

*Recommended
Esophageal/Gastric
Cancer Abstracts from
ASCO 2019*

RAS Lifescience Solutions

A single-arm, open phase II clinical trial of anti-PD-1 antibody SHR-1210 combined with nimotuzumab (anti-EGFR) as 2L treatment of advanced esophageal squamous cell carcinoma.

Abstract No: TPS4147

Background: Approximately 40% of patients (pts) with esophageal cancer are diagnosed with advanced unresectable or metastatic disease; the 5-year survival rate for advanced disease is 5%. No standard therapy is available in China for Advanced Esophageal Squamous Cell Carcinoma (ESCC) patients progressed after first-line chemotherapy. Inhibition of programmed cell death protein-1 (PD-1) has demonstrated promising antitumor activity and manageable safety in pts with advanced unresectable or metastatic ESCC. SHR-1210, a humanized IgG4 monoclonal antibody, has high affinity and specificity for PD-1 molecule. SHR-1210 was generally well tolerated and had preliminary antitumor effects in pts with solid tumors, including ESCC. Nimotuzumab, a humanized anti-epidermal growth factor receptor monoclonal antibody h-R3, has been shown to be effective and safe in the treatment of head and neck cancer, non-small cell lung cancer (NSCLC) and esophageal Cancer in several phase II studies. *The purpose of this study is to observe and evaluate the efficacy and safety of anti-PD-1 antibody SHR-1210 combined with nimotuzumab as second-line therapy in patients with advanced ESCC.*

Methods: Patients, age 18-75, with measurable tumor lesion, failed in or progression after 1st line chemotherapy, were enrolled in this study. Patients received SHR-1210 200 mg once every 2 weeks (Q2W) combined nimotuzumab 200 mg weekly until disease progression, death or unacceptable toxicity. Assessments included response by RECIST v1.1 every 6 wks and safety (physical examination, vital signs, ECOG PS, laboratory tests). The primary endpoint is the objective response rate (ORR), and the secondary end points include the disease control rate (DCR), duration of response (DOR), progression-free survival (PFS), and overall survival (OS). Additionally, we try to identify biomarker to predict efficacy of SHR-1210 and Nimotuzumab with target capture sequencing and gene expression profile as exploratory endpoints. Clinical trial information: [NCT03766178](https://clinicaltrials.gov/ct2/show/study/NCT03766178)

Phase 2 study of camrelizumab (anti-PD-1 antibody) combined with apatinib and chemotherapy for the first-line treatment of advanced esophageal squamous cell carcinoma.

Abstract No: 4033

Background: Both anti-PD-1 antibodies and molecular antiangiogenic agents have shown promising anti-tumor activities in patients with advanced esophageal cancer. We conducted this single-center phase 2 study to evaluate the efficacy and safety of camrelizumab (anti-PD-1 antibody) plus apatinib (VEGFR2-TKI) in combination with liposomal paclitaxel and nedaplatin in the first-line treatment of patients with esophageal squamous cell carcinoma (ESCC).

Methods: Patients with unresectable locally advanced or metastatic ESCC received camrelizumab 200mg d1, liposomal paclitaxel 150mg/m² d1, nedaplatin 50mg/m² d1 and apatinib 250mg d1-14. Treatments were repeated every 14 days for up to 6-9 cycles, followed by maintenance therapy with camrelizumab, apatinib, or both. The primary end point was progression-free survival (PFS) in the intention-to-treat population. Secondary end points included objective response rate (ORR), disease control rate (DCR), overall survival (OS) and safety. PD-L1 positivity, defined as a combined positive score (CPS) ≥1, was evaluated by immunohistochemistry (IHC).

Results: Between Aug 6th 2018 and Feb 6th 2019, a total of 29 patients were enrolled. The median age was 62 years (43-70). Most patients were male (22/29, 75.9%) with metastatic disease (25/29, 86.2%). Response evaluation by independent central review was available in 26 patients, with 19 achieving a best response of PR, 6 with SD, and 1 with PD. *The ORR and DCR were 73.1% (19/26) and 96.2% (25/26), respectively.* Data for PFS and OS were not matured. The most common grade 3/4 adverse events were leucopenia (21/29, 72.4%) and neutropenia (15/29,

51.7%). Two cases of treatment-related SAEs occurred, both led to hospitalization: one patient developed grade 3 febrile neutropenia, grade 4 leucopenia and grade 3 anorexia; another patient developed grade 4 toxic epidermal necrolysis.

Conclusions: [Camrelizumab plus apatinib in combination with liposomal paclitaxel and nedaplatin could be a new treatment option](#) for patients with unresectable locally advanced or metastatic ESCC. Clinical trial information: [NCT03603756](#)

Lactate dehydrogenase (LDH) and baseline markers associated with clinical outcomes of advanced esophageal squamous cell carcinoma patients treated with camrelizumab (SHR-1210), a novel anti-PD-1 antibody.

Abstract No: e15559

Background: A small proportion of patients with advanced esophageal squamous cell carcinoma (ESCC) could benefit from immune checkpoint inhibitors, and reliable peripheral blood biomarkers for outcomes of anti-PD-1 immunotherapy were not identified in ESCC.

Methods: A total of 43 patients were retrospectively reviewed in the ESCC cohort of a phase I trial from our center. All patients received intravenous camrelizumab (SHR-1210), a novel anti-PD-1 antibody, at a dose of 60 mg, 200 mg or 400 mg (4-week interval after first dose followed by a 2-week schedule) and repeated every two weeks until disease progression or intolerable toxicity. [The associations between lactate dehydrogenase \(LDH\) as well as other peripheral blood biomarkers at baseline and the efficacy of camrelizumab were also investigated.](#)

Results: With a median follow-up of 19.6 months, the overall response rate was 25.6% (11/43), including one complete response. Median progression-free survival (PFS) and overall survival were 2.0 months (95% CI: 0-4.1 months) and 8.0 months (95% CI: 7.2-8.8 months), respectively. Notably, [four patients achieved a PFS exceeding 12 months](#), including three patients with a long-lasting duration of response over 1 year. [Patients with an elevated baseline lactate dehydrogenase had lower tumor response rates \(8.3% vs. 32.3%, \$p = 0.02\$ \) as well as shorter PFS \(median: 1.8 vs. 4.0 months; HR 0.39, \$p = 0.002\$ \) and overall survival \(median: 4.2 vs. 10.4 months; HR 0.22, \$p < 0.0001\$ \) compared with patients with normal levels. An increase of lactate dehydrogenase level during treatment was significantly associated with disease progression \(\$p = 0.014\$ \). Multivariate Cox analysis identified LDH \(HR = 0.18\), C-reactive protein \(HR = 0.27\), number of involved organs \(HR = 0.31\), absolute monocyte count \(HR = 0.33\) and Eastern Cooperative Oncology Group performance status \(HR = 0.36\) as independent prognostic factors.](#)

Conclusions: Serum LDH, as is readily available in routine clinical practice, is a potential marker for response and a powerful independent factor for survival in advanced ESCC patients receiving anti-PD-1 treatment.

CA224-060: A randomized, open label, phase II trial of relatlimab (anti-LAG-3) and nivolumab with chemotherapy versus nivolumab with chemotherapy as 1L treatment in patients with GC or GEJC.

Abstract No: TPS4143

Background: Blockade of the immune checkpoint receptor programmed death-1 (PD-1) has shown clinical benefit in multiple tumor types. Nivolumab (anti-PD-1) has demonstrated a survival advantage versus (vs) placebo in patients (pts) with advanced gastric cancer (GC) or gastroesophageal junction cancer (GEJC) (Kang YK et al. *Lancet* 2017;390:2461–71). *Lymphocyte activation gene 3 (LAG-3) is an immune checkpoint molecule that negatively regulates effector T-cell function and is a marker of T-cell exhaustion.* Preliminary data in melanoma suggest that combining nivolumab with relatlimab (anti-LAG-3) could improve efficacy without substantially increasing toxicity vs nivolumab especially, but not exclusively, in LAG-3-expressing pts (Ascierto PA et al. *Ann Oncol* 2017;28(S5):LBA18). Furthermore, LAG-3 expression was as high as 33% in an analysis of solid tumors including GC (Edwards R et al. *J Immunother Cancer* 2017;5(S3):P510). Study CA224-060 will assess the clinical efficacy and safety of relatlimab and nivolumab with chemotherapy for first-line treatment of GC or GEJC.

Methods: This is a randomized, open-label, multicenter, phase 2 study of relatlimab and nivolumab with oxaliplatin-based chemotherapy vs nivolumab with oxaliplatin-based chemotherapy. Approximately 250 adult pts with untreated, locally advanced, unresectable or metastatic GC or GEJC will be enrolled. To be randomized, pts must have tumor tissue for analysis of biomarkers, LAG-3 status, and PD-L1 combined positive score. Key exclusion criteria include HER2-positive status, untreated CNS metastases, or significant cardiovascular disease. The primary endpoint is objective response rate (ORR) using RECIST v.1.1 by blinded independent central review in LAG-3-expressing pts. Other endpoints include investigator-assessed ORR, ORR in LAG-3-negative pts, duration of response, overall survival, progression-free survival, and safety and tolerability. Efficacy signals in biomarker subgroups will be explored. Currently, 26 sites are activated with 15 randomized pts. Clinical trial information: [NCT03662659](https://clinicaltrials.gov/ct2/show/study/NCT03662659)

Camrelizumab combined with capecitabine and oxaliplatin followed by camrelizumab and apatinib as 1L therapy for adv./met. GC or GEJC: Updated results from a multicenter, open label phase II trial.

Abstract No: 4031

Background: Capecitabine plus oxaliplatin (CAPOX) is one of the standard first-line treatments for advanced or metastatic gastric cancer. Camrelizumab (SHR-1210, an anti-PD-1 antibody) shows promising anti-tumor activity in patients (pts) with advanced or metastatic gastric or gastroesophageal junction (G/GEJ) cancer. Camrelizumab combined with CAPOX for untreated G/GEJ cancer was assessed as a part of an ongoing multicenter, open-label phase 2 trial (cohort 1), and encouraging preliminary results were reported. Here, we present the updated safety and efficacy data.

Methods: In this cohort, systemic treatment naïve pts with HER2- advanced or metastatic G/GEJ adenocarcinoma were given camrelizumab 200 mg on Day 1, capecitabine 1000 mg/m² bid on Days 1–14 and oxaliplatin 130 mg/m² on Day 1 of each 21-day-cycle for 4 to 6 cycles followed by camrelizumab 200 mg every 3 weeks plus apatinib 375 mg qd until disease progression or intolerable toxicity. The primary endpoint was objective response rate.

Results: At data cutoff (Jan 20, 2019), 43 of the 48 enrolled pts were evaluable. Partial response was observed in 28 pts (65%), and 19 (44%) were confirmed. *Stable disease in 14 pts and progressive disease in 10 pts were reported.* Median estimates for duration of response and progression-free survival were not reached. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 9 pts (21%), included neutropenia, diarrhea, rash and elevated ALT, whereas none of the TRAEs was fatal. *Ten pts without progression after 4–6 cycles of camrelizumab and CAPOX combination therapy all received camrelizumab plus apatinib as sequential therapy, and no new safety signals were observed.*

Conclusions: The updated results confirmed that camrelizumab plus CAPOX followed by camrelizumab plus apatinib was well tolerated with noteworthy responses as first-line therapy in advanced or metastatic G/GEJ cancer pts. Expansion of this cohort in a phase 3 study are under way. Clinical trial information: [NCT03472365](https://clinicaltrials.gov/ct2/show/study/NCT03472365)

Efficacy and safety of sintilimab in combination with XELOX in 1L GC or GEJC

Abstract No: 4042

Background: Immune checkpoint inhibitors have shown clinical benefit in advanced GC/GEJC. This phase 1b study evaluates the efficacy and safety of sintilimab, an anti-programmed cell death-1 antibody (PD-1 Ab) in combination with XELOX for GC/GEJC in first-line setting.

Methods: This phase 1b study enrolled treatment-naïve unresectable locally advanced or metastatic GC/GEJC patients without HER2 amplification in cohort F. Patients received sintilimab 200mg IV q3w until disease progression, unacceptable toxicity or death, in combination with XELOX regimen (oxaliplatin 130mg/m² IV D1 and capecitabine 1000mg/m² PO BID D1-14) for up to 6 cycles. *The primary objective was to evaluate the efficacy of the combination per RECIST v1.1 and safety and tolerability.*

Results: Totally 20 patients were enrolled in cohort F. As data cutoff (15 Jan 2019), median follow up was 5.8 months (range, 2.4 to 12.5). The median dose of sintilimab was 6.5 (range, 4 to 12). *The objective response rate (ORR) was 85.0% (95%CI, 62.1 to 96.8) and disease control rate (DCR) was 100.0% (95%CI, 83.2 to 100.0).* Among 17 patient with BOR of PR, two patients achieved a complete response (CR) of the target lesion. The median duration of response (DOR) and median progression free survival (PFS) had not been met. Three patients underwent resection of primary tumor after achieving a BOR of partial response (N=2) and stable disease (N=1). The incidence of treatment emergent adverse events (TEAEs) was 85.0%. Treatment-related AEs (TRAEs) occurred in 14 (70.0%) patients. The incidence of TRAE ≥ Grade 3 was 15%. AEs of immune-related etiology, occurred in 6 patients (30.0%). There were no AEs that resulted in death. As data cutoff, 12 patients were still in treatment and 8 had discontinued treatment and were under survival follow up. The biomarker analysis including PD-L1 expression in tumor specimen was ongoing.

Conclusions: *Sintilimab in combination with XELOX in first-line GC/GEJC shows promising anti-tumor efficacy and a tolerable safety profile.* The further randomized, phase 3 study of Sintilimab in combination with XELOX in this setting is ongoing (NCT03745170). Clinical trial information: [NCT02937116](https://clinicaltrials.gov/ct2/show/study/NCT02937116)

Tumor mutational burden identifies chemorefractory gastric cancer with overall survival advantage after receiving toripalimab, a PD-1 antibody.

Abstract No: 4021

Background: Tumor mutational burden (TMB) is correlated with enhanced objective response rate (ORR) and progression-free survival for certain cancers receiving immunotherapy. This study aimed to investigate the safety and activity of toripalimab, a humanized PD-1 antibody, in advanced gastric cancer (AGC), and the efficacy predictive value of biomarkers including TMB and PD-L1.

Methods: This study was a part of phase Ib/II trial evaluating the safety and activity of toripalimab as a single agent therapy or in combination with chemotherapy in chemo-refractory or treatment-naïve AGC, esophageal squamous cell carcinoma, nasopharyngeal carcinoma and head and neck squamous cell carcinoma. This report focused on the

chemo-refractory AGC cohort receiving toripalimab (3 mg/Kg d1, Q2W) as a single agent therapy. Primary endpoint was ORR. Biomarkers including tumor PD-L1 expression, TMB, microsatellite instability (MSI) and Epstein-Barr virus (EBV) infection status were evaluated for their correlation with clinical efficacy as preplanned. Tumor PD-L1 expression was assessed with the SP142 immunohistochemistry assay, and the other biomarkers were assessed with whole exome sequencing based on tumor samples.

Results: There were 58 subjects included in this cohort. The ORR was 12.1% and the disease control rate was 39.7%. Only 1 subject was MSI-H and achieved partial response. One out of 4 EBV positive subjects achieved partial response. **Significant higher ORR was observed in subjects with positive PD-L1 expression** (ORR 37.5%, 3/8) or TMB \geq 12 Mutations/Mb (ORR 33.3%, 4/8) than those with negative PD-L1 expression (ORR 8.5%) or TMB < 12 Mutations/Mb (ORR 7.0%). **The TMB-high subgroup showed significant superior OS than the TMB-low subgroup** (HR = 0.48 [96% CI 0.24 to 0.96], $p = 0.038$), while PD-L1 expression status failed to differentiate OS.

Conclusions: Toripalimab demonstrated promising anti-tumor activity in chemo-refractory AGC patients. **TMB might serve as a better predictive marker for OS than PD-L1 expression for chemo-refractory AGC patients receiving PD-1 blockade immunotherapy.** Clinical trial information: [NCT02915432](https://clinicaltrials.gov/ct2/show/study/NCT02915432)

Efficacy and safety of pembrolizumab (pembro) alone or in combination with chemotherapy (chemo) in patients (pts) with advanced gastric or gastroesophageal (G/GEJ) cancer: Long-term follow up from KEYNOTE-059.

Abstract No: 4009

Background: Interim analysis of a global, phase 2 KEYNOTE-059 study (NCT02335411) reported manageable safety and promising antitumor activity for pembro alone or pembro + chemo in pts with G/GEJ cancer. Here we report long-term efficacy and safety data of all cohorts.

Methods: Pts with recurrent or metastatic G/GEJ adenocarcinoma were enrolled in 3 cohorts. **Cohort 1** pts (PD-L1+ or PD-L1-) received pembro alone after \geq 2 prior lines of therapy. **Cohort 2** pts (PD-L1+ or PD-L1-) received pembro + cisplatin (80 mg/m² day 1) + 5-fluorouracil (800 mg/m² days 1-5 Q3W) or capecitabine (in Japan only, 1000 mg/m² twice daily) as first-line. **Cohort 3** pts (PD-L1+, combined positive score \geq 1% using the PD-L1 IHC 22C3 pharmDx assay) received pembro alone as first-line. All pts received pembro 200 mg Q3W for up to 2 years. End points included safety, ORR, DOR, and OS.

Results: At data cutoff (Aug 8, 2018), median (range) follow-up was 6 (1-38), 14 (2-40), and 21 (2-36) months for cohorts 1 ($n = 259$), 2 ($n = 25$), and 3 ($n = 31$), respectively. **In cohort 1, confirmed ORR (95% CI) was 11.6% (8-16) overall, 15.5% (10-22) in PD-L1+, and 6.4% (3-13) in PD-L1- tumors. In cohort 2, confirmed ORR was 60.0% (39-79) overall, 73.3% (45-92) in PD-L1+, and 37.5% (9-76) in PD-L1- tumors. In cohort 3, confirmed ORR was 25.8% (12-45).** Median (range) DOR in months was 16.1 (2-35+), 4.6 (3-37+), and not reached (2.1-32.5+) in cohorts 1, 2, and 3, respectively. **OS at 1 year/2 years was 24.6%/12.5%, 52%/32%, and 63.6%/40.1% in cohorts 1, 2, and 3, respectively.** In cohorts 1, 2, and 3, grade 3-5 treatment-related adverse event (TRAE) incidence was 46 (18%), 20 (80%), and 8 (26%) respectively. TRAEs led to discontinuation in 6 (2%) and 3 (12%) pts in cohorts 1 and 2, respectively, and to death in 2 (1%) pts in cohort 1. No TRAEs led to discontinuation or death in cohort 3.

Conclusions: **These updated results demonstrate manageable safety, durable clinically meaningful activity of pembro in heavily pretreated pts, and promising efficacy of first-line pembro (alone or + chemo) in pts with advanced G/GEJ cancer.** Clinical trial information: [NCT02335411](https://clinicaltrials.gov/ct2/show/study/NCT02335411)

Pembrolizumab versus chemotherapy as 2L therapy for advanced esophageal cancer: Phase 3 KEYNOTE-181 study.

Abstract No: 4010

Background: The phase 3 KEYNOTE-181 study compared pembrolizumab (pembro) vs chemo as second-line therapy for patients (pts) with advanced/metastatic squamous cell carcinoma (SCC) and adenocarcinoma (ACC) of the esophagus (NCT02564263).

Methods: Eligible pts were randomized 1:1 to pembro 200 mg Q3W for up to 2 years or choice of paclitaxel, docetaxel, or irinotecan. Randomization was stratified by histology (SCC vs adenocarcinoma) and region (Asia vs rest of world). Primary end points were OS in the SCC, PD-L1 combined positive score (CPS) ≥ 10 , and the ITT. Secondary end points included PFS, ORR, safety; exploratory end points included health-related quality of life (HRQoL) in CPS ≥ 10 .

Results: 628 pts were randomized (401 with SCC; 222 with CPS ≥ 10). As of Oct. 15, 2018, median follow-up was 7.1 mo (pembro) vs 6.9 mo (chemo). *In CPS ≥ 10 , OS was superior with pembro vs chemo (median 9.3 vs 6.7 mo; HR 0.69; 95% CI 0.52-0.93; P= 0.0074). In CPS ≥ 10 SCC, median OS was 10.3 mo vs 6.7 mo and in CPS ≥ 10 ACC, median OS was 6.3 mo vs 6.9 mo; 12-mo OS rates were higher with pembro vs chemo (Table). In SCC, median OS was 8.2 mo vs 7.1 mo; HR 0.78; 95% CI 0.63-0.96; P= 0.0095. In the ITT, median OS was 7.1 mo vs 7.1 mo; HR 0.89; 95% CI 0.75-1.05; P= 0.0560. Updated OS will be presented. Grade 3-5 drug-related AEs ($\geq 10\%$ incidence in either arm) included decreased white blood cells (0% vs 10%), decreased neutrophils (0.3% vs 10%). In CPS ≥ 10 , HRQoL improved with pembro vs chemo only for EQ-5D VAS (difference in LS mean change from baseline 5.57; 95% CI 0.58-10.56).*

Conclusions: *Pembro significantly improved OS vs chemo as second-line therapy for advanced esophageal cancer with PD-L1 CPS ≥ 10 , with a more favorable safety profile and stable and similar QOL. These data support pembro as a new second-line standard of care for esophageal cancer with PD-L1 CPS ≥ 10 . Clinical trial information: [NCT02564263](https://clinicaltrials.gov/ct2/show/study/NCT02564263)*

Health-related quality of life (HRQoL) of pembrolizumab (pembro) versus physician choice single-agent paclitaxel, docetaxel, or irinotecan in subjects with advanced/metastatic adenocarcinoma (ACC) or squamous cell carcinoma (SCC) of the esophagus that has progressed after first-line standard therapy (KEYNOTE-181).

Abstract No: 4048

Background: KEYNOTE-181 (NCT02564263) is an open-label, randomized, phase 3 trial in ACC and SCC of the esophagus that evaluated IV pembro 200 mg Q3W for up to 2 years vs investigator choice of single-agent paclitaxel/docetaxel/irinotecan (control). Pembro was superior to control for OS in patients with PD-L1 CPS ≥ 10 (N = 222; median 9.3 vs 6.7 months; P= 0.0074). Here we present results of prespecified HRQoL analyses in this population.

Methods: The EORTC QLQ-C30 and EORTC QLQ-OES18 were administered at baseline; weeks 2, 3, 4, 6, 9, 12, 18; every 9 weeks up to 1 year/end of treatment; and 30-day safety follow-up visit. Data from patients receiving ≥ 1 dose of study treatment and completing ≥ 1 HRQoL assessment were analyzed. Least squares mean (LSM) score change from

baseline to week 9, 95% CI, and nominal P values were calculated. Time to deterioration (TTD) (≥ 10 -point decline from baseline) was assessed by Kaplan-Meier method and Cox regression model. HRs, 95% CIs, and nominal P values are provided.

Results: The HRQoL population included 218 PD-L1 CPS ≥ 10 patients (107 pembro, 111 control). QLQ-C30 compliance at week 9 was 88.9% for pembro and 83.9% for control. There was no significant difference in LSM between arms (3.68; 95% CI -2.28, 9.64; $P=0.2248$) in global health status (GHS)/QoL score. Week 9 QLQ-OES18 compliance was 88.4% for pembro and 83.3% for control. QLQ-OES18 scores were not significantly different between arms. TTD for pain (HR 1.02; 95% CI 0.58, 1.81; $P=0.5282$), reflux (HR 1.69; 95% CI 0.83, 3.47; $P=0.9254$), and dysphagia (HR 1.81; 95% CI 0.97, 3.37; $P=0.9693$) subscales were not significantly different between arms.

Conclusions: Over 9 weeks, [patients treated with pembro had stable GHS/QoL scores similar to those of patients treated with single-agent docetaxel/paclitaxel/irinotecan](#). Combined with the superior OS and lower rate of treatment-related AEs seen with pembro, these data support clinically meaningful benefit of pembro in esophageal cancer patients with PD-L1 CPS ≥ 10 . Clinical trial information: [NCT02564263](#)

Pembrolizumab in previously treated metastatic esophageal cancer: Longer term follow-up from the phase 2 KEYNOTE-180 Study.

Abstract No: 4032

Background: In the phase 2, open-label, KEYNOTE-180 (NCT02559687) study, after a median follow-up of 5.8 months, pembrolizumab (pembro) provided antitumor activity with durable responses in pts with previously treated, advanced/metastatic adenocarcinoma (EAC) including Siewert type 1 adenocarcinoma of the gastroesophageal junction or squamous cell carcinoma (ESCC) of the esophagus. Here we present results of an additional 10 months of follow-up.

Methods: Eligible pts with metastatic esophageal cancer, ≥ 2 prior lines of therapy, and tumor samples evaluable for biomarker expression, received pembro 200 mg Q3W for up to 2 years, or until disease progression, unacceptable toxicity, or withdrawal. Tumor response was assessed Q9W (RECISTv1.1, central review). PD-L1+ pts had combined positive score ≥ 10 using IHC (22C3 antibody). Primary endpoint was objective response rate (ORR). Secondary endpoints included safety, DOR, PFS, and OS.

Results: Of 121 pts enrolled, 63 (52%) had ESCC and 58 (48%) had PD-L1+ (combined positive score ≥ 10) tumors. As of July 30, 2018, median follow-up duration, from randomization to data cutoff, was 5.8 mo (range, 0.2 mo to 27.8+ mo). ORR (CR+PR) was 10% (95% CI, 5%-17%); 2 (2%) CR, 10 (8%) PR, 25 (21%) SD. Median DOR was not reached ([NR] range, 2.1 mo to 25.1+ mo). [Median PFS was 2 mo](#) (95% CI, 1.9%-2.1%) with [9-mo PFS rate of 9%](#). [Median OS was 5.8 mo](#) (4.5-7.2) with [12 mo OS rate of 27%](#). [In ESCC, ORR was 14%](#) (95% CI, 7%-25%); 2 (3%) CR, 7 (11%) PR, with median DOR NR (range, 4.2 mo to 25.1+ mo). [In EAC, ORR was 5%](#) (95% CI, 1-14); 3 PR, with median DOR NR (range, 2.1 mo to 15.6+ mo). [In PD-L1+ pts, ORR was 14%](#) (95% CI, 6%-25%); 1 (2%) CR, 7 (12%) PR with median DOR NR (range, 4.2 mo to 25.1+ mo). [In PD-L1- pts ORR was 6%](#) (95% CI, 2%-16%); 1 (2%) CR, 3 (5%) PR; median DOR NR (range, 2.1 mo to 17.3+ mo). Overall, 19 (16%) pts had treatment-related grade 3-5 AEs. Seven (6%) pts discontinued due to a treatment-related AE. There was one treatment-related death from pneumonitis.

Conclusions: [Pembro continued to provide durable clinical benefit with a manageable safety profile for pts with heavily pretreated esophageal cancer](#), with conversions of PR to CR observed. Clinical trial information: [NCT02559687](#)

KEYNOTE-811 pembrolizumab plus trastuzumab and chemotherapy for HER2+ mGC/GEJC: A placebo-controlled phase 3 DBRCT.

Abstract No: TPS4146

Background: Combination therapy with the anti-HER2 antibody trastuzumab with fluoropyrimidine and platinum is the current standard for patients with HER2+ mGC/GEJC. We hypothesize that combination anti-PD-1 and anti-HER2 therapy will result in T-cell activation, augment ADCC, and potentiate antitumor immune response in HER2+ patients. This phase 2 study in HER2+ mGC/GEJC demonstrated the safety and [preliminary efficacy of trastuzumab /pembrolizumab/ chemotherapy; the overall response rate was 87%](#), and the disease control rate was 100% (Janjigian YY, ASCO GI 2019). KEYNOTE 811, a global, multicenter, randomized, placebo-controlled, phase 3 study, is underway.

Methods: Key eligibility criteria are age ≥ 18 years; previously untreated unresectable or metastatic HER2+ (centrally confirmed IHC 3+ or IHC 2+/ISH >2.0) G/GEJ adenocarcinoma; life expectancy >6 months with RECIST v1.1 measurable disease; adequate organ function and performance status. Patients will be randomly assigned 1:1 to receive chemotherapy with pembrolizumab 200 mg IV flat dose or placebo with trastuzumab 6 mg/kg (after 8 mg/kg load) Q3W up to 2 years or until intolerable toxicity or disease progression. Investigator choice chemotherapy will include day 1 cisplatin 80 mg/m² IV and /5-fluorouracil 800 mg/m²/day IV (days 1-5) or oxaliplatin 130 mg/m² IV and capecitabine 1000 mg/m² BID days 1-14 (Q3W). Primary end points are progression-free survival and overall survival. Secondary end points are objective response rate, duration of response, and safety and tolerability. Adverse events are graded per NCI CTCAE v4.0 and will be monitored for 30 or 90 days after treatment. Patients will be followed up for survival. Planned enrollment is approximately 692 patients. Clinical trial information: [NCT03615326](#)

TENERGY: Phase II study of atezolizumab monotherapy following definitive chemoradiotherapy with 5-FU plus cisplatin in patients with locally advanced esophageal squamous cell carcinoma.

Abstract
TPS4141

No:

Background: The standard treatment for patients with unresectable locally advanced esophageal squamous cell carcinoma (ESCC) is definitive chemoradiotherapy (CRT) using 5-FU plus cisplatin. However, complete response (CR) rates are only 11% to 25%, and median overall survival (OS) is 9 to 10 months. The improved therapeutic efficacy of combining immunotherapy with radiation has been gaining interest. Our basic research suggested that sequential treatment with anti-PD-L1 agents soon after completion of CRT is the best combination. Twelve months of anti-PD-L1 antibody following platinum-based CRT significantly improved progression-free survival (PFS) and OS in patients with locally advanced non-small cell lung cancer (Antonia SJ, et al. N Engl J Med. 2018). Based on this background information, we have planned a phase II clinical trial to evaluate the safety and efficacy of atezolizumab monotherapy following definitive CRT in patients with locally advanced ESCC.

Methods: The main inclusion criteria are unresectable locally advanced ESCC without distant metastasis, completion of treatment with 60 Gy of radiation plus two concomitant cycles of chemotherapy (cisplatin 70 mg/m² on day 1 and 5-FU 700 mg/m² on days 1–4, every 28 days), and adequate organ function. Within 4 weeks after CRT, patients will be registered in the study and started on 1200 mg of atezolizumab every three weeks until 12 months or disease progression. The primary endpoint is the CR rate by the investigator's assessment. Overall response rate, PFS, OS,

treatment-related adverse events, and CR rate by central assessment are secondary endpoints. A total of 50 patients will be enrolled, including 40 with primary locally advanced ESCC and 10 with postoperative loco regionally recurrent ESCC. As an exploratory biomarker study, biopsies from the primary site and blood collections will be performed at 3 time points (before CRT, after CRT, and four weeks after the start of atezolizumab). We will analyze the phenotype of immune-competent cells, neoantigens, tumor mutation burden, PD-L1 status, and Human Leukocyte Antigen haplotyping. Clinical trial information: [UMIN000034373](#).

Safety and efficacy of durvalumab following multimodality therapy for locally advanced esophageal and adeno-GEJC: Results from big ten cancer research consortium study.

Abstract No: 4058

Background: Concurrent chemoradiation (CRT) followed by esophagectomy is a standard of care for locally advanced esophageal (LA-EAC) and GEJ adenocarcinoma. Approximately 50% of patients (pts) experience disease relapse within the 1st yr after treatment(tx) completion. [No adjuvant tx has been shown to improve survival in these pts. Immune checkpoint inhibitors have activity in metastatic PD-L1 positive EAC.](#) Preclinical studies have shown upregulation of PD-1/PD-L1 pathway with RT +/- chemotherapy.

Methods: We conducted a phase II trial evaluating safety and efficacy of durvalumab (durva), a monoclonal antibody against PD-L1, in pts with LA-EAC and GEJ adenocarcinoma who have viable tumor in surgical specimen after neoadjuvant CRT and R0 resection. Pts received durva 1500mg IV every 4 weeks for up to 1yr.

Results: 24 pts were enrolled from 4/2016-1/2018 (median age: 60yrs (range, 43-70). 18 received carbo/paclitaxel and 6 received cis/5-FU concurrently with radiation. Staging at diagnosis: T2N0 (n=3, 12.5%), T2N2 (n=3, 12.5%), T3N0 (n=6, 25%), T3N1 (n=6, 25%), T3N2 (n=4, 17%), T3N3 (n=1, 4%), T3Nx (n=1, 4%). 19 pts (79%) had positive lymph nodes (LNs) at the time of surgery following CRT. 12 pts completed 1yr of tx, 12 came off tx before 1yr because of relapse(6), AEs(5), and consent withdrawal (1). Median number of tx cycles was 12.5 (range, 2-13). Most common AEs were fatigue (n=8, 33.3%) and nausea (n=6, 25%). 3pts (12.5%) developed grade 3 irAEs: pneumonitis (1), hepatitis (1), colitis (1). At median follow up of 14.5 mo (range, 1.7-24mo), 17 are disease free (including 5 who came off tx before 1yr). 7pts (29%) have relapsed (3 alive, 4 died). 6/7pts had distant relapse (lung, brain, bone, cervical LNs) and 1 had locoregional relapse. 1-yr RFS and OS were 79.2% and 95.5%, respectively. 2-yr OS was 59.2%. RFS probability at 26 mo was 67.9%. Median survival after relapse was 11.1 mo (range, 0.1-11.3mo).

Conclusions: [Adjuvant durvalumab following trimodality therapy for LA-EAC and GEJ adenocarcinoma was safe and feasible with improvement in 1-yr RFS to 79.2% compared to historical rate of 50%. OS results are encouraging in this high risk pt population.](#) Clinical trial information: [NCT02639065](#)

Modified FOLFOX versus modified FOLFOX plus nivolumab and ipilimumab in patients with 1L adv./met. GC/GEJC: MOONLIGHT, a phase 2 RCT of the German Gastric Group of the AIO.

Abstract No: TPS4144

Background: The majority of patients (pts) with gastroesophageal cancer present with inoperable or metastatic disease and there is a strong need for efficient and tolerable first-line (1L) treatment. Oxaliplatin-based regimens like FOLFOX have become one standard of care. However, median survival is still below 12 months. Results from trials using nivolumab plus ipilimumab treatment of subjects with advanced/metastatic GC and GEJ cancers demonstrated clinical activity, in pts whose tumors did or did not express PD-L1; in addition, nivolumab alone and in combination with ipilimumab demonstrated clinical benefits in various other tumor types. Based on this clinical experience, the AIO-STO-0417 trial (Moonlight) has been designed to evaluate the combination of chemotherapy with two checkpoint inhibitors in first-line therapy of pts with gastroesophageal adenocarcinoma.

Methods: This is a prospective, multicenter, randomized, investigator-initiated phase II trial. Pts with Her2-negative, inoperable, advanced or metastatic GC/GEJC will be randomized 1:1 to 1L treatment with FOLFOX (Oxaliplatin 85 mg/m²; Leucovorin 400 mg/m²; 5FU 400 mg/m² on d1 of each treatment cycle and 5FU 1200 mg/m² continuous infusion over 24 hrs d1 and d2) every 2 weeks plus Nivolumab 240 mg every 2 weeks and Ipilimumab 1mg/kg every 6 weeks (Arm A) or FOLFOX alone (Arm B). **Primary endpoint of the trial is progression-free survival based on the ITT population.** Main secondary endpoints are overall survival, objective response rate, Safety and Quality of life (EORTC QLQ-C30). 118 pts (59 per arm) will be enrolled to provide 80% power for detecting an average HR of 0.68 using the log rank test at a one-sided type I error of 10%. At the date of submission, (Feb 2019), 28 of planned 118 pts are randomized. Clinical trial information: [NCT03647969](https://clinicaltrials.gov/ct2/show/study/NCT03647969)

Phase II study of a telomerase-specific oncolytic adenovirus (OBP-301, Telomelysin) in combination with pembrolizumab in GC/GEJC.

Abstract No: TPS4145

Background: Although checkpoint inhibitors (CPIs) can produce durable responses in gastric cancer patients (pts) in the 3rd line setting, the response rate is only 10-15%. Therefore, there is a huge unmet need to enhance the response rate of CPIs to provide benefit to wide range of pts. A novel concept in immuno-oncology is the use of cancer specific oncolytic viral therapy. In addition to the specific killing of the tumor by the virus, these agents can induce an immunogenic cell death in the tumor to augment the immune activation driven by PD-1 inhibition. **OBP-301 is an oncolytic adenovirus genetically modified to be able to selectively replicate in cancer cells by introducing human telomerase reverse transcriptase (hTERT) promoter.** Results of a phase I study of OBP-301 in solid tumor pts demonstrated the safety and efficacy of intra-tumoral injection of OBP-301. A pre-clinical study of the combination of OBP-301 with anti-PD-1 antibody has also shown significant synergistic activity as well. Based on these encouraging pre-clinical and clinical data, we designed a phase II clinical trial to examine the safety and efficacy of combination of pembrolizumab and OBP-301 in the treatment of PD-L1 positive metastatic gastric/GEJ adenocarcinoma.

Methods: This is a multicenter, non-randomized phase II trial of OBP-301 with pembrolizumab in metastatic gastric/GEJ adenocarcinoma that has progressed on at least 2 lines of prior therapy. Eligibility criteria include PD-L1 positive tumors as defined by a combined positive score, performance status ≤ 1 , and good end organ function. The primary endpoints are to examine objective response rate and safety of OBP-301 with pembrolizumab. The secondary endpoints are to examine disease control rate, duration of response, overall survival and progression free survival. Correlative studies are planned to identify biomarkers for response to combination therapy by using multiparameter flowcytometry, single-cell transcriptional profiling and immunohistochemistry. All eligible pts will receive 1×10^{12} Viral Particles/mL of OBP-301 administered every 2 weeks for total of 4 injections, injected directly into tumor via upper endoscopy. Every pt will also receive pembrolizumab 200 mg IV every 3 weeks for 2 years or until progression. Pts will be enrolled in a Simon two stage design, with 18 pts in the first stage. If 3 or more pts respond to the combination therapy, the study will move forward to stage 2, with 19 more pts enrolled. The study is currently enrolling pts.

ARTIST 2: Interim results of a phase III trial involving adjuvant chemotherapy and/or chemoradiotherapy after D2-gastrectomy in stage II/III gastric cancer (GC).

Abstract No: 4001

Background: Adjuvant chemotherapy and/or chemoradiotherapy have been the standard of care in GC for years, supported by randomized trials. We compared the efficacy of different chemotherapy regimens and chemoradiotherapy in patients with D2-resected, stage II/III, node-positive GC.

Methods: From Feb 2013 through Nov 2018, we randomly assigned, in a 1:1:1 ratio, patients with pathologically-staged II or III, node-positive, D2-resected GC, to receive adjuvant S-1 (40-60 mg twice daily 4-weeks-on/2-weeks-off) for one year, S-1 (2-weeks-on/1-week-off) plus oxaliplatin 130 mg/m² (SOX) for six months, or SOX plus chemoradiotherapy 45 Gy (SOXRT). Randomization was stratified according to the type of surgery (total or subtotal gastrectomy), stage (II or III), and Lauren histologic classification (diffuse or intestinal). The primary endpoint was disease-free survival (DFS). A total of 900 patients had to be enrolled to demonstrate superiority of SOX or SOXRT to S-1 (hazard ratio [HR] 0.667), with 90% power at a two-sided significance level of 5%.

Results: A total of 538 patients were included for this interim efficacy analysis. Median age was 58 years, men constituted 65%, and stage II and III were 31% and 69%, respectively. Baseline tumor and patient characteristics were balanced between treatment arms. Adverse events were as anticipated in each arm, generally well-tolerated and manageable. DFS in the control arm (S-1) were significantly shorter than in SOX and SOXRT arms (stratified HR for recurrence): S-1 vs. SOX, 0.617 (P = 0.016) and S-1 vs. SOXRT, 0.686 (P = 0.057). **The DFS at 3-years was found to be 65%, 78% and 73% in S-1, SOX and SOXRT arms, respectively.** No difference in DFS between SOX and SOXRT was found (HR 0.910, P = 0.667). Based on the results after the observation of 145 recurrence events at the cutoff date of Dec 27, 2018, the independent data monitoring committee considered the results sufficient to meet the endpoint of the trial and recommended early stopping of the trial.

Conclusions: **In patients with curatively D2-resected, stage II/III, node-positive GC, adjuvant SOX or SOXRT was effective in prolonging DFS, when compared to S-1 monotherapy.** Clinical trial information: NCT0176146.

Epigenetic alternate promoter utilization and association with PD-L1 expression in EBV+ GC.

Abstract No: e15509

Background: We recently elicited the role of epigenetic promoter alterations as a mechanism of immune-evasion and primary resistance to immune checkpoint inhibition in gastric cancer. High prevalence of epigenetic modifications are known to occur in Epstein-Barr virus associated gastric cancer (EBVaGC). **EBVaGC has high response rates to anti-PD-1 immune checkpoint inhibitors** and is associated with high levels of PD-L1 expression. However, not all EBVaGC express PD-L1 and mechanisms that mediate these phenomena are unknown.

Methods: We performed NanoString profiling and PD-L1 immunohistochemistry (using Dako PD-L1 IHC 22C3) on tissue from gastric cancer patients undergoing primary tumor resections at Samsung Medical Centre, South Korea. NanoString panel was designed for 90 recurrent somatic alternate promoter-related genes, and immune-related genes including PD-L1. EBV status was determined using EBV-encoded RNA *in situ* hybridization and categorized as EBVaGC and EBV-negative. Samples in the top-quartile of alternate promoter utilization were classified as AP_{high} and the remaining AP_{low}.

Results: A total of 272 samples (EBVaGC n = 79; EBV-negative n = 193) were included in this study. EBVaGC had significantly higher PD-L1 expression ($p < 0.001$) compared to EBV-negative samples. AP_{high} group (n = 67) consisted of 61 EBV-negative and 6 EBVaGC samples. EBVaGC AP_{high} tumors had significantly lower PD-L1 transcript expression compared to EBVaGC AP_{low} tumors ($p = 0.011$, Wilcoxon-rank sum). Similar correlation was also found with PD-L1 IHC combined positive score (CPS)(median CPS score 1 vs 8, $p = 0.047$). *There was a trend towards poorer survival for EBVaGC AP_{high} tumors* (vs EBVaGC AP_{low}; HR 0.23, 95% CI: 0.046 – 1.23, $p = 0.087$). EBV-negative AP_{high} tumors also had lower PD-L1 expression (vs EBV-negative AP_{low}; $p = 0.046$, Wilcoxon-rank sum).

Conclusions: *Increased utilization of epigenetic alternate promoter isoforms correlates with lower transcriptomic and protein expression of PD-L1 in EBVaGC.* Here we describe a potential mechanism of immune-evasion to explain low immune-infiltration and PD-L1 expression that occurs in a group of EBVaGC that is traditionally considered highly immunogenic.

Investigation of enhanced antitumor effects via co-inhibition of Wnt/ β -catenin and PI3K/Akt/mTOR signaling pathways in human gastric cancer.

Abstract No: e15553

Background: Gastric cancer, a highly aggressive malignancy, frequently recurs despite curative surgery and metastasizes to lymph node and distant sites. Epithelial-mesenchymal transition (EMT) is the main phenomenon of cancer progression, including invasion and metastasis. It is regulated by cross talks between diverse intracellular signaling pathways such as Wnt/ β -catenin and phosphatidylinositol-3-kinase (PI3K)/Akt/ mammalian target of rapamycin (mTOR) pathways. Here, this study elucidated the effects of co-inhibition of Wnt/ β -catenin and PI3K/Akt/mTOR pathways on gastric cancer.

Methods: It is known that Wnt/ β -catenin signaling pathways are constitutively activated in two of gastric cancer cell lines, AGS and MKN-28. ICG-001 (β -catenin transcription inhibitor) and rapamycin (mTOR inhibitor) were used for dual blockade, and then the combinatory effects were examined.

Results: As a result, both cell lines were significantly affected by the β -catenin transcription inhibitor, ICG-001, and addition of the mTOR inhibitor, rapamycin induced marginal inhibitory effects on cancer cell proliferation and target gene expression. In addition, invasive activity was $62.3 \pm 15.7\%$ and $53 \pm 14.4\%$ inhibited by single treatment, but it was $79 \pm 13.3\%$ inhibited by co-treatment. Moreover, migratory activity was $33 \pm 13\%$, $42 \pm 9\%$ inhibited by single treatment, but it was $82 \pm 4\%$ by co-treatment. Interestingly, Snail, one of the important regulatory protein during EMT process, was significantly decreased by co-treatment.

Conclusions: Taken together, these results suggest that *co-inhibition of Wnt/ β -catenin and PI3K/Akt/mTOR pathways could effectively enhance antitumor effects on gastric cancer* via the inhibition of invasion and migration as well as decrease of Snail expression.

Effect of p-PAQR3^{Thr32} on PD-L1 expression and immune evasion in GC.

Abstract No: e15571

Background: Therapies targeted to the immune checkpoint mediated by PD-1 and PD-L1 show antitumor activity in some solid tumors. We have now examined PD-L1 expression and its regulation in gastric cancer with p-PAQR3^{Thr32} protein.

Methods: The expression of PD-L1 at the protein and mRNA levels in gastric cancer cell lines was examined by flow cytometry, real-time RT-PCR and western blot analysis, respectively. The expression of PD-L1 and p-PAQR3^{Thr32} protein in 319 surgically resected gastric cancer specimens was evaluated by immunohistochemical analysis.

Results: The PD-L1 expression level was higher in gastric cancer cell lines positive for p-PAQR3^{Thr32} protein induced by glucose starvation than in those negative for the p-PAQR3^{Thr32} protein. Forced expression of p-PAQR3^{Thr32} protein in gastric cancer cells markedly increased PD-L1 expression, whereas endogenous PD-L1 expression in p-PAQR3^{Thr32} protein positive gastric cancer cells was attenuated by treatment with PAQR3 siRNAs. Furthermore, expression of PD-L1 was downregulated by inhibitors of the IRF1 and STAT1 in IFNs-PDL1 signaling pathway in gastric cancer cells positive for p-PAQR3^{Thr32} protein. At clinical tissue level, the expression level of PD-L1 was positively associated with the presence of p-PAQR3^{Thr32} protein in gastric cancer specimens. Moreover, the expression level of p-PAQR3^{Thr32} protein was negatively correlated with CD3, CD8, GZMA (CD8 T cell secretory factor) and positively correlated with CD68 (macrophage marker).

Conclusions: Our findings that p-PAQR3^{Thr32} protein induced by glucose deficiency upregulate PD-L1 by activating IFNs-PDL1 signaling pathway in gastric cancer reveal a direct link between p-PAQR3^{Thr32} protein and PD-L1 expression. It is suggested that p-PAQR3^{Thr32} protein may be involved in tumor immunosuppression by inhibiting the proliferation and activity of CD8 T cells in gastric cancer tissues.

Association of frequent amplification of chromosome 11q13 in esophageal squamous cell cancer with clinical benefit to immune check point blockade.

Abstract No: 4036

Background: Esophageal squamous cell carcinoma (ESCC) is the predominant histological subtype of esophageal cancer in South America and East Asian countries and remains an unmet medical need worldwide. Previous studies have shown the efficacy of programmed cell death 1 (PD-1) targeted therapy in a subset of patients with metastatic ESCC. However, robust predictive biomarkers to PD-1 antibody-based immunotherapy remain undefined.

Methods: Patients included in this analysis were part of multi-center, phase Ib/II trial (NCT02915432) evaluating the safety and activity of toripalimab, a humanized PD-1 antibody in solid tumors. To identify molecular determinants of response, we performed whole exome sequencing (WES), messenger RNA sequencing and immunohistochemistry on patients' samples and evaluated genomic and transcriptional biomarkers, PD-L1 expression and tumor mutational burden (TMB) for correlation with clinical efficacy.

Results: Sixty advanced chemo-refractory ESCC patients were enrolled and 59 were treated with toripalimab. 94.9% (56/59) patients experienced at least one treatment related adverse event after 16 months; mostly grade 1 or grade 2. Treatment-related grade 3 or higher AEs occurred in 30.5% (18/59) of subjects. By the data cutoff date, 11 (18.6%; 95%CI 9.7 to 30.9) patients achieved an objective response, while the disease control rate was 47.5% (95%CI 34.3 to 60.9). Copy number analysis identified 24 out of 50 (48%) patients with amplifications of chromosome 11q13 region, which was consistent with elevated mRNA expression of amplified genes, including CCND1(Cyclin D1) and fibroblast growth factor family members (FGF3/4/19). Patients without 11q13 amplification, had significantly better objective response rate (ORR 30.8% versus 4.2%, $p = 0.024$) and progression free survival (3.7 versus 2.0 months, HR = 0.47 [95%CI 0.24 to 0.91], $p = 0.025$) when compared with 11q13 amplified individuals. In contrast, patients with high TMB (≥ 12 Mutations/Mb; 11/47, 23.4%) or positive PD-L1 expression (TC or IC 1%; 19/57, 33.3%) showed no significant advantage in ORR or survival.

Conclusions: Toripalimab has demonstrated a manageable safety profile and promising anti-tumor activity in chemo-refractory ESCC patients. Genomic amplification of 11q13 region may serve as a negative predictive marker for

advanced ESCC patients receiving anti-PD-1 based immunotherapy. Further interrogation of putative resistance genes that lie within this region is under study. Clinical trial information: [NCT02915432](https://clinicaltrials.gov/ct2/show/study/NCT02915432)

Immune biomarker expression in the tumor microenvironment in Chinese patients with esophageal squamous cell carcinoma was explored.

Abstract No: e15542

Background: Esophageal squamous cell carcinoma (ESCC) is one of the most common malignancies in China, of which the standard treatment of advanced esophageal cancer is chemotherapy followed by surgery. Recently, immunotherapy has shown great potential in ESCC treatment. The aim of this study was to explore the landscape of immune-related gene expression in the tumor microenvironment (TIME) and further explore the relationship between immune biomarkers and therapeutic effect.

Methods: We retrospectively analyzed PDL1(clone sp142)/PD1 expression in a cohort of Chinese patients (male = 92, female = 18; median age = 64, range from 36 to 84) with ESCC. Patient samples were detected in Genecast. Co. from February 2017 to November 2018. Another 6 patients (male = 4, female = 2) who accepted anti-PD1/PD-L1 antibody treatment were analyzed. PD-L1/PD-1 expression and the incidence of CD8, CD57, CD68, CD163 TILs were immunohistochemically.

Results: In tumor cells, more than 32% (36/110) samples of ESCC patients was stained with PDL1 ($\geq 1\%$), while 52.8% (21/36) of these patients highly expressed PDL1 ($\geq 10\%$, 10%-98%). In tumor infiltrating lymphocytes (TILs), 31.82% (35/110) patients expressed PDL1 ($\geq 1\%$) and 1.82% (2/110) highly expressed PDL1 ($\geq 10\%$, 10%-50%). For PD1 expression in TILs, 17.27% (19/110) samples were positively stained with PD1 antibody ($\geq 1\%$). In a subset of ESCC patients who received immune checkpoint blockade therapy (including 2 responders and 4 non-responders), the median percentage of CD163, CD68, PDL1, CD8, PD1 and CD57 were 1.49% (0.44%-9.98%), 0.40% (0.16%-19.08%), 3.74% (0%-45%), 9.52% (4.20%-13.79%), 4.51% (1.37%-33.43%) and 0.68% (0.08%-1.74%), respectively in tumor area and 4.14% (1.85%-15.99%), 1.62% (0.21%-11.47%), 4.87% (0.33%-18.97%), 7.74% (5.88%-14.35%), 3.93% (1.92%-20.54%) and 0.92% (0.27%-2.18%), respectively in stroma area. When compared with non-responders, samples from the responders showed higher CD8 expression in tumor area.

Conclusions: Percentage of PDL1/PD1 expression is relatively high in Chinese patients with ESCC. High levels of CD8 positive TILs might be beneficial to patients with ESCC. Clinical investigations with large sample sizes are warranted to prove our findings.

***Pembrolizumab +/- Chemo versus Chemo for advance
GC/GEJC: The phase III KEYNOTE-062 study.***

To be published on June 1, 2019 at 07.30 am EST

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