Plinabulin, a Novel Small Molecule That Ameliorates Chemotherapy-Induced Neutropenia, Is Administered on the Same Day of Chemotherapy and Has Anticancer Efficacy

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Plinabulin is a small molecule with tumor-inhibiting and immune-enhancing effects. Plinabulin induces dendritic cell maturation and cytokines interleukin-1β (IL-1β), IL-6, and IL-12 production, all of which are important in neutrophil survival. In preclinical studies, plinabulin prevented docetaxel- or cyclophosphamide-induced neutropenia via a mechanism of action different from that of granulocyte colony-stimulating factor (G-CSF) analogues. In phase 1 and 2 solid tumor trials of plinabulin, which included >140 patients, routine safety laboratory assessments revealed an unexpected protective effect against neutropenia.

In the phase 2 clinical trial, patients were randomized to receive docetaxel 75 mg/m² alone (n=73) or docetaxel 75 mg/m² followed by plinabulin (NPI-2358-101) at 30 mg/m² (n=50) or at 20 mg/m² (n=40), repeated every 3 weeks (clinicaltrials.gov NCT00630110). Plinabulin was given by a 30-minute intravenous (IV) infusion, starting 1 hour after administration of docetaxel. The primary efficacy endpoint was median overall survival. Secondary endpoints included safety assessments, such as complete blood count measurements, on Days 1, 8, and 15 of each cycle.

Compared to docetaxel treatment alone, the addition of plinabulin to docetaxel significantly (p<0.0003) reduced the proportion of patients with grade 4 neutropenia from 33.3% to 4.6% in Cycle 1. The figure shows the proportions of patients with grade 4 neutropenia (absolute neutrophil count [ANC] <0.5x10⁹/L) on Day 8, the approximate day after docetaxel administration corresponding to the largest reduction in neutrophil count (Blackwell Ann Oncol 2015). Plinabulin also reduced the clinical sequelae associated with docetaxel-induced neutropenia (sepsis, infections, hospitalizations, need for docetaxel dose reduction, and G-CSF use). Bone pain was reported in 4% of patients receiving plinabulin. Plinabulin had a favorable safety profile; the most prominent finding was grade 3 transient hypertension in 20% and 5% of patients receiving 30 mg/m² and 20 mg/m² plinabulin, respectively.
Plinabulin is a novel small molecule that is being developed for the mitigation of chemotherapy-induced neutropenia. Administered by IV infusion on the same day of (approximately 1 h after) chemotherapy, plinabulin will be given in a single dose of 20 mg/m² per cycle. Plinabulin has the potential to be an effective, safe (with much less bone pain), cost-effective, and convenient alternative to G-CSF for the prevention of chemotherapy-induced neutropenia.
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