Plinabulin (Plin), a small molecule with anti-cancer activity and a novel mechanism of action (MoA) in docetaxel (Tax) induced neutropenia: Phase (φ) 2 results from a head-to-head comparison with Pegfilgrastim (Peg)

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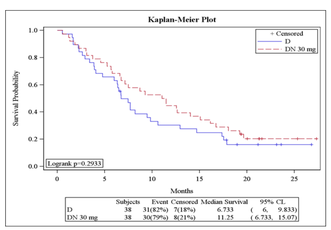
Study BPI-2358-105 (NCT03102606): Phase 2/3, Multicenter, Randomized, Double Blind Study to Evaluate Duration of Severe Neutropenia with Plinabulin Versus Pegfilgrastim in Patients with Solid Tumors Receiving Docetaxel Myelosuppressive Chemotherapy

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:
ANC 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.
Here we report the final study results from the phase 2 portion of Study BPI-2358-105.

Results

Figure 1. Plinabulin exposure by dose level.

Key findings:
1. Plinabulin exposure is higher with Plinabulin dose

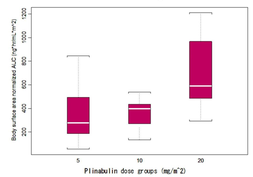


Figure 3. Mean (95% CI) Neutrophil Count over Time

Key Finding:

1. Mean (95% CI) Absolute Neutrophil Count with Plinabulin remains at levels higher than 0.5x10E9/L (Grade 4 Neutropenia)

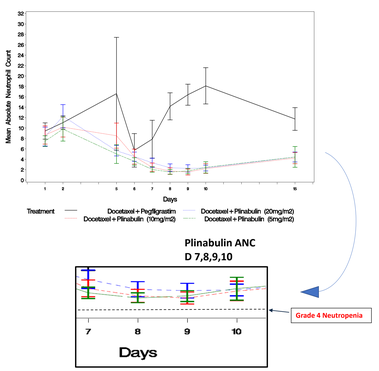


Table 1. DSN Summary

Key Finding:

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

		Docetaxel + Pegfilgrastim	Docetaxel + Plinabulin (20mg/m^2)
Parameter	Statistic	DSN	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
	JT p-value	0.7554	

Figure 2: Neutropenia by Grade and by treatment arm.

Key findings:
1. The 20 mg/m2 Plinabulin dose is the most effective dose
2. 20 mg/m2 Plinabulin and Pegfilgrastim are equally effective

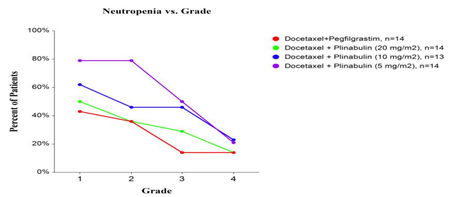


Table 2: Grade 4 Neutropenia in Cycle 1,2,3 and 4

Key Finding:

1. Plinabulin 20 mg/m2 and Pegfilgrastim are equally effective in the prevention of Grade 4 Neutropenia over Cycles 1,2,3,4

Cycle	Docetaxel + Pegfilgrastim n/N (%)	Docetaxel + Plinabulin (20 mg/m2) n/N (%)
1	2/14 (14.29%)	2/14 (14.29%)
2	0/13 (0.00%)	0/13 (0.00%)
3	0/9 (0.00%)	0/9 (0.00%)
4	0/3 (0.00%)	0/5 (0.00%)

Figure 5. Bone Pain with Plinabulin and Pegfilgrastim.

Only patients are included who had no Bone Pain at baseline.

Key Finding:

1. Plinabulin caused less Bone Pain vs Pegfilgrastim

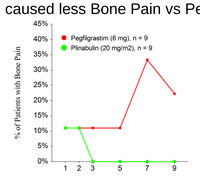
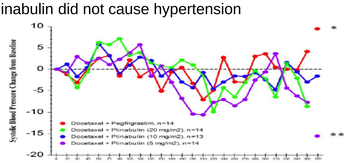


Figure 6. Systolic Blood Pressure Over Time

Key Finding:

1. Plinabulin did not cause hypertension



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**

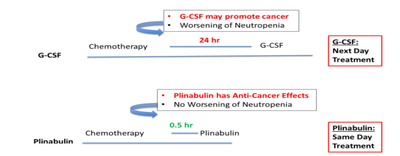
For Production
- **Potential for large commercial opportunity** in an already-established and underserved market
- **Opportunity for significantly lower COGs** (small molecule vs. biologic)

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 has a Superior Product Profile vs Pegfigrastim:**
   - **a. Plinabulin has Anti-Cancer Activity**
   - **b. Plinabulin has less Bone Pain**
   - **c. Plinabulin is given on the 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 biological Pegfilgrastim**
3. **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.**

Clinical trial supported by BeyondSpring, Inc.

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