P-43 Correlation of mesothelin expression with recurrence in colorectal cancer (CRC) patients

M. Malla[1], J. Fuqua[1], D. Olevian[1], J. Avalon[1], C. Wakefield[1], J. Karakiozis[2], B. Patel[1], B. Boone[1], C. Schmidt[1], S. Wen[1], Y. Agazie[1], L. Hazelhurst[1], R. Goldberg[1]

[1]West Virginia University, Morgantown, United States; [2]West Virginia University School of Medicine, Morgantown, United States

Background: Mesothelin (MSLN) is a membrane bound protein that can promote survival, proliferation and invasion of cancer cells. Our previous work had shown a significant association between MSLN expression on resected localized CRC (Stage I-III) and future development of peritoneal carcinomatosis (PC) ($p < 0.001$). MSLN expression in early stage CRC was also associated with an inferior overall survival. We expanded this work by examining an additional cohort of patients at West Virginia University (WVU), WV, USA.

Methods: This is a retrospective study of patients with localized CRC who underwent surgical resection from 2005-2019 at WVU. The patients were categorized into two groups based on whether they had a recurrence. Metastatic group comprised of patients who recurred and control group constituted patients who did not have a recurrence after a minimum of 5 years of surveillance. Metastatic group is further subdivided into 2 subgroups; SOM: patients who developed metastases in solid organs only; PC group: patients who developed PC at any time. MSLN staining with immunohistochemistry was performed using Rockland (MN1) mouse monoclonal antibody and scored based on intensity (0, 1+, 2+, and 3+) and percent positivity (0: 50%). MSLN total score was defined as the sum of intensity and percent positivity, with a total score of 3 or greater considered "positive" for MSLN expression. Fisher's exact test was performed to determine the association of MSLN score and future recurrence of CRC.

Results: Out of a total of 484 patients diagnosed with localized CRC, 88 patients had a recurrence. Out of 88 patients, SOM and PC groups comprised 48 (54%) and 19 (22%) patients respectively while 21 patients (24%) had local recurrence. Control group comprised 126 patients. MSLN staining was completed on 70 patients in the entire cohort and the results are presented here. Among 70 patients, 14 patients had a recurrence in either solid organs (n-9) or peritoneum (n-5) and 56 patients did not recur. Positive MSLN score was demonstrated on resected CRC tissues in 8 out of 14 patients who had a recurrence; Five of them from the SOM group (5 out of 9 patients (55.6%)) and 3 from the PC group (3 out of 5 patients (60%)). Contrastingly, only 16 out of 56 patients (28.5%) in the control group had a positive MSLN score. Based on Fisher's exact test, a near significant association was observed between positive MSLN score and future development of cancer recurrence (p: 0.06). No statistical significance was observed between positive MSLN score and location of metastases (SOM vs PM) likely due to limited sample size.

Conclusions: A higher proportion of patients who had a recurrence (SOM+PC groups) had a positive MSLN score on their resected CRC specimens compared to the patients who did not recur (control group) (p: 0.06). MSLN staining results on the remaining patients is ongoing. Precision medicine informatics to identify patients at highest risk of development of future recurrence is key to personalize treatment for patients with colorectal cancer.

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P-44 Impact of regorafenib dose optimization on clinical outcomes compared to best supportive care and TAS-102 in the treatment of relapsed/refractory metastatic colorectal cancer

T. Bekaii-Saab[1], H. Burnett[2], I. Proskorovsky[2], S. Yoon[3], Y. Wang[2], H. Ostojic[4], L. Gaianu[5], Y. Su[4]

[1]Mayo Clinic Hospital, Phoenix, United States; [2]Evidera, Saint-Laurent, Canada; [3]Evidera, San Francisco, United States; [4]Bayer US, Whippany, United States; [5]Bayer Public Limited Company, Reading, United Kingdom

Background: In a randomized controlled trial (RCT) ReDOS of relapsed/refractory metastatic colorectal cancer (mCRC) patients, regorafenib dose optimization (rego 80+), starting at 80 mg/day with 40 mg weekly increments to the standard dose of 160 mg/day, was found to improve tolerability and clinical outcomes compared to regorafenib at standard dose (rego 160), 160 mg/day for 21 days of a 28-day cycle. This network meta-analysis (NMA) aims to further investigate the impact of rego 80+ on efficacy and safety compared to best supportive care (BSC) and trifluridine/tipiracil (TAS-102).

Methods: RCTs included in the NMA were identified via a systematic literature review conducted in April 2021. A feasibility assessment was performed to ensure that the included trials did not differ significantly with respect to treatment effect modifiers. Bayesian fixed effect NMAs were performed to simultaneously synthesize hazard ratios (HRs) for overall survival (OS) and progression-free survival (PSF) and odds ratios for safety endpoints of interest, and their respective 95% credible intervals (CrI). The HRs from the NMA were applied to the rego 80+ OS and PFS Kaplan Meier Curves from the ReDOS trial to estimate predicted median OS and PFS for each treatment.

Results: Three global or US-only RCTs (ReDOS, CORRECT, RECOURSE) and three Asian-only RCTs (TERRA, Yoshino 2012, and CONCUR) were included in the NMA. When all trials were analyzed, rego 80+ was associated with statistically significant improvements in OS and PFS vs. BSC (HR [95% CrI]: 0.49 [0.33, 0.73] and 0.35 [0.24, 0.53], respectively) and numerically favorable improvements in OS and PFS vs. rego 160 (0.72 [0.49, 1.05] and 0.84 [0.56,1.25]), and TAS-102 (0.71 [0.47, 1.08] and 0.78 [0.52, 1.18]). Median OS (95% confidence interval [CI]) was estimated to be 9.8 (7.5, 11.9) months for rego 80+, 7.5 (4.6, 11.9) months for rego 160, 7.5 (4.4, 11.9) months for TAS-102, and 6.4 (2.5, 10.3) months for BSC. Median PFS (95% CI) was 2.80 (2.0, 2.5) months for rego 80+, 2.07 (1.89, 5.85) months for rego 160, 1.98 (1.8, 5.76) months for TAS-102, and 1.89 (1.17, 2.16) months for BSC. For grade 3+ adverse events (AEs), BSC was the most favorable, with the exception of increased aspartate transaminase (AST). Compared to rego 160, rego 80+ was numerically favorable in all AEs analyzed including hand-foot skin reactions (HSFR), diarrhea, fatigue, hypertension, and increased AST. Compared to TAS-102, rego 80+ had higher incidence of HSFR, comparable fatigue and hypertension, and numerically lower incidence of diarrhea, increased AST, neutropenia, febrile neutropenia, leukopenia, and anemia. All NMA findings were consistent when Asian-only trials were excluded from the analyses.

Conclusions: Findings from this NMA indicate that rego 80+ provides additional survival benefits (over standard dose rego 160) when compared to BSC and TAS-102; with gains of median OS of 3.4 months (~50% risk reduction), and 2.3 months (~30% risk reduction), respectively. Results also suggest that rego 80+ delays disease progression in comparison. With its more favorable safety profile, rego 80+ should be considered a preferred option for optimizing clinical outcomes in patients with relapsed/refractory mCRC.

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P-45 Microsatellite instability and HER2 status in radically resectable locally advanced esophago-gastric adenocarcinoma: A single-center experience

L. Gervaso[1], L. Bottiglieri[1], M. Meneses[2], S. Pellicori[1], R. Biffi[1], U. Fumagalli Romario[1], I. Sala[1], V. Bagnardi[1], C. Cella[1], N. Fazio[3]

[1]European Institute of Oncology, IEO, IRCCS, Milan, Italy; [2]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico; [3]European Institute of Oncology, IEO, IRCCS, Milan, Italy, Milan, Italy

Background: Peri-operative systemic chemotherapy significantly improved the prognosis of patients with resectable locally advanced gastric cancer (LAGC) but, despite that, relapse-related death remains a major challenge. Neoadjuvant chemotherapy (NAC) plays a crucial role and is currently recommend by international guidelines. Several biomarkers, including human epidermal growth factor receptor-2 (HER2) and mismatch repair (MMR) or microsatellite instability (MSI) are crucial for treatment decision in metastatic setting. However, currently, no biomarkers can guide the choice of NAC in clinical practice. In addition, most of available data derived from surgical specimens, harboring potential confusing factors after NAC. Our aim was to evaluate correlations between MSI and HER2 status and clinical outcomes in resectable LAGC treated with perioperative chemotherapy.

Methods: We conducted a retrospective cohort study of resectable LAGC patients treated with NAC and surgery +/- adjuvant chemotherapy from 2006 to 2018, for whom endoscopic pre-NAC and surgical post-NAC samples were available. A uniform small cohort of patients receiving adjuvant chemotherapy only was added for general prognostic analyses. Clinical parameters were collected including patient and tumor characteristics. Determinations of HER2 and MMR status were carried out on endoscopic pre-NAC and surgical samples. Pathologic complete response (pCR) rate, Overall survival (OS) and event-free survival (EFS) were estimated and evaluated for association with histologic downstaging and MSI status using Cox proportional hazard