PS13 Late breaking

Paclitaxel poliglumex vs. docetaxel for the second-line treatment of non-small cell lung cancer (NSCLC): the STELLAR 2 phase III study

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Background: Virtually all patients with advanced NSCLC will have progressive disease after initial treatment, however, therapeutic options for second-line therapy are limited. Paclitaxel poliglumex (PPX; XYOTAX™) is a macromolecular drug conjugate that links paclitaxel with a biodegradable polymer, poly-L-glutamic acid. Hyperpermeable angiogenic tumor vasculature and the reduced lymphatic clearance associated with malignancy facilitate retention of macromolecules, such as PPX, within the interstitial tumor space. This results in higher intratumoral drug concentrations for a prolonged period of time. In addition, PPX is water soluble and can be administered as a short infusion without premedication.

Methods: This open-label, multinational, phase III study randomized NSCLC patients with disease progression on or after a single platinum-containing regimen to either: (A) PPX 210 mg/m^2 (PS0/1 patients) or 175 mg/m^2 (PS2 patients) or (B) docetaxel 75 mg/m^2. Patients were treated until disease progression or intolerable toxicity. Stratifications included disease stage, PS, time since start of front-line therapy, gender, and prior taxane therapy. The primary endpoint was overall survival (OS). Secondary endpoints included response rate, time to progression, and quality of life.

Results: A total of 849 patients enrolled with a median age of 62 years (range: 30–87), 71% were male, 72% had stage IV disease, and 14% were PS2. Treatment resulted in a 6.9 month median survival for both arms. Disease control, defined as CR, PR, or stable disease, was not statistically different between treatment arms (40% vs 45%, $p = 0.096$). Patients treated with PPX had significantly fewer hematologic side effects than patients on the docetaxel arm, including grade 3/4 neutropenia (14% vs 37%, $p < 0.001$), febrile neutropenia (2% vs 6%, $p = 0.002$), anemia (17% vs 26%, $p = 0.002$), and infections (25% vs 32%, $p = 0.03$). This was associated with a significant reduction in patients requiring supportive care measures. PPX also resulted in a significant reduction in alopecia ($p < 0.001$), fatigue ($p = 0.01$), asthenia ($p = 0.015$), respiratory adverse events ($p = 0.021$), mucositis ($p < 0.001$), and gastrointestinal adverse events ($p = 0.012$). As expected, the occurrence of neuropathy in the PPX-arm (210 mg/m^2) was higher than in the docetaxel arm (50% vs 30%, $p < 0.001$); neuropathy was limited to 33% in those patients treated with PPX 175 mg/m^2 ($N = 24$).

Conclusions: PPX demonstrated similar efficacy associated with a significant reduction in many toxicities compared to docetaxel, and can be delivered in a convenient 10–20 minute infusion without the need for premedication.