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1300 The phase III, randomized, double-blind, placebo-controlled KEYNOTE-811 study of pembrolizumab plus trastuzumab and chemotherapy for HER2+ metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma

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Background: In a prior analysis of the phase 3 KEYNOTE-811 study, pembrolizumab (pembro)/trastuzumab and chemotherapy (chemo) vs placebo (pbo)/trastuzumab and chemo provided an ORR of 74% vs 52% in the first 264 pts. These data led to FDA approval of first-line pembro/trastuzumab and chemo for HER2+ mG/GEJ adenocarcinoma. We present results of a prespecified interim analysis.

Methods: Eligible patients (pts) aged ≥18 years with first-line, locally-advanced unresectable or metastatic HER2+ mG/GEJ adenocarcinoma irrespective of PD-L1 were randomized 1:1 to pembro 200 mg IV Q3W or pbo IV Q3W plus chemo (5-FU and cisplatin [FP] or capecitabine and oxaliplatin [CAPOX] and trastuzumab [SOC]). Randomization was stratified by region, PD-L1 status, and chemo choice. Treatment continued for ≤2 years or until disease progression or intolerable toxicity. Dual primary end points were PFS (RECIST v1.1, BICR) or OS. Data cut-off for this interim analysis was Mar 29, 2023.

Results: At data cut-off, 698 pts were randomized (350 pembro + SOC; 348 pbo + SOC). Median follow-up was 38.5 mo. In all pts, pembro + SOC vs pbo + SOC significantly improved PFS (median 10.0 vs 8.1 mo; HR 0.73; 95% CI 0.61-0.87; p=0.0002). In pts with PD-L1 CPS ≥1, median PFS was 10.9 vs 7.3 mo (HR 0.71; 95% CI, 0.59-0.86). OS was longer with pembro + SOC vs pbo + SOC in all pts (median 20.0 vs 16.8 mo; HR 0.84; 95% CI, 0.70-1.01), and in pts with PD-L1 CPS ≥1 (median 20.0 vs 15.7; HR 0.81; 95% CI, 0.67-0.98). As the prespecified criteria for significance was not met, OS continued to final analysis. ORR was 72.6% vs 60.1% with pembro + SOC vs pbo + SOC (73.2% vs 58.4% [PD-L1 CPS ≥1]); median DOR was 11.3 mo vs 9.5 mo. Grade ≥3 drug-related AE rates were 59% vs 51%. Grade 5 drug-related AEs occurred in 4 (1%) vs 3 (1%) pts, respectively.

Conclusions: First-line pembro plus trastuzumab and chemo significantly improved PFS, and improved ORR with durable responses vs pbo plus trastuzumab and chemo in pts with unresectable, HER2+ mG/GEJ adenocarcinoma, specifically in pts with PD-L1 CPS ≥1. These data support use of this regimen as a standard option for HER2+ and PD-L1-positive tumors.

Clinical trial identification: NCT03615326.

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131O Long-term outcomes of indocyanine green fluorescence imaging-guided versus conventional laparoscopic lymphadenectomy for gastric cancer: A randomized clinical trial

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Background: Radical lymph node (LN) dissection is the cornerstone of surgical treatment for gastric cancer (GC). Indocyanine green (ICG) fluorescence imaging-guided lymphadenectomy has been proven effective in increasing the number of LNs retrieved in laparoscopic gastrectomy for GC. However, the long-term oncological efficacy of ICG fluorescence imaging in laparoscopic gastrectomy remains unclear.

Methods: In this open-label, randomized clinical trial, 266 eligible patients with potentially resectable GC (cT1-4a, N0/+, M0) were enrolled from November 2018 to July 2019. Patients were randomly (1:1 ratio) assigned to either the ICG or non-ICG group. The primary outcome was the number of retrieved lymph nodes. The secondary outcomes were three-year overall survival (OS), three-year disease-free survival (DFS), and recurrence patterns.

Results: Among the 266 patients, 258 were included in the per-protocol analysis (ICG [n=129] vs. non-ICG group [n=129]). The mean (SD) total retrieved LNs in the ICG group was significantly more than that in the non-ICG group (50.5 (15.9) vs 42.0 [10.3], $P<0.001$). The 3-year OS rate in the ICG group was 86.0%, which was significantly higher than that in the non-ICG group (73.6%; $P=0.015$). The 3-year DFS rates in the ICG and non-ICG groups were 81.4% and 68.2%, respectively, with an absolute risk difference of 13.2% ($P=0.012$). There was a significant difference in the overall recurrence rates between the ICG and non-ICG groups (17.9% vs 31.0%; $P=0.014$). The LN noncompliance rate in the ICG group (31.8%) was lower than that in the non-ICG group (57.4%; $P<0.001$), while the LN noncompliance rate in patients with locoregional recurrence was significantly higher (75.0%) than those without locoregional recurrence (43.1%, $P=0.030$).

Conclusions: Compared with conventional lymphadenectomy, ICG guided laparoscopic lymphadenectomy is safe and effective in prolonging survival among patients with resectable GC.

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Legal entity responsible for the study: This study was approved by the institutional review board of FMUUH (IRB number: 2016YF015-02).

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132MO Zanidatamab (ZW25; Zani) in patients (pts) with previously treated advanced human epidermal growth factor receptor 2 (HER2)-amplified biliary tract cancer (BTC): Asia subgroup analysis of the phase IIb HERIZON-BTC-01 study

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Background: Zani, a HER2-targeted bispecific antibody, has shown antitumor activity and a tolerable and manageable safety profile in pts with HER2-amplified, treatment (Tx)-refractory, advanced BTC (HERIZON-BTC-01; NCT04466891). Here, we report a post-hoc analysis of the Asia subgroup in predetermined cohort 1 (HER2 immunohistochemistry 2+ or 3+) comprising pts from China and South Korea.

Methods: This phase 2b, open-label, single-arm study evaluated Zani monotherapy (20 mg/kg IV Q2W) in adults with HER2-amplified, inoperable, locally advanced/metastatic BTC. Pts had received ≥1 prior systemic Tx for advanced disease, including gemcitabine. The primary endpoint was confirmed objective response rate. Secondary endpoints included disease control rate, duration of response, progression-free survival, and adverse events (AEs).

Results: Of 80 pts enrolled in cohort 1, 50 were from Asia (median age 63.5 years; 29 [58%] gallbladder cancer, 11 [22%] intra-, and 10 [20%] extra-hepatic cholangiocarcinoma). At data cutoff (Oct 10, 2022), median study follow-up was 11.3 months (range 6.9-22.3); 7 (14%) pts remained on Tx. Pts had median 1 prior line (range 1-5) of Tx for advanced disease. Efficacy is summarized in the table. Tx-related AEs (TRAEs) were experienced by 70% of pts, the most common being infusion-related reactions (42%), diarrhea (28%), and decreased ejection fraction (EF; 12%). In all, 10% of pts experienced grade 3 TRAEs (decreased EF [4%]; diarrhea, increased blood bilirubin, and enteritis [all 2%]); none had grade 4/5 TRAEs. A total of 4% of pts had serious TRAEs and 2% discontinued Tx due to decreased EF.

Table: 132MO

	Asia subgroup (n=50)
Objective response rate[a], % (95% CI)[b]	42 (28, 57)
Best overall response[a], n (%)	
Complete response	0 (0)
Partial response	21 (42)
Stable disease	13 (26)
Progressive disease	15 (30)
Not evaluable	1 (2)
Disease control rate[a], % (95% CI)[b]	68 (53, 81)
Median duration of response, months (95% CI)[c]	7.4 (3.9, not estimable)
Duration of response ≥16 weeks, n (%) (95% CI)[b]	16 (76) (53, 92)
Median progression-free survival, months (95% CI)[c]	5.5 (3.3, 7.0)

CI, confidence interval

[a]Confirmed by independent central review per RECIST v1.1; [b]Estimated using Clopper-Pearson method; [c]Estimated using Brookmeyer & Crowley method with log-log transformation.