common being decreased neutrophil count. Patients with PD-L1 TPS ≥1% showed a higher ORR (66.7% *vs.* 25.0%), as well as longer median PFS (6.3 *vs.* 5.3 months) and median OS (18.8 *vs.* 9.9 months). Fibrosis-associated signatures (such as ECM-myCAF and IL-iCAF) and pSMAD2/3 level were associated with anti-tumor activity.

Conclusions: SHR-1701 combined with AG showed positive antitumor activity and controllable safety in advanced pancreatic cancer.

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1527P GnP vs mFOLFIRINOX or S-IROX in metastatic pancreatic cancer: 1-year follow-up updated data from the GENERATE (JCOG1611)

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Background: We previously reported that the superiority of modified FOLFIRINOX (mFOLFIRINOX) and S-IROX (S-1, irinotecan, and oxaliplatin) compared with Gemcitabine (G) plus nab-paclitaxel (nP) (GnP) were not demonstrated as first-line treatment for metastatic pancreatic cancer (MPC). We report the final follow-up updated data.

Methods: This randomized, open-label, phase 2/3 trial was done in 45 Japanese centers. Eligible patients (pts) were aged 20—75 years and had an ECOG PS of 0—1 with pathologically confirmed metastatic or recurrent pancreatic cancer. Pts were randomly allocated (1:1:1) to receive GnP (G 1,000 mg/m^2 and nP 125 mg/m^2 on days 1, 8, 15, every 4 weeks), mFOLFIRINOX (oxaliplatin 85 mg/m^2, irinotecan 150 mg/m^2,and l-leucovorin 200 mg/m^2 on day 1, and 5-FU 2,400 mg/m^2 on days 1—3, every 2 weeks), or S-IROX (oxaliplatin 85 mg/m^2 and irinotecan 150 mg/m^2 on day 1, and S-1 80 mg/m^2/day on days 1—7, every 2 weeks). The primary endpoint was overall survival (OS).

Results: From Apr 2019 to Mar 2023, 527 pts were included and analyzed for the final analysis. The median OS was 15.3 mo in the GnP arm, 12.5 mo in the mFOLFIRINOX arm (HR 1.27, 95% CI 1.01—1.61), and 13.2 mo in the S-IROX arm (HR 1.23, 95% CI 0.98—1.56). The median progression-free survival was 6.5 mo in the GnP arm, 5.9 mo in the mFOLFIRINOX arm (HR 1.06, 95% CI 0.86—1.32), and 6.0 mo in the S-IROX arm (HR 0.96, 95% CI 0.77—1.20). Subsequent anti-cancer therapy was administered in 85.8% of GnP arm, 86.9% of mFOLFIRINOX arm, and 87.5% of S-IROX arm. Nal-IRI-based regimens were administered as the 2nd-line setting in 22.2% of the GnP arm, 1.1% of the mFOLFIRINOX arm, and 0.6% of the S-IROX arm. In the BRCA mutated pts, OS was longer than that in wild type pts in all 3 arms (GnP 25.9 mo, mFOLFIRINOX 18.4 mo, S-IROX 33.2 mo). Grade 3 or higher anorexia was more frequent in the mFOLFIRINOX (22.8%) and S-IROX (27.6%) arm than in the GnP arm (5.2%).

Conclusions: In the final analysis as well as in the interim analysis, GnP is recommended as the first-line treatment for pts with MPC compared to mFOLFIRINOX or S-IROX.

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1528P TCOG T5221 trial: A phase II randomized study of gemcitabine and nab-paclitaxel in combination with S- 1/LV (GASL) or oxaliplatin (GAP) as first-line treatment for metastatic pancreatic cancer

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Background: Gemcitabine plus nab-paclitaxel (GnP), given weekly for consecutive 3 weeks every 4 weeks, is one of the standard treatment for metastatic pancreatic adenocarcinoma (mPDAC); however, the objective response rate (ORR) is only 23% and the standard GnP is too toxic for Asian (71% grade 3—4 neutropenia in the Japanese study). Prior study showed biweekly GnP could reduce toxicities, which provided the opportunity to add other agents to overcome tumor heterogeneity. This study aims to assess the efficacy and safety of biweekly GnP plus either S-1/LV (GASL) or oxaliplatin (GAP).

Methods: The major inclusion criteria were histologically confirmed mPDAC with adequate organ functions. The primary endpoint was ORR. Utilizing a 'pick the winner' approach, a parallel Simon two-stage design was employed to test if ORR could achieve 41% in either arm. The study arm would proceed to the second stage if there were 6 or more responders among the first 24 patients in each arm. Both arm consisted of nab-paclitaxel 125 mg/m^2, gemcitabine 800 mg/m^2 on day 1 in a 2-week

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