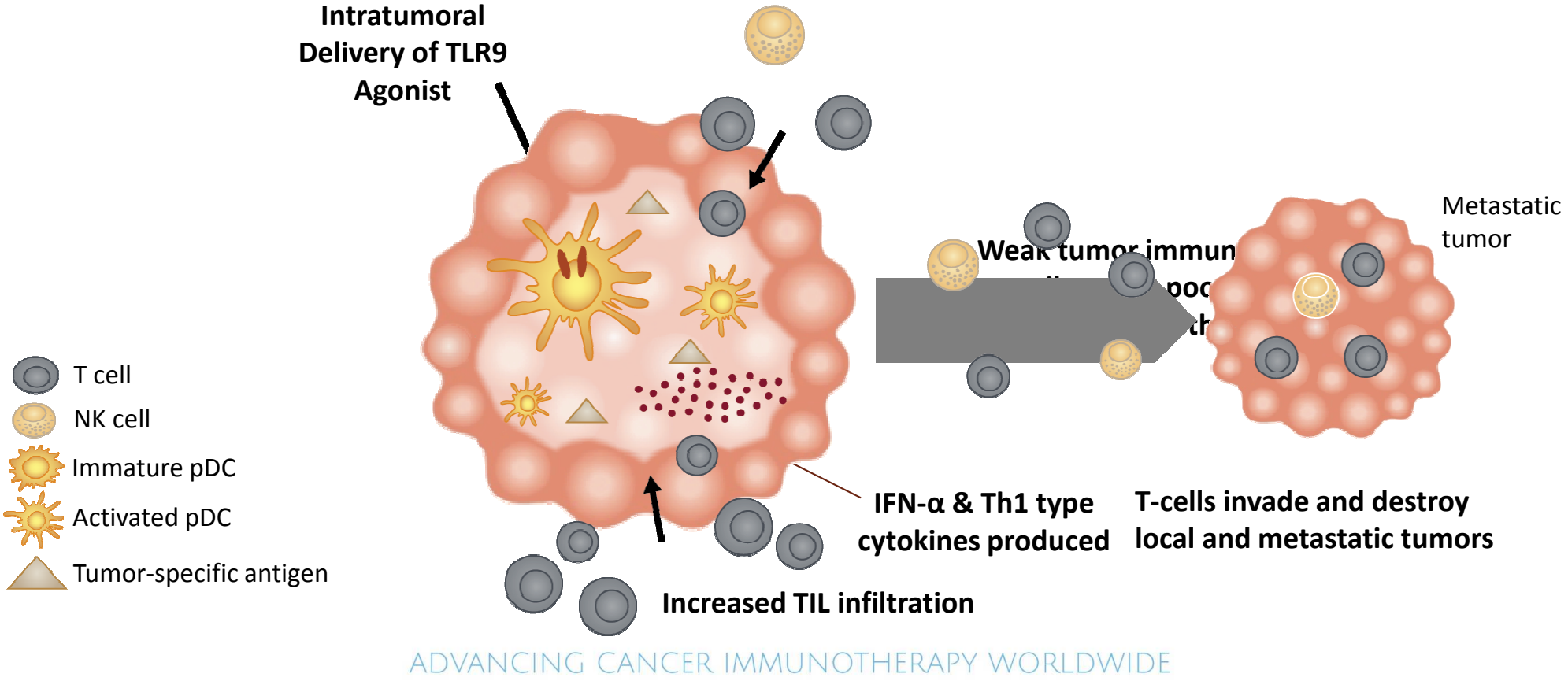
- IMO-2125 at doses ranging from 0.04 to 0.48 mg/kg administered subcutaneously weekly in Hepatitis C infected subjects
- Treatment was well-tolerated
- Immune response parameters showed activation





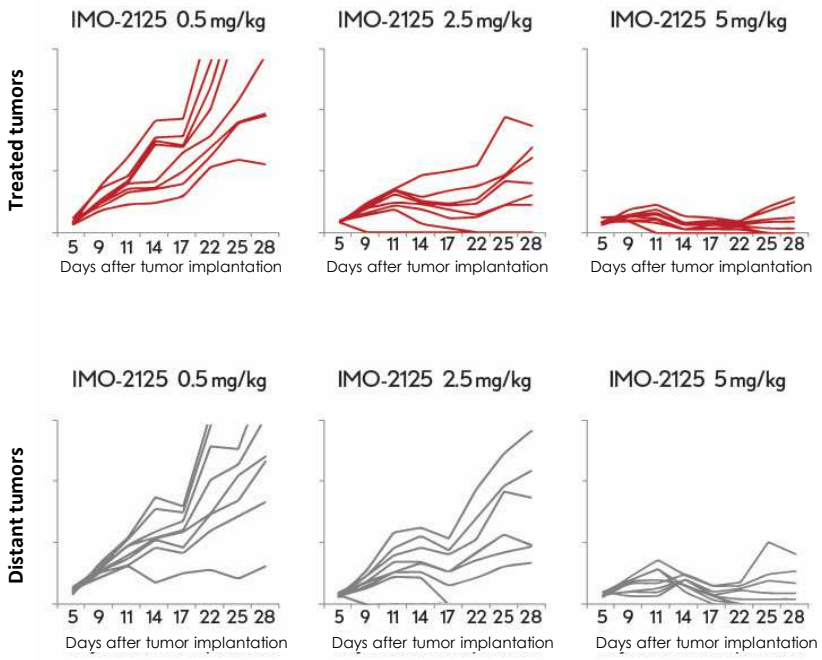
Data presented at EASL 2010, AASLD Liver Meeting 2010

Modulation of the tumor microenvironment by intratumoral administration of IMO-2125



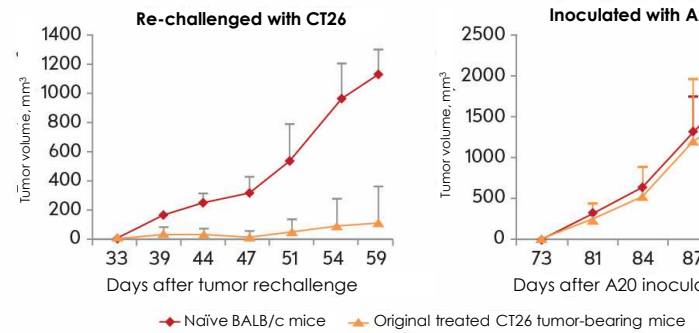
Intratumoral IMO-2125 exerted local and systemic anti-tumor activity

Dose-dependent antitumor activity in injected and distant tumors (abscopal effect)



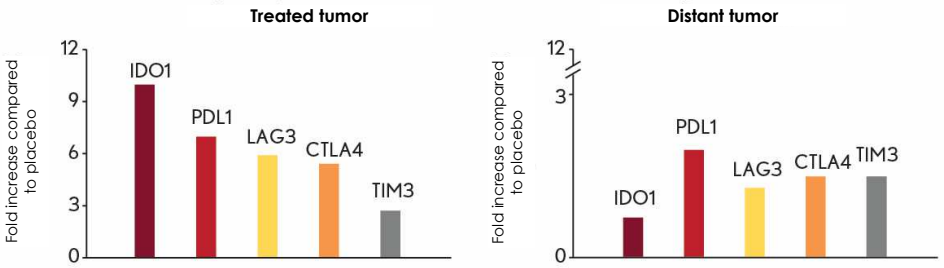
BALB/c mice (n=8 per group) implanted with CT26 colon carcinoma cells on right and left flank. IMO-2125 i.t. treatment on right flank on days 5, 8, 11 and 14.

Specific and durable cytotoxic T-cell responses to tumor antigen



Six BALB/c mice whose CT26 tumors completely or partially regressed following treatment were rechallenged with CT26 cells on day 33 and inoculated with A20 lymphoma cells on Day 73.

Changes in checkpoint gene expression

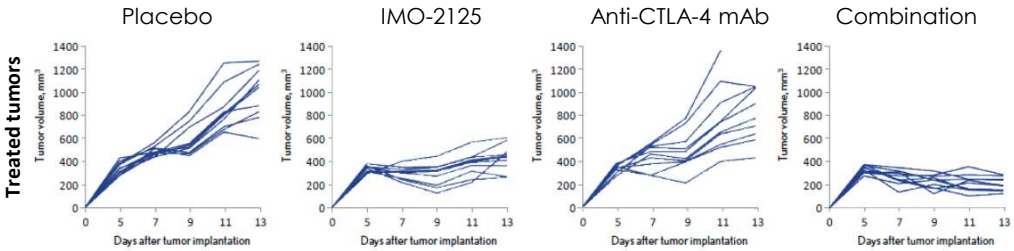


C57BL/6 mice (n=9) implanted with B16 melanoma cells on right and left flank. IM-2125 treatment on left flank on days 7, 9, 11, 13, and 15. One week post last dose, samples collected and analyzed for checkpoint expression by qPCR.

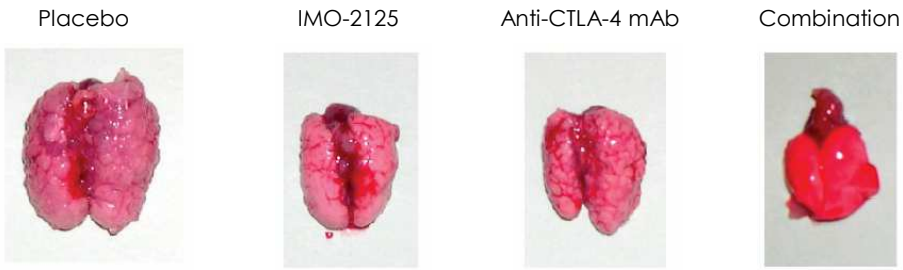
All data from presentation CRI-CIMT-EATI-AACR Cancer Immunotherapy Conference 2015

Intratumoral IMO-2125 potentiated systemic anti-tumor activity of anti-CTLA-4 and anti-PD-1 in preclinical models

Antitumor activity of IMO-2125 and anti-CTLA-4 mAb



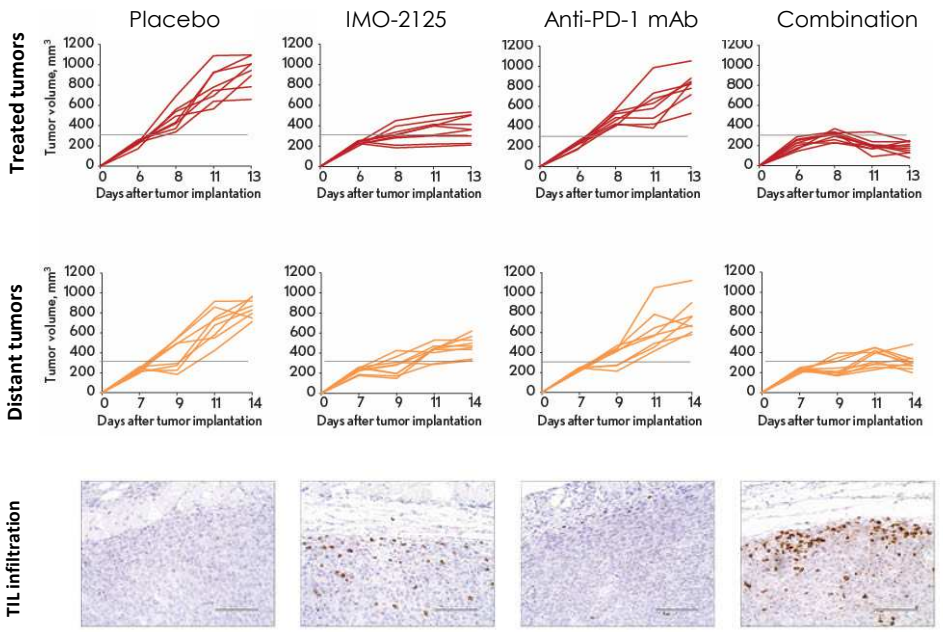
Effects on distant lung metastases



BALB/c mice (n=10 per group) implanted with CT26 colon carcinoma cells s.c. on right flank and i.v. to form lung metastases. IMO-2125 and anti-CTLA-4 treatment on days 5, 6, 8, and 9. Lung pictures taken on day 13.

Data from presentation CRI-CIMT-EATI-AACR Cancer Immunotherapy Conference 2015

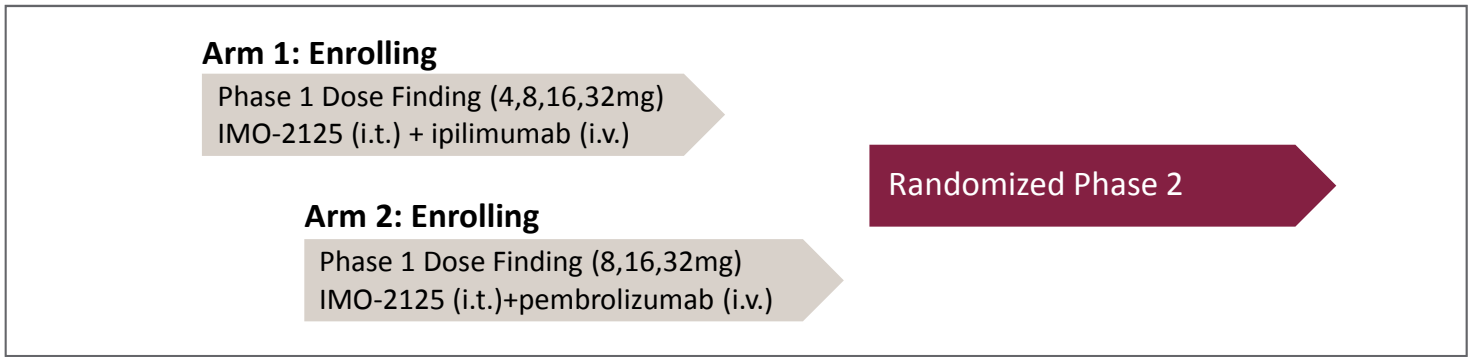
Antitumor activity of IMO-2125 and anti-PD-1 mAb



BALB/c mice (n=8 per group) implanted with CT26 colon carcinoma cells s.c. on right and left flank and i.v. to form lung metastases. IMO-2125 and anti-PD-1 treatment on days 7, 8, 11, and 12. Magnification of tumor samples x400.

Data from presentation AACR-NCI-EORTC International Conference 2015

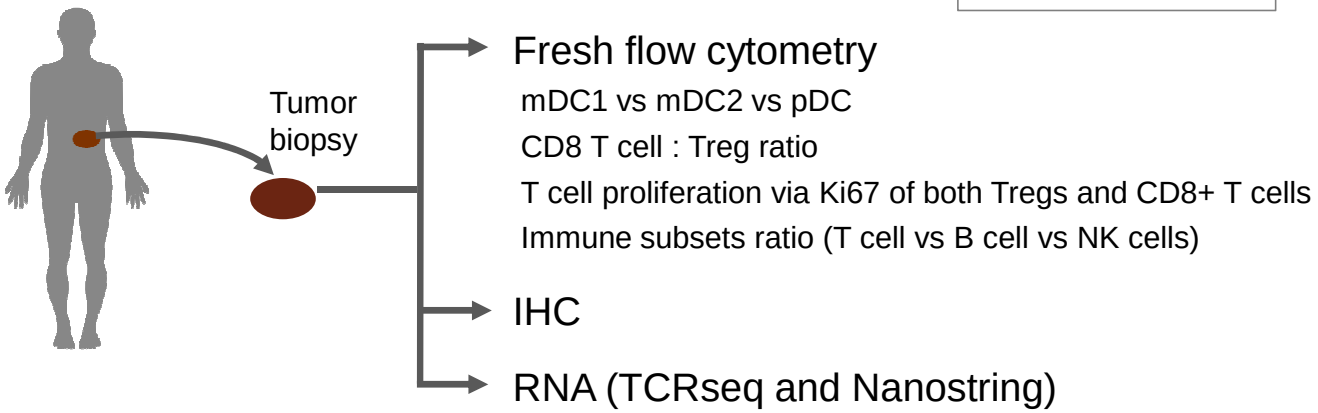
Study 2125-204: Phase 1/2 study of intratumoral IMO-2125 in combination with ipilimumab or pembrolizumab in patients with metastatic melanoma following prior PD-1 directed therapy (NCT02644967)



Trial design

- Population: relapsed on or after 12 wks PD-1 directed therapy (alone or in combination)
- IMO-2125 administered as a single intratumoral injection weeks 1, 2, 3, 5, 8, 11
- Ipilimumab and pembrolizumab administered per label (commercial supply)
- Bayesian dose-escalation (Phase 1); Randomized Phase 2 at RP2D's
- Endpoints: Safety, investigator assessed ORR (irRC)
- Exploratory: markers of immune activation with serial biopsy of injected and distant tumors

Study 2125-204: Immune response monitoring to correlate with mechanism of action



SITC 2016

Preliminary safety, clinical activity and translational results to be presented at SITC annual meeting:

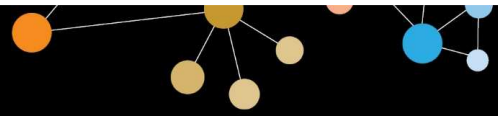
Reactivating the Anti-tumor Immune Response by Targeting Innate and Adaptive Immunity in a Phase I/II Study of Intratumoral IMO-2125 in Combination with Systemic ipilimumab in Patients with Anti-PD-1 Refractory Metastatic Melanoma

Cara Haymaker, PhD – University of Texas MD Anderson Cancer Center

Session: State-of-the-Art Immunotherapies: Challenges and Opportunities
Friday, November 11 – 2:00-4:15 p.m.

IMO-2125 development program

- Goals of IMO-2125 and checkpoint inhibitor (CPI) combination immunotherapy
  - Stimulate host antitumor immune responses
  - Break tumor-related immune tolerance
  - Increase potential for curative treatment
- Opportunity to establish clinical POC in anti-PD-1 refractory melanoma
  - Anti-PD-1 established as standard of care, with no clear consensus on treatment after failure
- Future potential opportunities in CPI addressable tumors with low PD-L1 expression and non-immunogenic tumors unadressable with current CPI class



Backup

Modulation of the tumor microenvironment by intratumoral administration of IMO-2125