P-30 First-line (1L) treatment patterns in advanced gastric, gastroesophageal junction, and esophageal adenocarcinoma (GC/GEJC/EAC): Data from the Spanish AGAMENON-SEOM registry

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Background: Data on treatment patterns and outcomes in patients with advanced gastroesophageal adenocarcinoma in daily clinical practice are scarce. Using real-world data from the Spanish AGAMENON-SEOM registry, this retrospective study assessed patient characteristics, treatment patterns, and outcomes for 1L advanced GC/GEJC/EAC.

Methods: Adult patients diagnosed with locally advanced unresectable or metastatic GC/GEJC/EAC between 2008 and 2021 were identified from 34 centers. This analysis only included patients who received ≥1 cycle of 1L polychemotherapy. Primary endpoints included description of demographic and clinical characteristics at initial diagnosis (equivalent to 1L therapy initiation), 1L treatment patterns, progression-free survival (PFS) and overall survival (OS) from 1L therapy initiation. Secondary endpoints included subgroup analyses in patients with human epidermal growth factor receptor 2 (HER2)-negative status and in patients who met the eligibility criteria of the CheckMate 649 study (Janjigian YY et al, Lancet 2021;398:27-40) and were treated with FOLFOX or XELOX (hereafter, CheckMate 649-matched subgroup). The proportion of patients who received second-line (2L) or third-line (3L) therapy and the reasons for not receiving subsequent therapy were explored.

Results: Overall, patients initiating 1L treatment (n=3,110) had a median (range) age of 65 (20–89) years, were mostly male (71.0%), had an ECOG performance status (PS) of 1 (61.7%) or 0 (23.7%), and had normal (>35 g/dL) basal albumin levels (64.8%). The most prevalent comorbidities were diabetes (15.3%) and chronic cardiopathy (11.6%). The most common primary tumor location was the stomach (77.7%) versus GEJ (13.4%) or esophagus (8.7%). 5.6% of patients had unresectable locally advanced disease and 94.4% of patients had metastatic disease, primarily synchronous (77.6%); the number of metastastic sites was unknown in 13 (synchronous) and 4 (metachronous) patients. The most frequent metastatic locations were lymph nodes (46.4%) or peritoneum (43.7%). In the HER2-evaluable population (n=2,650), 73.3% of patients had HER2-negative tumors. Clinical characteristics of patients in the HER2-negative (n=2,385; includes 460 patients with unknown HER2 status) and CheckMate 649-matched (n=383) subgroups were generally similar to those of the overall population. The most common 1L treatments for HER2-negative tumors were FOLFOX6 (20%) and XELOX (19%). In the overall population, 1,588 patients received 2L therapy and 218 patients received 3L therapy. The primary reason for patients not receiving 2L or 3L therapy was poor ECOG PS (68.0% and 79.8%, respectively). At a median follow-up of 57.0 months in the overall population (n=3,037), the median (95% confidence interval [CI]) PFS and OS were 6.0 (5.8–6.2) and 10.8 (10.4–11.2) months, respectively. Median OS was 10.1 (95% CI 9.7–10.5) months in the HER2-negative subgroup (n=2,346). At a median follow-up of 32 months in the CheckMate 649-matched subgroup, median (95% CI) PFS and OS were 6.4 (5.7–7.2) and 11.7 (10.6–12.8) months, respectively.

Conclusions: In this real-world observational study of the Spanish AGAMENON-SEOM registry, PFS and OS outcomes for 1L treatment of advanced GC/GEJC/EAC were comparable to those of historical studies. With an estimated median OS of < 1 year from 1L therapy initiation, better treatment options for patients with advanced GC/GEJC/EAC remain an unmet need and deserve further investigation.

Clinical trial identification: NCT04958720.

Editorial acknowledgement: Writing and editorial assistance was provided by Thai Cao, MS, of Evidence Scientific Solutions, funded by Bristol Myers Squibb.

Legal entity responsible for the study: Bristol Myers Squibb, Princeton, NJ, USA.

Funding: Bristol Myers Squibb, Princeton, NJ, USA.

Disclosures: M. Moreno Gutierrez: Shareholder / Stockholder / Stock options: Bristol-Myers Squibb; Full / Part-time employment: Bristol-Myers Squibb. C. Polanco Sanchez: Full / Part-time employment: Bristol Myers Squibb. H. Xiao: Full / Part-time employment: Bristol-Myers Squibb, Bristol-Myers Squibb, Bristol-Myers Squibb. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.121

P-32 Different regimens of the 1st line chemotherapy in patients (pts) with metastatic anal cancer: Results of the multicenter observational study

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Background: Combination of paclitaxel with carboplatin and cisplatin with fluoropyrimidines are the standards of the 1st and 2nd lines of treatment in pts with metastatic anal cancer. Regimen mDCF (docetaxel 40 mg/m2 d1, cisplatin 40 mg/m2 d1, 5-FU 2400 mg/m2 46-h d1-3, two-weekly) showed promising activity in the 1st line in the nonrandomized study. We performed an analysis of a prospective multicentric database of metastatic anal cancer pts to evaluate the efficacy of different regimens as 1st line systemic treatment in a real-life clinical practice setting.

Methods: We analyzed a database of pts with metastatic anal cancer in 3 cancer centers in Russia. The primary endpoints were progression free survival (PFS) and overall response rate (ORR). Analysis was performed with the SPSS v.20 software package.

Results: The study included 68 pts with metastatic anal cancer. Sixty three (93%) pts received systemic treatment; female — 87%, average age - 68 years (20-83), ECOG 0-1/2/3/NA — in 22%/33%/31%/13%; synchronous metastases - in 30%; local relapse or primary tumor — in 60%; radiotherapy or chemoradiotherapy of primary tumor were previously? administered in 70%; lung metastases in 18%, liver - 38%, retroperitoneal lymph nodes metastases — 27%; peritoneal metastases — in 3% pts; average number of metastatic zones — 2 (1-5); metastasectomy was performed in 32% pts. The first line was weekly paclitaxel and carboplatin (CP) in 29 (46%), mDCF - in 10 (16%), platinum compounds with fluoropyrimidines (CF) — in 18 (29%), others regimen — in 6 (9%). Median PFS was 6 months in CP group, 3 months — in CF group, 10 months - in mDCF group, and 3 months — in other regimens group (HR 1,02, 95% CI 0,76-1,37, p=0,8); ORR was 9%, 10%, 50%, 0%, respectively (p=0,01).

Conclusions: In the 1st line mDCF regimen shows the best ORR and numerically the longest median PFS, which warranted conducting of prospective randomized study to compare mDCF and paclitaxel with carboplatin.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.123

P-33 Prognostic impact of single organ pulmonary metastasis in metastatic colorectal cancer patients treated with FOLFIRI and vascular endothelial growth factor inhibitors as second-line chemotherapy

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Background: The impact of single-organ metastases to lung on progression free survival (PFS) and overall survival (OS) in patients with metastatic colorectal cancer (mCRC) has not been studied. Recognizing the differences in prognosis and chemotherapeutic efficacy by metastatic organs can help optimize treatment strategy.

Methods: Consecutive mCRC patients who were treated with second-line FOLFIRI and vascular endothelial growth factor (VEGF) inhibitorswere retrospectively enrolled. Overall response rate (ORR), PFS, OS were assessed according the presence of single organ pulmonary metastasis.

Results: A total of 289 patients were treated with FOLFIRI +VEGF inhibitors.26 patients (9.0%) have a single organ pulmonary metastasis. Characteristic of patients with single organ pulmonary metastasis were tended to be high frequency of left sided primary site (P = 0.076) and significantly low level of tumor markers at initiation of chemotherapy (CEA: P = 0.0044, CA19-9: P = 0.00008). Patients with single organ pulmonary metastasis had significantly longer PFS and OS than those without (Median PFS: 29.6 months vs 6.1 months P = 0.00025, Median OS: 35.3 months vs 18.7 months P = 0.0001). In multivariate analysis, single organ pulmonary metastasis was independent predictor of longer PFS and OS (PFS: HR 0.36, P = 0.0009, OS: HR 0.28, P = 0.0004).

Conclusions: Single organ pulmonary metastasis has better impact on PFS and OS in mCRC patients treated with FOLFIRI and VEGF inhibitors as second-line chemotherapy.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: K. Yamaguchi: Honoraria (Institution): Taiho pharm; Speaker Bureau / Expert testimony: Daiichi Sankyo, Eli lily Japan, Bristol Mayers Sqibb. E. Shinozaki: Honoraria (self): Merck biopharma. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.124

P-34 Does the chemotherapeutic efficacy of trifluridine/tipiracil plus bevacizumab change depend on pre-treatment vascular endothelial growth factor inhibitors?

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Background: Trifluridine/tipiracil (FTD/TPI) plus bevacizumab (BEV) is widely used as one of salvage line treatment options in metastatic colorectal cancer (mCRC) patients. In Japan, three vascular endothelial growth factor (VEGF) inhibitors, BEV, ramucirumab (RAM), and aflibercept (AFL), are approved for mCRC patients with second-line chemotherapy including irinotecan. It remains unclear the effect of the difference of pretreatment VEGF inhibitors in clinical outcomes of FTD/TPI plus BEV.

Methods: Consecutive mCRC patients who were treated with FTD/TPIplus BEV were retrospectively enrolled. Disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and safety were compared according to the pretreatment VEGF inhibitors. Subgroup analyses of prognostic and predictive efficacy markers were performed.

Results: In total,156 patients (median age, 61.5 years) were included. The DCR was 52.6%, median PFS was 4.2 months (3.2-4.9), and median OS was 12.9 months (10.7-15.3). A total of 73 (46.8%), 50 (32.0%), and 33 patients (21.2%) were treated with FOLFIRI +BEV, RAM, or AFL, respectively. DCR, PFS, OS showed no significant differences between three groups. The most common grade 3 or 4 AEs were neutropenia (29.1%), proteinuria (16.0%) respectively. There were also no significant differences about grade 3 or 4 adverse events rates between three groups.Multivariate analysis revealed poor performance status and liver metastasisas an independent predictor for shorter both PFS and OS (Liver metastasis, PFS: P = 0.002, OS: P = 0.001, Performance status, PFS: P = 0.001, OS: P = 0.00002).

Conclusions: Chemotherapeutic efficacy and safety of FTD/TPIplus BEV did not differ regardless of the pre treatment VEGF inhibitors.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: K. Yamaguchi: Honoraria (Institution): Taiho pharm; Speaker Bureau / Expert testimony: Daiichi Sankyo, Eli lily Japan, Bristol Mayers Sqibb. E. Shinozaki: Honoraria (self): Merck biopharma. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.125

P-35 An observational study of health-related quality of life (HRQoL) with electronic patient-reported outcome (ePRO) monitoring during nivolumab therapy for advanced gastric cancer as the 3rd or later line treatment: NIVO-G QoL study

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Background: Nivolumab is the first immune checkpoint inhibitor that proves efficacy in advanced gastric or gastroesophageal junction cancer and is approved as the 3rd or later line treatment. However, the patients (pts)'s HRQoL has not been evaluated in this setting. We thus investigated how adverse events (AEs) affect HRQoL decline during nivolumab treatment and assessed the feasibility of symptom monitoring at home using the patient's own smartphone.

Methods: Eligible pts were aged ≧20 years with ECOG-PS of 0-2, diagnosed as advanced gastric cancer, and were scheduled to receive nivolumab every two weeks as the 3rd or later line treatment. Pts assessed symptomatic AEs by themselves with PRO-CTCAE and HRQoL with FACT-Ga weekly through ePRO system using pts' own smartphones or rental devices. Objective AEs were evaluated with NCI-CTCAE v5 at the time of consultation. The observation period was 12 weeks. The primary endpoint was the association between each AE and HRQoL decline. The impact of AE deterioration on HRQoL decline was determined by the longitudinal data analysis using a general linear model. The response variable was FACT-Ga total score changes from baseline for each time point. Explanatory variables were FACT-Ga total score at baseline, time point, and composite grade of each AE based on PRO-CTCAE. After ePRO monitoring, the pts completed the questionnaire about its usability.

Results: Between April 2019 and April 2020, 30 pts were enrolled, out of which 29 were evaluable. Twenty pts had completed ePRO monitoring by the end of the observation period, of which 10 pts had still continued nivolumab. The median age of pts was 71 years, and 58% were male. 97% of the pts were PS 0-1 and treated after the third line of treatment. 37.9% of pts do not use their smartphones on a regular basis, and 52.4% were aware of the difficulty of using them. As a result, only 0.95% of the total timepoints were missing data due to no ePRO input, indicating good compliance. The median time until the definitive deterioration of the FACT-Ga total score was nine weeks (95%CI: 3-NA). AEs such as stomatitis ($p<0.0001$), dysgeusia ($p<0.0001$), pain ($p<0.0001$, malaise ($p<0.0001$, nausea ($p=0.0006$, depression ($p=0.0011$, insomnia ($p=0.0035$), loss of appetite ($p=0.0047$, shortness of breath ($p=0.0052$, and vomiting ($p=0.0123$) were associated with worsening HRQoL, but peripheral neuropathy, diarrhea, and constipation were not. For the questionnaire about the usability of ePRO, no pts answered "not satisfied", but only 33.4% of pts were answered "satisfied". While 33.4% of pts wanted to continue using ePRO, 22.2% did not.

Conclusions: Symptom monitoring with ePRO revealed that certain AEs may be responsible for the decrease in HRQoL in pts with advanced gastric cancer during the 3rd or later line nivolumab treatment. Although compliance in the ePRO input was sufficient, there are still challenges in implementing it in daily practice to meet pts expectations.

Legal entity responsible for the study: The authors.

Funding: The study was supported by Bristol Myers Squibb.

Disclosures: H. Kawakami: Honoraria (self): Taiho Pharmaceutical Co. Ltd, Ono Pharmaceutical Co. Ltd., Bristol-Myers Squibb Co. Ltd., Daiichi-Sankyo Co. Ltd.; Advisory / Consultancy: Daiichi-Sankyo Co. Ltd.; Research grant / Funding (institution): Taiho Pharmaceutical Co. Ltd, Bristol-Myers Squibb Co. Ltd, Eisai Co. Ltd., Kobayashi Pharmaceutical. Co., Ltd. N. Izawa: Honoraria (self): Chugai Pharmaceutical, Lillly, Takeda, Taiho Pharmaceutical, Daiichi Sankyo, Bristrol Myers Squibb. T. Miyaji: Research grant / Funding (institution): ONO PHARMACEUTICAL CO., LTD. T. Yamaguchi: Advisory / Consultancy: ONO PHARMACEUTICAL CO., LTD.; Speaker Bureau / Expert testimony: 3H Clinical Trial Inc.. T. Nakajima: Honoraria (self): Taiho Pharm; Research grant / Funding (self): Chugai Pharm, Taiho Pharm. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.126

P-36 Real-world outcomes in BRAFV600E metastatic colorectal cancer – the Glasgow experience

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Background: Approximately 8 - 10% of metastatic colorectal cancers (mCRC) have a BRAF V600E mutation. BRAF V600E mutant mCRC represents a distinct clinical subset with a poor prognosis. Previous treatment guidelines have been derived from subgroup analyses of non-designated BRAF V600E trials. Real world studies have shown that outcomes and treatment practices can vary widely. Here, we report on our regional practices and outcomes.

Methods: We undertook a retrospective analysis of all mCRC patients with confirmed BRAF V600E mCRC diagnosed in NHS Greater Glasgow and Clyde Health Board (Scotland, UK) between 01/01/2015 - 31/12/2020. Clinical and pathological features were obtained from electronic records. Univariate analysis of prognostic factors was performed using Kaplan Meier analysis and log-rank test. Multivariate analysis was performed using Cox regression.

Results: A total of 139 patients were identified for study with 1 excluded for missing follow up information. Median age at metastatic diagnosis was 69 years, with a female preponderance (59% female, 41% male). 31% of tumours also had deficient mismatch repair (dMMR) or high levels of microsatellite instability (MSI-H). Primary tumour site was mostly right-sided (n=102, 74%), with less left-sided (n=20, 15%) and rectal (n=15, 11%) tumours. 1 patient had 2 synchronous primaries (1 right colon and 1 rectal). 64% presented with de novo metastatic disease. For those with initial loco-regional disease, the median time to metastatic progression was 10 months. The most common metastatic sites were liver (54%), peritoneal (33%), lymph node (31%), and lung (28%). 36% of patients did not receive any systemic treatment, 36% received 1 line, and 28% received 2 or more lines of treatment. Most (69%) received a cytotoxic chemotherapy doublet as first-line treatment, and 6% received triplet cytotoxic chemotherapy. 7% received immunotherapy. Among the treated patients, only 19% received some form of targeted therapy over their full treatment course, usually a combination containing an anti-EGFR inhibitor. The median overall survival was poor at 7.2 months. Features significantly associated with shorter survival were