Plinabulin, a Novel Small Molecule in Development for Chemotherapy-Induced-Neutropenia (CIN) Prevention, Mobilizes CD34+ Cells through a Mechanism of Action Different from G-CSF and from CXCR4 Inhibition

Plinabulin Overview:
- Small Molecule
- Given by IV infusion, on the same day of the chemotherapy
- More than 300 Patient Data from Phase I/II
- Currently in Phase III for CIN and NSCLC

Plinabulin is a small molecule activator of GEPH1, and represents a novel signaling pathway leading up to activation of Dendritic Cells. Plinabulin is developed for Chemotherapy-Induced-Neutropenia (CIN) and as an anti-agent in NSCLC.

• CD34+ mobilization is achieved with G-CSF and CXCR4-inhibitors (Plerixafor).
• Plinabulin is not a G-CSF and does not inhibit CXCR4 (19% inhibition at 10μM).

We evaluated whether Plinabulin mobilizes CD34+ progenitor cells

Target Patient Population
- Arm a: TAC + Pegfilgrastim
- Arm b: TAC + Pegfilgrastim
- Arm 1: Docetaxel (75 mg/m²) + Pegfilgrastim (6 mg)
- Arm 2: Docetaxel (75 mg/m²) + Plinabulin (20 mg/m²)
- Arm 3: Docetaxel (75 mg/m²) + Plinabulin (10 mg/m²)
- Arm 4: Docetaxel (75 mg/m²) + Plinabulin (5 mg/m²)

Study 105
Figure 1. D0 & D8 CD34+ count with Plinabulin Doses

Study 106
Figure 5. Plinabulin and Neulasta Have Complimentary Protection against TAC-Induced Neutropenia

Table 1. Neulasta Alone, and Plinabulin / Neulasta Combination CIN and Bone Pain Summary Results

Table 2. Plinabulin Superior Profile compared with Pegfilgrastim

Plinabulin vs. Pegfilgrastim

Conclusion
- Plinabulin Monotherapy is an Equally Effective Single-Dose-per-Cycle Agent as Pegfilgrastim for CIN
- With Combining Plinabulin to Pegfilgrastim:
  • Superior Efficacy for Neutropenia
  • Almost Eradicates Pegfilgrastim-Induced Bone Pain
- Plinabulin Mobilizes CD34+ Progenitor Cells through a MoA Independent from G-CSF of CXCR4
- Plinabulin can Potentially Mobilize CD34+ Cells from the Bone Marrow prior to HCT, in Particular in Patients Failing to Respond to G-CSF or G-CSF/Plerixafor

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