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BeyondSpring

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By attending this presentation, you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of our business.

Investment Highlights

Plinabulin: Safety & Efficacy	Lead Asset Plinabulin: >700 cancer patients treated with good tolerability; Positive Phase 3 data in 2 indications
Plinabulin Potential	Plinabulin: Dual Benefit in anti-cancer and prevention of CIN; Potential in re-sensitizing in PD-1/PD-L1 progressed patients in multiple cancers
SEED: Novel TPD Platform & Pipeline	SEED: 8 Disclosed Pipeline Assets with 1 expected to enter IND in 2024
Premier Partnerships	SEED: Investment and R&D Collaboration from Eli Lilly
Intellectual Property	Strong Intellectual Property and Technology Protection

Leading Expert Speaker Biography

Dr. Steven Lin, MD Anderson Cancer Center

Dr. Steven Lin is a Professor and Physician Scientist, with joint appointments in the Departments of Radiation Oncology and Experimental Radiation Oncology. Dr. Lin's practice focuses on thoracic malignancies, and he oversees several clinical trials including the use of proton beam therapy for esophageal cancer and in the combination of immunotherapy with radiotherapy in lung and esophageal cancers.

Dr. Lin runs a translational research team that evaluates biomarkers for treatment response and disease outcomes after chemoradiation therapy and immunotherapy. On the basic science side, Dr. Lin's main interests lie in identifying novel approaches that could enhance radiotherapy and immunotherapy combinations in lung cancer that could be translated to innovative clinical trials for patients.

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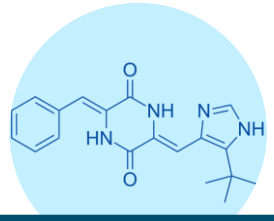
Preclinical and Clinical POC immunomodulating activity of Plinabulin inducing Dendritic Cell maturation and Re-sensitization in Immunotherapy Refractory Tumors when Combined with Radiation and PD-1/PD-L1 Inhibitors

November 7, 2023

Presented at SITC 2023 (Poster #732)

Executive Summary: Plinabulin, Combined with Radiation and Immune Checkpoint Inhibitors, Induces DC Maturation and Re-sensitizes IO-refractory Tumors to Immune Checkpoint Blockade



Plinabulin is a Unique Tubulin Binder

Plinabulin's tubulin binding site is distinct from that of other tubulin binding agents such as taxanes, vinca alkaloids, and colchicine.

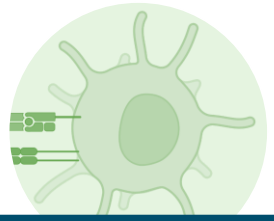
Strong Preclinical Proof of Concept

Plinabulin in combination with radiation and anti-PD-1 **activates DCs, stimulates T-cell proliferation**, and achieves **abscopal effects**.

Clinical Evidence of Efficacy

In 10 IO-refractory patients, 80% disease control rate and durable responses in heavily pre-treated patients,

Demonstrates **clinical efficacy in a growing high-unmet need IO-refractory population**.



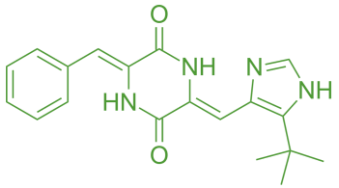
Clinical Evidence of Immune Activation

Responding patients exhibit early immune activation with DC maturation and proinflammatory monocytes in the peripheral blood.

These IO effects are observed across six different cancer types indicating **broad applicability**.

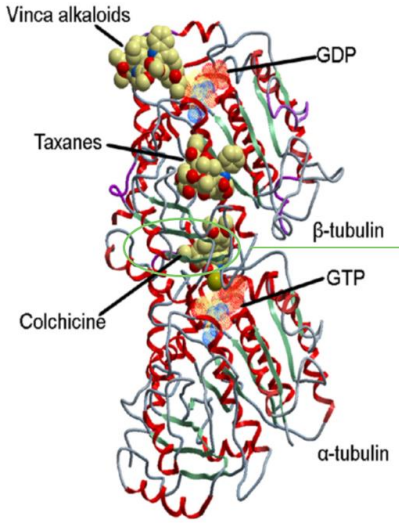
As a Unique Tubulin Binder, Plinabulin Effectively Liberates GEF-H1 from Microtubules Leading to DC Maturation, M1-polarization and T-cell Activation

Plinabulin is a unique tubulin binder

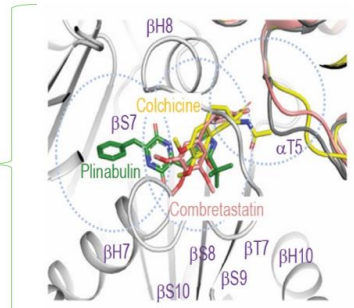


Plinabulin (NPI-2358)

Tubulin Binding Sites



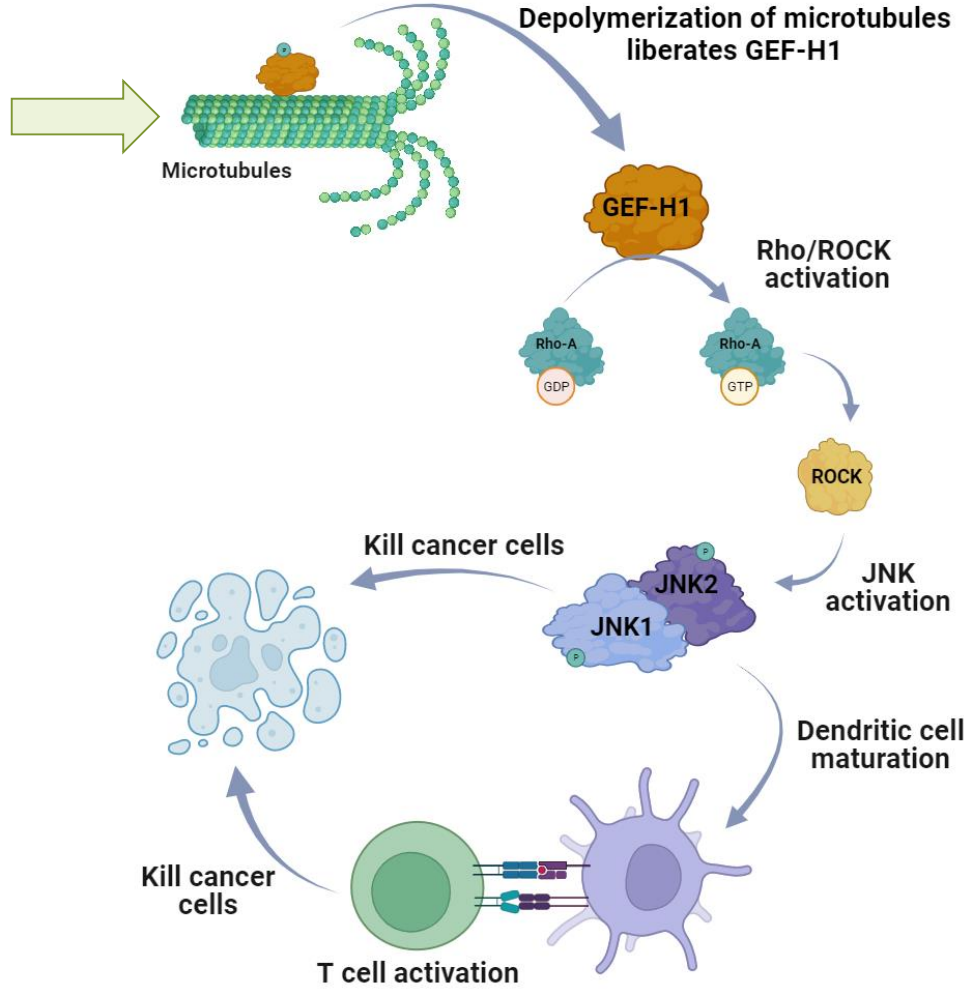
Plinabulin Binds to β-Tubulin, Near the Colchicine Site[1]



Plinabulin's tubulin binding site is distinct *from other classes of tubulin binding agents such as tubulin stabilizing taxanes (paclitaxel, docetaxel, cabazitaxel) and tubulin destabilizing vinca alkaloids (vinblastine, vincristine, vinorelbine) and colchicine.*

Plinabulin

Depolymerization of microtubules



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[1] La Sala et al., 2019 Chem

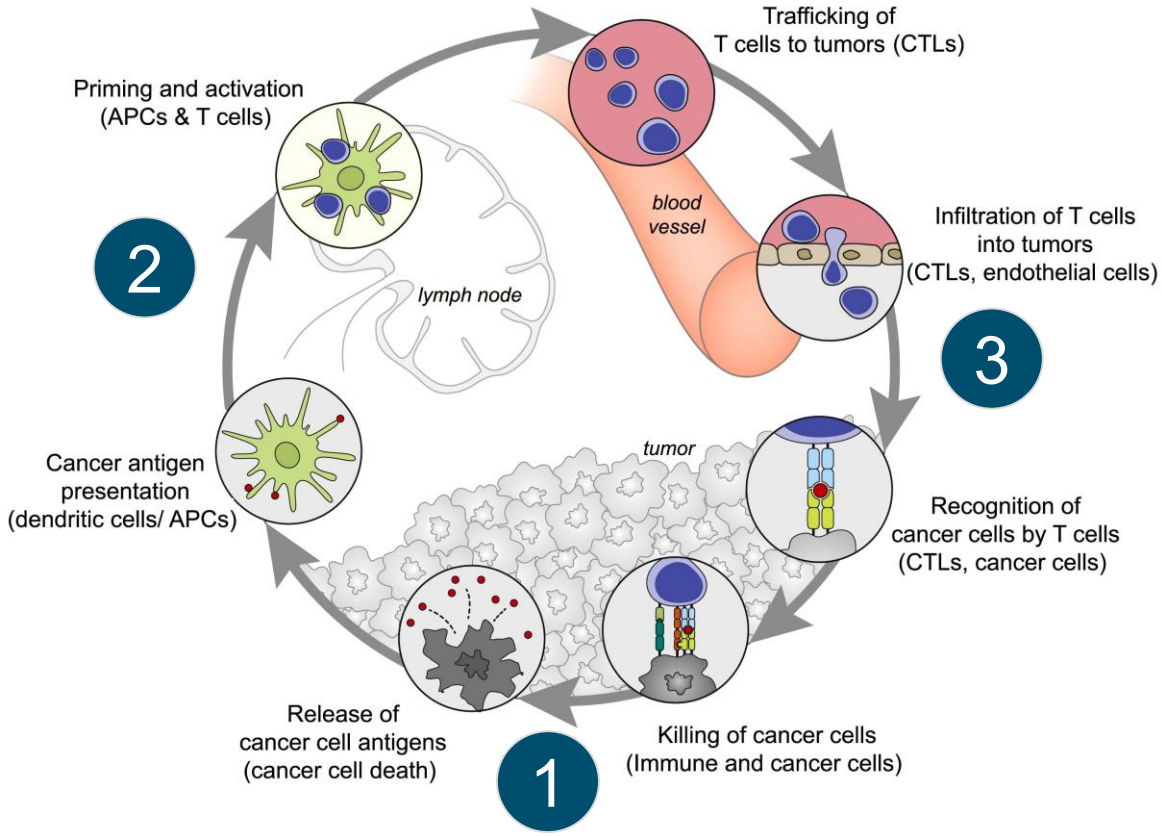
GEF-H1 is a Rho guanine nucleotide exchange factor.

Plinabulin is Hypothesized to Synergize with Radiation and Anti-PD1 to Generate an Optimal Anti-tumor Response

② Plinabulin

Improved antigen presentation
Stimulate maturation of dendritic cells to increase antigen presentation.

Induce polarization and proliferation of anti-tumor M1-like macrophages



③ Checkpoint Inhibitors

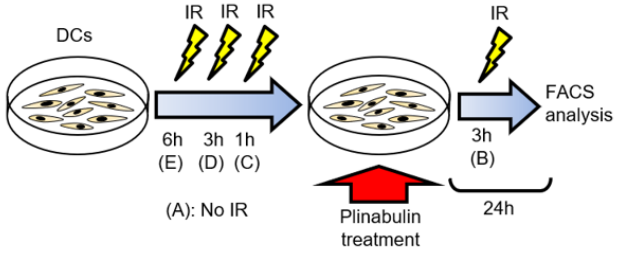
Anti-tumor T cell activation
Optimize T cell response

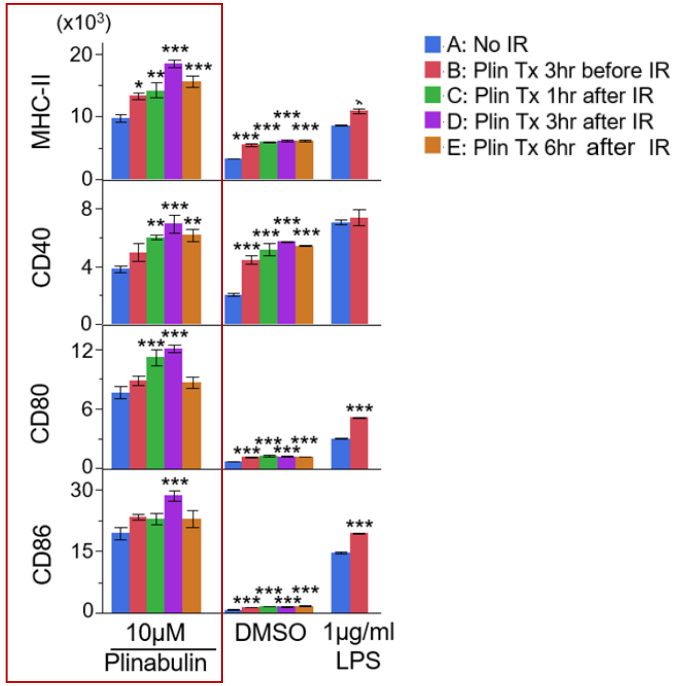
① Radiation/Chemotherapy

Release tumor antigens
For more potent anti-cancer effect

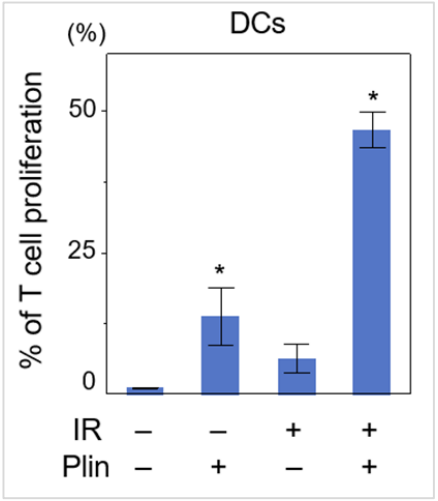
Preclinical Proof-of-Concept (PoC): Plinabulin plus Radiation and Anti-PD-1 led to DC Activation, T-cell Proliferation, and Abscopal Effects

Plinabulin induces DC maturation, with most potent effect observed when administered after IR

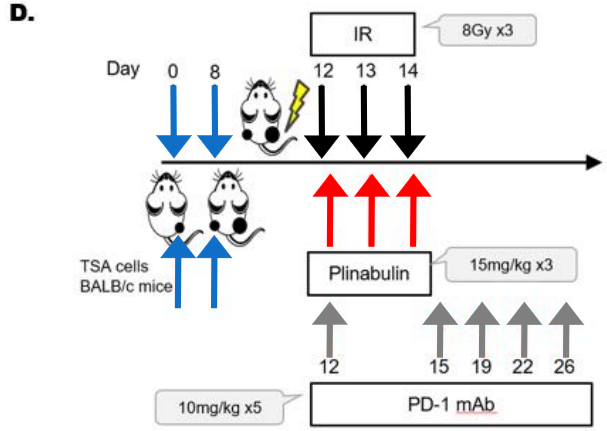


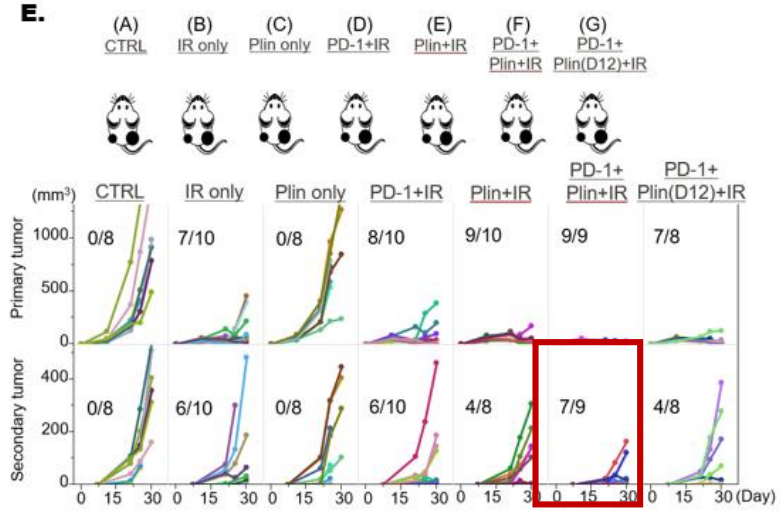


Plinabulin-treated DCs stimulate T cell proliferation, enhanced by combining with IR



The triple combination of plinabulin, IR, and anti-PD-1 led to control of secondary tumors



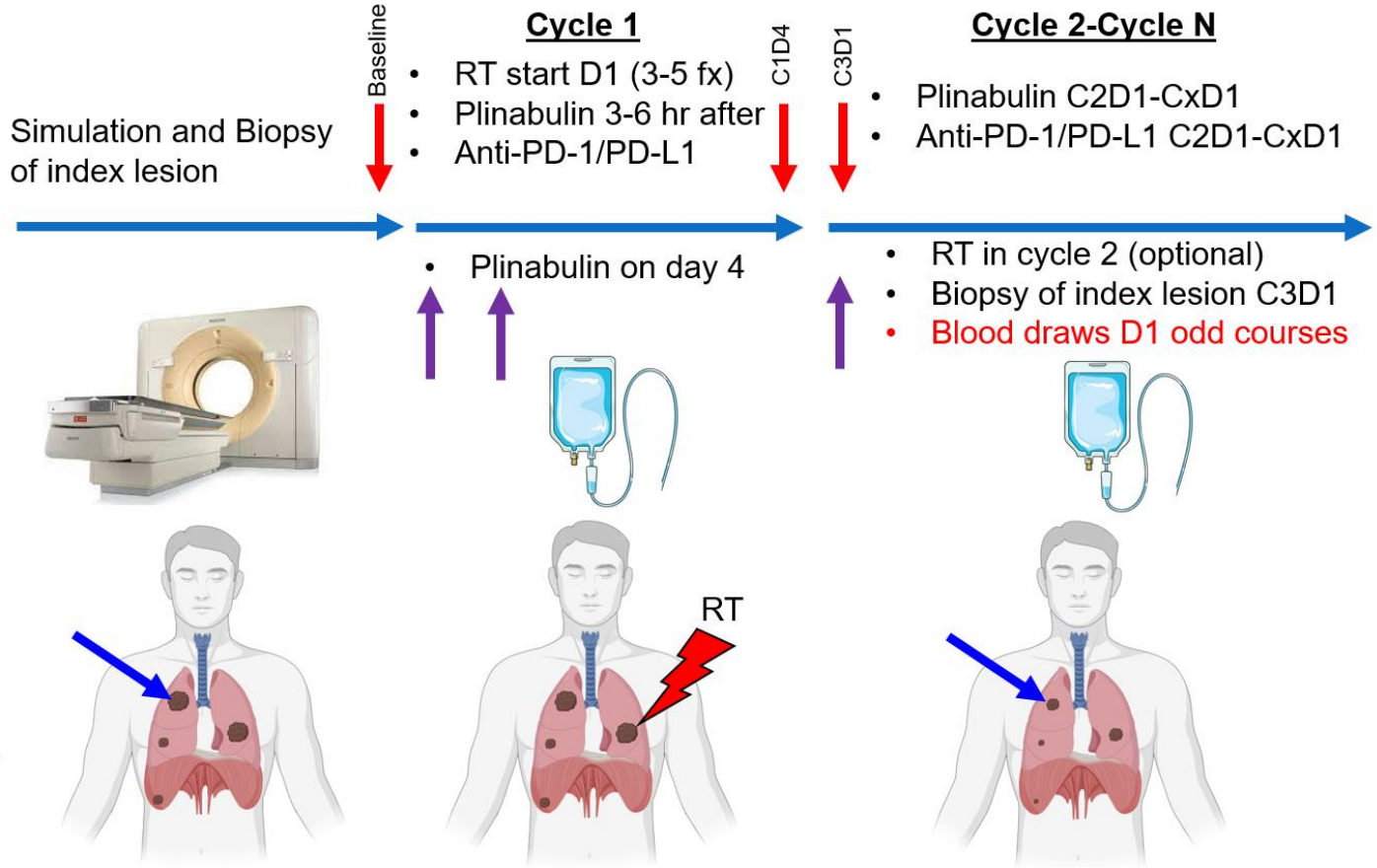


Phase 1 Study: Plinabulin in Combination with Radiation and PD-1/PD-L1 Inhibitors for Patients who have Progressed on Immunotherapies

Eligibility:
Any cancer w/ progression on prior SOC anti-PD-1/PD-L1 agents

Must have at least one site to be treated with RT and biopsy, with another metastatic site to assess response outside of index lesion

Study Design:
Open label, single-center
Phase Ib
3+3 design, DLT w/in 30 days



Primary objectives

Safety and tolerability
ORR

Secondary objectives

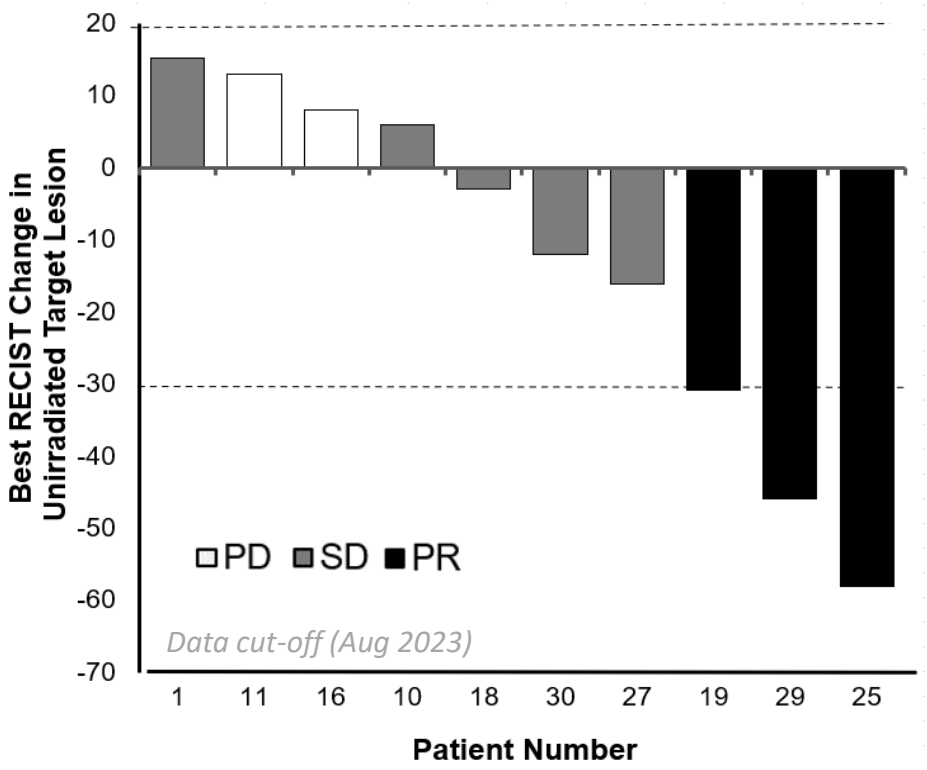
DCR, PFS, OS

Exploratory objectives

Immune phenotypes
(tumor and peripheral blood)
Dendritic cell activation
Biomarkers

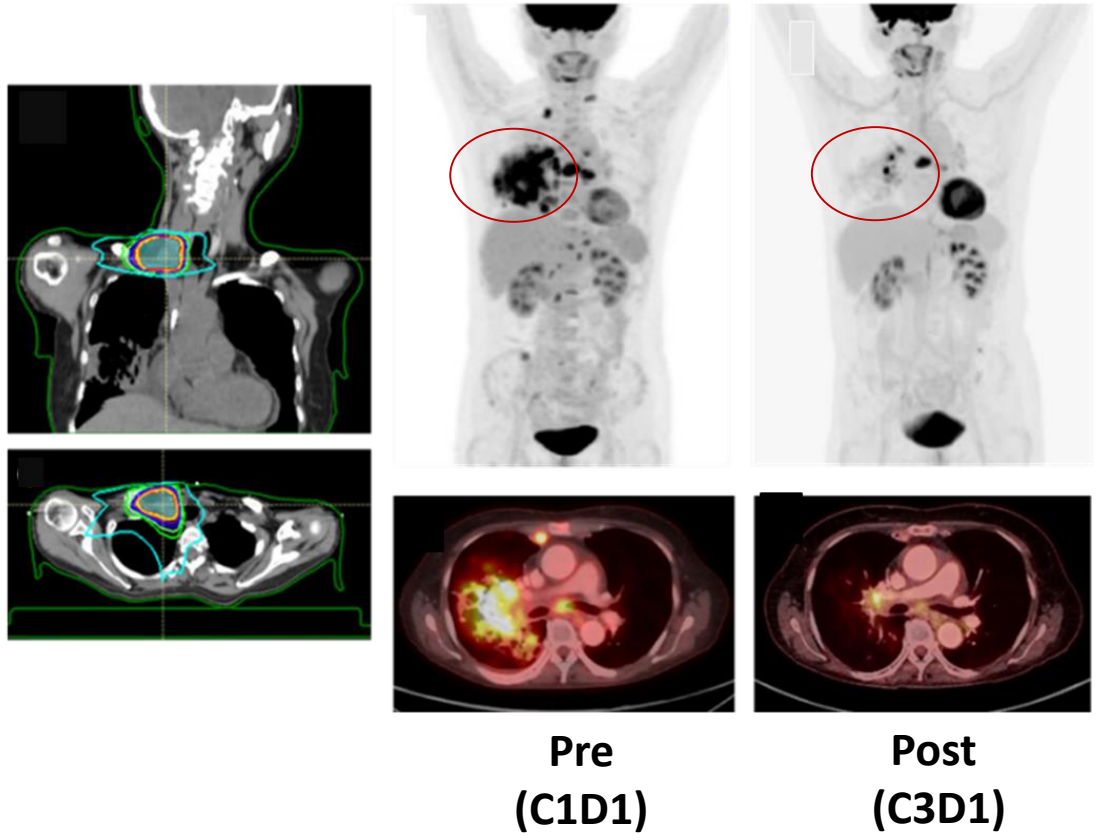
Clinical PoC in Efficacy: Plinabulin Triple Combo Produces Clinically Meaningful Responses in the Non-Irradiated Tumor Across Multiple IO-refractory Cancers

Plinabulin triple combination led to 80% DCR (3 PR, 5 SD, 2 PD) in 10 IO-refractory patients



Durable response has been observed in 2 Hodgkin lymphoma patients who progressed after 12 or 16 prior lines of therapy

Systemic abscopal effect seen comparing baseline and C3D1 for one Hodgkin lymphoma patient



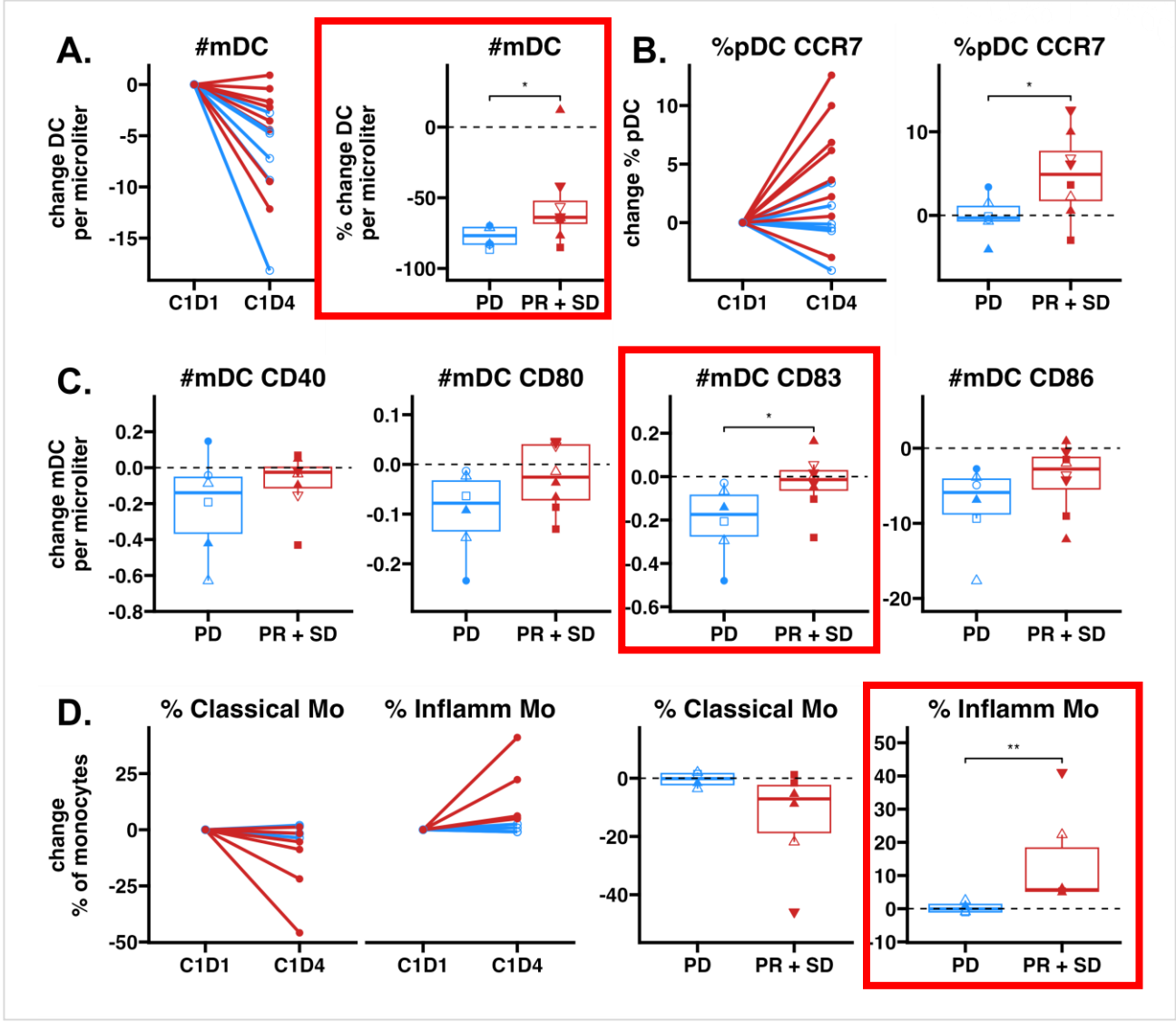
Pre (C1D1) | Post (C3D1)

Six IO-refractory cancers: NSCLC (Patient #1, #19); Merkel cell (#11); RCC (#16, #18); FL-HCC (#10); HNSCC (#27, #29); Hodgkin (#25, #30)

Clinical PoC in MOA: Plinabulin-Responding Patients Show Early Immune Activation Evidenced by DC Maturation and Proinflammatory Monocytes in the Peripheral Blood

Plinabulin induces DC Maturation

In 6 different cancers, DC maturation was observed in responding patients.



Summary

Plinabulin, in combination with radiation and immune checkpoint inhibitors, demonstrates induction of DC maturation and re-sensitization to anti-PD(L)1 in IO refractory tumors.

Plinabulin was shown to induce DC maturation on cycle 1 day 4 in blood samples of responding patients across **6 different cancer types**.

The overall results were impressive showing high **disease control rate (80%) in ICI refractory and heavily pre-treated patients**.

These preliminary but **encouraging results** warrant further clinical studies of **Plinabulin/IO combinations** in IO-refractory settings, such as Hodgkin Lymphoma and NSCLC.

"It's compelling to see activity at different points of the cancer immunity cycle and to make sure that we have non-redundant mechanisms of action. And here with the one agent, I think you're hitting different points on that cycle."

- Immuno-oncology Expert