Plinabulin, a Potent Inducer of Haptoglobin Production for the Prevention of Tissue Iron Overload in Patients Receiving Blood Transfusions Chronically

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Abstract JNCCN-320

Introduction

Transfusion Iron Overload in Cardiac, Hepatic, Endocrine tissues and Bone Marrow causes increased morbidity in Cancer Survivors

MoA - First-in-class agent with GEF-H1 as new target

Blood Transfusion Intensity is directly related to Iron Overload (Ruccione et al. Pediatric Blood Cancer 2011)

Haptoglobin is our Natural Defense Mechanism to prevent Transfusion Iron Overload:
- Haptoglobin safely binds/neutralizes free Hemoglobin. The Haptoglobin/Hemoglobin complex is internalized in Macrophages through the CD163 receptor and Fe is safely processed through Transferrin.
- During Hemolysis, Haptoglobin is depleted quickly, and once depleted, Iron is deposited in tissues leading to tissue Iron Overload.

Haptoglobin is our Natural Defense Mechanism to prevent Transfusion Iron Overload:
- Myelosuppressive Chemotherapy causes Neutropenia and Anemia
- Prevents Chemotherapy-Induced Neutropenia (CIN)
- myelopoiesis

MoA - Plinabulin - First-in-class agent with GEF-H1 as new target

Plinabulin Mitigates Chemotherapy-Induced Consequences of Myelosuppression Broadly

Plinabulin's Neutropenia Benefit

Plinabulin's Anti-Cancer Activity

Conclusion

Plinabulin Pipeline

Study BPI-2358-106 Phase 3 Status

Randomized: 100 pts (Target: 222 pts)
Countries: China; US; Ukraine
Expected first interim analysis: Q2 2020

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See more on our website

Plinabulin Mechanism of Action

Plinabulin is a Novel Immune-Enhancing Agent with:
- Anticancer Activity (ASCO-GTC 2018)
- Avoidance of Thrombocytopenia (JASLC 2018)

Here we provide evidence that Plinabulin has the potential to prevent Transfusion Iron Overload by increasing Haptoglobin levels.

Plinabulin was evaluated at 3 dose levels:
- 10 mg/m^2
- 20 mg/m^2
- 30 mg/m^2

Plinabulin caused a dose-dependent increase (P=0.0006) in Neutrophil Count

Plinabulin's Haptoglobin Benefit

Plinabulin's Anti-Cancer Activity

- Myelosuppressive Chemotherapy causes Neutropenia and Anemia
- The Anti-Cancer Agent Plinabulin, given as a single dose per Cycle also:
  - Induces a rapid (<3 days) and sustained (f>3 weeks) increase in Haptoglobin, to levels double of baseline that Might Prevent Organ Fe-Overload and Related Morbidity in Cancer Survivors Requiring Frequent Blood Transfusions.