BeyondSpring PHARMACEUTICALS

Overcoming PD-1/L1 Resistance: Translational Insights with Plinabulin

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- The market data and certain other statistical information used throughout this presentation are based on independent industry publications, governmental publications, reports by market research firms or other independent sources. Some data are also based on our good faith estimates. Although we believe these third-party sources are reliable, we have not independently verified the information attributed to these third-party sources and cannot guarantee its accuracy and completeness. Similarly, our estimates have not been verified by any independent source.
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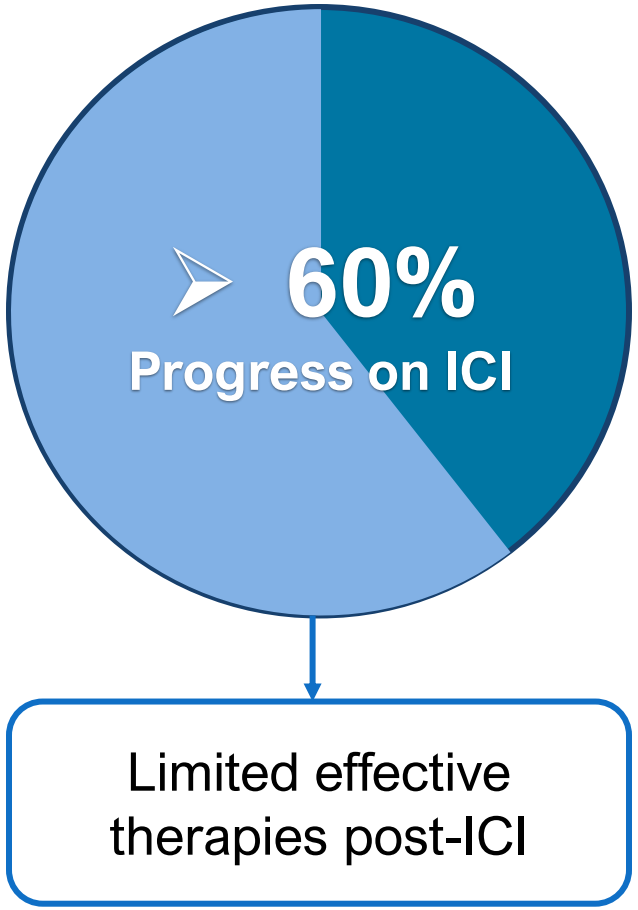
Mechanism of Acquired Resistance to Immune Checkpoint Inhibitors (ICI)



Immune Checkpoint Inhibitors (ICIs, PD-1/L1 Inhibitors) Have Transformed Cancer Care

- Approved in 20+ cancer types
- Have redefined first-line treatment in NSCLC and other solid tumors

"Acquired Resistance" to ICI

- >60% patients develop "**acquired resistance**" due to T cell exhaustion and/or antigen presenting cell (APC) pathway alterations.[1]
- After progression, ICIs are no longer recommended alone owing to limited efficacy

Urgent Opportunity

- Current options include chemotherapy, which is associated with severe neutropenia
- Significant clinical and commercial opportunity

1. Memon et al. Cancer Cell 42, 209–224 (2024).

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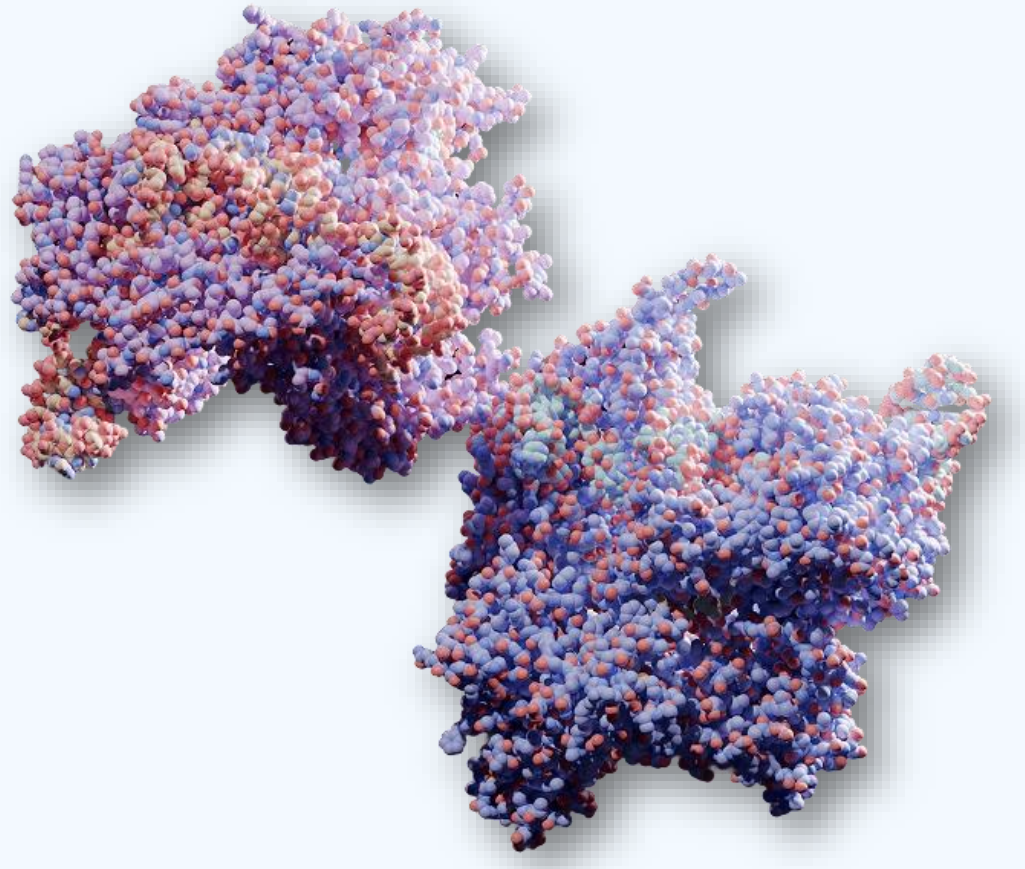


Plinabulin: Unique Dual Mechanism with Immune and Safety Benefits

- **Reversible tubulin binder** – distinct from taxanes, vincas, or colchicine; does not disrupt microtubule dynamics
- **Immune modulation** – induces **dendritic cell maturation** and primes T cells by activating GEF-H1
- **Neutropenia mitigation** – reduces chemotherapy-induced neutropenia by stimulating GMP progenitor cells

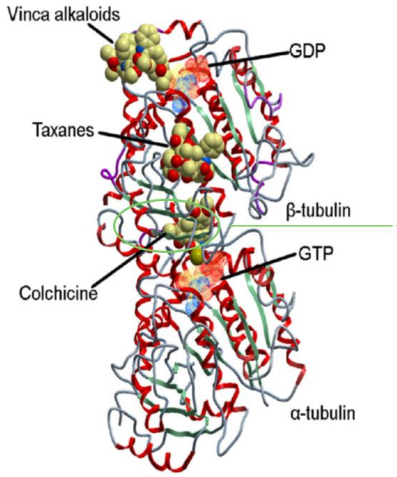
Plinabulin Monohydrate is a Brain-Penetrant, Unique Tubulin Depolymerizing Agent which induces “Dendritic Cell or DC Maturation via GEF-H1 release”

Plinabulin Monohydrate is a unique tubulin binder[1]

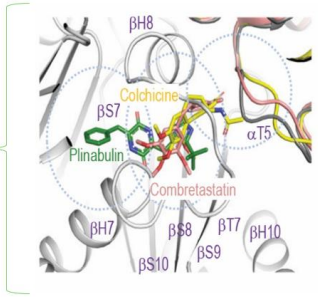
Plinabulin release GEF-H1 from microtubule, activates RhoA/ROCK pathway, leading to DC Maturation[2,3]

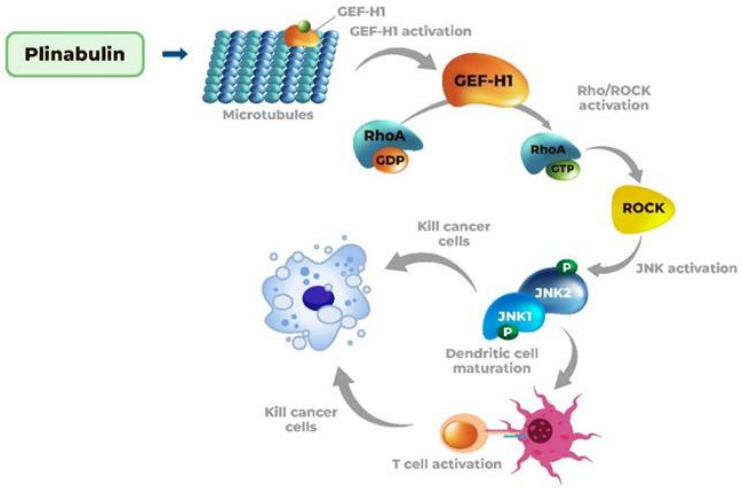
In WT DC cells, plinabulin can induce DC maturation, but not in GEF-H1 deleted DC cells[2]

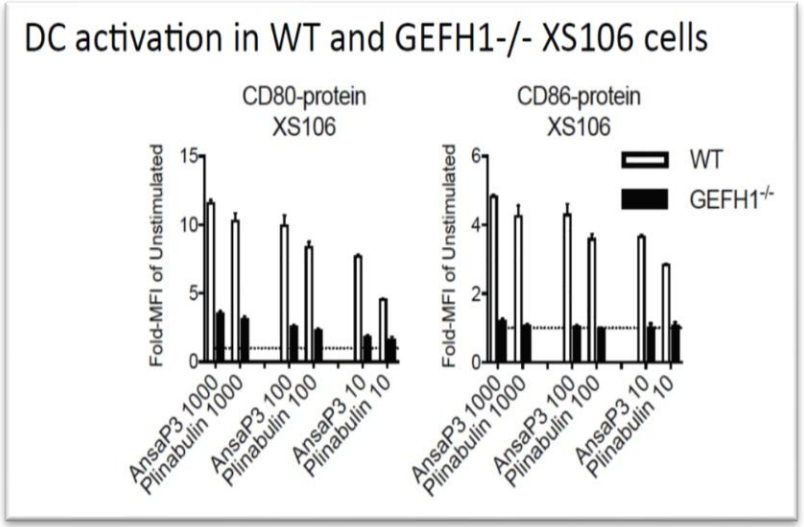
Tubulin Binding Sites



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





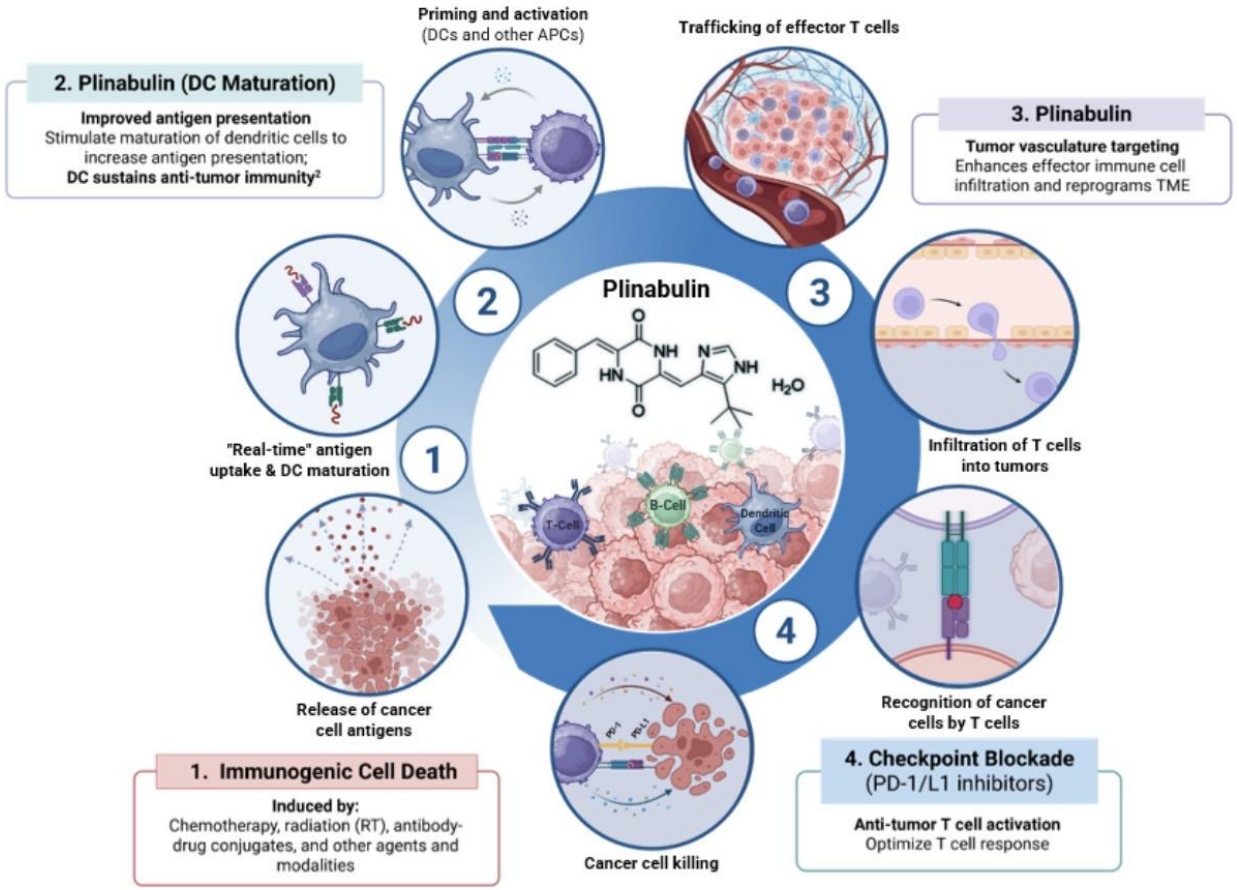


1. La Sala et al., Chem 5(11): 2969-2986 (2019); 2. Kashyap et al., Cell Reports 28(13): 3367-3380 (2019); 3. Choi et al. Cell 189 (2): 461-477 (2026)

Plinabulin's DC Maturation MoA has the Potential to Mitigate Acquired Resistance to PD-1/L1 Inhibitors

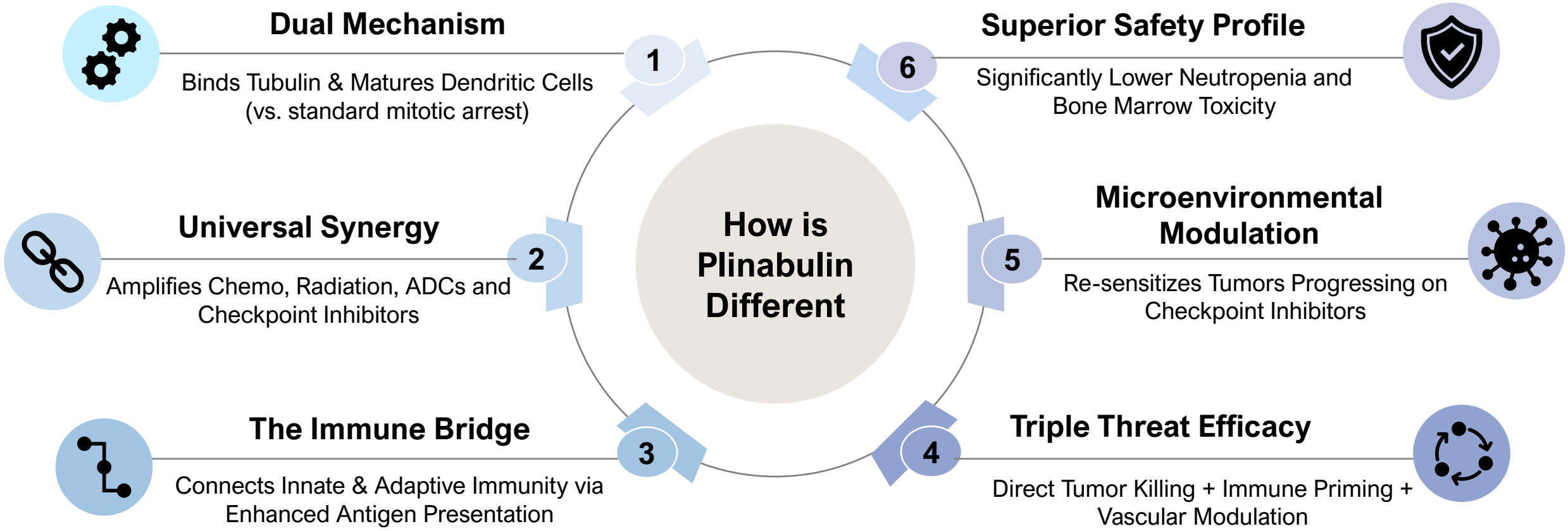
- **Plinabulin MoA DC maturation:** Dendritic cells (DCs) are the most potent antigen-presenting cells and can prime T cell function to strengthening the cancer-immunity cycle.

- **Synergistic anti-cancer benefit** by combining with chemo, ADC, or radiation to take advantage of the real-time tumor antigen from these agents.



Plinabulin Differentiated Profile

Mechanism Supported | Clinically Validated | Favorable Safety | Scalable Opportunity



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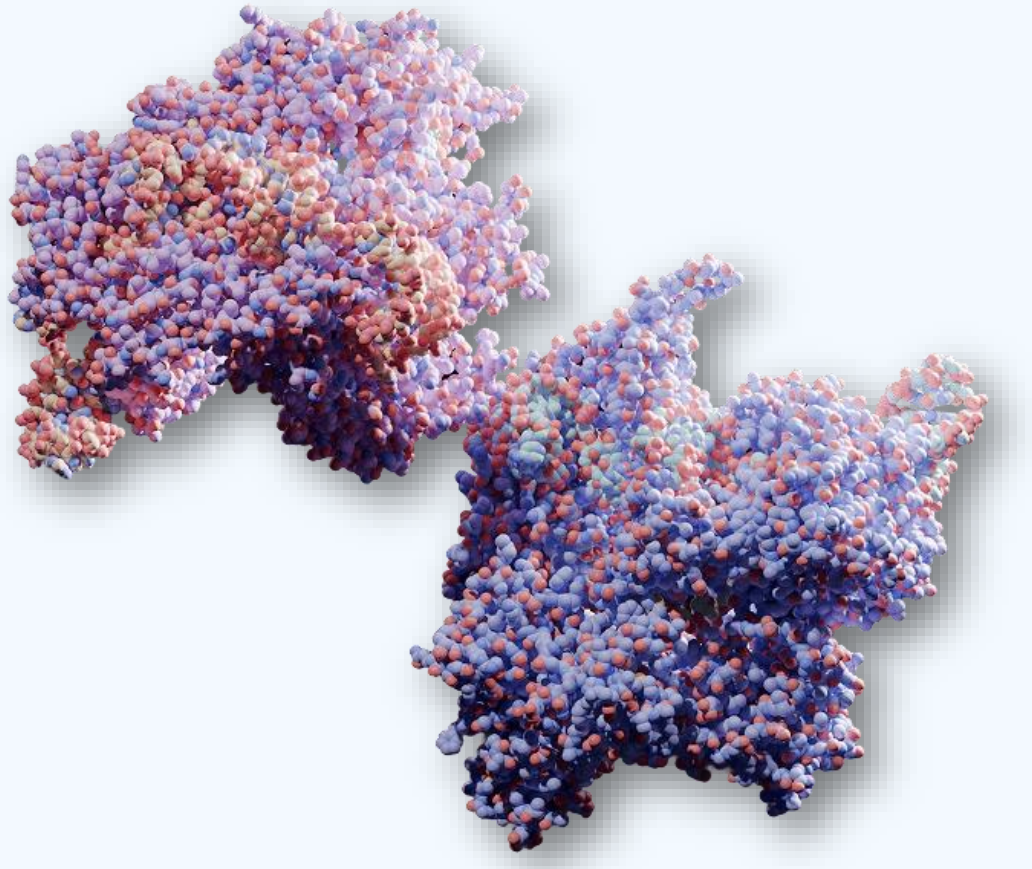


Post-ICI NSCLC: A Large, Growing and Unmet Clinical Challenge

- Limited treatment options after PD-1/L1 inhibitor progression
- Chemotherapy remains the main option, with poor outcome and high toxicity
- Urgent need for differentiated therapy with immune re-sensitization

Docetaxel Remains a Global Standard of Care (SOC) in Post-ICI NSCLC, EGFR WT, Despite Limited Benefit and Substantial Toxicity

Current Standard of Care

Docetaxel Overview

- Approved >25 years ago
- Remains the NCCN-recommended standard of care for 2L/3L NSCLC with no targetable alterations
- Used after progression on anti-PD-(L)1 antibody ± chemotherapy
- Used in real world practice across U.S., EU, Japan, and China

Limitations

- Median OS: ~9-11 months
- 40% experience severe neutropenia

Industry-wide Phase 3 Trials Summary

11 Phase 3 Studies: no OS Benefit vs. Docetaxel

- **7 global trials** including ADCs and anti-PD-(L)1 combos did not improve OS vs. docetaxel [1]
- **#8 global trial** PRAGMATICA-LUNG (SWOG S2302) — ASCO 2025 [2]
  - N=838, randomized 1:1, Ramucirumab + pembrolizumab (mOS 10.1 Mo) vs. SOC (mOS 9.3 Mo), HR 0.99, p=0.46
- **#9 global trial** COSTAR (GSK) – 07/2025
  - N=758, TIM-3 + PD-1 + docetaxel vs. PD-1 + docetaxel vs. docetaxel. Triple combo & combo did not improve OS vs. docetaxel
- **#10 global trial** LATIFY (AZ) – 12/2025
  - N=594, Durvalumab + Ceralasertib (ATR inhibitor) did not improve OS vs. docetaxel.
- **#11 trial ended ABBIL1TY** (Genmab) – 12/2025
  - N=702, Acasunlimab (PD-L1x4-1BB) + Pembro vs Doc

1. Malinou J et al., ASCO 2024; 2. Dragnev KH etal. ASCO 2025

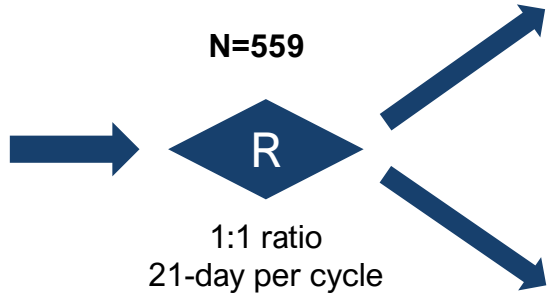
Dublin-3: “Plinabulin and Docetaxel” vs. Docetaxel in a Global Phase 3 Study with Stage IIIb/IV NSCLC EGFR WT Patients

Docetaxel + Plinabulin vs. Docetaxel + Placebo in Patients with EGFR Wild-Type NSCLC

Study Plan	Primary endpoint	Secondary endpoints
• Global, randomized, single-blinded (to patients) • Stratified by region (Asia/non-Asia), prior line (2L or 3L), ECOG (0-1/2), Prior PD-1/PD-L1 (yes/no)	**Overall survival (OS)**	• ORR, PFS • Percent of patients without severe neutropenia (Day 8, cycle 1) • Month 24 and 36 OS rate • DoR • Q-TWiST; QoL • Proportion of patients who received docetaxel >8 cycles, >10 cycles and >12 cycles

Inclusion Criteria:

- Non-squamous or squamous NSCLC
- Stage IIIb/IV
- ECOG ≤ 2
- Progression during or after treatment with one or two treatment regimens containing a platinum
- Must have at least one measurable lung lesion
- Prior checkpoint inhibitor therapy allowed



1:1 ratio
21-day per cycle
Plinabulin IV Infusion: 1 or 2 dose per cycle

DP:
Docetaxel
(75 mg/m2, day 1)
+ **Plinabulin**
(30 mg/m2, day 1, 8)

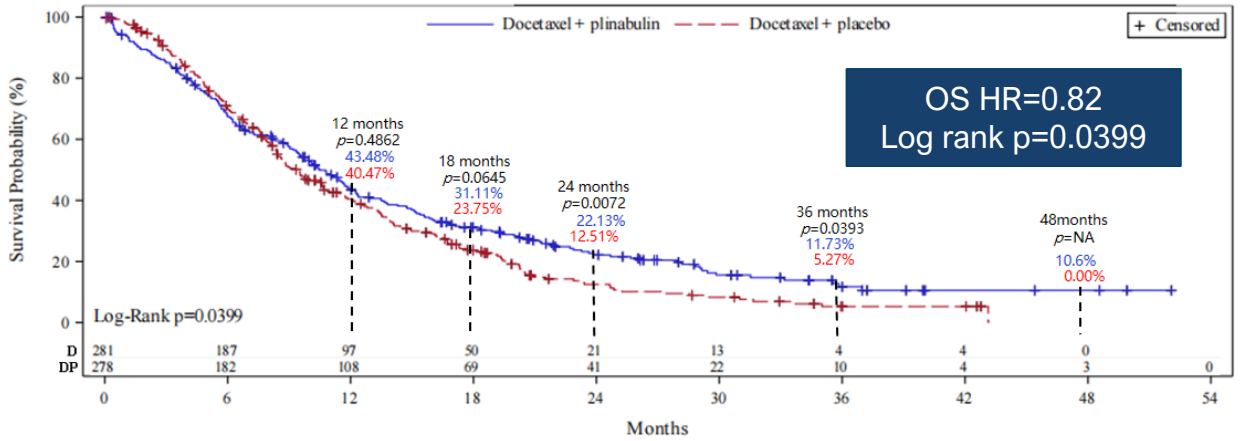
D:
Docetaxel
(75 mg/m2, day 1)
+ Placebo (day 1, 8)

Publication: Lancet Respir Med 12(10): 775-786 (2024)

Plinabulin + Docetaxel vs. Docetaxel (n=559) Met its Primary Endpoint of OS and Secondary Endpoints of PFS, ORR, and Grade 4 Neutropenia Reduction

Plinabulin and Docetaxel Showed Significant Improvement in Long-term OS Rate

- Double 2-year, 3-year OS Rate



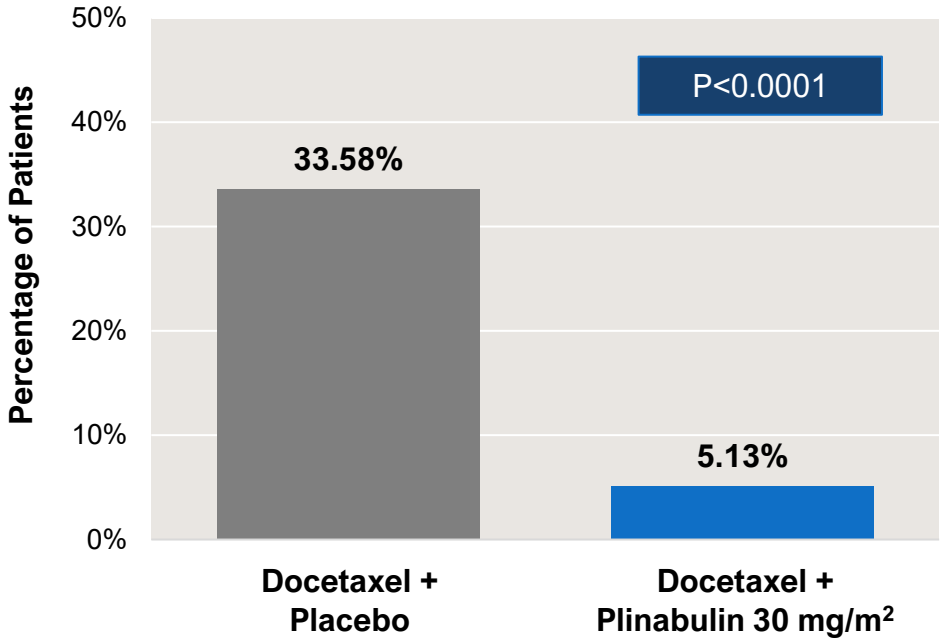
Treatment	Subjects	Event	Censored	Median (95% CI)	HR (95% CI)
Docetaxel + placebo	281	230 (81.9%)	51 (18.1%)	9.40 (8.38,10.68)	
Docetaxel + plinabulin	278	214 (77.0%)	64 (23.0%)	10.49 (9.34,11.87)	0.822(0.681,0.991)

	Mean OS (SE)	Median OS (95% CI)	HR
Docetaxel	12.77 (0.676)	9.4 (8.4, 10.7)	
Plinabulin + Docetaxel	15.05 (0.848)	10.5 (9.3, 11.9)	0.82 (0.68, 0.99)

Publication: Lancet Respir Med 12(10): 775-786 (2024)

Plinabulin Significantly Reduced Grade 4 neutropenia of Docetaxel

Grade 4 neutropenia, **All Cycles** Day 8

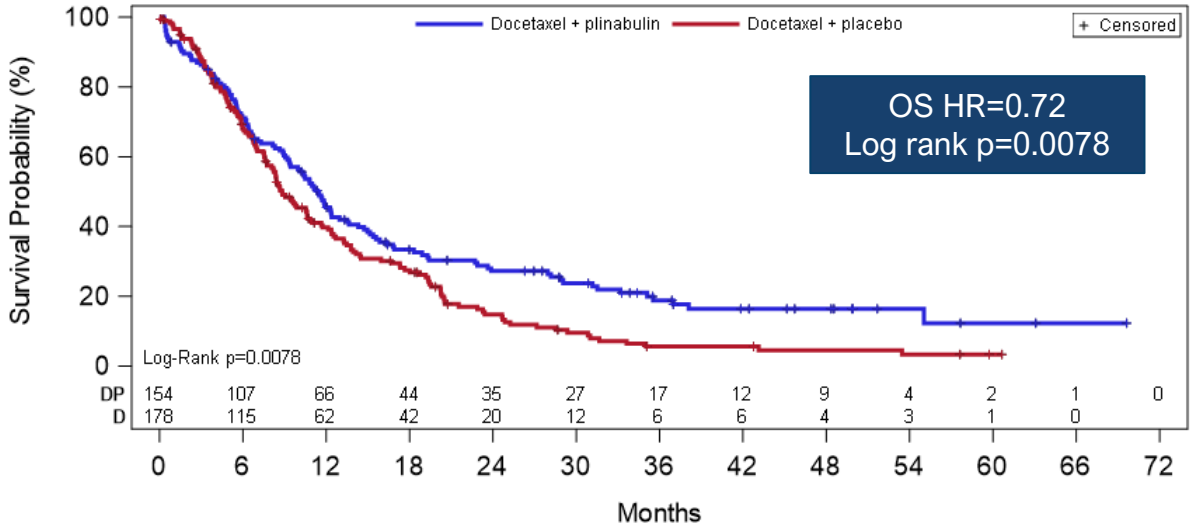


Similar results for Grade 4 neutropenia on Cycle 1 Day 8
- Day 8 is ANC Nadir for Docetaxel

Dublin-3: Post-hoc Analysis in Plinabulin Mechanism-Based Population in 2L/3L Non-squamous EGFR WT NSCLC, Progressed on PD-1/L1 Inhibitors

Non-squamous

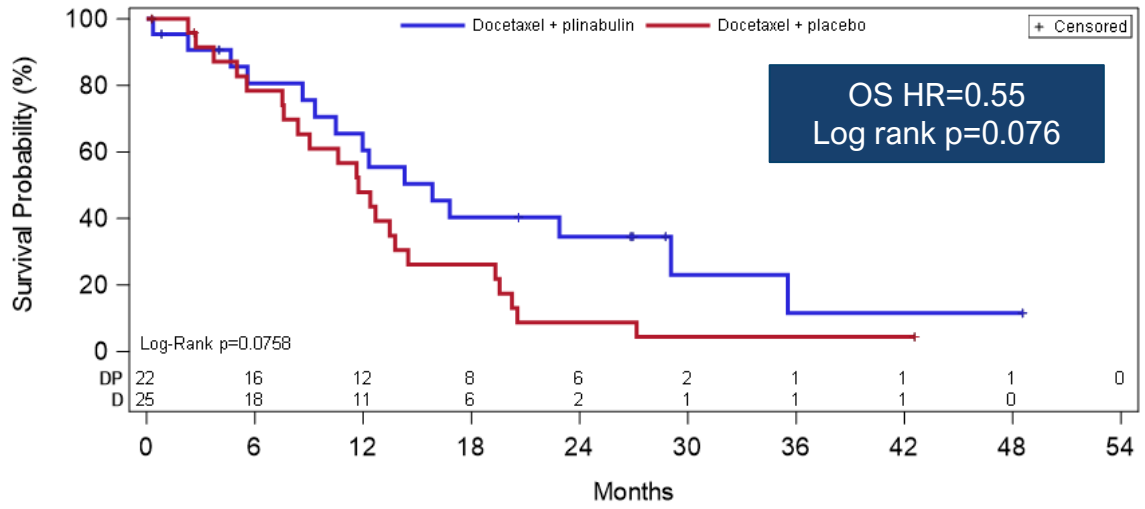
mOS extension of 2.5 months
(DP 11.4 vs. D 8.8 months, HR 0.72)



Non-squamous	N	Median OS (95% CI)	HR	Log rank P value
Docetaxel	178	8.81 (7.73, 10.65)		
Plinabulin + Docetaxel	154	11.37 (9.37, 12.95)	**0.72 (0.57, 0.92)**	**P = 0.0078**

Non-squamous, Progressed on ICI

mOS extension of 4.1 months
(DP 15.8 vs. D 11.7 months, HR 0.55)



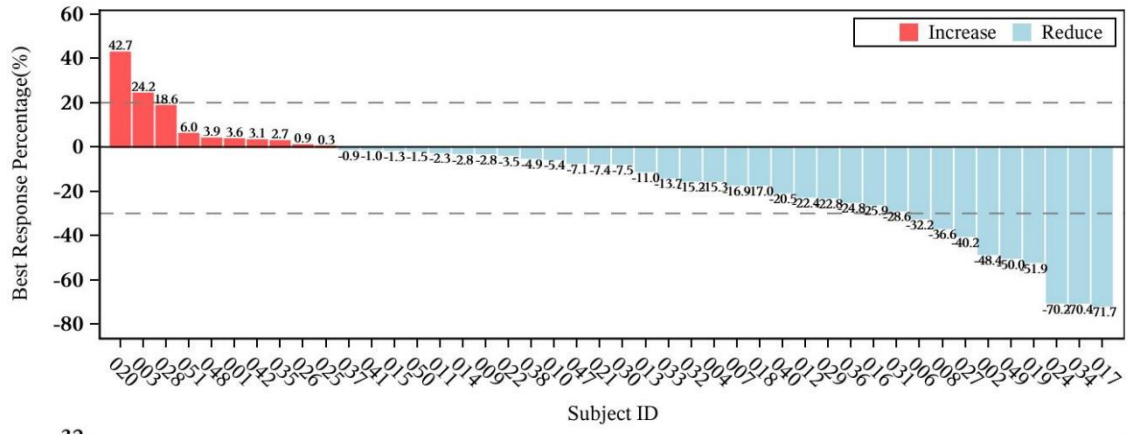
Non-squamous, post-ICI	N	Median OS (95% CI)	HR	Log rank P value
Docetaxel	25	11.7 (7.59, 13.77)		
Plinabulin + Docetaxel	22	15.8 (9.34, 29.06)	**0.55 (0.28, 1.07)**	**P = 0.076**

Publication: Lancet Respir Med 12(10): 775-786 (2024); NACLC 2025

Study 303 (Plinabulin + Docetaxel + PD-1) in 2L/3L Metastatic NSCLC, Immediately Progressed on PD-1/L1 Inhibitors – Phase 2 IIT Study with Merck

Primary Endpoint (n=47)	
Confirmed ORR（RECIST 1.1）	**18.2%**
Secondary Endpoint	
Median PFS（RECIST 1.1）	**7.0 months**
Median OS	**16 months+, Not reached**
Median DoR（RECIST 1.1）	7.2 months
Disease Control Rate (DCR)	**85.1%**
12 months OS%	79%
24 months OS%	**66%**

Best Change (%) in Target Lesions



Presentation at SITC 2025:

- Median follow-up at data cutoff (30 September 2025) was 14.3 months.
- Median age was 67 (44-83); 80.9% male and 19.1% female. 72.3% were current or former smokers.
- Histology included 63.8% with non-squamous cell carcinoma, 36.2% with squamous cell carcinoma.

Plinabulin + Docetaxel: Addressing Unmet Needs in 2L/3L NSCLC, EGFR WT, After Prior PD-1/L1 Failure with Positive Benefit/Risk Ratio

Severity of Unmet Need	Current SOC - Docetaxel	Potential Solution - Plinabulin + Docetaxel
●●●	Lack of durable response post-immunotherapy	Strong immune re-priming, durable OS benefit
●●●	Immune exhaustion, “cold” tumors	Converts tumors to “hot”
●●	Limited efficacy with Docetaxel	More cycles and more dose of docetaxel; Improved OS, PFS, and ORR
●●	High chemo-induced neutropenia	Reduces Grade 4 neutropenia
●●	EGFR wild-type population underserved	Target EGFR and other wild-type patients

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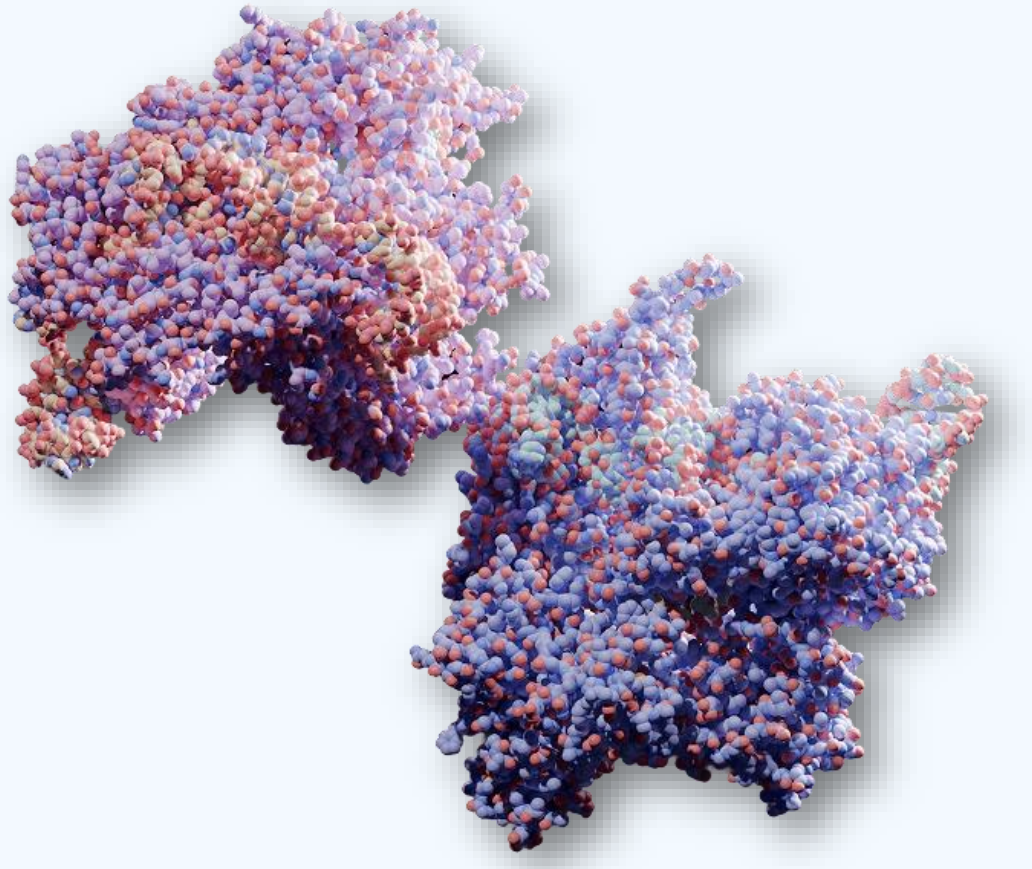
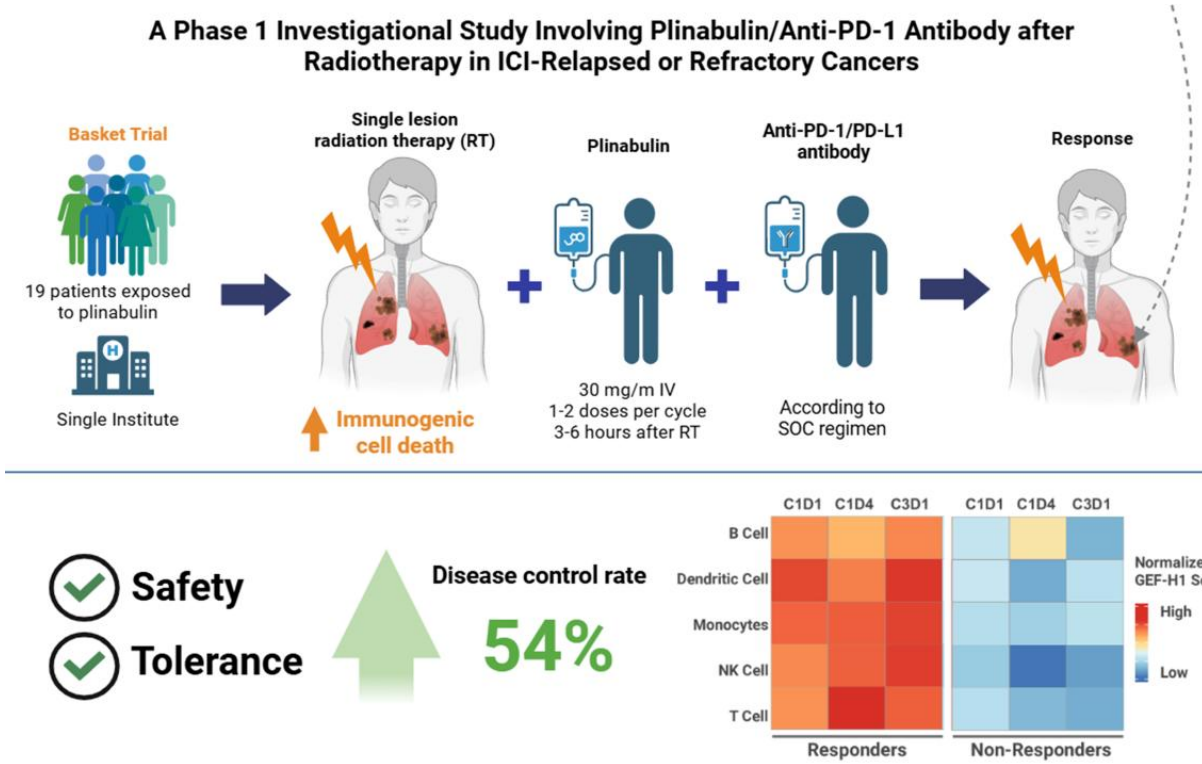


Translational Biomarker: DC maturation in Responding Patients in Multiple Cancers who Failed ICI

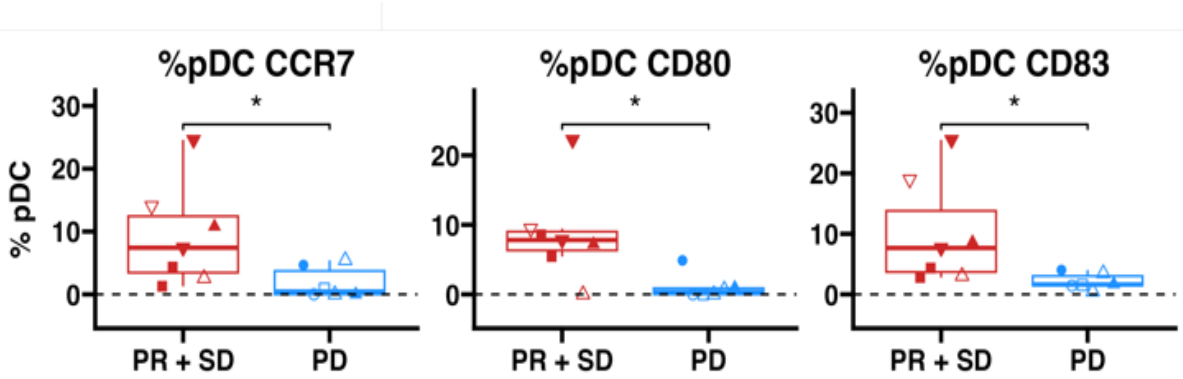
- Collaboration with MD Anderson
- Publication: Lin et al., Med 6(10):100752 (2025)

Plinabulin-Responding Patients Show Early Immune Activation Evidenced by Rapid DC Maturation in the Peripheral Blood

CCR7, CD80 and CD83 are rapidly upregulated at cycle 1 Day 4 in responding (PR + SD) patients[1]



Dendritic Cell Maturation & Migration



▽ Fibrolamellar HCC ● Melanoma □ MSI-H CRC △ RCC PD

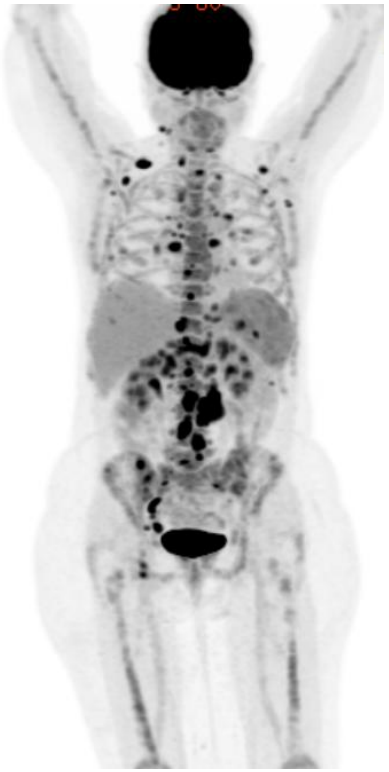
■ Hodgkin lymphoma ○ Merkel Cell Carcinoma ▽ NSCLC ▲ SCCHN PR + SD

1. Lin et al., Med 6(10):100752 (2025)

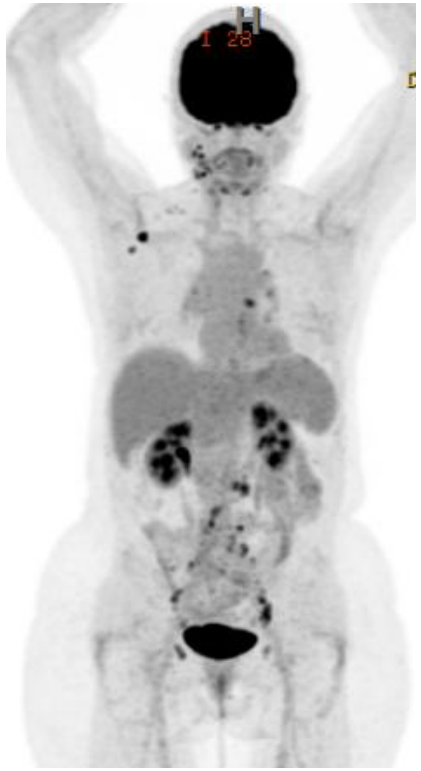
Clinically Meaningful Responses in the Non-Irradiated Tumor in Hogkins Lymphoma, with Prolonged Duration of Response

Patient #2: 59yoF relapsed refractory cHL diagnosed 2005. Prior treatments (**16 prior lines**) including ABVD x 8, ICE x 3, **autoSCT** with Bu/Mel, brentuximab, sirolimus and vorinostat, **nivolumab**, Revlimid, bendamustine, Ibrutinib, ADCT 301, CD30 CAR-T, HMPL-523, gemcitabine

- Plinabulin/Nivolumab C1D1 2/2023 - C14 3/2024, RT 20Gy in 5 fractions to LT axilla (2/2023)
- Best response PR/irPR
- EOS 3/2024: Treatment discontinued by pt choice
- Progressive disease 9/2024
- **Duration of response 19 months**



Pre-treatment PET



PR/irPR with plinabulin/RT/nivo

First-in-Class Agent Plinabulin: Potentially Transforming Oncology Treatment with Novel Mechanisms and Clinically Meaningful Benefits in ICI-Progressed Patients in NSCLC and Beyond

SIMPLE

Easy to use

Day 1 or Day 1+ 8 use in a cycle, intravenous infusion of 30-60 minutes

SAFE

Safety Benefit

Reduce AEs including chemotherapy-induced neutropenia

DURABLE

Clinical Benefit

Overall survival and durable response

thank you!

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