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

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Study BPI-2388-105 (NCT03102686): 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 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-2017).

Primary objectives:
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, and 10. 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 CTI, CBC, andneral Chemist.

Study Design:
This was the phase 2 portion of the phase 2/3 BPI-2388-105, and was designed as a multicenter, open-label, randomized study. A total of 1161 NSCLC patients were enrolled in this study. Patients were randomly assigned to the following arms:
Arm 1: Docetaxel (75 mg/m2) + Pegfilgrastim (6 mg) (N=14);
Arm 3: Docetaxel (75 mg/m2) + Plinabulin (5 mg/m2) (N=13);
Arm 2: Docetaxel (75 mg/m2) + Plinabulin (20 mg/m2) (N=14);
Arm 4: Docetaxel (75 mg/m2) + Plinabulin (10 mg/m2) (N=14)

Target Patient Population:
Patients with advanced or metastatic NSCLC who have failed platinum-based therapy.

Results

Table 1. DSN Summary

Table 2. Neutropenia Results

Table 3. Plinabulin Superior Profile compared with Pegfilgrastim

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 Pegfilgrastim:
   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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Figure 1. Neutropenic Count Mean (95% CI) (Cycle 1)

Figure 2. Bone Pain with Plinabulin and Pegfilgrastim.

Figure 3. Platelet Count Change from Baseline (Cycle 1)

Figure 4. Percentage Patients with >30% Decrease in Platelet Count (Cycle 1-4) per Treatment Arm

Figure 5. Thrombocytopenia per Cycle (1-4)