Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

P-149 Impact of COVID-19 pandemic and total neoadjuvant therapy (TNT) implementation in pathological complete response (pCR) rates in patients (pts) with locally advanced rectal cancer (LARC)

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Background: Strategies for locally advanced rectal cancer LARC usually consisted of neoadjuvant concomitant chemoradiotherapy (CRT) followed by adjuvant chemotherapy, or short-course radiotherapy (SCRT). TNT is a novel approach for LARC, with several randomized clinical trials exploring its role and paving the way for implementation in clinical practice. Nevertheless, the COVID-19 pandemic represented a challenge for a timely diagnosis, implementation and follow-up of new treatment strategies in these pts.

Methods: Records of all the pts diagnosed with LARC and stage IV rectal cancer evaluated in the Oncology department of Vall d'Hebron Hospital between Jan 1st, 2017 and Dec 31th 2021 were included. The period 2017-19 was considered pre-pandemic (PP) and 2020-2021 during-pandemic (DP). Patients with LARC receiving neoadjuvant and/or adjuvant treatment were analyzed, including those treated with SCRT, CRT, and TNT. Data regarding demographics, diagnosis and staging, preoperative treatment received, surgical outcomes, including treatment response, and pathological stage were collected.

Results: 390 patients were included (31.28% female, 68.71% Male, median age 69). LARC pts characteristics included 123 (31.54%) either cT4 or cN2, 59 low rectal cancers, 4 with signet ring cells. Neoadjuvant treatment was done in 160 pts (CRT) and 59 pts (TNT). pCR was achieved in 20% and 22% for CRT, and TNT respectively (p0.84). 32 pts received only SCRT with 6.25% pCR. An increased ratio of stage IV pts compared to LARC was evident during the pandemic (stage IV 26.38% 2017-2019, 37.14% 2020-2021, p=0.044). The proportion of high risk LARC increased during pandemic (34.89% PP vs 39.04% DP, p=0.041). No difference was found in terms of pCR amongst the PP and DP patients (25.3% vs 27%, p=0.83) nor different strategies (TNT: 26.47% PP and 26.6% PD, p=0.98 and CRT 23.89% PP and 27.27 % PD, p=0.82).

Conclusions: Efficacy of LARC neoadjuvant treatment measured by pCR was maintained in pts before and during COVID-19 pandemic despite an increasing proportion of new LARC high-risk pts. Evaluation of TNT impact in LARC outcomes was challenging because of pandemic confounding role. Real-world data in a post-pandemic setting is essential to evaluate outcome trends in LARC pts; an increase in high-risk LARC and metastatic pts should be expected.

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P-150 Targeting loss of heterozygosity in colorectal cancer

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Background: The 8p22 chromosomal locus commonly suffers loss of heterozygosity (LOH) in advanced colorectal cancer (CRC) in about 21 % of cases (1,2). The gene encoding N-acetyltransferase-2 (NAT2) is located on 8p22 and thus frequently lost as a by-stander gene. NAT2 is a highly polymorphic gene with at least X alleles which encode products with slow, normal or rapid metabolic activity (3). Half of tumors in subjects heterozygous for a slow and a rapid allele with LOH at 8p22 will retain only the slow NAT2 allele. This can be exploited in treatment as CRC cancer cells with LOH and remaining NAT2-slow allele cannot efficiently metabolize certain drugs, whereas normal heterozygous cells can. This was shown with 6-(4-aminophenyl)-N-(3,4,5-trimethoxyphenyl)pyrazin-2-amine (APA), which killed cells with NAT2-slow alleles (NAT2*6A, NAT2*5, NAT2*14) but not with the rapid (NAT2*13A) (4,5). Our aim here was to identify additional compounds which selectively kill cancer cells with slow NAT2 acetylator phenotype.

Methods: Previously established CRC cell modes (4), expressing NAT2-slow or NAT2-rapid variant alleles and empty vector control were used for drug screening (5). Resazurin-based MTT or Cell-Titer Glo cell viability assays were used to assess differential cell kill between cells lines with different NAT2 activity. A set of FDA approved cancer drugs (147), NCI chemical library (503), compounds engineered as potential NAT2 substrates (879), and kinase inhibitors libraries (378) were used for screening at concentrations ranging from 1 pmol to 10 micromol.

Results: In the FDA approved cytotoxic drugs we found 7 compounds that were selectively toxic to cells having high NAT2 activity. 5 of them are alkaline agents like doxorubicin and others, 1 is multikinase inhibitor Afatinib, 1 topoisomerase inhibitor Teniposide. This might be useful for individual dosage for better drug safety. In the kinase inhibitors libraries and NCI chemical compounds library we found 9 and 6 substances respectively with enhanced toxicity towards cells with low NAT2 activity. These compounds are now in validation face. In the library of potential NAT2 substrates 256 toxic compounds are selected for further experiments.

Conclusions: Clinically used as well as novel compounds whose cytotoxicity was modulated by NAT2 activity were identified. The results can improve the use of existing drugs and enable collateral lethality targeting of NAT loss.

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P-151 PRO-based symptom management for patients with gastric and esophageal cancer who have undergone previous surgery

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Background: The incidence of gastric cancer and esophageal cancer ranks second and third respectively in China. Patients with previously surgically resected gastric and esophageal cancers often suffer from malnutrition, anorexia, gastroesophageal reflux and depression which have a serious implication on their subsequent treatment. However, due to the specificity of the current medical situation in China and the heavy treatment workload of clinicians, there is no efficient and easy way to manage the symptoms of these patients.

Methods: Patients were randomized in a 1:1 ratio after enrollment into the Patient-Reported Outcome (PRO) symptom management group and the conventional care group. The PRO group were assessed for anorexia, gastroesophageal reflux, depression, nutritional status (assessment scales are FAACT A/CS, GERD-Q, SDS and NRS2002 respectively), weight and BMI in the hospital before each cycle of chemotherapy via an electronic data platform. The doctors responded the assessment results and provided interventions, including advice for home care, drug prescription, and telephone follow-up, before patients are discharged from the hospital. Patients were assessed and managed every 3-4 weeks at the time of return for chemotherapy during 16 weeks. Patients in the usual care group underwent symptom assessment only at the first and the 16th weeks, during which the surgeons only managed the symptoms with usual care modalities. The primary endpoint is number of symptoms at the 16th weeks and the secondary endpoints are the incidence of each symptom at the 16th weeks.

Results: From Apr. 2021 to Mar. 2022, 97 pts completed the clinical observation, including 49 pts in the PRO group and 48 pts in the conventional care group. Baseline results of all were not statistically different ($P>0.05$). After 16 weeks of symptom management, the number of overall symptoms in the PRO group was significantly lower than in the conventional care group (1 (0-1) vs 2.5 (1-4), $P < 0.001$). The incidence of nutrition risk (24.5% vs 64.6%, $P < 0.001$), anorexia (24.5% vs 66.7%, $P < 0.001$), gastroesophageal reflux (12.2% vs 56.3%, $P < 0.001$) and depression (4.1% vs 16.7%, P=0.042) in the PRO group was significantly lower than that in the conventional care group, and there was no statistically significant difference about underweight (defined: BMI < 18.5, 16.3% vs 33.3%, P=0.052). The NRS2002 (2 [1-2] vs 3 [2-4], $P < 0.001$), FAACT A/CS (40 [37.5-44] vs 34 [27.3-39.8], $P < 0.001$), GERD-Q (6 [6-7] vs 8 [6-9], $P < 0.001$), SDS (32.5 [28.8-37.5] vs 45 [36.6-48.8], $P < 0.001$) scores of the PRO group were statistically significantly different from those of the conventional group ($P < 0.001$), while there was no statistical difference in the weight(54.39±8.07 vs 52.06±7.55, P=0.146), BMI (20.45±2.38 vs 19.62±2.44, P=0.095). Of note, although the weight was same, it was found that weight loss was less severe in the PRO group by comparing the weight loss rate (2.04% [-2.97%-3.96%] vs 5.32% [1.84%-9.22%], $P < 0.001$).

Conclusions: Compared to conventional care, the rates of nutritional risk, anorexia, gastroesophageal reflux, depression and weight loss were effectively controlled in patients with previously surgically resected gastric and esophageal cancers through 16 weeks of patient-reported outcome-based symptom management, which providing clinicians with an easy-to-operate and effective means of symptom management.

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