Protective-2 (BPI-2358-106): a Confirmatory Trial to Demonstrate Superiority of the Plinabulin (Plin) + Pegfilgrastim (Peg) Combination versus Standard of Care Pegfilgrastim for the Prevention of Chemotherapy-Induced Neutropenia in Breast Cancer Patients

San Antonio Breast Cancer Symposium® - December 8-11, 2020

Program Number: OT-06-02

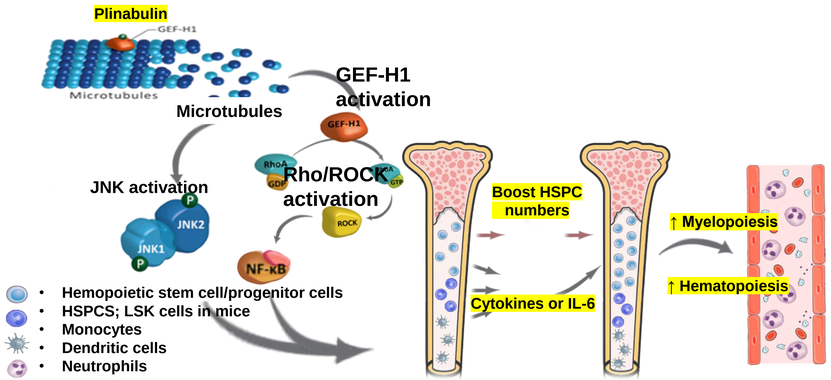
Douglas W. Blayney[1], Lan Huang[2] and Ramon Mohanlal[2].
[1]Stanford Cancer Institute, Stanford, CA;
[2]BeyondSpring Pharmaceuticals, Inc, New York, NY

INTRODUCTION

- Breast Cancer patients are potentially curable if receiving optimal chemotherapy and optimal prevention of clinical sequelae from CIN
- Standard of care for CIN is Pegfilgrastim does not fully prevent CIN (Masuda 2015).
- Plinabulin is a novel non-GCSF small molecule agent with dual activity:
  - ➢**Anti-cancer activity**
  - ➢**Prevention of Chemotherapy-Induced-Neutropenia (CIN)**
- Plinabulin has preventive CIN efficacy predominantly in week 1 of the chemotherapy Cycle, whereas Pegfilgrastim exerts CIN preventive effects primarily in week 2 of the Cycle (Blayney, ASCO 2019).
- Therefore there is a strong rationale to combine Plinabulin with Pegfilgrastim.
- Plinabulin is given as a single dose 30-minute infusion on the same day as chemotherapy. Pegfilgrastim is given on Day 2 of the Cycle.

MECHANISM OF ACTION

Plinabulin - First-in-Class Agent with GEF-H1 as a new target



RATIONALE

- Plinabulin exerts its CIN preventive effects predominantly in week 1 of the cycle
- Pegfilgrastim Primarily exerts its CIN preventive effects in week 2 of the cycle
- This was the rationale to combine these two agents, to obtain superior CIN protection throughout the entire cycle (Blayney ASCO 2019).
- Data from Phase (Ph) 2 portion of PROTECTIVE-2 (NCT0329457) with the Plin/Peg combination demonstrated superiority in CIN protection vs Peg alone, with a favorable safety/tolerability profile (Blayney, St Gallen 2019).
- The Ph 3 portion of PROTECTIVE-2 aims to confirm superiority of the Plin/Peg combination vs Peg standard of care for avoidance of CIN and Bone Pain-prevention

METHODS

Trial Design

- PROTECTIVE-2 is a global, multicenter, randomized, double-blind study to Evaluate Severe Neutropenia.

Arms
- ❑ Day 1: TAC chemotherapy, Plinabulin 40 mg
- ❑ Day 2: Neulasta 6 mg
- ❑ Day 1: TAC chemotherapy, Placebo
- ❑ Day 2: Neulasta 6 mg

Study population

- Target of approximately n=222 pts in early stage (Stage I and II) and Stage III BC (node positive or node negative with a high risk of recurrence) pts with
- ECOG status 0 or 1 receiving myelosuppressive Chemo with Docetaxel (75 mg/m2), Doxorubicin (50 mg/m2), and Cyclophosphamide (500 mg/m2) (TAC).

Data Collection

- TAC and Plin were given on Day (D)1 and Peg on D2.ANC (Covance Central Laboratory) was assessed before and after during Cycle 1 on D 1, 2, 3, 6, 7, 8, 9, 10, 11, 12, 13, and 15.
- Bone Pain was assessed by a validated & regular timepoints in Cycle 1 with a validated PRO questionnaire.

OBJECTIVES

Primary objective :

- **T**o compare the percentage of pts with a Duration of Severe Neutropenia (DSN) of 0 days in treatment Cycle 1 between the Plin/Peg vs Peg alone.

Secondary objectives:

In Cycle 1

- mean DSN,
- mean ANC NADIR,
- average change in Bone Pain from baseline,
- the rate of composite risk (infection, FN, hospitalization, significant disability, life threatening and death).
- Bone Pain

Over 4 Cycles,

- The percentage of patients with Relative Dose Intensity (RDI) < 85% and clinical sequelae of CIN (FN, Hospitalizations, Infection rate, Antibiotic use).

TRIAL STATUS

- A non-binding Interim Analysis was a planned and data was reported previously.
- Following the pre-planned Interim Analysis, the DSMB recommended the trial to continue without modifications.
- **Current Status**: Patient accrual has been completed.
- **Final data read out in 2020.**

CONTACT

Disclosures: The first author received project support to his institution, and travel support from BeyondSpring during the conduct of the study. Dr Huang and Dr Mohanlal are employees of BeyondSpring Pharmaceuticals.

Corresponding Author : **Douglas W. Blayney, MD** DBlayney@stanfordhealthcare.org
Ramon Mohanlal, MD, PhD rmohanlal@beyondspringpharma.com