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Body composition dynamics and impact on clinical outcome in gastric and gastro-esophageal junction cancer patients undergoing perioperative chemotherapy with the FLOT protocol

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Background: Perioperative chemotherapy with FLOT constitutes a standard of care approach for locally advanced, resectable gastric or gastro-esophageal junction (GEJ) cancer. We aimed at investigating anthropometric, CT-based and FDG-PET-based body composition parameters and dynamics during this multidisciplinary approach and the impact on clinical outcome.

Methods: This retrospective, single-center study was based on medical records and (FDG-PET)-CT images among gastric/GEJ cancer patients undergoing perioperative FLOT chemotherapy.

Results: Between 2016 and 2021, 46 gastric/GEJ cancer patients started perioperative FLOT at our tertiary cancer center (Salzburg, Austria). At a median follow-up of 32 months neither median PFS nor median OS were reached. The skeletal muscle index (SMI, cm2/m2) turned out to be the only body composition parameter with a statistically significant decrease during pre-operative FLOT (51.3 versus 48.8 cm2/m2, p=0.02). Neither pre-FLOT body mass index (BMI), nor SMI had an impact on the duration of pre-operative FLOT, time interval from pre-operative FLOT initiation to surgery, necessity of pre-operative or post-operative FLOT de-escalation or the likelihood of the start of postoperative chemotherapy. Pre-FLOT BMI (overweight versus normal, HR: 0.06, 95% CI: 0.01-0.59, p=0.02) was statistically significantly associated with PFS in the multivariable analysis and pre-FLOT SMI showed a trend towards an association with PFS (sarcopenia versus no sarcopenia; HR: 4.95, 95%CI: 0.97-25.29, p=0.05).

Conclusions: The statistically significant SMI loss during pre-operative FLOT and the meaningful impact of baseline SMI and BMI on PFS argue for the implementation of a nutritional screening and support program prior to the initiation of pre-operative FLOT in clinical routine.

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Real-world data of trastuzumab in metastatic cancer

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Background: Gastric cancer (GC) has usually a quite aggressive behaviour and many patients present with advanced or metastatic disease at diagnosis. Evidence supports a doublet/triplet of platinum/fluoropyrimidine combinations as standard of care in fit patients. In 2010, the phase III ToGA trial, showed benefit, in the addition of trastuzumab to chemotherapy, in Her2-positive advanced GC patients. Our goal is to evaluate the results of the use of trastuzumab and chemotherapy, with real-world data from a central hospital.

Methods: This is a retrospective unicentric cohort of patients diagnosed with GC, from January 2016 to December 2021. We analysed the prevalence of Her2-positive metastatic gastric cancer, the overall survival (OS) and the progression-free survival (PFS) of these patients.

Results: A total of 371 patients were identified, from these, 94 were tested for Her2 status with immunohistochemistry (IHC). Fluorescence in-situ hybridisation (FISH) was used in case of a 2+ result in IHC. There was a total of 9 metastatic Her2-positive patients. The median age at the start of treatment was 55.9 years (range 32-79 years) and most of the patients were males (66%). In five of the patients the chemotherapy regimen used was the combination of 5-fluorouracil, cisplatin and trastuzumab. In the other four patients the fluoropyrimidine was substituted by capecitabin. The median of cycles completed were 9 cycles (range 1-18 cycles). On the matter of OS our data provided a median of 15.6 months (range 1.5-29.5 months). Regarding the PFS, our median was 12 months (range 1.5-26.1 months).

Conclusions: The prevalence of Her2-positive gastric cancer in our analysis was 9.6%, rather alike the prevalence described in the literature (10-15%). Moreover, our data meets the results of the ToGA trial where the median OS was 16 months, very similar to our results (15.6 months). The sub-analyse of the median PFS in the Her2-positive group was not carried out in the ToGA trial, only the median PFS of the total sample was determined (6.7 months), and therefore we cannot compare results. However, our median PFS (12 months) leads us to believe that much like the OS was better in the HER2-positive subgroup, so must the PFS improve in this subgroup. We can hence infer that our data support the benefit from the addition of trastuzumab to the conventional chemotherapy regimen in such context.

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Unrecognized development of chemoresistance and/or distant metastases during induction chemotherapy for pancreatic adenocarcinoma

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Background: Induction Chemotherapy (IC) is often used in the treatment of pancreatic cancer (PC) and concurrent chemoradiotherapy (CRT), when given, usually follows the complete delivery of IC. We aim in this study to determine the incidence of CA19-9 rise during IC that is not associated with radiological/US progression, when patients are referred for CRT. Such progression may indicate the development of occult distant metastases and/or chemoresistance.

Methods: We retrospectively reviewed all charts of patients diagnosed with PC and referred for CRT following IC during the period of 2015-2021. Patients were eligible for this study if they met all of the following criteria: received IC, Staging/restaging imaging studies demonstrated no evidence of distant metastases or progression of locoregional disease at any point prior to CRT referral, availability of serial CA19-9 and bilirubin measurements during the IC phase. CA19-9 progression is defined as an increase in CA19-9 by at least 25% compared to prior measurement in the absence of elevated bilirubin.

Results: Thirty four patients, 21 males and 13 females, met the eligibility criteria with a median age of 69 years. PC was located in the head/neck or body of the pancreas in 21 and 10 cases respectively. The location of the tumor could not be determined in 3 cases. The disease was considered resectable, borderline resectable or unresectable in 5, 23 and 6 cases, respectively. Three patients had tumors with complete radiological clinical response at the time of referral for CRT. Partial response was noticed in 15 cases and stable disease was seen in 16 cases. Chemotherapy regimens included FOLFIRINOX (22 cases), Gemcitabine-Abraxane (10 cases) or Gemcitabine alone (2 cases). CA19-9 was rising by more than 25% (26%-337%, median 47%) with total bilirubin levels of less than 1, before referral for CRT in 10/34 cases (29%).

Conclusions: There may be high incidence of unrecognized chemical tumor progression, as measured by a CA19-9 rise, and/or development of chemoresistance during IC and before the delivery of CRT. This phenomenon may explain the lack of impact of CRT when delivered after completion of IC when only radiological studies are used to restage patients prior to initiation of CRT. Our findings need to be confirmed in a larger database and if confirmed would suggest the inclusion of CA19-9 levels in the restaging process and possible demonstration of a better impact of CRT if patients with CA19-9 rise are not included in the analysis to evaluate the potential benefit of CRT.

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