P-69 Anal squamous cell carcinoma (ASCC) outcomes in clinical practice: From localized to metastatic setting

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Background: Anal cancer is an infrequent neoplasm, usually diagnosed at localized stages. A multidisciplinary approach involving chemoradiotherapy (CRT) and surgery is necessary. Real-world data in both locally advanced and metastatic setting is needed to support therapeutic decisions.

Methods: Patients with ASCC diagnosis between 2004 and 2022 in three tertiary care centers in Spain were reviewed. Demographic, clinical, pathological, and therapeutic variables were collected. Comparative analyses have been performed by Chi-squared tests. Survival estimates have been calculated by Kaplan-Meier method and comparations have been made using Cox proportional hazards model.

Results: 111 patients were included (45.9% males, median age 61y, 9.9% metastatic at initial diagnosis). Preferred treatment in localized stage was CRT (88.1%) with 5-fluorouracil and mytomicin-C (5FU-MMC) (55%) or 5FU-Cisplatin (33%). Response in patients treated with CRT was assessed by MRI at 3 and/or 6 months after CRT in 60.4% and 53.1% respectively. 19.6% of patients needed surgical intervention due to persistent or progressive disease after CRT. There were no significant differences between 5FU-MMC or 5FU-Cisplatin in terms of complete radiological response (45,28% vs. 51,61%; $p = 0.58$), need of surgical rescue (18,85% vs. 19,35%; $p = 0.96$), distant or localized relapse (30,18% vs. 25,80%; $p = 0.67$), median disease-free survival (DFS) (50,00 months vs. non reached (NR); $p = 0.24$) or overall survival (117,26 months vs. NR; $p = 0.45$). OS was significantly improved in patients who achieved a complete radiological response vs. patients who not (117,26 months vs. 29,01 months p 42,57% of all patients treated with curative intent relapsed locally (44.2%) or distant (55.8%), being regional nodes most common place of recurrence. The median OS of metastatic patients at diagnosis was 14,75 months. Considering all metastatic patients (de novo or relapsed), no significant differences in OS were found between patients who received treatment with curative intent (surgery, CRT) and patients only candidate to palliative chemotherapy 15,97 months vs. 13,11 months; $p = 0.072$). Median progression-free survival (PFS) of Carboplatin-Paclitaxel was 4,76 months. 62,85% of metastatic patients received a 2nd line of treatment. 48,57% of metastatic patients received immunotherapy. PD-(L)1 was only determined in 11,42% of metastatic patients. PFS of immunotherapy was 2,27 months. One patient receiving immunotherapy achieved a complete response and two patients achieved a PFS > 12 months. Other regimens used in latter lines included oxaliplatin (5,71%) and irinotecan-based (14,28%) regimens.

Conclusions: Real world data in ASCC population reveals a complex scenario with significant heterogeneity in response to treatments and outcomes. Multidisciplinary collaboration is essential. Role of immunotherapy in ASCC patients in clinical practice is still unknown. More research is needed in the refractory setting after Carboplatin-Paclitaxel to increase OS.

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P-70 Outcomes following FGFR inhibitor therapy in patients with cholangiocarcinoma: Multi-center single institution cohort experience

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Background: Cholangiocarcinomas (CCA) are a group of heterogeneous tumors arising from the biliary system. Significant sequencing efforts have provided further insights on the molecular mechanisms of this disease including fibroblast growth factor receptor (FGFR) alterations, which occurs in approximately 15-20% of intrahepatic cholangiocarcinomas. There is lack of data on outcomes of patients following cessation of FGFR inhibitor (FGFRi) therapy. Herein, we described the patient characteristics and treatment outcomes among patients with cholangiocarcinoma harboring FGFR alterations treated with chemotherapy, another targeted therapy or a second FGFRi following treatment with a first FGFRi from a multi-center single institution experience.

Methods: We conducted a retrospective study of patients with pathologic confirmed diagnosis of cholangiocarcinoma treated at the Mayo Clinic Enterprise. The study was reviewed and approved by the institutional review board. The identified patients had FGFR alterations obtained from clinical genomic reports. The primary outcome was overall survival (OS) and progression free survival (PFS).

Results: Our group identified 88 advanced or metastatic cholangiocarcinoma patients, 28 males (31.8%) and 60 females (68.2%), harboring FGFR alterations who received FGFRi. Median progression free survival (PFS) on first FGFRi was 6.6 months for all patients (95% CI: 5.5 – 8.3). Following cessation of first FGFRi therapy 55% of patients received systemic therapy as next line: 67% chemotherapy or other targeted treatment and 33% received another FGFRi therapy. Median PFS for patients who received chemotherapy or other targeted agent was 2.1 months (95% CI: 1.6 – 5.7) and for patients who received a second FGFRi following first FGFRi therapy was 3.7 months (95% CI: 1.5 – not evaluable). 28% (N=25) of the patients received another FGFRi as any line after first FGFRi therapy and median PFS was 4.0 months.

Conclusions: This is a large multi-center single institution cohort study assessing the outcomes among patients with cholangiocarcinoma treated with a second FGFRi or chemotherapy after initial treatment with FGFR inhibitors. This data reflects the real-world experience at a tertiary cancer center. Following FGFRi treatment, almost half of the patients are able to receive next line of therapy. As more novel agents are being introduced and the optimal sequencing of FGFRi is under investigation, detailed understanding of outcomes following treatment with an FGFRi is essential.

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P-71 Treatment outcome comparisons of first-line targeted therapy in patients with KRAS wild-type metastatic colorectal cancer: A nationwide database study

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Background: It remains controversial regarding whether bevacizumab or anti-epidermal growth factor receptor (anti-EGFR) monoclonal antibody (mAb) is the better companion of a chemotherapy doublet as the first-line treatment for inoperable KRAS wild-type metastatic colorectal cancer (mCRC).

Methods: We established a cohort of patients with KRAS wild-type mCRC who initiated first-line targeted therapy plus doublet chemotherapy between 2013 and 2018 from the database of National Health Insurance, Taiwan. Patients were classified according to the targeted therapy agents used in the first-line treatment regimen into the bevacizumab group and the anti-EGFR mAb group. The definition of secondary surgeries included resections of primary tumors, liver metastases, or lung metastases and radiofrequency ablation.

Results: A total of 6,482 patients were included; the first-line targeted therapy was bevacizumab and anti-EGFR mAb in 3334 (51.4%) and 3148 (48.6%) patients, respectively. Patients who received anti-EGFR mAb, compared with patients who received bevacizumab, exhibited significantly longer overall survival (OS) (median, 23.1 vs. 20.2 months, $p = 0.012$) and time-to-treatment failure (TTF) (median, 11.3 vs. 10.0 months, $p < 0.001$). We further analyzed the treatment outcomes according to the sidedness of the primary tumor. Among patients with left-sided mCRC, those who received anti-EGFR mAb in first-line systemic therapy, compared with those who received bevacizumab, exhibited significant longer OS (median, 24.9 vs. 22.9 months, $p = 0.021$) and TTF (median, 12.2 vs. 10.4 months, $p < 0.001$). Among patients with right-sided mCRC, those who received anti-EGFR mAb and those who received bevacizumab in first-line systemic therapy exhibited similar OS (median, 15.6 vs. 16.1 months, $p = 0.385$) and TTF (median, 7.6 vs. 8.8 months, $p = 0.146$). In the multivariate analyses, first-line anti-EGFR mAb remained an independent predictor for longer OS and TTF for left-sided primary tumors. Among the 6,482 patients in the study, 1,685 (26.0%) received secondary surgeries after initiation of the first-line systemic therapy. Patients who received secondary surgeries exhibited significantly longer OS than patients who never received secondary surgeries (median, 37.9 vs. 17.2 months, $p < 0.001$). Patients who received anti-EGFR mAb were more likely to

receive secondary surgeries (29.6% vs. 22.6%, $p < 0.0001$) than patients who received bevacizumab.

Conclusions: In this nationwide cohort study, we demonstrated that among patients who received first-line chemotherapy doublets for inoperable KRAS wild-type mCRC, the combination with anti-EGFR mAb, compared with the combination with bevacizumab, led to significantly longer OS and TTF. This benefit mainly came from patients with left-sided primary tumors. In the multivariate analysis, anti-EGFR mAb treatment remained an independent predictor of longer OS and TTF for the left-sided primary tumors. To our knowledge, this is the largest (n = 6,482) cohort study focusing on this issue.

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P-72 Real-world treatments and outcomes for biliary tract cancer patients using administrative databases in Ontario, Canada

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Background: There is a paucity of literature on treatment patterns and outcomes in biliary tract cancer (BTC) patients in Canada. The aim of this study was to better understand treatment patterns and survival outcomes of BTC patients in Ontario.

Methods: We conducted a retrospective population-level study in Ontario using ICES datasets on patients diagnosed with de novo or recurrent, advanced BTC (including: gallbladder cancer, intrahepatic and extrahepatic cholangiocarcinoma [IHC and EHC, respectively], Ampulla of Vater [AoV]) between January 1, 2010 and December 31, 2019. Follow-up data were available until December 31, 2020. Patients were categorized as de novo if they had stage IV disease at the time of first diagnosis, and as recurrent if they had a prior diagnosis of early stage (I-III) or unknown/missing (UNK/M) disease and received a BTC treatment (proxy for progression). Patients were excluded if they died before BTC diagnosis or had a prior cancer diagnosis. To determine the longitudinal trajectory of care for BTC patients, linkages were made between 8 national/provincial data sets.

Results: A total of 2,666 advanced BTC patients were identified, of which 471 (17.7%) were gallbladder, 785 (29.4%) were IHC, 864 (32.4%) were EHC, 304 (11.4%) were AoV and 242 (9.1%) had an unspecified BTC diagnosis. Out of 2,666, 828 (31.1%) were diagnosed with de novo and 1,838 (68.9%) were diagnosed with recurrent disease. The median age at diagnosis was 67 (interquartile range [IQR] 59-74) that significantly ($p<0.001$) varied between de novo and recurrent patients, and a majority (50.5%) of the patients were male. A total of 2,307 (86.5%) patients received first-line (1L) treatment. The most common 1L treatments were a platinum and gemcitabine combination — cisplatin and gemcitabine (gem/cis) (50.1%) and carboplatin and gemcitabine (gem/carbo) (4.9%), followed by gemcitabine monotherapy (gemmono) (17.5%), and capecitabine- or fluorouracil-based treatments (fluoropyrimidine [FP]) (16.5%). For AoV patients, the most common 1L treatment was gemmono (47.6%). Of those treated with 1L treatments, 38.7% received subsequent treatment(s). The most common treatment in second line (2L) was FP (32.1%). Among the 2,307 treated patients, 1,132 (49.1%) of patients received a stenting procedure. The mean (standard error [SE]) and median (IQR) overall survival (OS) for all advanced BTC patients from diagnosis was 28.8 months (0.83) and 13.1 months (5.7-32.0), respectively. Mean and median OS from diagnosis was longer for patients who received a 1L treatment (32.3 months [0.93] and 16.4 months [IQR 7.8-37.0], respectively) versus untreated patients (6.2 months [0.71] and 2.8 months [1.7-5.6], respectively). Mean and median OS from initiation of treatment was 16.7 months [0.71] and 9.2 months (IQR 4.0-18.9), respectively for non-AoV patients who received gem/cis.

Conclusions: This is the first comprehensive, Canadian-specific, real-world evidence study of advanced BTC patients. This study showed that 1L treatment options vary between AoV and non-AoV BTC patients, and patients who receive 1L treatment have greater survival than those who do not. The short OS in advanced BTC patients highlight the need for novel and more effective first-line therapies.

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P-73 Survival outcomes of surgical resection in perihilar cholangiocarcinoma in endemic area of O. Viverrini, Thailand

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Background: Perihilar cholangiocarcinoma is an intractable malignancy and still remain the most challenge for surgeon. This study aims to investigate survival outcomes and prognostic factors in perihilar cholangiocarcinoma patient receiving surgical treatment in single center in Thailand, endemic area of O. Viverrini.

Methods: From October 2013 to December 2018, 240 consecutive patients with perihilar cholangiocarcinoma underwent surgical exploration with or without adjuvant treatment at Sunpasitthiprasong hospital were retrospectively reviewed from medical recording system. The clinicopathological parameters and surgical outcomes were extracted. Patients were divided into two groups: unresectable and resectable group. The restricted mean survival time between two groups were analyzed. Factors associated with overall survival in resectable group were explored with multivariable Cox regression analysis.

Results: Of the 240 patients, 201 (83.75%) were received surgical resection. The survival outcomes of resectable group was better than unresectable group significantly. The restricted mean survival time difference were 0.5 (95%CI 0.22-0.82) months, 1.8 (95%CI 1.15-2.49) months, 4.7 (95%CI 3.58-5.87) months, and 9.1 (95%CI 7.40-10.78) months at four landmark time points of 3, 6, 12 and 24 months, respectively. The incidence of major complications and 90-day mortality in resectable group were 35.82% and 11.44%, respectively. Bismuth type IV, vascular resection, positive resection margin, lymph node metastasis, and distant metastasis were all predictive factors for long-term survival in univariable analysis. However, multivariable analysis revealed that Bismuth type IV (HR:4.43, 95%CI 1.853-10.599), positive resection margin (HR:4.24, 95%CI 1.741-10.342), and lymph node metastasis (HR:2.29, 95%CI 1.046-4.999) were all independent predictors of long-term survival. For pM0, R0 and pN0 patients, the median survival time was better than pM0, R1 or pN1/2 patients and pM0, R1 and pN1/2 patients (32.4, 10.4 and 4.9 months, respectively; $p < 0.001$).

Conclusions: Surgical resection increased survival in perihilar cholangiocarcinoma. Bismuth type IV, positive resection margin and lymph node metastasis were independent factors for long-term survival. Patients with R0 and pN0 had a good prognosis, but those with R1/2 and/or pN1/2 had a bad prognosis. As a result, aggressive resection are essential.

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P-74 SGNTUC-019: Phase 2 basket study of tucatinib and trastuzumab in previously treated solid tumors with HER2 alterations: Biliary tract cancer cohort (trial in progress)

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Background: Tucatinib (TUC), a highly selective HER2-directed tyrosine kinase inhibitor approved in multiple regions for HER2+ metastatic breast cancer, is being investigated as a novel therapy for patients with metastatic colorectal cancer, gastric cancer, and other GI tumors. In xenograft models of HER2+ and HER2-mutated tumors, dual targeting of HER2 with TUC + trastuzumab (Tras) showed superior activity to either agent alone. (Kulukian 2020) Interim results from the MOUNTAINEER study have shown promising activity for TUC + Tras in HER2+ colorectal cancer. In 23 response-evaluable patients, an objective response rate (ORR) of 52% was observed with a median progression-free survival (PFS) of 8.1 months. (Strickler 2019) The prognosis for patients with biliary tract cancers (BTCs) remains poor, and treatment options are limited. Given that approximately 12%-15% of BTC patients are HER2+, and 1%-8% have HER2 mutations, TUC + Tras warrants further evaluation in this patient population. The SGNTUC-019 basket study (NCT04579380) is evaluating TUC + Tras in patients with previously treated, locally advanced, unresectable or metastatic solid tumors, including BTC, that display HER2 overexpression/amplification or activating mutations. We describe the design of the BTC cohort.

Trial design: SGNTUC-019 is a multi-cohort, open-label, international phase 2 study. Patients must be $\geq$18 years old; have an ECOG PS of $\leq$1; have adequate hepatic, hematological, renal, and cardiac functions; and have no previous exposure to HER2-directed therapy. Exceptions for prior Tras treatment are allowed in patients with uterine serous carcinoma or HER2-mut gastroesophageal junction. Patients must have