

Plinabulin, a Potent Inducer of Haptoglobin Production for the Prevention of Tissue Iron Overload in Patients Receiving Blood Transfusions Chronically

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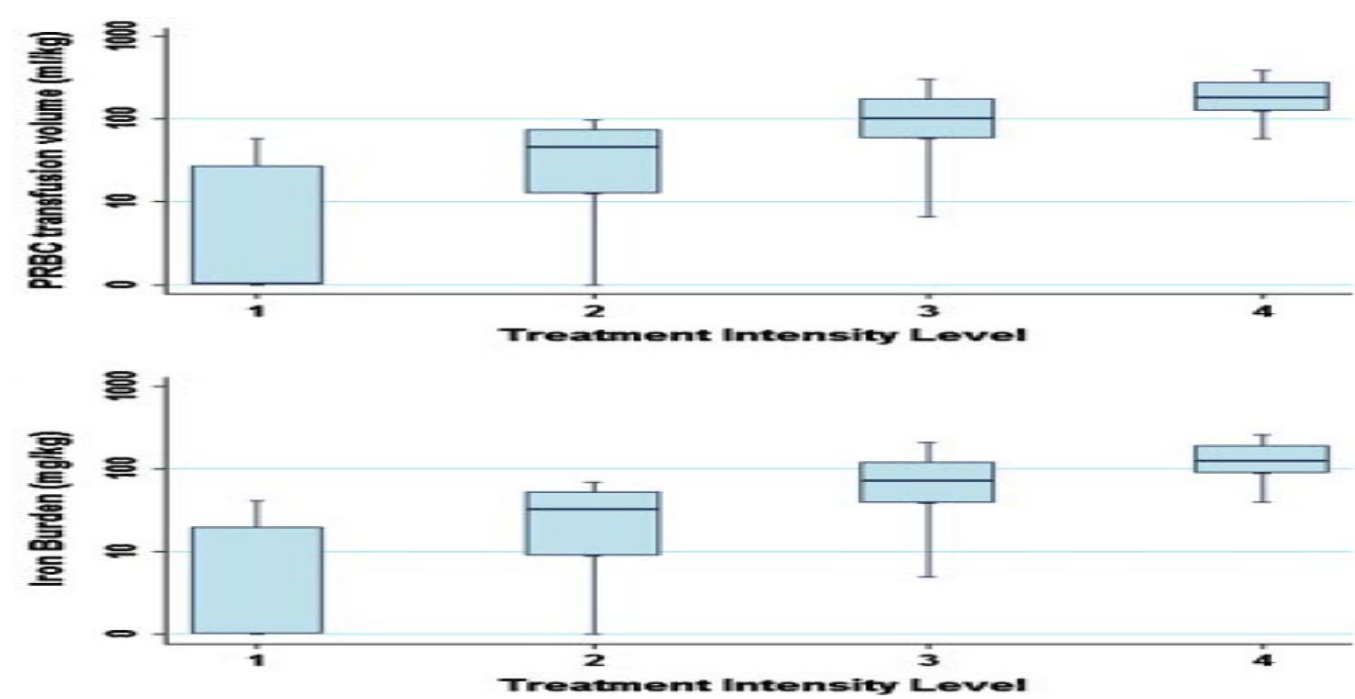


Introduction

Transfusion **Iron Overload** in Cardiac, Hepatic, Endocrine tissues and Bone Marrow causes Increased Morbidity in Cancer Survivors



Blood Transfusion Intensity is directly Related to Iron Overload (Ruccione et al. Pediatric Blood Cancer 2011)



Tissue Iron Overload in Heart, Liver, and Endocrine tissues and Bone Marrow, leads to progressive organ dysfunction.

Haptoglobin is our Natural Defense Mechanism to prevent Transfusion Iron Overload:

- Transfused Blood has a high degree of Hemolysis, resulting in increased Free Hemoglobin that contains Fe.
- Haptoglobin safely binds/neutralizes free Hemoglobin. The Haptoglobin/Hemoglobin complex is internalized in Macrophages through the CD163 receptor and Fe is safely processed through Transferrin
- During Hemolysis, Haptoglobin is depleted quickly, and once depleted, Iron is deposited in tissues leading to tissue Iron Overload

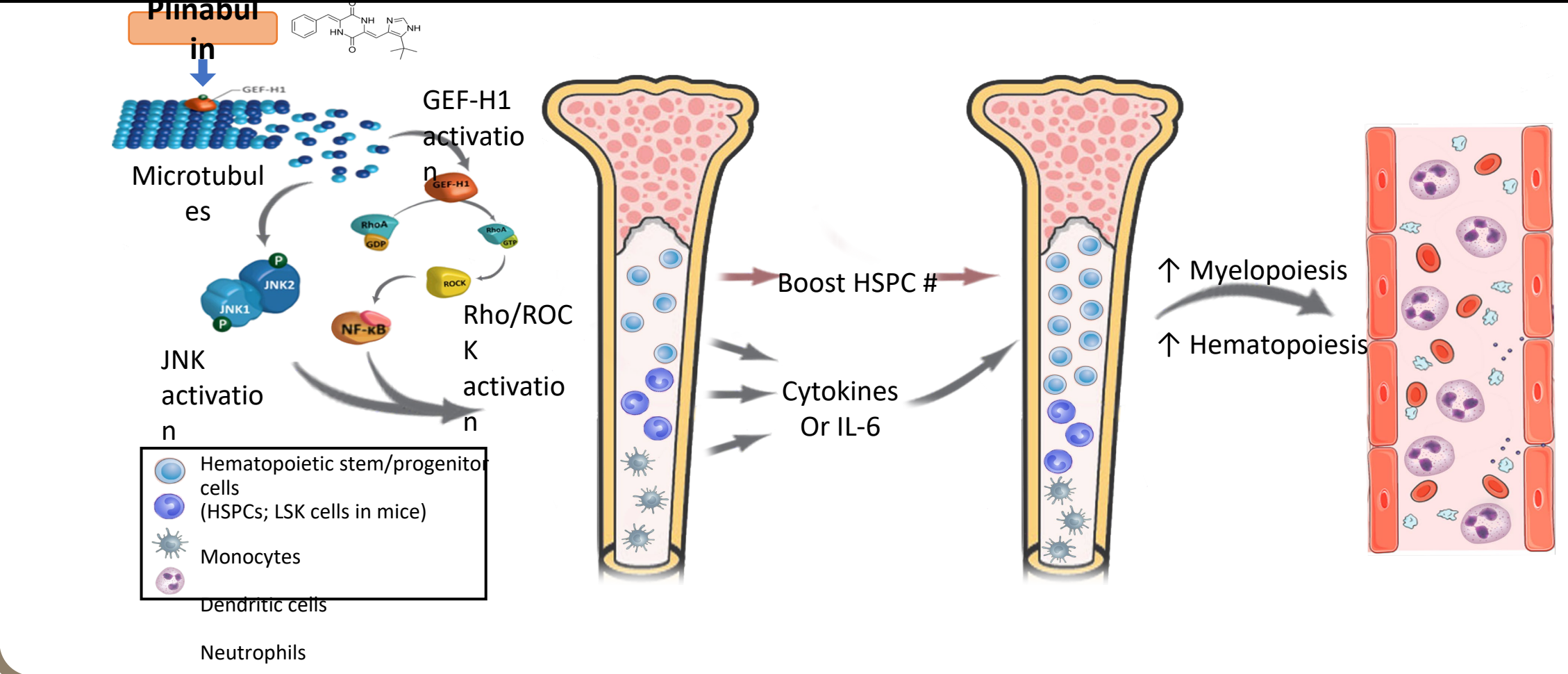
Plinabulin is a Novel Immune-Enhancing Agent with:

- Anticancer Activity (ASCO-CITC 2018)
- Prevention of Chemo-Therapy-Induced Neutropenia (ASH 2018, ASCO 2018,2019)
- Avoidance of Thrombocytopenia (IASLC 2018)

Here we provide evidence that **Plinabulin** has the potential to prevent Transfusion Iron Overload by increasing **Haptoglobin** levels

Plinabulin Mechanism of Action

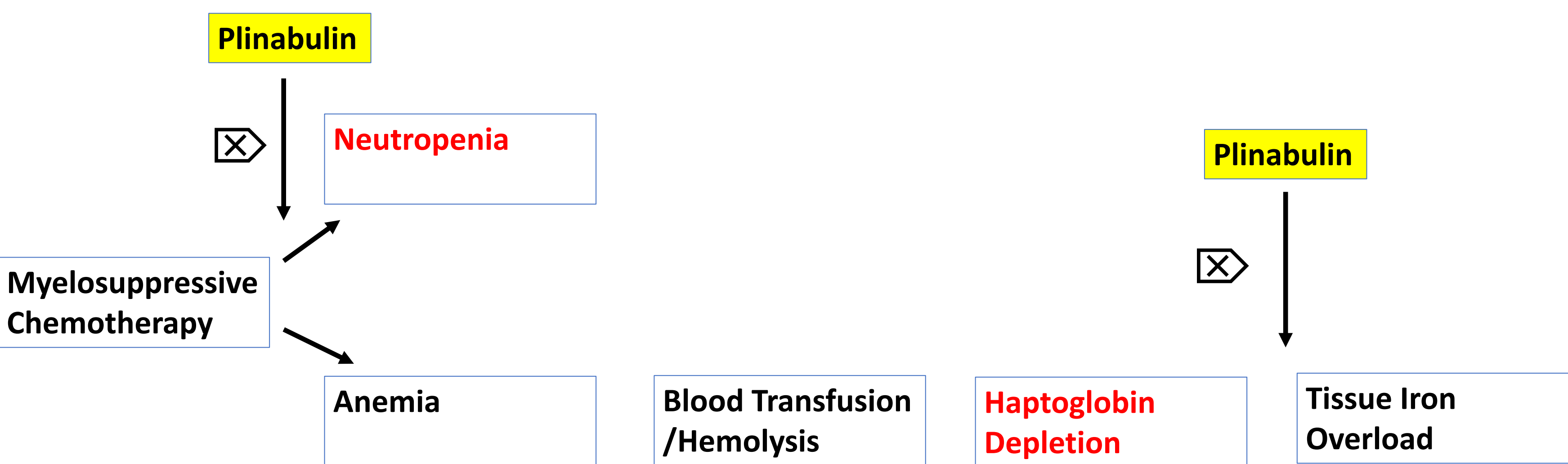
MoA - Plinabulin - first-in-class agent with GEF-H1 as new target



Plinabulin Pipeline

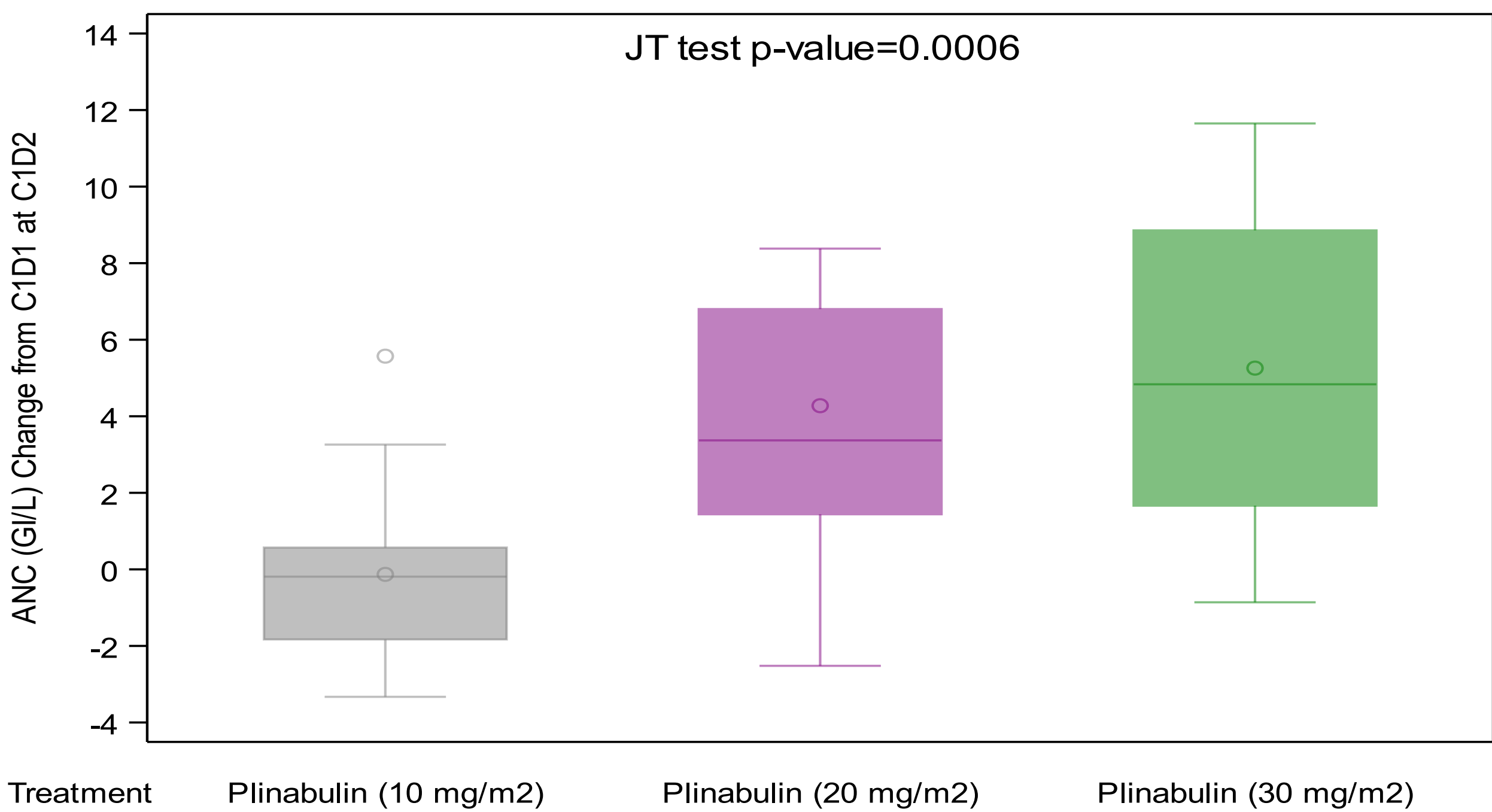
	Program	Indication	Trial name	Preci nical	Phase 1	Phase 2	Phase 3	Commercial rights	China NDA filing	U.S. NDA filing
Late stage	Plinabulin + docetaxel	NSCLC (2 nd /3 rd line)	Study 103		Phase 3 primary end point met at interim analysis			Global ¹	Q1 2020	2020
	Plinabulin	CIN	Study 105		Phase 3 first interim data analysis completed			Global ¹	Q1 2020	2020
	Plinabulin + pegfilgrastim	CIN	Study 106					Global ¹	Q1 2020	2020
Investigator-initiated IO	Plinabulin + nivolumab	NSCLC (2 nd /3 rd line)	Fred Hutch/Univ. Washington/UCSD					Global ¹		
	Plinabulin + nivolumab + ipilimumab	SCLC	Rutgers University					Global ¹		
	Plinabulin + PD-1/PD-L1 + radiation/chemo	Various cancers (2 nd /3 rd line)	MD Anderson					Global ¹		

Plinabulin Mitigates Chemotherapy-Induced Consequences of Myelosuppression Broadly



Plinabulin's Neutropenia Benefit

Absolute Neutrophil Count (g/L) Change from Baseline on Day 2



Signed Rank test P-value 0.6257 0.0015 0.0015

Breast Cancer Patients received Severe Myelosuppressive Chemotherapy with: Taxotere + Doxorubicin + Cyclophosphamide

Plinabulin was evaluated at 3 dose levels:

- 10 mg/m2
- 20 mg/m2
- 30 mg/m2

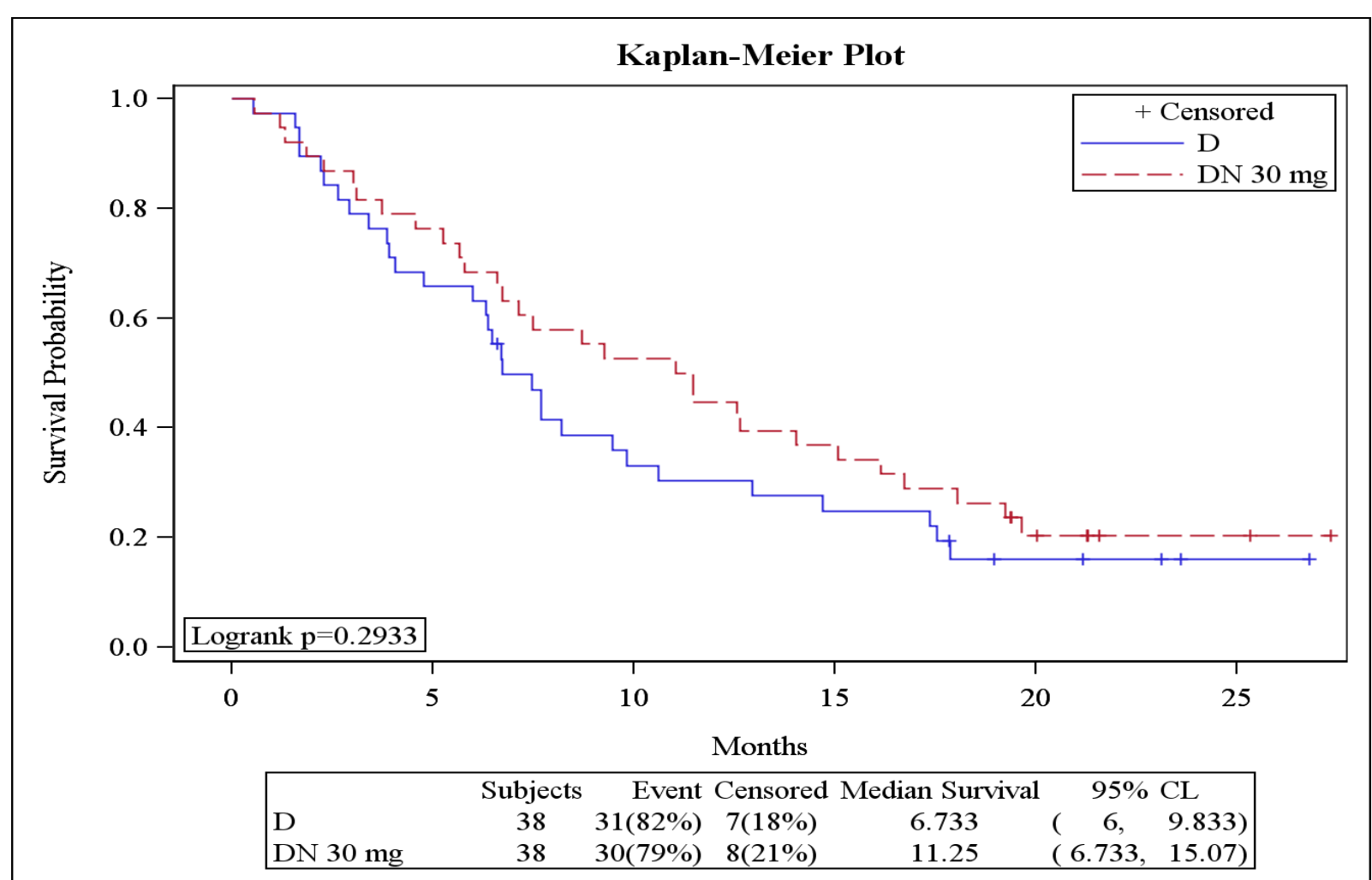
Methods

Blood draws for Absolute Neutrophil Count (ANC) and Haptoglobin (Hp) in the hematology panel were taken prospectively at Day (D) 0, 2,3,6,7,8,9, 10,11,12,13,15, 22 in cycle 1.

Plinabulin caused a dose-dependent increase (P=0.0006) in Neutrophil Count

Plinabulin's Anti-Cancer Activity

Durable Response and Extended Survival Benefit of 4.6 Month



	Plinabulin + Docetaxel (DN)	Docetaxel (D)
N	38	38
mOS	11.3 M	6.7 M
P	P = 0.29 *	
DOR	12.7M	1.0 M
P	P < 0.05	
ORR	18.4%	10.5%
PFS	3.7M	2.9M

Study BPI-2358-106 Phase 3 Status

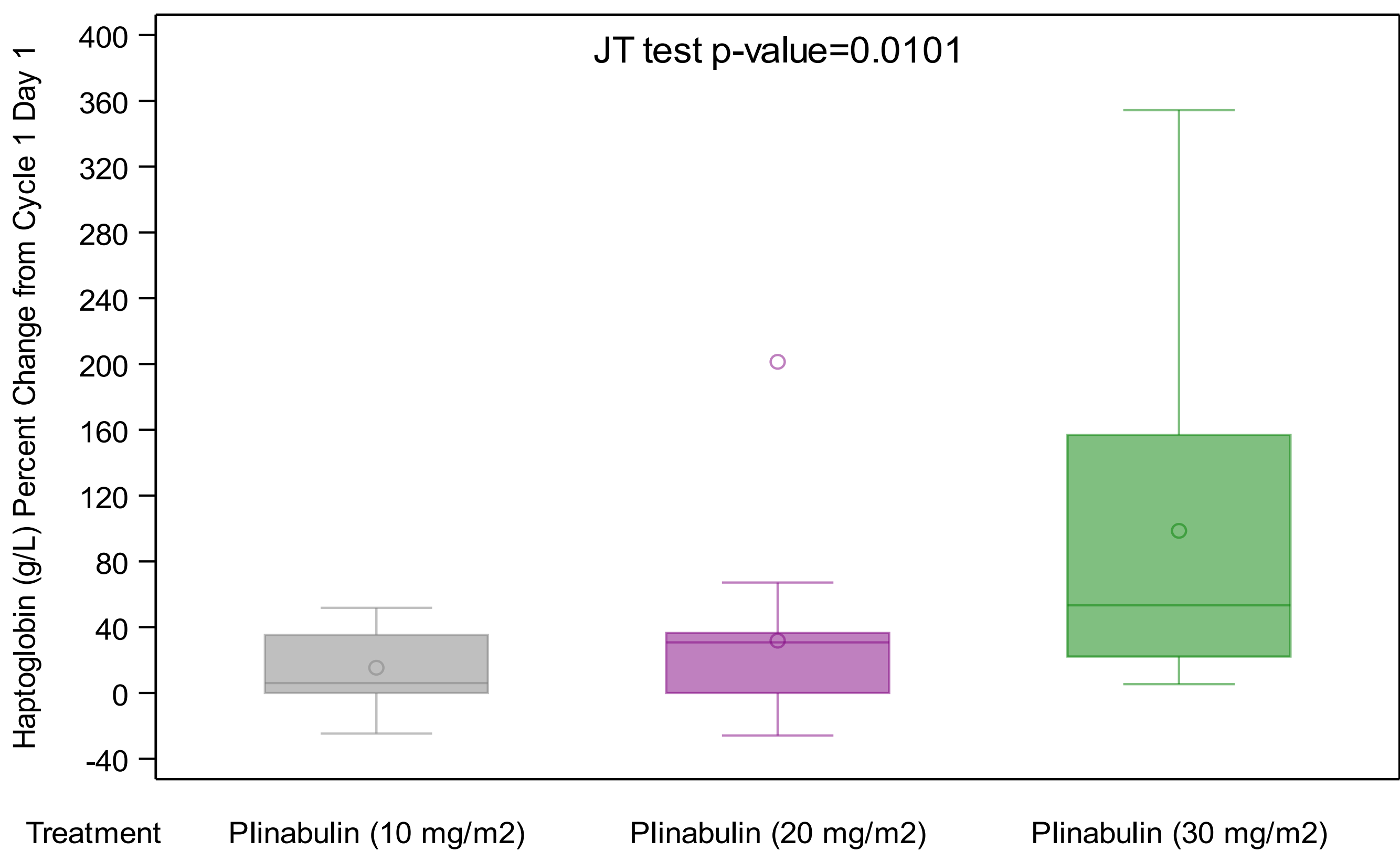
Randomized: 100 pts (Target: 222 pts)

Countries: China; US; Ukraine

Expected first interim analysis: Q2 2020

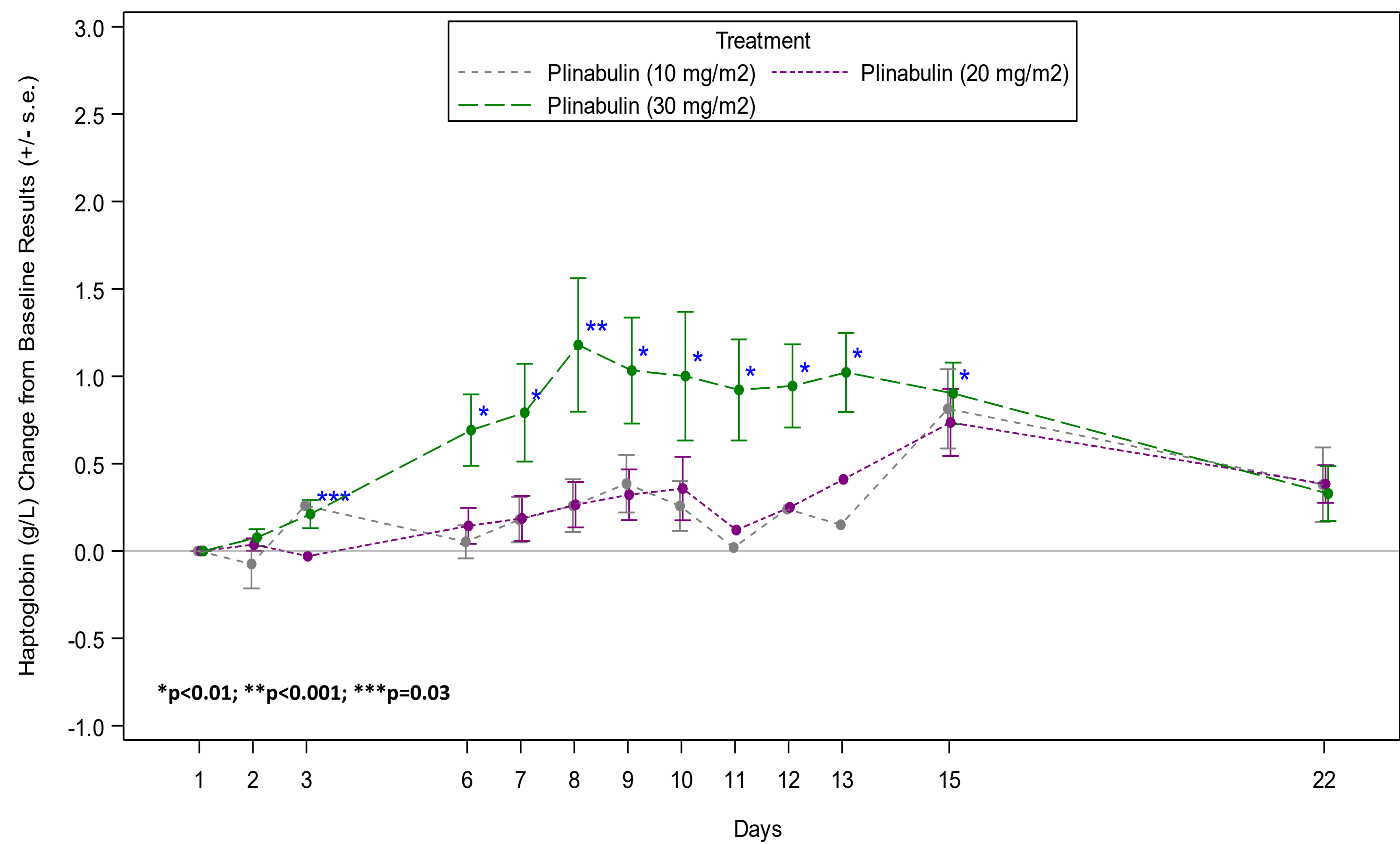
Plinabulin's Haptoglobin Benefit

Haptoglobin (g/L) Change from Baseline on Day 8



Signed Rank test P-value 0.0425 0.0105 0.0005

Haptoglobin (g/L) Change from Baseline Time Course



Haptoglobin normal range is 0.3 to 2 g/L

Conclusion

- Myelosuppressive Chemotherapy causes Neutropenia and Anemia
- The Anti-Cancer Agent **Plinabulin**, given as a single dose per Cycle also:
 - Induces a rapid (<3 days) and sustained (>3 weeks) increase in Haptoglobin, to levels double of baseline that May Prevent Blood Transfusion Iron Overload in Tissue Organs
 - Prevents Chemotherapy- Induced- Neutropenia (CIN)

Co-Administration of Chemotherapy with the Anti-Cancer Agent Plinabulin May Prevent Organ Fe-Overload and Related Morbidity in Cancer Survivors Requiring Frequent Blood Transfusions.



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