# Plinabulin, a Novel Immuno-Oncology Agent mitigates Docetaxel Chemotherapy - Induced-Neutropenia and -Thrombocytopenia in NSCLC Patients

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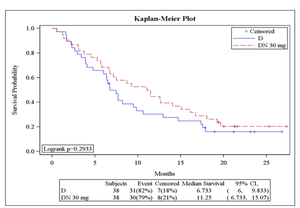
## Study BPI-2358-105 (NCT03102606): Phase 2/3, Multicenter, Randomized, Double Blind Study to Evaluate Duration of Severe Neutropenia with Plinabulin Versus Pegfilgrastim in Patients with Solid Tumors Receiving Docetaxel Myelosuppressive Chemotherapy

**Plinabulin Overview:**
- **Small Molecule**
- **Inexpensive to manufacture**
- **Given by IV infusion, on the same day of the chemotherapy**
- **More than 300 Patient Data from Phase I,II,III**
- **Currently in Phase III in NSCLC**

Plinabulin is a small molecule activator of GEFH1,and represents a novel signaling pathway leading up to activation of Dendritic Cells. Plinabulin has Anti-Cancer Activity, as demonstrated previously (ASCO-SITC 2017).




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

**Primary objective:**
**To establish the Recommended Phase 3 Dose (RP3D) based on PK/PD analysis.**

## Methods

**Assessments:**
Absolute Neutrophil Count (ANC) and platelet count was assessed at baseline (prior to Cycle 1 docetaxel dose) and during Cycle 1 on Days 1, 2, 6, 7, 8, 9, 10, and 15; Blood pressure was measured semi-continuously with 15-minute intervals, starting 15 minutes pre-Plinabulin dose and lasting ~ 4.5 hours after start of infusion with Plinabulin; Bone Pain was assessed with a validated questionnaire (Bone Pain Inventory, Short Form); Pharmacokinetics of Plinabulin were assessed with bioanalytical methods ; Safety was evaluated through AEs, CBC, and Hematology.

**Study Design**
This was the phase 2 portion of the phase 2/3 BPI-2358-105, and was designed as a multicenter, open label, randomized study. A total of N=55 patients were enrolled in this study. Patients were randomly assigned to the following arms:
Arm 1: Docetaxel (75 mg/m$^2$) + Pegfilgrastim (6 mg) (N=14); Arm 3: Docetaxel (75 mg/m$^2$) + Plinabulin (10 mg/m$^2$) (N=13);
Arm 2: Docetaxel (75 mg/m$^2$) + Plinabulin (20 mg/m$^2$) (N=14); Arm 4: Docetaxel (75 mg/m$^2$) + Plinabulin (5 mg/m$^2$) (N=14)

**Target Patient Population**:
Patients with advanced or metastatic NSCLC after failing platinum-based therapy.

## Results

### Neutropenia Results

***Figure 1. Neutrophil Count Mean (95% CI) (Cycle 1)***
Mean (95% CI) ANC with Plinabulin Stays above Gr 4 Neutropenia)

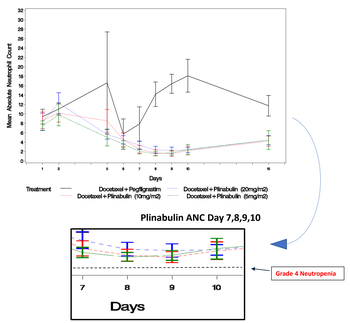
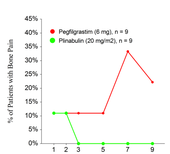



***Table 1. DSN Summary***
DSN is similar for 20 mg/m2 Plinabulin and Pegfilgrastim

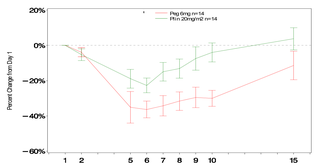
| | | Docetaxel + Pegfilgrastim | Docetaxel + Plinabulin (20mg/m$^2$) |
|---|---|---|---|
| Parameter | Statistic | DSN | DSN |
| | N | 14 | 14 |
| | Mean | 0.51 | 0.54 |
| | Std. Dev | 1.413 | 1.392 |
| | Median | 0.0 | 0.0 |
| | Minimum | 0.0 | 0.0 |
| | Maximum | 5.0 | 4.3 |
| | P=NS | | |

***Figure 2. Bone Pain with Plinabulin and Pegfilgrastim.***
Plinabulin caused less Bone Pain vs Pegfilgrastim




### Thrombocytopenia Results

***Figure 3. Platelet Count Change from Baseline (Cycle 1)***
Plinabulin Significantly Ameliorates Thrombocytopenia




| | Day 2 | Day6 | Day 7 | Day 8 | Day 9 | Day 10 | Day 15 |
|---|---|---|---|---|---|---|---|
| Difference: Pegfilgrastim – Plinabulin 20mg/m2 | 1.42 | -13.66 | -19.34 | -18.44 | -22.07 | -26.05 | -14.14 |
| P-value from 2-sided t-test, unequal variances | 0.7340 | 0.0446 | 0.0257 | 0.0221 | 0.0211 | 0.0012 | 0.1733 |

***Figure 4. Percentage Patients with >30% Decrease in Platelet Count (Cycle 1-4) per Treatment Arm***
Plinabulin Significantly Prevented Thrombocytopenia over All Doses

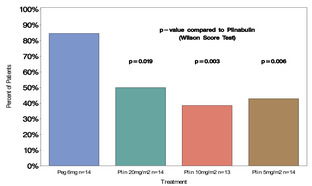
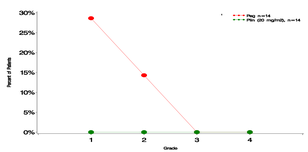



***Figure 5. Thrombocytopenia per Grade (Cycle 1)***
Plinabulin, but not Pegfilgrastim Prevented Thrombocytopenia




## Plinabulin vs. Pegfilgrastim

***Table 3. Plinabulin Superior Profile compared with Pegfilgrastim***

***Target Indication: Prevention of all chemo-induced neutropenia in all cancers***

**For Patients**
- **High Quality of Life** (less bone pain)
- **Ease of Use** (first day dosing)

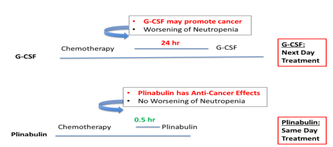
**For Physicians**
- **Potential for Improved Efficacy** (durable anti-cancer benefit, more chemo cycles of treatment)
- **Potentially Fewer ER Visits**

**For Payers**
- **Lower cost** with lower hospitalization admissions rate and duration of stay
- **Maintain pricing similar to G-CSFs**

**For Production**
- **Potential for large commercial opportunity** in an already-established and underserved market
- **Opportunity for significantly lower COGs** (small molecule vs. biologic)

**Compelling Safety Profile To-Date**
**Plinabulin AEs**: nausea, vomiting, diarrhea, and transient hypertension
**G-CSF AEs**: bone pain, splenic rupture and splenomegaly, acute respiratory distress syndrome, glomerulonephritis, and capillary leak syndrome

**G-CSF Must Wait 24 Hours after Last Chemotherapy**




## Conclusion

1. **Plinabulin 20 mg/m2 is equally effective as Pegfilgrastim for the prevention of Grade 4 Neutropenia**
2. **Plinabulin, but not Pegfilgrastim Prevents Docetaxel-Induced Thrombocytopenia**
3. **Plinabulin has a Superior Product Profile vs Pegfigrastim:**
   a. **Plinabulin has Anti-Cancer Activity**
   b. **Plinabulin has Less Bone Pain**
   c. **Plinabulin has Same Day dosing vs Next Day dosing with Pegfilgrastim**
   d. **Both Plinabulin and Pegfilgrastim are given as a single agent per Cycle**
   e. **Plinabulin is a Low cost small molecule vs high cost Pegfilgrastim**
4. **Phase 3 has been initiated with the RP3D of 20 mg/m2.**
   **This Plinabulin dose will be given as a fixed Plinabulin dose of 40 mg.**

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