P-91 Landscape of BRAF-V600E mutant colorectal cancer management in Latin America

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Background: BRAF-V600E mutated metastatic colorectal cancer (BRAF-V600E mCRC) has a 4-12% prevalence in Latin America (LA). Novel therapeutics have recently improved BRAF-mutated mCRC outcomes for patients globally. However, delayed regulatory approvals and affordability compromise treatment access in LA. In this narrative, we characterize the landscape of BRAF-V600E mCRC treatment management in LA and recommend opportunities for improving treatment and patient outcomes.

Methods: A meeting of Latin American clinical oncologists was held to address the barriers to BRAF testing in colorectal cancer and provide treatment recommendations for the region's context. During a three-day conference, the experts reviewed the current testing and treatment landscape for BRAF mCRC through a literature search and personal experience to construct recommendations for improvement.

Results: Equanimous access to molecular diagnostics and optimum medical and surgical treatment for CRC must be promoted and ensured in LA. The region's lack of access to effective screening programs and evidence-based surgical and clinical treatments hinders optimal patient outcomes. Recommendations include, 1. Local guidelines to manage advanced mCRC patients should be created. 2. Multidisciplinary Boards should be created to discuss and manage patient care plans. 3. All patients with mCRC should have tumor tissue genotyped for BRAF mutations individually or as part of a multiple genes panel. 4. The test should be performed in the primary tumor and/ or in the metastasis and routinely performed in relapsed/ unresectable or metastatic disease (stage IV). 5. Liquid biopsies are acceptable in the absence of tissue availability to use for BRAF testing. 6. First-line systemic treatment to BRAF-V600E mutated pMMR tumors should include oxaliplatin/ irinotecan − fluoropyrimidine as doublets or triplets plus bevacizumab. 7. Patients with dMMR BRAF-mutated tumors should receive pembrolizumab as first-line systemic treatment. 8. Second-line systemic treatment should include BRAF inhibitors + Anti-EGFR combinations. 9. Non-V600E-BRAF mutations can have different clinical characteristics and/or prognosis, and the appropriate treatment is yet to be defined. 10. Curative or citorreductive surgical procedures should be considered in multidisciplinary board's decisions. BRAF-mutational status should prevent interventions in patients with curative potential.

Conclusions: Treating patients with BRAF-V600E mCRC remains a challenge across LA, with opportunities for improvement in access, adoption innovative testing and treatment, and engaging in clinical trials. Favorable results of chemotherapy-free regimen, with a purely targeted dual blockade should be incorporated in the care in adult patients with BRAF-V600E mCRC who have received prior systemic treatment, in order to improve the overall survival in this poor prognosis subgroup of patients.

Editorial acknowledgement: We thank Ms. Thais Vidal, BS for English language editing the manuscript.

Legal entity responsible for the study: The authors.

Funding: This study was funded through an unrestricted grant from the Pfizer Foundation. The Pfizer Foundation had no involvement in the design, development, and content of this study.

Disclosure: G. Mendez: Honoraria (self): Merck, MSD, BMS, Roche, Amgen, Servier, Biotoscana Lab, Eli Lilly, Pfizer; Advisory / Consultancy: Merck, BMS, MSD, Pfizer; Speaker Bureau / Expert testimony: Merck, MSD, BMS, Roche, Amgen, Servier, Biotoscana Lab, Eli Lilly, Pfizer; Travel / Accommodation / Expenses: Servier, Pfizer, Amgen, Merck. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.04.147

P-92 Is preoperative chemosensitivity associated with improved outcomes in locally advanced gastric cancer? A multicentric retrospective real-world study

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Background: Perioperative chemotherapy (PCT) is the standard of care for locally advanced gastric cancer (LAGC) in western countries. However, less than 60% of patients complete the adjuvant part of treatment due to postoperative complications, toxicity and disease progression (DP). This study aim is to evaluate if preoperative chemosensitivity (POCS) is associated with improved overall survival (OS) and disease free survival (DFS).

Methods: Retrospective, multicentric study of 175 consecutive patients with LGAC treated with PCT and curative resection in 7 Portuguese hospitals from 2016 to 2021. We defined POCS as sensitive (partial or complete pathological responses) and refractory (no pathological response or disease progression).

Results: One hundred seventy-five medical records were reviewed. Nineteen patients were excluded because surgery was not performed due to DP. The median age was 66 years, and 114 (73.1%) were male. All patients were ECOG 0-1. Regarding neoadjuvant chemotherapy, 117 patients (75%) received FLOT, 16 (10.3%) received ECF, 11(7.1%) received FOLFOX, 9 (5.7%) received EOX, and 3 patients (1.9%) received EOF. Forty-nine patients (31.4%) were classified as refractory and 107 (68.6%) as sensitive (94 had partial pathological response and 13 had complete pathological response). Fifteen patients did not complete the preoperative chemotherapy due to toxicity. At a median follow-up of 27 months, sensitive POCS resulted in a statistically significant 51% reduction in the risk of death (HR 0.49; 95% CI, 0.24-0.71; p=.001). Median OS was 31 months (95% CI, 17.5-44.5) in the refractory group and was not reached in the sensitive group ($p < .001$). Mean DFS was 22 months (95% CI, 16.3-27.7) in the refractory group was not reached in the sensitive group (HR for disease progression or death, 0.40; 95% CI, 0.25-0.65; $p < .001$).

Conclusions: Despite the limitations due to our sample size, the sensitive POCS was associated with an improved OS and DFS in patients with LAGC treated with perioperative chemotherapy and surgery. These results need to be validated with more real-life evidence based studies and may help inform future studies to personalise postoperative therapy.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2023.04.148

P-93 Safety and feasibility of irradiation and nivolumab in esophageal cancer − a phase I/II study

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Background: Immune check point inhibition (ICI) with programmed death-1 (PD-1) inhibitors has recently been included in first-line standard-of-care (SOC) treatment for advanced esophageal cancer and in adjuvant therapy after chemoradiotherapy (CRT) and surgery of localized esophageal cancer. Radiotherapy (RT) may increase interaction between immune cells and cause immunogenic cell death of tumor cells. We designed a signal-finding clinical study to assess the safety and feasibility of adding the PD-1 inhibitor nivolumab to three different SOC radiotherapy regimens in esophageal cancer.

Methods: This was a single center, open-label, non-randomized, signal finding phase Ib/II study with three parallel cohorts of previously untreated esophageal adeno- or squamous cell carcinoma. Starting with concurrent RT, nivolumab was in cohort A added to SOC palliative radiotherapy, in cohort B SOC definitive chemoradiotherapy (dCRT) and in cohort C SOC neoadjuvant CRT. In A, nivolumab was added to palliative RT (30-50Gy, 15-25fx) and continued after RT until nontolerance, progression or up to 2 years using one of the dosing schedules; 240mg Q2W, 360mg Q3W or 480mg Q4W. In B, induction chemotherapy (Carboplatin AUC5/Paclitaxel 175mg/m2) preceded dCRT (50,4Gy-23fx, Carboplatin AUC2/Paclitaxel 50mg/m2 Q1W) with concurrent nivolumab 240mg Q2W and then continued with 480mg Q4W for up to one year after dCRT. In C, neoadjuvant CRT (41,4Gy-28fx, Carboplatin AUC2/Paclitaxel 50mg/m2 Q1W) with concurrent nivolumab 240mg Q2W and after surgery 480mg Q4W for up to one year/12 courses. Primary endpoints were treatment feasibility and incidence of treatment related adverse events (CTCAE v5).

Results: Thirty patients started study treatment and were included in analyses. In cohort A, 6 patients in each of the three dosing schedules were included, in total 18 patients. In B and C, 6 patients were included in both cohorts. Patients were males in 90% (27/30), mean age was 63.8 years in cohort A, 60.5 years in B and 57.3 years in C. In total, 83% (25/30) had adenocarcinoma and 17% (5/30) squamous cell carcinoma. Concurrent nivolumab was completed in 94% (17/18) in cohort A, 100% (6/6) in B and in 67% (4/6) of the patients in cohort C. In cohort A, planned radiotherapy was completed in 89% (16/18) of patients, 80% (4/5) in B and 80% (4/5) in C. Mean radiation doses were 37.8 Gy in A, 49.8 Gy in B and 39.2 Gy in C. Frequencies of most severe AEs; no AE in 3% (1/30), grade 1: none (0/30), grade 2: 17% (5/30), grade 3: 67% (20/30), grade 4: 7% (2/30) and grade 5; 7% (2/30). In cohort A, there was a tendency to more severe AEs when treated with 240mg Q2W than for 360mg Q3W and 480mg Q4W. In cohort A, the overall objective response rate (ORR) was 33% (6/18). In cohort B, ORR was 67% (4/6) and in cohort C pathology complete response (pCR) was 33% (2/6).