Plinabulin/Docetaxel vs. Docetaxel in 2L/3L EGFR WT NSCLC after Platinum Regimens (DUBLIN-3): a Phase 3 Randomized Controlled Trial

Asian subset (n=488)

Dr. Baohui Han, Shanghai Chest Hospital

6 Dec. 2025

DECLARATION OF INTERESTS

Dr. Baohui Han

BeyondSpring, Eli Lilly, AstraZeneca, Merck, and Chia Tai Tianqing Pharma

Unmet Medical Needs in 2/3L NSCLC, EGFR WT

Docetaxel remains SOC with limited benefit

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 months
- 40% experience severe neutropenia

Industry-wide Phase 3 Trials Summary

- **7 global trials** including ADCs and anti-PD-(L)1 combos **did not improve OS vs. docetaxel** [1]
- **#8 failed global trial** PRAGMATICA-LUNG (SWOG S2302) — ASCO 2025 [2]
  - ➢ Enrolled advanced NSCLC patients post-ICI (≥84 days ICI treatment) + platinum chemo
  - ➢ ITT population (n=838) randomized 1:1;
  - ➢ OS: Ramucirumab + pembrolizumab (10.1 Mo) vs. Standard of care (9.3 Mo), HR 0.99, p=0.46
- **#9 failed global trial** COSTAR (GSK) – 07/2025
  - ➢ N=758, TIM-3 + PD-1 + docetaxel vs. PD-1 + docetaxel vs. docetaxel
  - ➢ OS: Triple combo & combo did not improve OS vs. docetaxel

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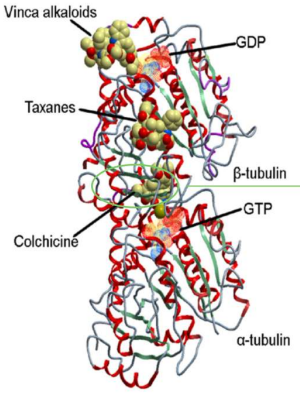
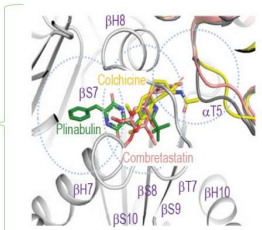
Plinabulin Mechanism in Dendritic Cell Maturation

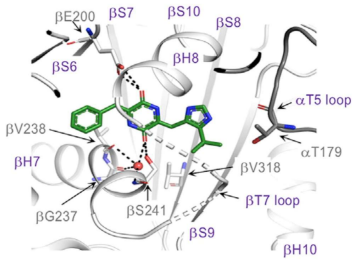
As a Unique Tubulin Binder, Plinabulin monohydrate (small molecule, NCE) Effectively Liberates GEF-H1 from Microtubules Leading to DC Maturation and T-cell Activation

Tubulin Binding Sites

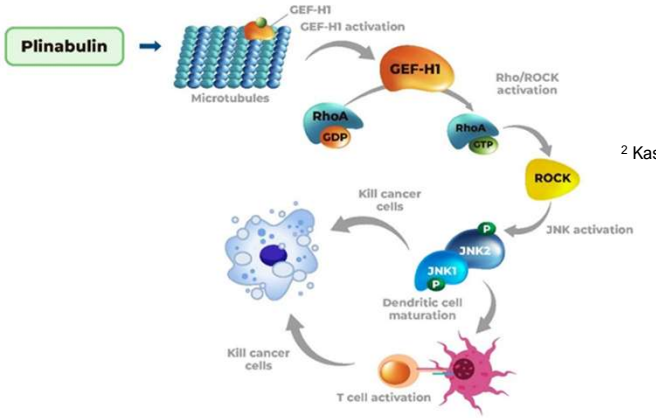


Plinabulin Binds to β-Tubulin, Near the Colchicine Site[1]



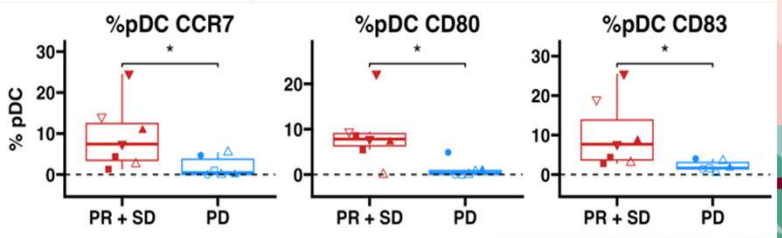


[1] La Sala et al., 2019 Chem 5(11): 2969-2986



[2] Kashyap et al., Cell Reports 28(13): 3367-3380 (2019)

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



[3] Lin et al., Med, Online now, 100752, June 27, 2025

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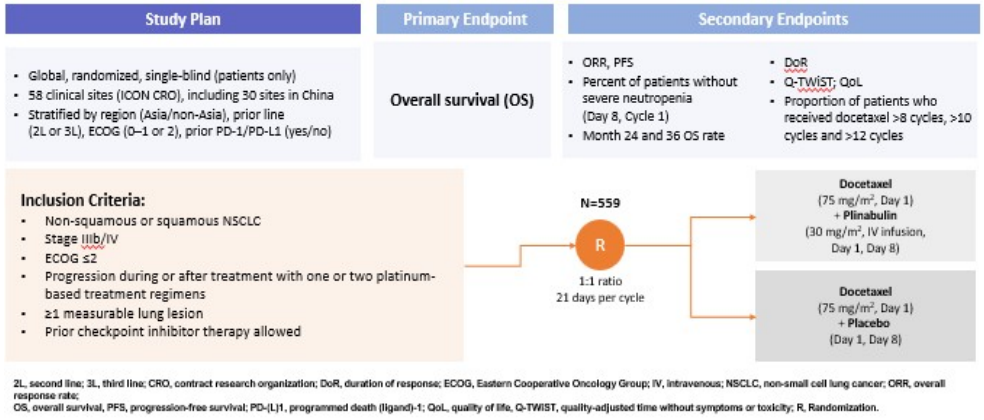
DUBLIN-3 Study Design

Plinabulin + Docetaxel vs Docetaxel in 2/3L NSCLC, EGFR WT

Study Design



2L, second line; 3L, third line; CRO, contract research organization; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; NSCLC, non-small cell lung cancer; ORR, overall response rate; OS, overall survival, PFS, progression-free survival; PD-(L)1, programmed death (ligand)-1; QoL, quality of life, Q-TWIST, quality-adjusted time without symptoms or toxicity; R, Randomization.

Balanced Baseline Characteristics (Asian Subset)

Characteristics	Docetaxel + placebo (D group) N=245	Docetaxel + plinabulin (DP group) N=243
Median age, years (range)	59.0(25.0-78.0)	61.0(37.0-76.0)
<65	169(69.0%)	166(68.3%)
≥65	76(31.0%)	77(31.7%)
Sex		
Male	189 (77.1%)	181 (74.5%)
Female	56 (22.9%)	62 (25.5%)
Smoking status		
Current smoker	10(4.1%)	15(6.2%)
Past smoker	121(49.4%)	118(48.6%)
Never smoked	93(38.0%)	93(38.3%)
Missing	31(12.7%)	32(13.2%)
Tumor histology		
Squamous	96 (39.2%)	107 (44.0%
Non-squamous	146 (59.6%)	132 (54.3%)
Missing	3 (1.2%)	4 (1.6%)
Metastatic organs		
Brain	11 (4.5%)	13 (5.3%)
Liver	35 (14.3%)	26 (10.7%)
Bone	74 (30.2%)	44 (18.1%)
ECOG score		
0	34 (13.9%)	32 (13.2%)
1	204 (83.3%)	206 (84.8%)
2	6 (2.4%)	5 (2.1%)
Missing	1 (0.4%)	0 (0.0%)
Cancer stage		
IIIB	39 (15.9%)	43 (17.7%)
IV	204 (83.3%)	197 (81.1%)
Missing	2 (0.8%)	3 (1.2%)
Line of previous therapy		
First-line	195 (79.6%)	189 (77.8%)
Second-line	50 (20.4%)	54 (22.2%)
Prior treatment history for NSCLC		
Surgery	113 (46.1%)	93 (38.3%)
Radiotherapy	67 (27.3%)	64 (26.3%)
Chemotherapy	245(100%)	243(100%)
PD-1 /PD-L1 inhibitor		
Yes	24 (9.8%)	21 (8.6%)
No	221 (90.2%)	222 (91.4%)

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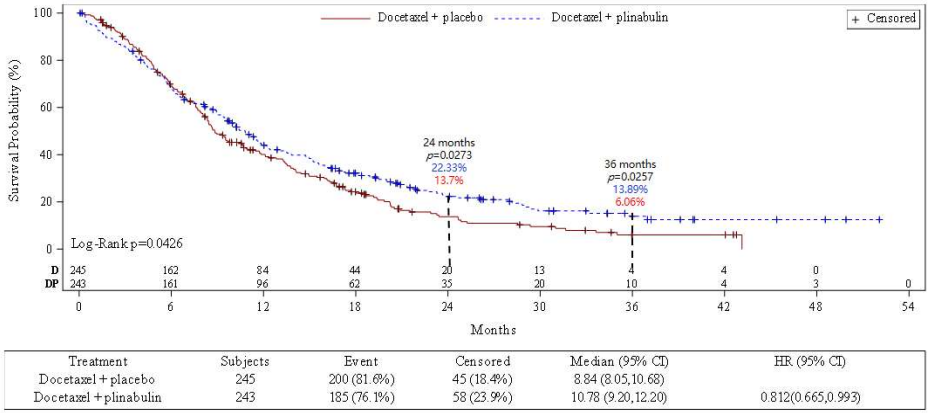
DUBLIN-3 Study Asian Subset Primary Endpoint (OS)

Plinabulin/Docetaxel Met its Primary Endpoint (OS) with Significant Improvement in Long-term OS Rate; More Pronounced OS benefit in Non-squamous patients (HR 0.69)

Asian Subset (ITT, n=488)

Double 2-year and 3-year OS rate



ITT Chinese Pts	mOS Mo [95% CI] DB lock	DB lock + 24 Mo All	DB lock + 24 Mo NSQ	ORR %	DOR Mo	mPFS Mo [95% CI]	24-Mo OS-Rate (%)	36-Mo OS-Rate (%)	Gr4N Rate (%)
DP (n=243)	10.8	10.8	11.4	14.0% (34/243)	8.4	3.2	22.3%	13.89%	3.9%
D (n=245)	8.8	8.8	8.4	6.9% (17/245)	5.4	2.8	13.7%	6.06%	26.5%
HR	0.81	0.80	0.69	N/A	0.47	0.77	NA	NA	NA
P value	0.0426	0.0300	0.0064	0.010	0.0296	0.0111	0.0273	0.0257	<0.0001

	Mean OS (SE)	Median OS (95% CI)	HR
Docetaxel (D)	12.96 (0.755)	**8.8 (8.05,10.68)**	0.812(0.665,0.993) Log rank p=0.0426
Plinabulin + Docetaxel (DP)	15.45 (0.931)	**10.8 (9.20,12.20)**	

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DUBLIN-3 Study Asian Subset Safety (>=10%) TEAE

Term	D group (n=244)			DP group (n=240)		
Preferred term	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
At least one AEs	242(99.2%)	71(29.1%)	107(43.9%)	239(99.6%)	126(52.5%)	43(17.9%)
Anaemia	116(47.5%)	13(5.3%)	0(0.0%)	124(51.7%)	11(4.6%)	0(0.0%)
Constipation	68(27.9%)	0(0.0%)	0(0.0%)	85(35.4%)	1(0.4%)	0(0.0%)
Diarrhoea	48(19.7%)	**3(1.2%)**	0(0.0%)	95(39.6%)	**20(8.3%)**	**1(0.4%)**
Nausea	57(23.4%)	0(0.0%)	0(0.0%)	80(33.3%)	1(0.4%)	0(0.0%)
Vomiting	35(14.3%)	1(0.4%)	0(0.0%)	68(28.3%)	4(1.7%)	0(0.0%)
Abdominal distension	12(4.9%)	0(0.0%)	0(0.0%)	28(11.7%)	2(0.8%)	0(0.0%)
Abdominal pain	8(3.3%)	1(0.4%)	0(0.0%)	30(12.5%)	0(0.0%)	0(0.0%)
Pyrexia	56(23.0%)	0(0.0%)	0(0.0%)	83(34.6%)	0(0.0%)	0(0.0%)
Malaise	54(22.1%)	2(0.8%)	0(0.0%)	64(26.7%)	1(0.4%)	0(0.0%)
Non-cardiac chest pain	27(11.1%)	3(1.2%)	0(0.0%)	31(12.9%)	2(0.8%)	0(0.0%)
Lung infection	26(10.7%)	17(7.0%)	0(0.0%)	19(7.9%)	11(4.6%)	1(0.4%)
White blood cell count decreased	175(71.7%)	93(38.1%)	30(12.3%)	154(64.2%)	44(18.3%)	30(12.5%)
Neutrophil count decreased	171(70.1%)	39(16.0%)	92(37.7%)	126(52.5%)	41(17.1%)	31(12.9%)
Platelet count decreased	45(18.4%)	1(0.4%)	1(0.4%)	66(27.5%	10(4.2%)	4(1.7%)
Alanine aminotransferase increased	42(17.2%)	0(0.0%)	0(0.0%)	40(16.7%)	2(0.8%)	0(0.0%)
Aspartate aminotransferase increased	24(9.8%)	1(0.4%)	0(0.0%)	30(12.5%)	1(0.4%)	0(0.0%)
Weight decreased	20(8.2%)	0(0.0%)	0(0.0%)	28(11.7%)	1(0.4%)	0(0.0%)
Decreased appetite	76(31.1%)	6(2.5%)	0(0.0%)	89(37.1%)	3(1.3%)	0(0.0%)
Hypoalbuminaemia	44(18.0%)	0(0.0%)	0(0.0%)	50(20.8%)	1(0.4%)	0(0.0%)
Hyponatraemia	37(15.2%)	4(1.6%)	0(0.0%)	43(17.9%)	8(3.3%)	6(2.5%)
Hyperglycaemia	27(11.1%)	3(1.2%)	0(0.0%)	40(16.7%)	9(3.8%)	0(0.0%)
Pain in extremity	37(15.2%)	1(0.4%)	0(0.0%)	31(12.9%)	1(0.4%)	0(0.0%)
Arthralgia	21(8.6%)	0(0.0%)	0(0.0%)	24(10.0%)	1(0.4%)	0(0.0%)
Back pain	25(10.2%)	2(0.8%)	0(0.0%)	18(7.5%)	2(0.8%)	0(0.0%)
Insomnia	28(11.5%)	1(0.4%)	0(0.0%)	28(11.7%)	1(0.4%)	0(0.0%)
Cough	47(19.3%)	1(0.4%)	0(0.0%)	43(17.9%)	0(0.0%)	0(0.0%)
Dyspnoea	37(15.2%)	4(1.6%)	2(0.8%)	26(10.8%)	3(1.3%)	0(0.0%)
Haemoptysis	24(9.8%	1(0.4%)	0(0.0%)	31(12.9%)	4(1.7%)	1(0.4%)
Alopecia	106(43.4%)	0(0.0%)	0(0.0%)	110(45.8%)	0(0.0%)	0(0.0%)
Hypertension	15(6.1%)	**7(2.9%)**	0(0.0%)	84(35.0%)	**46(19.2%)**	0(0.0%)

D group = Docetaxel + placebo. DP= Docetaxel + plinabulin. TEAE=treatment-emergent adverse event. WBC=white blood cell

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Conclusion

Plinabulin + Docetaxel with durable anti-cancer benefit and significantly reduced severe neutropenia; a potential practice-changing treatment for 2/3L non-squamous NSCLC, EGFR WT

The addition of Plinabulin as a single agent added to SOC Docetaxel led to improved anti-cancer efficacy, in terms of OS, PFS and ORR; and enhanced safety in reducing docetaxel-induced severe neutropenia.

Efficacy

- Significant survival benefit in ITT (OS *HR*=0.81).
  - Doubled 2-year, 3-year survival rate;
  - More pronounced OS benefit in non-squamous patients (HR 0.73)
- Significant PFS and ORR benefit. Significant reduction in grade 4 neutropenia in cycle 1 day 8 ($p<0.0001$).
- Plinabulin and docetaxel arm had more exposure to docetaxel (16 vs 3 pts in >12 cycles).
- The OS benefits with > 4 treatment cycles improved in DP vs D (mOS=22.72 months vs 14.43 months; HR 0.51; p=0.0022)

Safety and Tolerability

- The regimen was well tolerated with similar TEAE rate and lower Grade 4 TEAE rate.
- Side effects included transient hypertension, which resolved in 4–6 hours, nausea, vomiting and GI side effects.
- Docetaxel-induced neutropenia was significantly reduced, allowing increased treatment exposure. Exposure adjusted grade 3 and 4 events were significantly lower in the combination arm.

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