SAFETY DATA ANALYSES FOR FIRST-LINE PEMETREXED PLUS CARBOPLATIN (PEM + CB) IN NONSQUAMOUS NON-SMALL CELL LUNG CANCER (NS-NSCLC)


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Aim: The safety profiles of Pem + Cb for the two Cb doses (area under the curve [AUC] 5 and 6 mg/ml·min) most widely used in clinical practice have not been compared in the clinical-trial setting.

Methods: A total of 486 patients (pts) with advanced ns-NSCLC were identified from the safety populations of 5 historical phase II-IV Lilly-sponsored trials of first-line Pem + Cb (Cb: AUC 5, 105 pts [22%]/1 trial; AUC 6, 381 pts [78%]/4 trials). Pts received Pem + Cb for up to 4 or 6 cycles. The primary objective was to compare the safety profiles (selected drug-related treatment-emergent adverse events [TEAEs]) of first-line Pem + Cb AUC 5 vs. AUC 6. The safety profiles between Cb doses were compared using frequency table analysis (FTA). The generalized linear mixed effect model (GLMM) and the propensity score (PS) method were also used to compare hematologic (hem) toxicity.

Results: FTA comparison showed that Pem + Cb AUC 5 vs. Pem + Cb AUC 6 was associated with a statistically significant lower incidence of all-grade TEAEs including thrombocytopenia (20.0% vs. 57.0%), anemia (32.4% vs. 62.2%), fatigue (11.4% vs. 47.5%), and vomiting (15.2% vs. 25.2%), as well as a lower rate of grade 3/4 thrombocytopenia (11.4% vs. 29.1%) (all P <.05; Fisher’s exact test). The incidence of all-grade neutropenia and grade 3/4 neutropenia, anemia, fatigue, and vomiting was numerically lower for Cb AUC 5. GLMM results revealed a numerically favorable, but not statistically significant, odds ratio (OR) for Cb AUC 5 vs. AUC 6 for all-grade and grade 3/4 hem TEAEs (OR <1; P > .05), except grade 3/4 leukopenia (OR >1). After 1:1 PS matching of pts in AUC groups (105 pts/group), FTA showed Pem + Cb AUC 5 vs. AUC 6 had significantly less all-grade and grade 3/4 hem TEAEs (P <.05), except grade 3/4 leukopenia. A PS regression adjustment revealed the Cb AUC 5 vs. AUC 6 group was less likely to experience all-grade hem TEAEs and grade 3/4 thrombocytopenia and anemia (all OR <1; all P <.05).

Conclusions: Overall, Pem + Cb AUC 5 showed a better safety profile than Pem + Cb AUC 6, which was consistent across three statistical approaches. Due to the heterogeneity of the trials analyzed, this trend should be confirmed in a randomized prospective trial.

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