Poster

[P25-10] P25-10: Oncologic drugs (2)

Chair: Takuya Iwamoto, Japan

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[P25-10-5] Open-label randomized study of individualized pharmacokinetically (PK)-guided dosing versus body surface area (BSA) dosing of paclitaxel (PTX) in advanced non-small cell lung cancer (NSCLC) NCT02058433

Salvatore Joseph Salamone[1], Jie Zhang[2], Huiwei Qi[3], Huijuan Ni[4], Yunying Li[5], Jodi Courtney[6], Caicun Zhou[7]
(1.Saladax Biomedical, Inc., 2.Shanghai Pulmonary Hosptial, 3.Shanghai Pulmonary Hosptial, 4.Shanghai Pulmonary Hospital, 5.Saladax Biomedical, Inc, 6.Saladax Biomedical, Inc, 7.Shanghai Pulmonary Hosptial)
Keywords: paclitaxel, non-small cell lung cancer, Pharmacokinetically guided dosing, randomized trial

Background

Variability of PTX exposure using BSA dosing is well documented and often leads to severe toxicities. While carboplatin is dosed to obtain a specific exposure, paclitaxel is conventionally dosed by BSA, leading to a wide range of exposure. This study compared PTX PK-guided dosing to BSA dosing in PTX-carboplatin regimen in treating stage IIIB/IV NSCLC. This is the final analysis of interim results presented at ASCO 2015 (Poster #375).

Methods

309 patients with stage IIIB/IV NSCLC were randomized to receive up to 4 cycles of first line 3-weekly carboplatin (AUC 5) and a PTX dose of 175 mg/m^2 (Arm A), or a PTX PK-guided dose (Arm B) to achieve a time above a PTX plasma concentration of 0.05M ($T_{c>0.05}$) for 26 to 31 hours. Response was classified according to Response Evaluation Criteria in Solid Tumors Group. PTX concentrations were measured by immunoassay; $T_{C>0.05}$ was calculated with PK software. Primary endpoint was reduction of grade 4 hematological toxicities.

Results

There were 164 patients in Arm A and 155 patients in Arm B, with 191 males and 128 females participating. PK-guided dose adjustment resulted in doses that were widely distributed 73 –175 mg/m^2, and statistically lower than in the BSA arm (by 24%, p<0.001). Compared to Arm A, PK-guided dosing significantly reduced grade 4 neutropenia by 35% (p = 0.002, 23% vs.16%) over 4 cycles. The incidence of severe (grade 3) neutropenia was also significantly reduced by 25% in Arm B over all cycles (p=<0.001). Additionally, neuropathy (grade 2) was reduced from 20% in Arm A to 8% in Arm B (p=0.008), representing a 60% reduction over all cycles. Response rates were not significantly different; objective response rates were 23% in Arm A and 29% in Arm B (p=0.285); stable disease rates were 49% in Arm A and 42% in Arm B (p=0.0.240).

Conclusions

Results of this study are in agreement with a previous report, and present further evidence that PK-guided dosing reduces severe toxicities. This is accomplished by an overall lowering of dose intensity, while still maintaining efficacy. PK-guided dosing personalizes chemotherapy, and may be useful in patient management.