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LBA-1 Phase 3 APACT trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + Gem) vs gemcitabine (Gem) alone in patients with resected pancreatic cancer (PC): Updated 5-year overall survival

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Background: The APACT trial evaluated the safety and efficacy of adjuvant nab -P + Gem vs Gem alone in patients with resected PC. Between April 2014 and April 2016, 866 patients were randomized. As previously reported, APACT did not meet the primary endpoint of independently assessed disease-free survival (DFS); however, the prespecified sensitivity analysis for median investigator-assessed DFS was 16.6 months with nab -P + Gem and 13.7 months with Gem (HR, 0.82; 95% CI, 0.694—0.965; nominal P=0.0168). The overall survival (OS; secondary endpoint) at the time of the primary analysis trended in favor of nab -P + Gem: median 40.5 vs 36.2 months (427 events; 68% mature; HR, 0.82; 95% CI, 0.680—0.996; nominal P=0.045). The post hoc updated follow-up survival analysis outcomes were consistent with those observed in the primary analysis of nab -P + Gem vs Gem: median 41.8 vs 37.7 months (511 events; 81% mature; HR, 0.82; 95% CI, 0.687—0.973; nominal P=0.0232). Safety outcomes as previously presented were consistent with those reported in the treated population for the entire trial. Here, we present updated 5-year OS in the intent-to-treat population.

Trial design: Treatment-naive patients with histologically confirmed pancreatic adenocarcinoma, macroscopic complete resection (R0 or R1), Eastern Cooperative Oncology Group performance status 0 or 1, and carbohydrate antigen 19-9 levels $<$ 100 U/mL were eligible. Stratification factors were resection status (R0 vs R1), lymph node status (positive vs negative) and region (North America, Europe, and Australia vs. Asia Pacific). Treatment was initiated $\leq$12 weeks postsurgery. Patients received nab-P 125 mg/m2 + Gem 1000 mg/m2 or Gem 1000 mg/m2 on days 1, 8, and 15 of six 28-day cycles. The primary endpoint was DFS by independent review. Secondary endpoints were OS and safety.

Methods: Treatment-naive patients with histologically confirmed pancreatic adenocarcinoma, macroscopic complete resection (R0 or R1), Eastern Cooperative Oncology Group performance status of 0 or 1, and carbohydrate antigen 19-9 levels nab -P 125 mg/m2 + Gem 1000 mg/m2 or Gem 1000 mg/m2 on days 1, 8, and 15 of six 28-day cycles. The primary endpoint was DFS by independent review. Secondary endpoints were OS and safety.

Results: As of the data cutoff date (9 April 2021), all patients had been followed up for $\geq$5 years or discontinued from the study. The median follow-up time for OS was 63.2 months. In the intent-to-treat population, 268 and 287 events occurred in the nab -P + Gem and Gem arms, respectively (88% mature). The median OS in the nab -P + Gem arm was 41.8 months compared with 37.7 months in the Gem arm (HR, 0.80; 95% CI, 0.678—0.947; nominal P=0.0091). Five-year OS rates were 38% with nab -P + Gem and 31% with Gem. Patterns of OS in the prespecified subgroups were generally consistent with observations from the intent-to-treat population: R0 (HR, 0.85; 95% CI, 0.698—1.034); R1 (HR, 0.73; 95% CI, 0.534—1.003); LN+ (HR, 0.77; 95% CI, 0.636—0.922); LN− (HR, 0.97; 95% CI, 0.667—1.415).

Conclusions: The 5-year OS outcomes in the APACT trial were consistent with those observed in both the primary analysis and the prior post hoc updated analysis for nab -P + Gem vs Gem alone. Although APACT did not meet its primary endpoint of independently assessed DFS in the primary analysis, these OS data suggest improved outcomes with nab -P + Gem.

Clinical trial identification: EudraCT (2013-003398-91) and ClinicalTrials.gov (NCT01964430).

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