

# Abstract #1813P

## The Effect of Increasing Doses of Pegfilgrastim (Peg) on Thrombocytopenia (T) in Breast Cancer (BC) Patients (pts) Receiving Taxotere (Doc), Doxorubicin, Cyclophosphamide (TAC) and Plinabulin (Plin)

D. Blayney<sup>1</sup>, I. Bondarenko<sup>2</sup>, Y. Shi<sup>3</sup>, S. Ogenstad<sup>4</sup>, L. Du<sup>5</sup>, L. Huang<sup>6</sup>, R. Mohanlal<sup>7</sup>; <sup>1</sup>Oncology, Stanford Cancer Institute, Stanford, CA, United States of America, <sup>2</sup>Oncology and Medical Radiology Department, Dnipropetrovsk city multidisciplinary clinical hospital №4, Dnipro, Ukraine, <sup>3</sup>Oncology, Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China, <sup>4</sup>Medicine (Oncology), Statogen Consulting, LLC, Zebulon, United States of America, <sup>5</sup>Clinical Operation, Wanchun Bulin Pharmaceuticals Limited, Dalian, China, <sup>6</sup>Clinical Operation, BeyondSpring Pharmaceuticals, Inc, New York, NY, United States of America, <sup>7</sup>Clinical Operation, BeyondSpring Pharmaceuticals, New York, United States of America



### Introduction

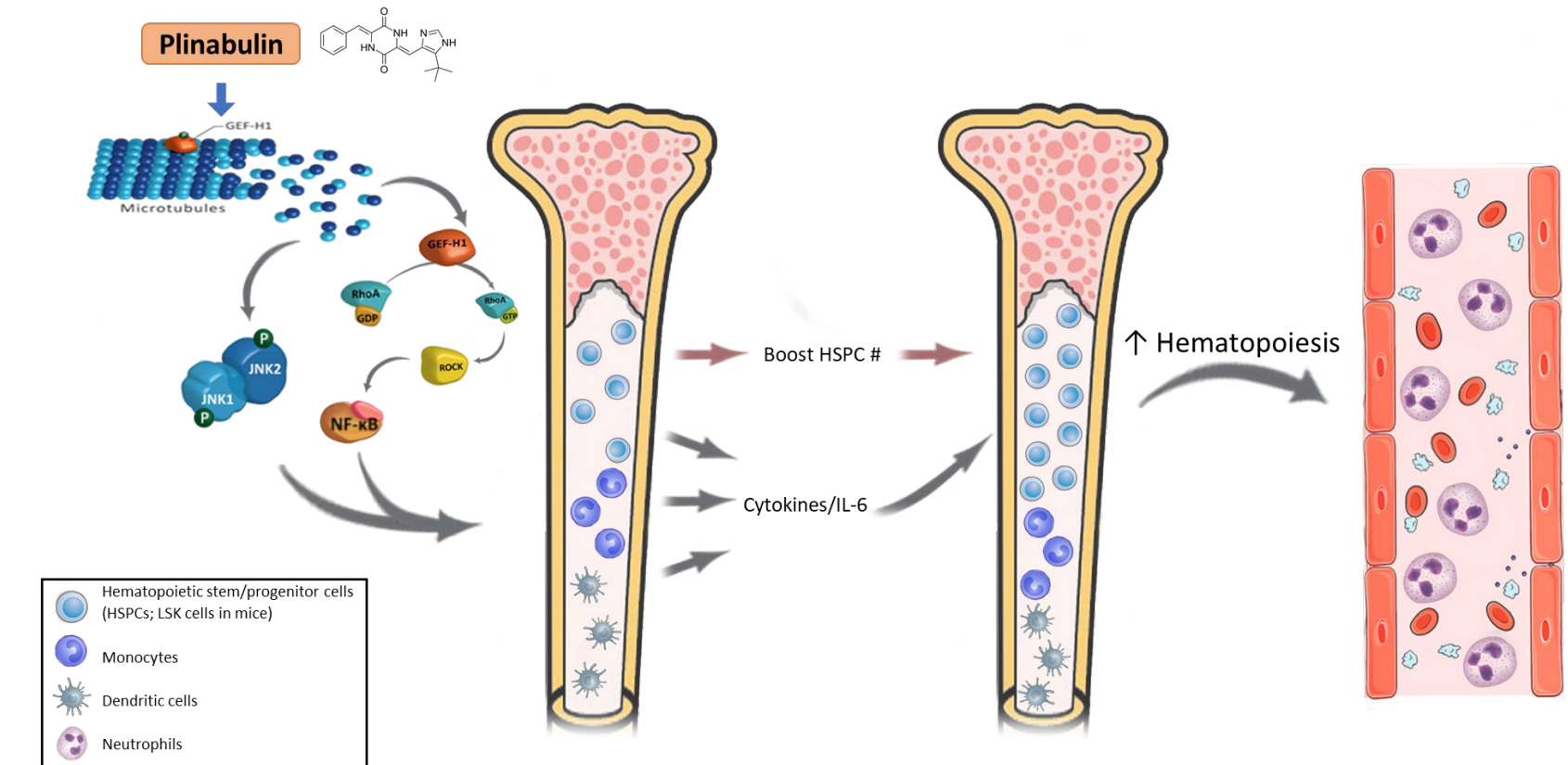
- Plinabulin is a novel non-G-CSF small molecule, in development for the prevention of Chemotherapy-Induced Neutropenia (CIN) and is differentiated from Pegfilgrastim:
  - Plinabulin has anticancer activity
  - Plinabulin does not cause bone pain
  - Plinabulin does not cause an immune-suppressive Neutrophil profile (i.e. NLR>5; Blayney ASCO 2018, ESMO 2018, SITC 2018).
  - Plinabulin is dosed 30 minutes after chemotherapy, on the same day of chemotherapy
- Plinabulin as single agent was equally effective vs single agent Pegfilgrastim standard dose (6mg) for Docetaxel (75 mg/m<sup>2</sup>) induced CIN in the Intermediate (10-20%) risk category for Febrile Neutropenia (FN).
- For High (> 20%) Risk FN induced by TAC, the combination of Plinabulin with Pegfilgrastim 6mg was superior vs single agent Pegfilgrastim 6mg for Neutropenia prevention (Blayney ASCO 2019; St Gallen 2019).
- Plinabulin combined with half-dose Pegfilgrastim (3 mg) was non-inferior vs full-dose Pegfilgrastim (6 mg), with respect to CIN (Blayney ASCO 2019; St Gallen 2019).
- Adding Plinabulin to any dose of Peg eradicated Peg-induced bone pain (Blayney St Gallen 2019).

Due to their differences in MoA, there is a strong rationale to combine Plinabulin and Pegfilgrastim, as this offers the potential of better protection against CIN in both week 1 and 2 in the chemo cycle.

Here we evaluated effects of Pegfilgrastim and Plinabulin on absolute platelet count by analyzing thrombocytopenia frequency.

### Plinabulin Background

- MoA - Plinabulin - first-in-class agent with GEF-H1 as a novel target**
- Plinabulin has a different mechanism of action (MoA) than G-CSF
  - Plinabulin induces:
    - Neutrophil demargination and reduced neutrophil transit time from the bone marrow that is consistent with IL-6 signaling, and
    - Plinabulin increases bone marrow LSK hematopoietic stem/progenitor cells (HSPC), 2 days after dosing in tumor bearing Balb/c mice
  - The absolute neutrophil count (ANC) nadir with Plinabulin occurs in week 2 and with Pegfilgrastim in week 1 after chemotherapy



### Methods

In the Phase II portion of Study 106, patients with breast cancer (BC) with TAC (docetaxel 75, doxorubicin 50, cyclophosphamide 600 mg/m<sup>2</sup>) and in a randomized manner to:

- Monotherapy 6 mg Pegfilgrastim (Peg6)
- Combination Therapy with Pegfilgrastim 6mg + Plinabulin 20 mg/m<sup>2</sup>
- Combination Therapy with Pegfilgrastim 3mg + Plinabulin 20 mg/m<sup>2</sup>
- Combination Therapy with Pegfilgrastim 1.5mg + Plinabulin 20 mg/m<sup>2</sup>
- Monotherapy Plinabulin (including the 20 mg/m<sup>2</sup> dose)

#### Endpoints:

- Neutropenia frequency
- Bone pain
- Neutrophil and Platelet Count was obtained on days 0, 1, 3, 6, 7, 8, 9, 10, 11, 12, 13, 15 of Cycle 1.
- Bone Pain was assessed by a validated questionnaire on days 1, 2, 3, 4, 6, 7, 8, 9, and expressed as % of patients reporting bone pain.

### Neutropenia Results

Figure 1: Time Course of Absolute Neutrophil Count (Median, ANC Log-Scale)

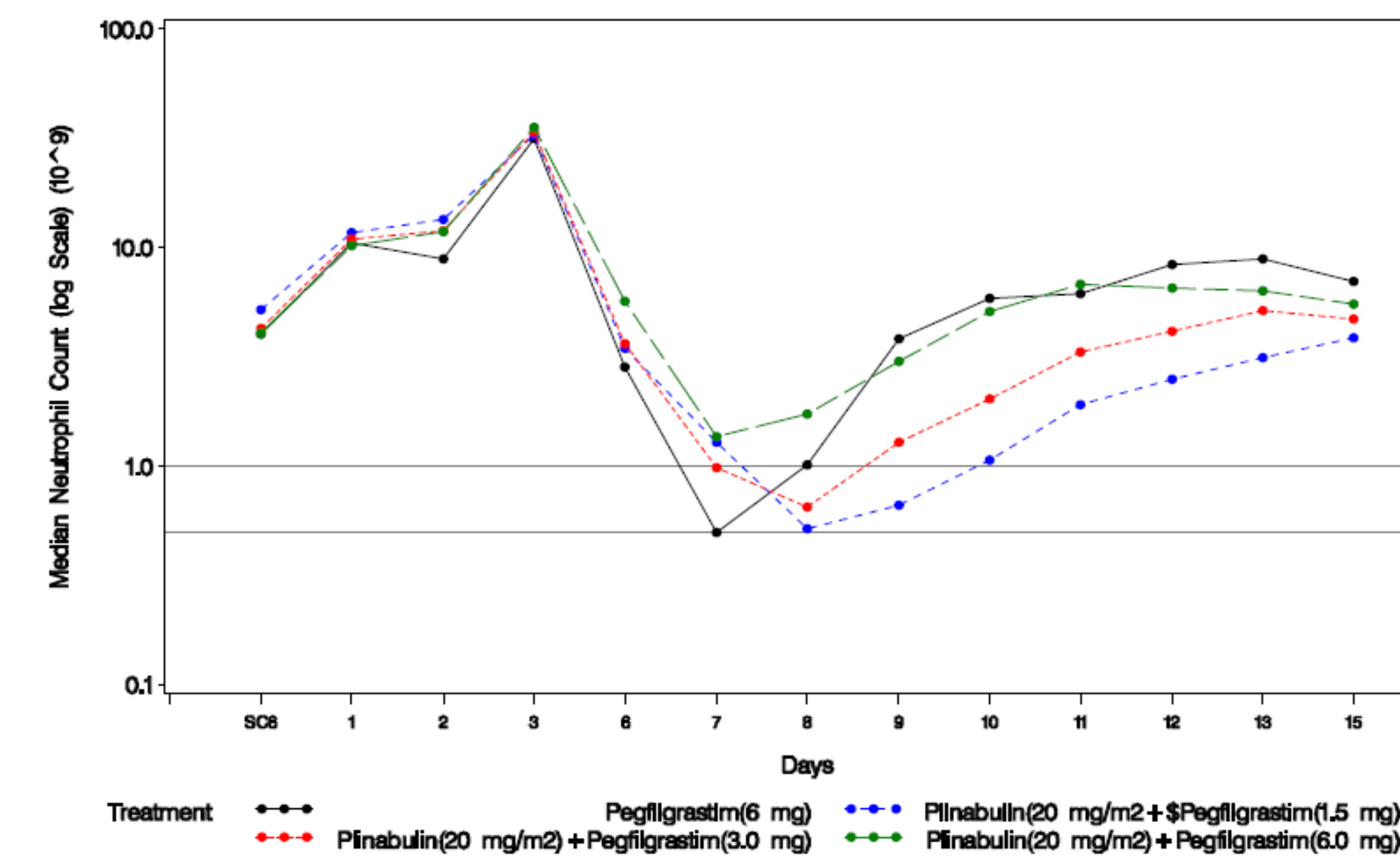


Figure 2: Grade 3/4 Neutropenia Frequency (%)

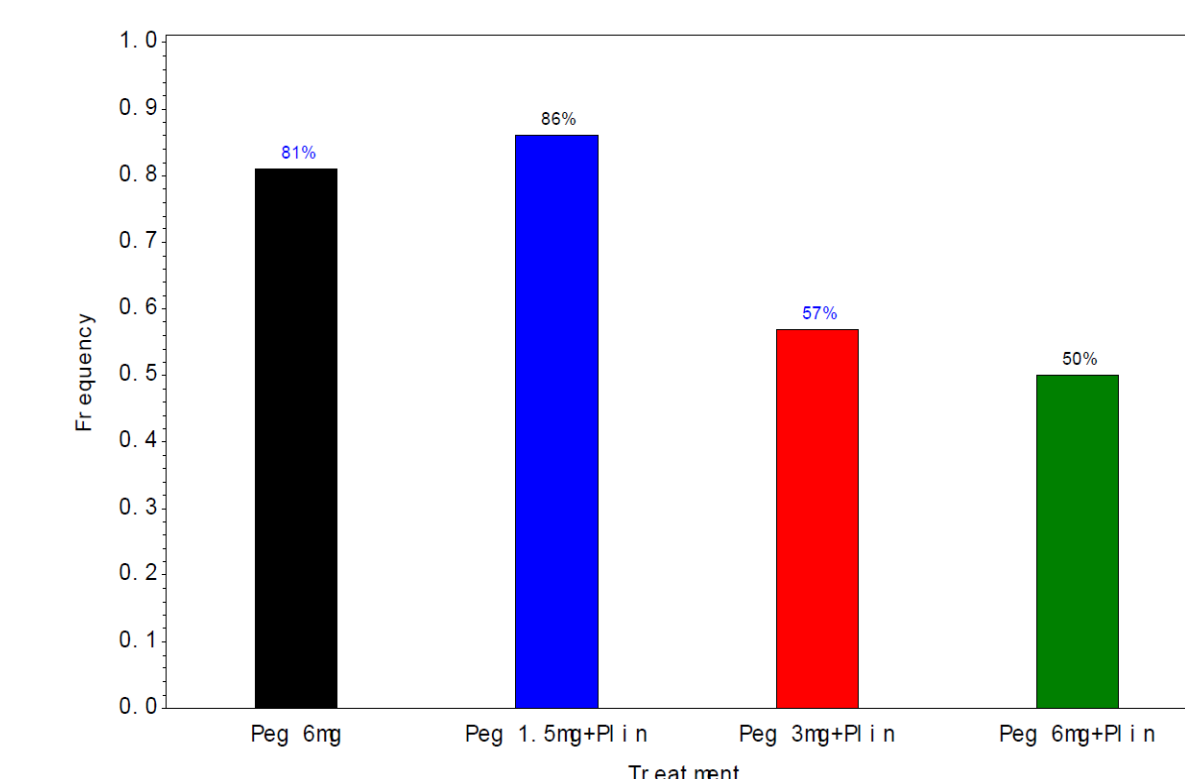


Figure 3: Grade 4 Neutropenia Frequency (%)

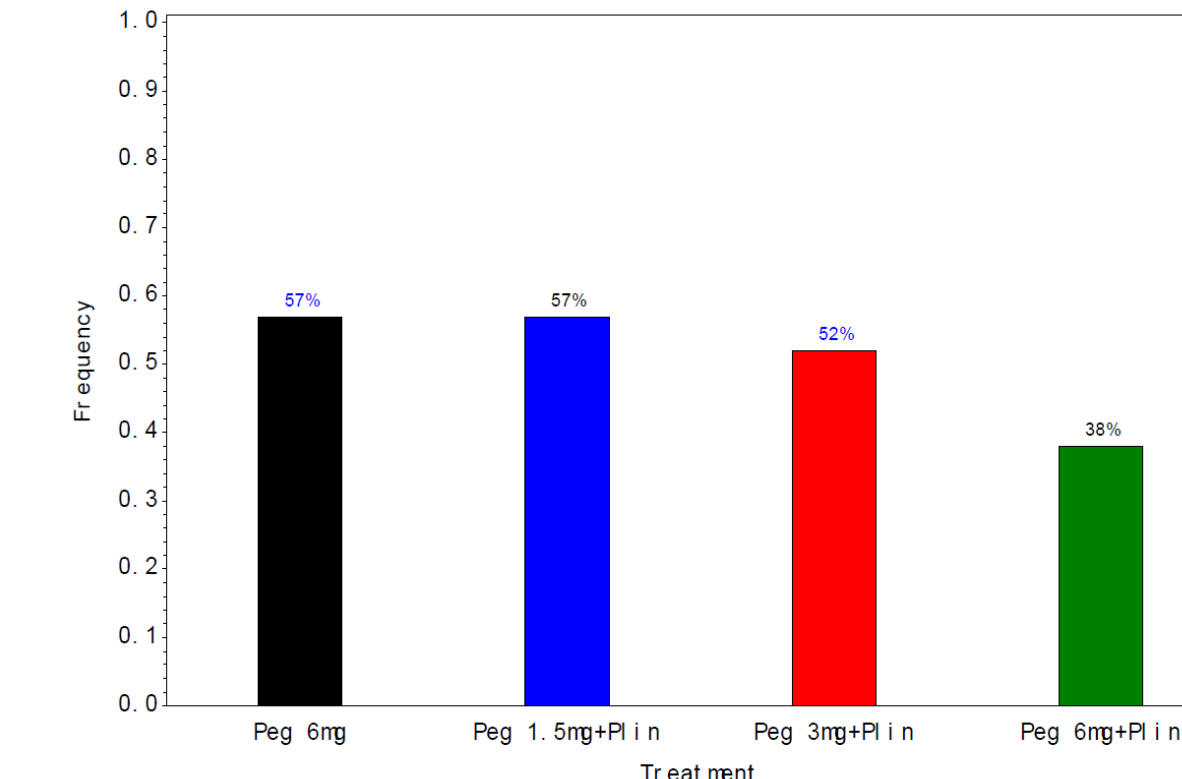


Figure 4: Nadir (Mean +/- SD) Absolute Neutrophil Count (Cellsx10E9/L)

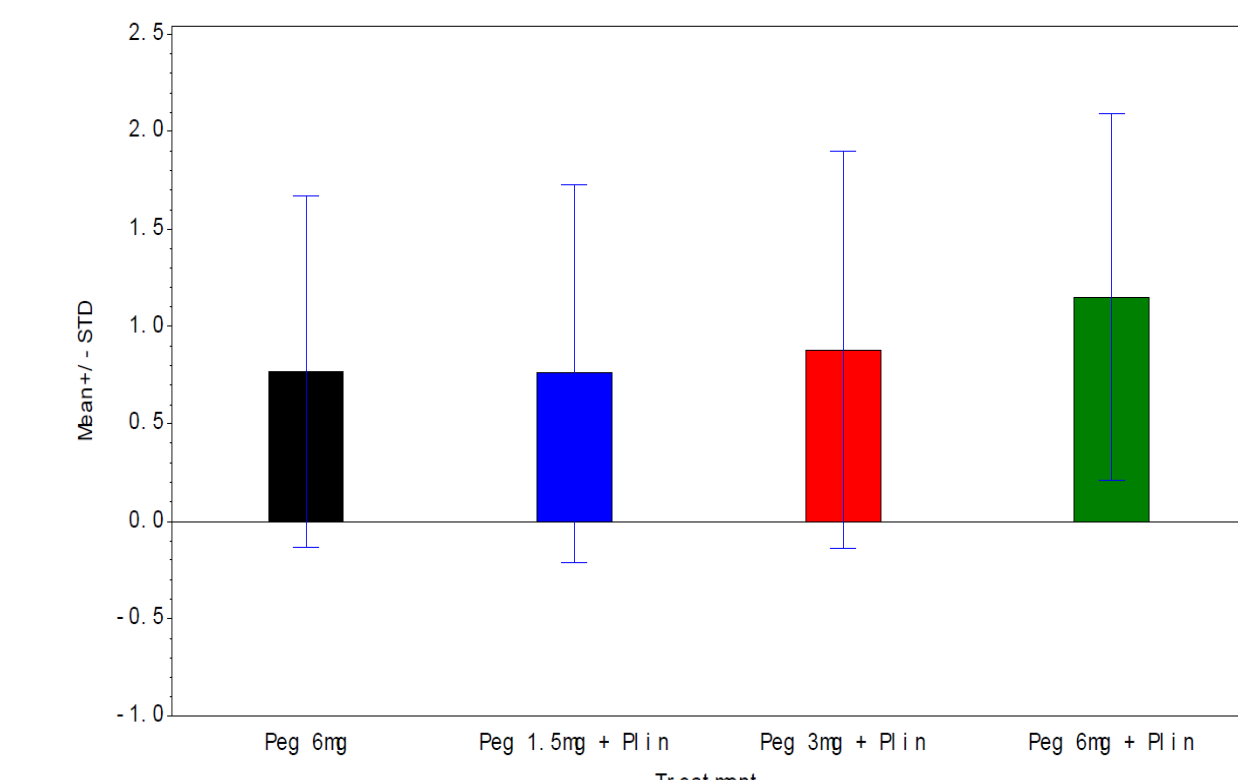
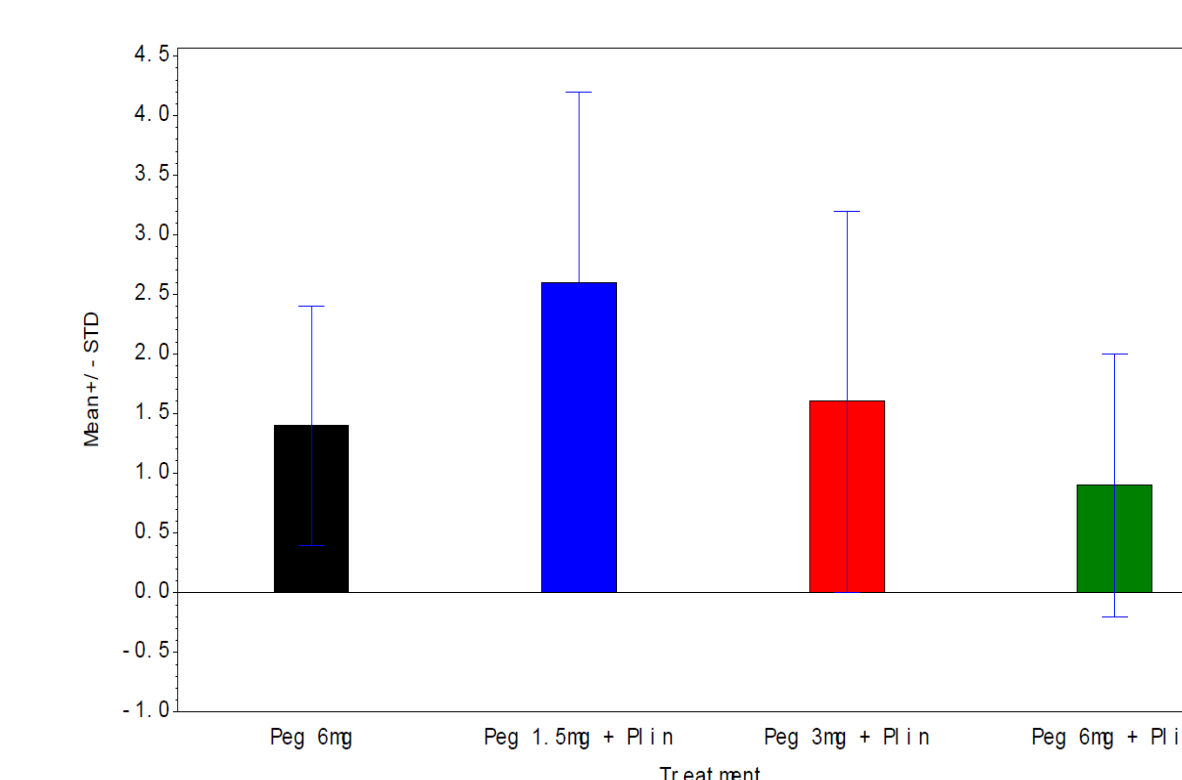
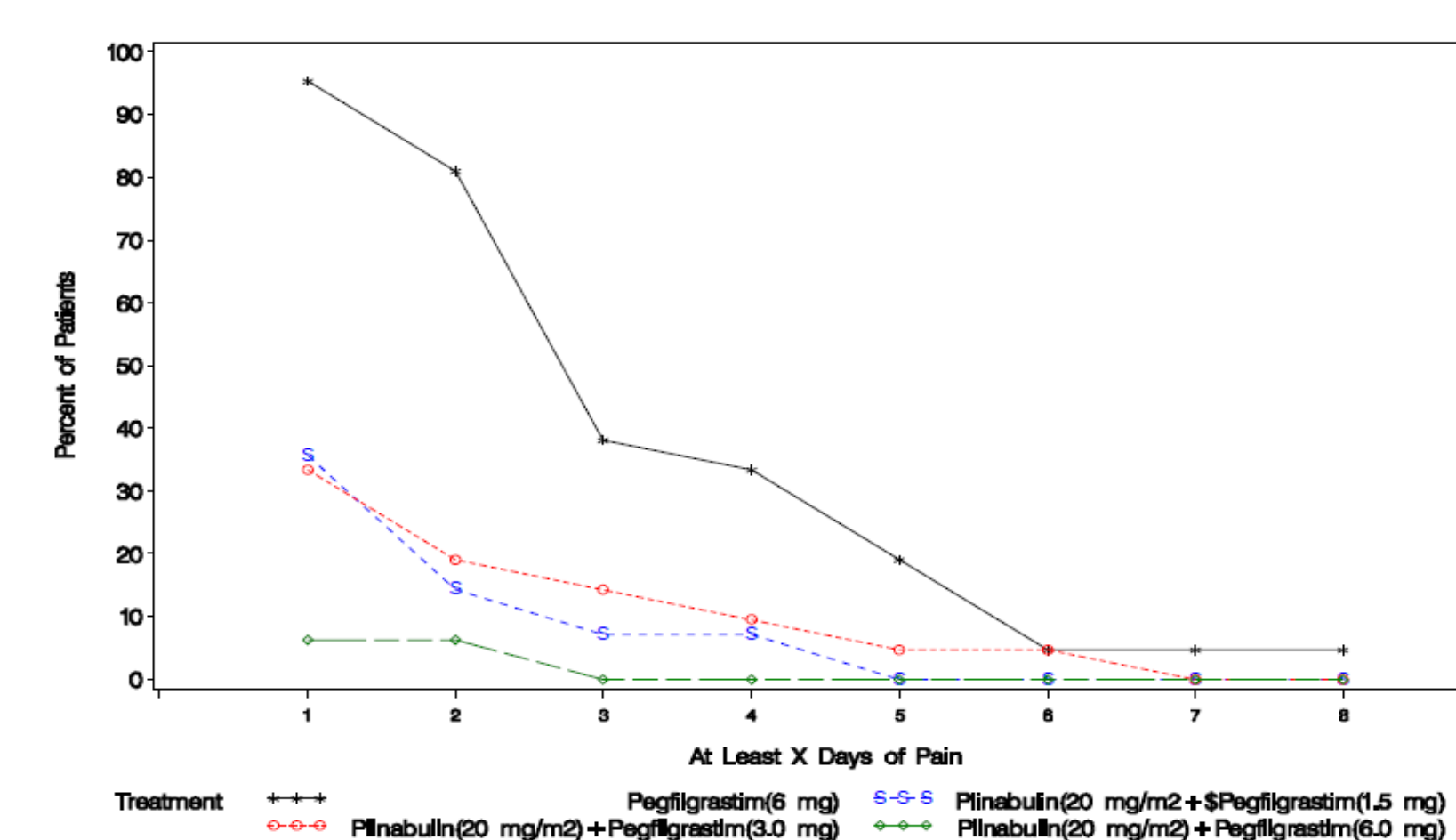


Figure 5: DSN (Mean +/- SD) (Days)



### Bone Pain Results

Figure 6: Time Course of Bone Pain



	Bone Pain ≥1 day	Bone Pain ≥4 days
Peg 6mg (N=21)	95%	33%
Peg 6mg+Plin (N=16)	6%**	0%***
Peg 3mg+Plin (N=21)	33%**	9.50%
Peg 1.5mg+Plin (N=14)	36%**	7.10%

\*p<0.05; \*\*p<0.001; \*\*\*P<0.01 Peg+Plin vs Peg 6mg

### Thrombocytopenia Results

Figure 7: Significant Thrombocytopenia with Pegfilgrastim, but not with Plinabulin

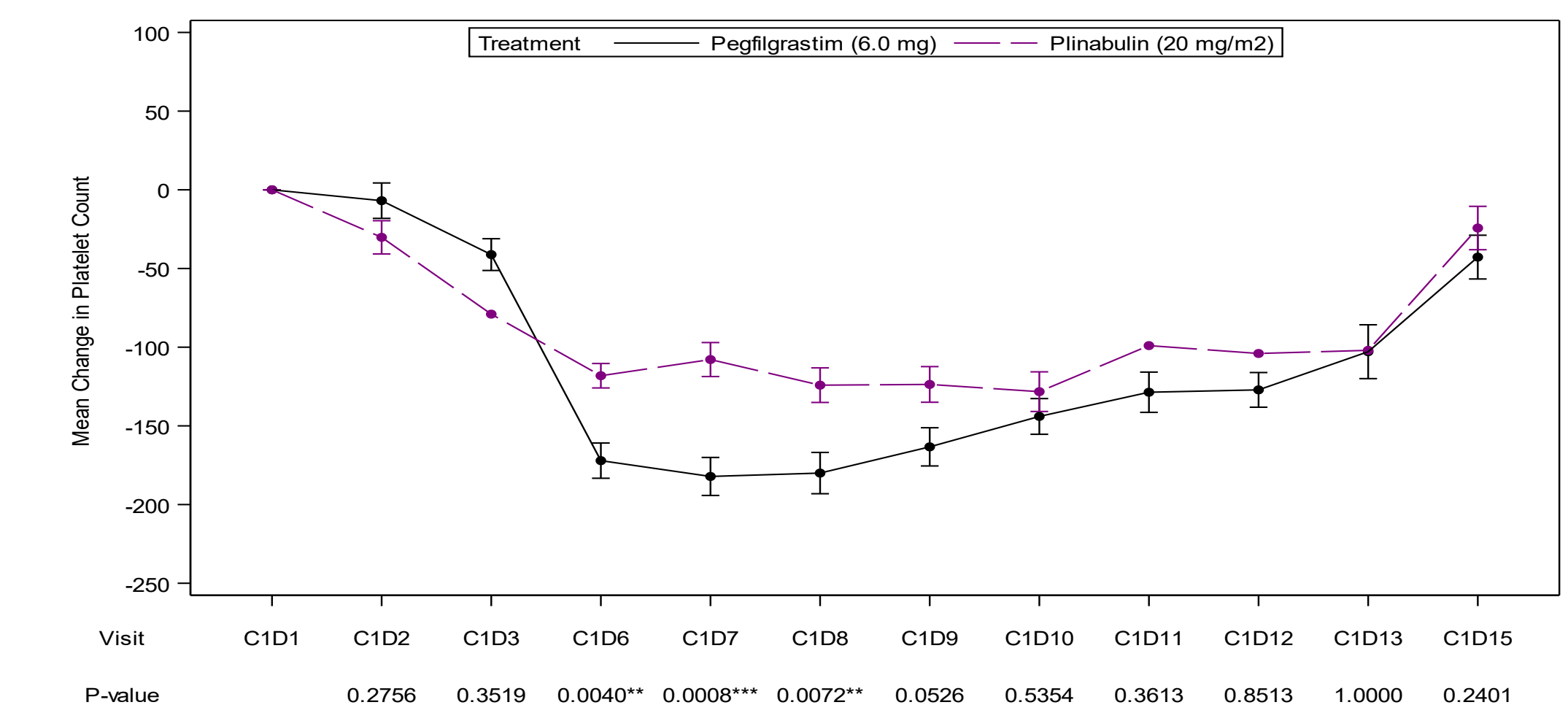
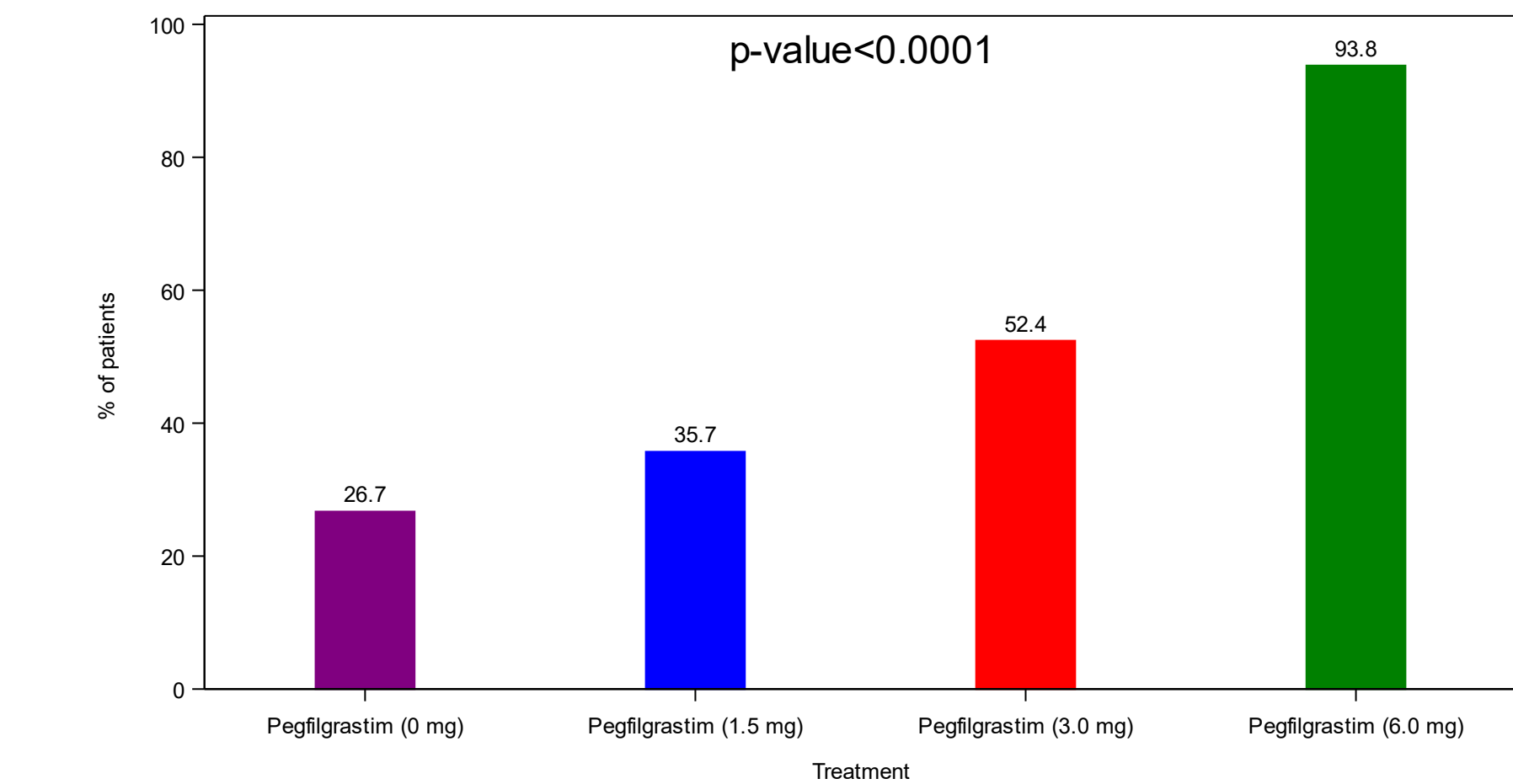


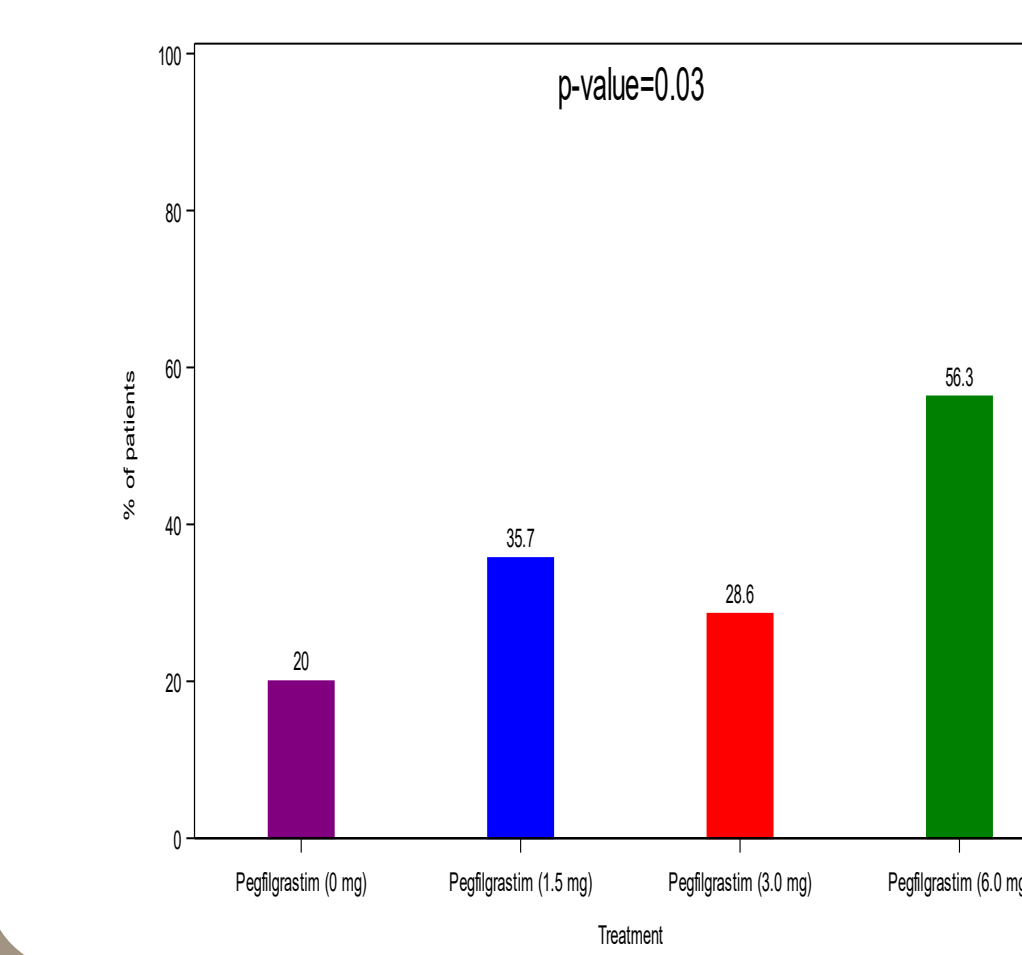
Figure 8: Thrombocytopenia with Increasing Doses of Pegfilgrastim

**Key Finding:** Dose-Dependent Increase in Thrombocytopenia with Increasing Pegfilgrastim Dose. All patients also received 20 mg/m<sup>2</sup> Plinabulin

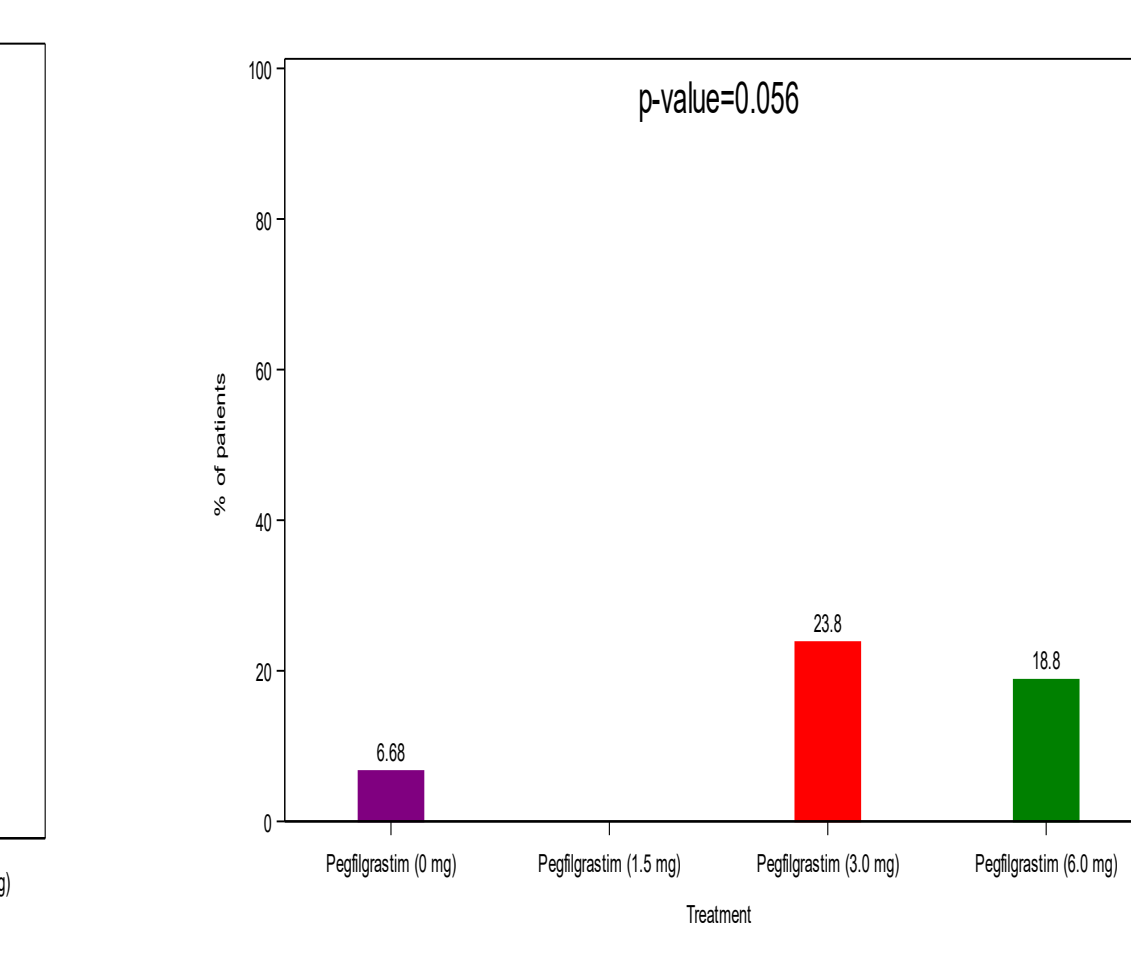
#### All Grade Thrombocytopenia



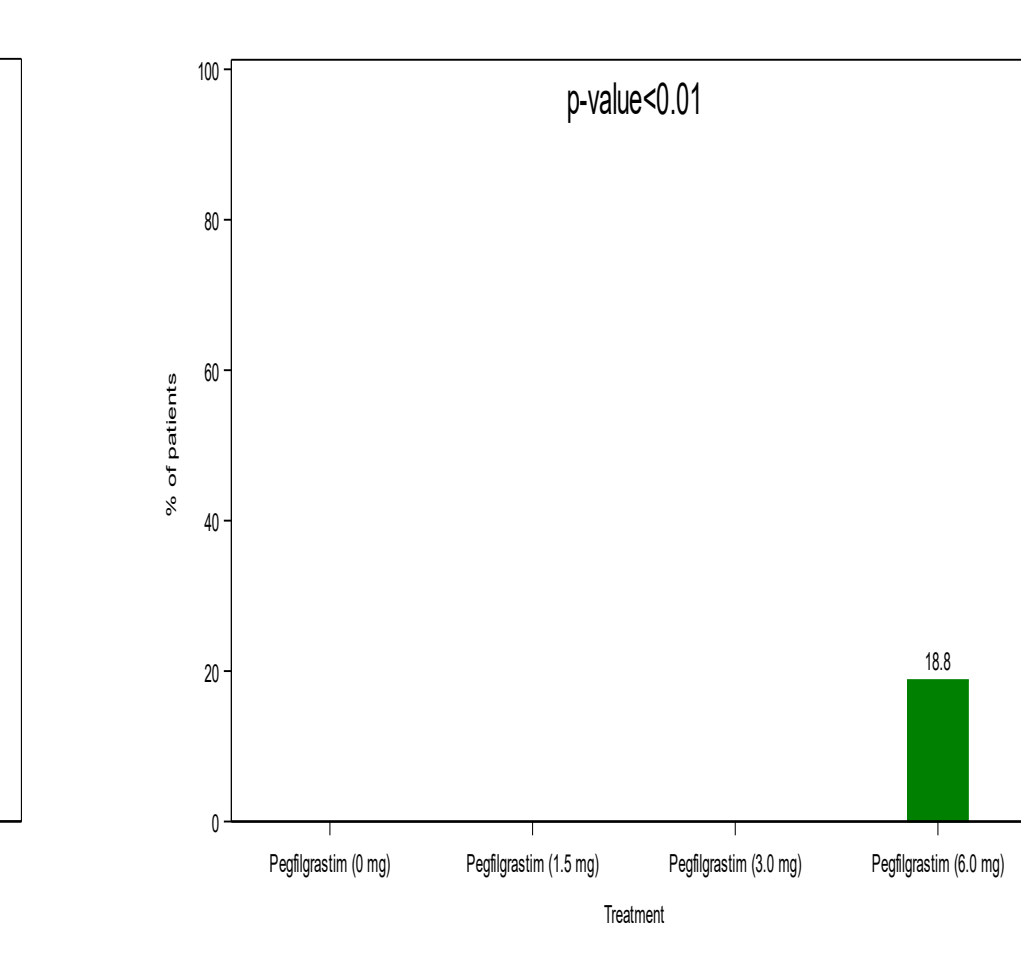
#### Grade 1



#### Grade 2



#### Grade 3



### Conclusion

- Plinabulin 20 mg/m<sup>2</sup> (Recommended Phase III dose) did not induce Thrombocytopenia
- Pegfilgrastim caused a statistically and clinically significant dose-dependent increase in Thrombocytopenia.
- A Phase III confirmatory trial is underway.

Contact  
dblayney@stanford.edu

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