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CA19-9 decrease at 8 weeks as a predictor of overall survival in a randomized phase III trial (MPACT) of weekly *nab*-paclitaxel plus gemcitabine versus gemcitabine alone in patients with metastatic pancreatic cancer

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Background: A phase I/II study and subsequent phase III study (MPACT) reported significant correlations between CA19-9 decreases and prolonged overall survival (OS) with *nab*-paclitaxel plus gemcitabine (*nab*-P + Gem) treatment for metastatic pancreatic cancer (MPC). CA19-9 changes at week 8 and potential associations with efficacy were investigated as part of an exploratory analysis in the MPACT trial.

Patients and methods: Untreated patients with MPC ($N = 861$) received *nab*-P + Gem or Gem alone. CA19-9 was evaluated at baseline and every 8 weeks.

Results: Patients with baseline and week-8 CA19-9 measurements were analyzed (*nab*-P + Gem: 252; Gem: 202). In an analysis pooling the treatments, patients with any CA19-9 decline (80%) versus those without (20%) had improved OS (median 11.1 versus 8.0 months; $P = 0.005$). In the *nab*-P + Gem arm, patients with ($n = 206$) versus without ($n = 46$) any CA19-9 decrease at week 8 had a confirmed overall response rate (ORR) of 40% versus 13%, and a median OS of 13.2 versus 8.3 months ($P = 0.001$), respectively. In the Gem-alone arm, patients with ($n = 159$) versus without ($n = 43$) CA19-9 decrease at week 8 had a confirmed ORR of 15% versus 5%, and a median OS of 9.4 versus 7.1 months ($P = 0.404$), respectively. In the *nab*-P + Gem and Gem-alone arms, by week 8, 16% (40/252) and 6% (13/202) of patients, respectively, had an unconfirmed radiologic response (median OS 13.7 and 14.7 months, respectively), and 79% and 84% of patients, respectively, had stable disease (SD) (median OS 11.1 and 9 months, respectively). Patients with SD and any CA19-9 decrease (158/199 and 133/170) had a median OS of 13.2 and 9.4 months, respectively.

Conclusion: This analysis demonstrated that, in patients with MPC, any CA19-9 decrease at week 8 can be an early marker for chemotherapy efficacy, including in those patients with SD. CA19-9 decrease identified more patients with survival benefit than radiologic response by week 8.

Key words: CA19-9, pancreatic cancer, chemotherapy, *nab*-paclitaxel, MPACT

introduction

Metastatic pancreatic adenocarcinoma is one of the most aggressive cancers, with <25% of patients alive 1 year after diagnosis [1]. Carbohydrate antigen 19-9 (CA19-9), a Lewis blood group antigen, is one of the most widely studied tumor markers in patients with advanced pancreatic cancer [2–5] due to its utility in determining prognosis and response to treatment [5–12]. In general, higher versus lower CA19-9 levels at baseline and increasing versus decreasing CA19-9 levels during therapy are associated with worse prognosis [5, 6]. However, the predictive value of decreasing CA19-9 levels during treatment for assessment of response and survival has not been clearly defined [6, 13]. In a pooled analysis of six phase II trials of patients with advanced pancreatic cancer

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