e16311 Publication Only

Correlation of therapy-induced neutropenia with survival in patients with metastatic pancreatic cancer treated with GSK-3 inhibitor elraglusib (9-ING-41) in combination with gemcitabine/nab-paclitaxel in the 1801 phase 2 study.

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Background: Previously, elraglusib (9-ING-41), an inhibitor of Glycogen Synthase Kinase-3 (GSK-3), was shown to potentiate the anticancer effects of chemotherapeutic drugs in pre-clinical models of cancer. The combination of elraglusib and gemcitabine/nab-paclitaxel (GnP) is currently being investigated in a randomized, open-label 1801 phase 2 study as a first-line therapy for patients with metastatic pancreatic ductal adenocarcinoma (mPDAC). Chemotherapy-induced neutropenia is a common dose-limiting toxicity resulting in dose reductions and/or treatment interruptions. Present evidence shows that therapy-induced neutropenia (TIN) grade 3-4 correlates with survival and is a potential marker for improved clinical outcome in elraglusib/GnP-treated patients. **Methods:** We correlated overall survival (OS) and time-to-treatment discontinuation (TTD) with TIN grade 3-4 in 72 (GnP arm) and 155 (elraglusib/GnP arm) mPDAC patients previously untreated for advanced disease (1801 Part 3 Arm B study; NCT03678883). TTD was defined as the date of first dose to the date of treatment discontinuation or death. The Kaplan-Meier log-rank test was used for statistical analysis. A p-value < 0.05 was considered statistically significant. **Results:** The rate of grade 3-4 TIN was 22% (16/72 patients) and 47% (72/155 patients) in the GnP and elraglusib/GnP groups, respectively. Based on 28% of all recorded death events in elraglusib/GnP group and 36% in GnP group, we found that grade 3-4 TIN was significantly associated with improved OS in patients treated with elraglusib/GnP (median OS: 14.4 vs 5.9 months; $P < 0.05$) but not in patients treated with GnP (median OS: 7.6 vs 7.2 months). In the elraglusib/GnP group, patients with grade 3-4 TIN stayed on treatment significantly longer (median TTD: 7.9 months; $P < 0.05$) as compared to the patients who did not develop TIN grade 3-4 (median TTD: 1.7 months). **Conclusions:** Our preliminary results identified grade 3-4 TIN as a potential marker of improved clinical outcome for elraglusib/GnP therapy in previously untreated patients with mPDAC. Recruitment for the 1801 Part 3 Arm B phase 2 trial has been completed. Another interim analysis of OS and its correlation to grade 3-4 TIN will be available by April 2024 and will be included in the final presentation. Clinical trial information: NCT03678883. Research Sponsor: None.