Supplementary Online Content

Blayney DW, Mohanlal R, Adamchuk H, et al. Efficacy of plinabulin vs pegfilgrastim for prevention of docetaxel-induced neutropenia in patients with solid tumors: a randomized clinical trial. *JAMA Netw Open*. 2022;5(1):e2145446. doi:10.1001/jamanetworkopen.2021.45446

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Patient Disposition and Demographics

Parameter	Peg (N=53) n (%)	Plin (N=52) n (%)	All Patients (N=105) n (%)
All Subjects			135
All Randomized Subjects	53 (100.0)	52 (100.0)	105 (100.0)
Stratification Category			
Breast Cancer and Asia	18 (34.0)	18 (34.6)	36 (34.3)
Breast Cancer and Non-Asia	8 (15.1)	9 (17.3)	17 (16.2)
HRPC and Non-Asia	10 (18.9)	9 (17.3)	19 (18.1)
NSCLC and Asia	7 (13.2)	7 (13.5)	14 (13.3)
NSCLC and Non-Asia	10 (18.9)	9 (17.3)	19 (18.1)
Analysis Population[a]			
ITT Population	53 (100.0)	52 (100.0)	105 (100.0)
Safety Population	53 (100.0)	52 (100.0)	105 (100.0)
Treatment Completion			
Completed	39 (73.6)	45 (86.5)	84 (80.0)
Early Discontinued	14 (26.4)	7 (13.5)	21 (20.0)
Reason for Discontinuation[b]			
Adverse Event	1 (4.8)	1 (4.8)	2 (9.5)
Other[c]	8 (38.1)	3 (14.3)	11 (52.4)
Prohibited Concomitant Medication or Therapy	1 (4.8)	0	1 (4.8)
Protocol Prohibited Dose Delay	1 (4.8)	0	1 (4.8)
Withdrawal by Subject	3 (14.3)	3 (14.3)	6 (28.6)
Age (Years)			
Mean (SD)	58.9 (10.85)	57.0 (10.79)	58.0 (10.81)
Median	60.0	58.5	59.0
Min, Max	36, 81	31, 81	31, 81
Age Category: n (%)			
<65 Years	34 (64.2)	40 (76.9)	74 (70.5)
≥65 Years	19 (35.8)	12 (23.1)	31 (29.5)
Sex: n (%)			
Male	21 (39.6)	19 (36.5)	40 (38.1)
Female	32 (60.4)	33 (63.5)	65 (61.9)
Risk Factors: n (%)			
Prior chemotherapy or radiation treatment	49 (92.5)	51 (98.1)	100 (95.2)
Bone marrow involvement by tumor	0	1 (1.9)	1 (0.95)
Surgery and/or open wounds within 4 weeks of first administration of study drug	2 (3.8)	2 (3.8)	4 (3.8)
Age >65 years of age and receiving full chemotherapy dose intensity	19 (35.8)	12 (23.1)	31 (29.5)
1 Risk factor only	36 (67.9)	38 (73.1)	74 (70.5)
2 Risk factors	17 (32.1)	14 (26.9)	31 (29.5)

Abbreviations: ECOG: Eastern Cooperative Oncology Group; HRPC: Hormone-refractory (androgen-independent) prostate cancer; ITT: Intent to treat; N: Total number of patients; n: Number of patients; NSCLC: Non-small cell lung cancer; Peg: Pegfilgrastim; Plin: Plinabulin; SD: Standard deviation.

Peg: Docetaxel (75 mg/m^2) + pegfilgrastim (6 mg); Plin: Docetaxel (75 mg/m^2) + plinabulin (40 mg)

a. For the treatment assignments, ITT included patients that had been randomized in the study, while Safety included patients that had been randomized in the study and had received at least one dose of study medication

b. Percentages based on the total number of discontinuations

c. Details regarding what was categorized as "Other" are provided in **eTable 2 in the Supplement**.

eTable 2. Reasons for Discontinuations Categorized as Other

Subject	Treatment Group	Reason for Discontinuation
1	Pegfilgrastim	Other: General Health Deterioration. ECOG 2
2	Pegfilgrastim	Other: Disease Progression
3	Pegfilgrastim	Other: Progressive Disease
4	Pegfilgrastim	Other: Death (Study Disease)
5	Plinabulin	Other: Disease Progression
6	Pegfilgrastim	Other: Violation of Standard Inclusion/Exclusion
7	Pegfilgrastim	Other: Volundary Refund Group
8	Plinabulin	Other: Disease Progression
9	Pegfilgrastim	Other: Disease Progression
10	Pegfilgrastim	Other: Disease Progression
11	Plinabulin	Other: Disease Progression

eTable 3. Listing of All-Cause Hospitalizations

Subject	Treatment Group	Reported Term	Reasons for Hospitalization	Details for Hospitalization	Cycle	Start Date	End Date
1	Plinabulin	Hospitalization	AE	AE25_anemia	Cycle 4	2018-12-26	2018-12-27
2	Plinabulin	Hospitalization	AE	AE4_status asthmaticus	Cycle 4	2018-10-13	2018-10-20
3	Plinabulin	Hospitalization	AE	AE9_massive thrombembolia of the L	Follow-up	2018-11-16	2018-11-22
4	Plinabulin	Hospitalization	Other	Due to neutrophil count decreased and white blood cell count decreased	Cycle 1	2018-06-22	2018-06-25
5	Plinabulin	Hospitalization	AE	AE10_vomiting	Cycle 1	2018-08-03	2018-08-15
		Hospitalization	AE	AE11_febrile neutropenia[a]	Cycle 1	2018-08-03	2018-08-15
6	Plinabulin	Hospitalization	AE	AE12_aspartic aminotransferase increase	Cycle 2	2018-09-04	2018-09-13
7	Plinabulin	ICU stay	AE	AE10_lung infection	Cycle 1	2018-09-09	2018-09-25
8	Pegfilgrastim	Hospitalization	AE	AE3_febrile neutropenia[a]	Cycle 1	2018-08-20	2018-08-21
9	Pegfilgrastim	Hospitalization	Other	The subject was hospitalized for follow-up treatment[b]	Cycle 4	2018-08-31	2018-09-18
10	Pegfilgrastim	Hospitalization	AE	AE1_lung infection	Cycle 4	2018-10-17	2018-11-10
11	Pegfilgrastim	Hospitalization	AE	AE7_hepatic injury	Cycle 2	2018-08-30	2018-09-21
12	Pegfilgrastim	Hospitalization	AE	AE1_vaginal hemorrhage		2018-07-25	2018-08-01

Abbreviation: AE: Adverse event.
a. AE3 and AE11: Febrile neutropenia was reported as an AE and not defined as per NCCN criterion
b. Sites may have hospitalized patients for treatment per institutional protocol or socio-economic factors

eTable 4. Summary of Infections

Subject	Treatment Group	Infection	Viral or Bacterial
1	Plinabulin	Upper respiratory tract infection	Unknown
		Atypical pneumonia	Unknown
2	Pegfilgrastim	Bronchitis viral	Viral
3	Pegfilgrastim	Respiratory tract infection viral	Viral
4	Plinabulin	Respiratory tract infection viral	Viral
5	Pegfilgrastim	Respiratory tract infection viral	Viral
		Tracheobronchitis	Unknown
6	Pegfilgrastim	Influenza	Viral
7	Pegfilgrastim	Subcutaneous abscess	Unknown
		Subcutaneous abscess	Unknown
		Subcutaneous abscess	Unknown
		Skin infection	Viral (herpes zoster)
		Lung infection	Viral
		Lung infection	Unknown
8	Pegfilgrastim	Hepatitis B reactivation	Viral
9	Pegfilgrastim	Herpes zoster	Viral
		Herpes zoster	Viral
10	Pegfilgrastim	Lung infection	Unknown
		Lung infection	Unknown

Subject	Treatment Group	Infection	Viral or Bacterial
		Lung infection	Unknown
11	Plinabulin	Lung infection	Unknown
12	Plinabulin	Lung infection	Unknown
		Lung infection	Unknown

eTable 5. Summary and Analysis of Patients With Neutrophil-to-Lymphocyte Ratio (NLR) >5 After Days 7-15 in Cycle 1

Parameter	Visit	Pegfilgrastim (N=53) n (sample size, %)	Plinabulin (N=52) n (sample size, %)	Docetaxel + Plinabulin-40 vs Docetaxel + Pegfilgrastim -6 (95% CI)	Aspin-Welch Unequal-Variance T-Test p-value
NLR >5	Cycle 1 Day 8	23 (50, 46.00%)	2 (52, 3.85%)	-42.15 (-56.92, -27.38)	<0.0001
	Cycle 1 Day 9	30 (51, 58.82%)	0	-58.82 (-72.33, -45.32)	
	Cycle 1 Day 10	34 (52, 65.38%)	0	-65.38 (-78.32, -52.45)	
	Cycle 1 Day 15	24 (51, 47.06%)	2 (52, 3.85%)	-43.21 (-57.87, -28.55)	

Abbreviations: CI: Confidence interval; ITT: Intent-to-treat; N: Total number of patients; n: Number of patients; NLR: Neutrophil-to-lymphocyte ratio.
Pegfilgrastim Arm: Docetaxel (75 mg/m^2) + pegfilgrastim (6 mg); Plinabulin Arm: Docetaxel (75 mg/m^2) + plinabulin (40 mg)

eTable 6. Summary and Analysis of Patients With Promyelocyte Plus Myelocyte Counts >0 After Days 7-15 in Cycle 1—ITT Analysis Set

Parameter	Visit	Pegfilgrastim (N=53) n (sample size, %)	Plinabulin (N=52) n (sample size, %)	Plinabulin vs Peg (95% CI, %)	Aspin-Welch Unequal-Variance T-Test p-value
Promyelocytes plus myelocytes >0	Cycle 1 Day 8	22 (50, 44.00 %)	0	-44.00 (-57.76, -30.24)	0.00026
	Cycle 1 Day 9	25 (51, 49.02 %)	4 (51, 7.84 %)	-41.18 (-56.75, -25.60)	
	Cycle 1 Day 10	20 (52, 38.46 %)	3 (51, 5.88 %)	-32.58 (-47.29, -17.86)	
	Cycle 1 Day 15	3 (51, 5.88 %)	1 (52, 1.92 %)	-3.96 (-11.42, 3.50)	

Abbreviations: CI: Confidence interval; ITT: Intent-to-treat; N: Total number of patients; n: Number of patients. Pegfilgrastim Arm: Docetaxel (75 mg/m^2) + pegfilgrastim (6 mg); Plinabulin Arm: Docetaxel (75 mg/m^2) + plinabulin (40 mg)

eTable 7. Summary and Analysis of Patients With Thrombocytopenia (All Grades) in Cycles 1-4

Parameter	Cycles	Docetaxel + Pegfilgrastim 6.0mg (N=53) n (sample size, %)	Docetaxel + Plinabulin 40 mg (N=52) n (sample size, %)	Docetaxel + Plinabulin 40 mg vs Docetaxel + Pegfilgrastim 6.0mg (95% CI)	Barnard's Test p-value
Thrombocytopenia (All Grades)	Cycle 1	19 (53, 35.85%)	10 (52, 19.23%)	-16.62 (-33.39, 0.16)	0.062
	Cycle 2	4 (51, 7.84%)	5 (51, 9.80%)	1.96 (-9.04, 12.96)	0.818
	Cycle 3	2 (45, 4.44%)	6 (46, 13.04%)	8.60 (-2.85, 20.04)	0.162
	Cycle 4	2 (39, 5.13%)	4 (45, 8.89%)	3.76 (-7.06, 14.58)	0.595
	Cycles 1 to 4	19 (53, 35.85%)	10 (52, 19.23%)	-16.62 (-33.39, 0.16)	0.062

Abbreviations: CI: Confidence interval; N: Total number of patients; n: Number of patients.

eTable 8. Summary and Analysis of EQ-5D-5L Evaluation—Safety Analysis Set

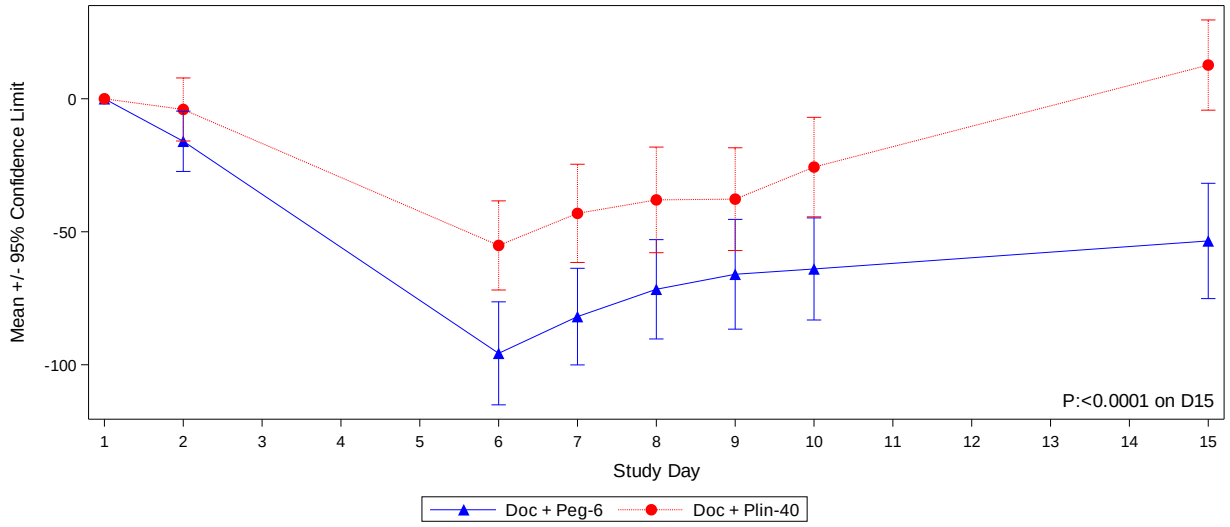
Parameter	Study Day	Analysis	Docetaxel + Pegfilgrastim-6 (N=53)	Doc + Plin-40 (N=52)
EQ5D02-EQ VAS Score	Across all Timepoints	LS Means (SE)	79.1 (1.01)	78.5 (1.00)
		Mean (95% CI)		-0.5 (-3.4, 2.3)
		p-value		0.7117
Health Utility	Across all Timepoints	LS Means (SE)	0.812 (0.0094)	0.816 (0.0093)
		Mean (95% CI)		0.004 (-0.022, 0.030)
		p-value		0.764

Abbreviations: CI: Confidence interval; LS: Least squares N: Total number of patients; SE: Standard error.
LS Means, SE, Mean (95% CI), and p-value computed using the following repeated measures mixed model: score = treatment arm + baseline score.

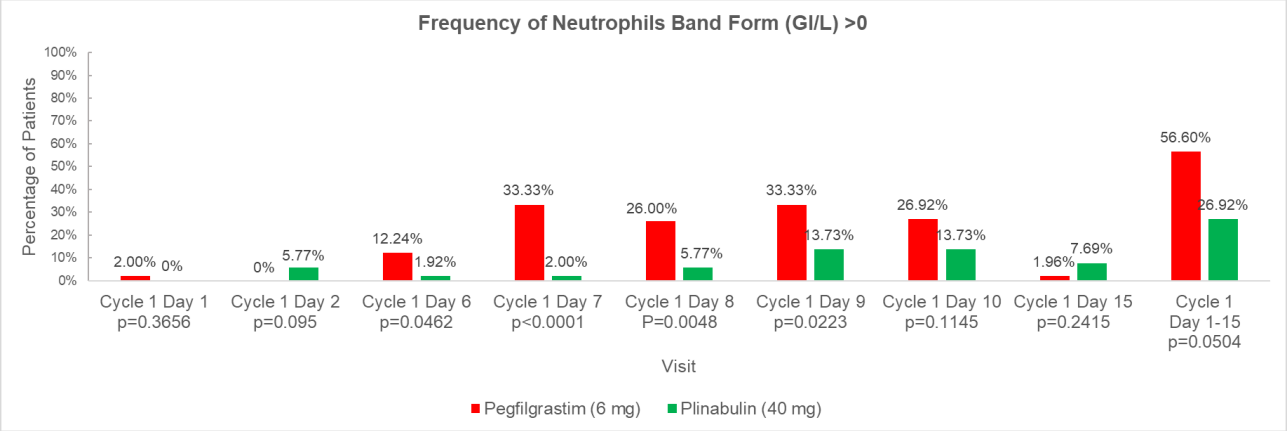
eTable 9. Summary of Patients With Bone Metastasis

Subject	Treatment Group	Medical History Term
1	Plinabulin	Bone Metastasis
2	Pegfilgrastim	Back Pain due to Bone Metastasis from Prostate Cancer
		Bone Metastasis from Prostate Cancer
3	Plinabulin	Bone Metastasis
		Meningioma TH1/2 of the Spine
4	Plinabulin	Bone Metastasis
5	Plinabulin	Bone Metastasis
6	Plinabulin	Bone Metastasis
7	Pegfilgrastim	Bone Metastasis
8	Pegfilgrastim	Bone Metastasis
9	Plinabulin	Ache (Osseious Metastasis)
10	Plinabulin	Extensive Bone Metastasis

eFigure 1. Mean Change From Baseline for Platelets (Gi/L) by Study Day for Cycle 1—ITT Analysis Set



eFigure 2. Summary and Analysis of Patients With Band Counts >0, Cycle 1, Days 1-15



P-value based on Aspin-Welch Unequal-Variance T-Test.

Pegfilgrastim Arm: Docetaxel (75 mg/m^2) + pegfilgrastim (6 mg); Plinabulin Arm: Docetaxel (75 mg/m^2) + plinabulin (40 mg)