Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: a phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine


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Introduction: Patients with mPDAC frequently experience a significant symptom burden. This in turn negatively impacts their QoL. Nal-IRI, a nanoliposomal formulation of irinotecan, was evaluated with or without 5-FU/LV vs 5-FU/LV in a randomized phase 3 study in patients with mPDAC previously treated with gemcitabine-based therapy (NAPOLI-1). Results showed nal-IRI + 5-FU/LV significantly improved overall survival compared with 5-FU/LV (6.1 vs 4.2 months; unstratified hazard ratio 0.67; \( P = 0.012 \)) (Wang-Gillam et al., Lancet. 2016). QoL was a secondary endpoint of the study.

Methods: QoL was assessed using the European Organization for Research and Treatment of Cancer quality-of-life core questionnaire (EORTC-QLQ-C30), which includes functional scales (physical, role, cognitive, emotional, and social); symptom scales (appetite loss, constipation, diarrhea, dyspnea, fatigue, insomnia, nausea and vomiting, and pain); and a global health and quality-of-life scale. Patients were to complete the questionnaire at treatment start, every 6 weeks, and 30 days post-follow-up visit. The population analyzed included all patients who provided baseline and at ≥1 subsequent EORTC-QLQ-C30 assessment. Linear transformations were applied to the raw scores to produce reported scores in the 0-100 range. In the responder analysis, patients were classified as improved (≥10% increase in scale of breadth at a post-baseline time point and remained above baseline for ≥6 weeks), worsened (did not meet improvement criteria and died, or had ≥10% decrease from baseline in scale of breadth at a post-baseline time point), or stable (did not meet criteria for improvement or worsening) for each subscale. Pairwise treatment group comparisons on response classification were performed for each subscale using Cochran-Mantel-Haenszel testing adjusted for multiplicity with a Benjamini-Hochberg correction to control false discovery rate at 0.05 level for the 15 comparisons.

Results: A total of 154 patients (nal-IRI + 5-FU/LV, n = 71; 5-FU/LV, n = 83) comprised the population for this analysis of which 69% (49/71) of patients in the nal-IRI + 5-FU group and 53% (44/83) in the 5-FU/LV group had evaluable data at 12 weeks. At baseline, median Global Health Status scores were near the midpoint of the scoring range, median Functional Scale scores were high, and Symptom Scale scores were low, with baseline values similar between groups. The observed median change in score at 12 weeks was 0 for both treatment groups for Global Health Status and for the following subscale scores: role functioning, emotional functioning, cognitive functioning, social functioning, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties. For subscale scores for which the median change was not 0 (nal-IRI + 5-FU/LV: physical functioning and fatigue), the between-group differences were not substantial. Additionally, there were no significant differences in the proportion of patients classified as improved, worsened, or stable between the treatment groups. Across subscales, adjusted \( P \) values for the comparisons were >0.05 (NS).

Conclusion: In NAPOLI-1, evaluable nal-IRI + 5-FU/LV-treated patients with data through 12 weeks tended to maintain baseline QoL over 12 weeks, and there were no significant differences versus the 5-FU/LV-treated patients in QoL response despite the addition of a second cytotoxic agent. These results are limited by the small number of patients and variability in QoL subscale scores.