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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Efficacy of second line immunotherapy in advanced upper gastrointestinal tract malignancies: A pooled analysis of randomized clinical trials

P. Ntella1, K.V. Kamospioras2, I. Gazouli3, K. Dadouli4, T. Germatsis5, G. Zarkavelis6, A.L. Amylidi7, S. Gkoura8, L. Mavroeidis9, F.L. Kostadima6, A. Sotirios Papadaki10, M. Papadaki11, A. Valderrama2, L. Yin3, S. Zhang4, C-S. Shih5, C. Gu6, P. Bhagia6, Z. Wainberg7

1Medical Oncology, University Hospital of Ioannina, Ioannina, Greece; 2Medical Oncology Dept., The Christie NHS Foundation Trust, Manchester, West Yorkshire, UK; 3Medical Oncology Department, University Hospital of Ioannina, IOANNINA, Greece; 4Laboratory of Hygiene and Epidemiology, Faculty of Medicine, University of Thessaly, Larisa, Greece; 5Medical Oncology Dept., The Christie NHS Foundation Trust, Manchester, UK; 6Medical Oncology Dept., University Hospital of Ioannina, Ioannina, Greece; 7Oncology, University Hospital of Ioannina, Ioannina, Greece; 8Oncology Department, University Hospital of Ioannina, Ioannina, Greece; 9Medical Oncology Dept., University Hospital of Ioannina, Ioannina, Greece; 10Medical Oncology Department, University Hospital of Ioannina, Ioannina, Greece; 11Department of Radiotherapy, School of Medicine, University of Crete, Heraklion, Greece

Background: The use of immune checkpoint inhibitors in upper track gastrointestinal malignancies is a major and rapidly evolving field of research. As a result in the last 5 years a lot of data have emerged from randomized clinical trials and even more are expected in the future.

Methods: The aim of the study was to systematically review and examine in a pooled analysis all the data from randomized clinical studies on the use of immune checkpoint inhibitors compared to chemotherapy in the second line of treatment for advanced upper gastrointestinal cancers.

Results: Systematic literature search revealed five randomized, multicenter clinical trials, comparing the use of immunotherapy against chemotherapy in the second-line treatment of upper gastrointestinal carcinoma. Overall a total of 2190 patients were randomized between 1056 of whom received immunotherapy and 1034 standard chemotherapy. In the overall population immunotherapy demonstrated an improved overall survival with a significant 16% lower risk of death compared to chemotherapy (HR 0.84, 95% CI 0.76 to 0.93, p = 0.0004). The benefit of immunotherapy was even more prominent for patients with CPS score > 1 or > 10 and for those with squamous cell histology. In contrast, there was no survival benefit confirmed in patients with esophageal or GEJ adenocarcinoma (HR 0.99, 95% CI 0.85 to 1.15, p = 0.89). Also, a benefit of immunotherapy in progression free survival was only evident in patients CPS score > 10 (HR 0.71, 95% CI 0.56 to 0.89, p < 0.003), but not in the overall population (HR 1.06, 95% CI 0.79 to 1.42, p = 0.70).

Conclusions: The above findings highlight the benefit of second-line immunotherapy, but further investigation is needed in future studies to discover the patient populations that will benefit the most from such an approach.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

Real world outcomes of locally advanced gastric/GOJ cancers receiving perioperative chemotherapy with FLOT regimen during the COVID-19 pandemic: Results from a regional cancer care centre in the UK

S. Bose1, R. Chowdhary1, A. Menon1, T. Hafeez1, M. Joseph1

1Medical Oncology, Deanesly Centre - New Cross Hospital - The Royal Wolverhampton NHS Trust, Wolverhampton, UK; 2Clinical Oncology, Deanesly Centre - New Cross Hospital - The Royal Wolverhampton NHS Trust, Wolverhampton, UK

Background: In locally advanced gastroesophageal and gastric cancers, which constitute the majority of the presentation, the postoperative 5 year survival rate remains only 30-40%. It is in these patients that perioperative chemotherapy has helped improve radical resection rates control preoperative micrometastases and improve survival. Since 2017 FLOT based chemotherapy has largely replaced ECF/ECX in this setting. We did a retrospective analysis on our patients treated with FLOT regimen during the COVID-19 pandemic to assess its efficacy, tolerance and pathologic response (TRG).

Methods: Patients with resectable gastric and GOJ cancers who presented to us from August 2019 – March 2020 and treated with FLOT based perioperative chemotherapy were analyzed with SPSS (version 26, IBM, Armonk, NY). Pathologic assessment of tumour regression was done by Mandar’s TRG scoring. A total of 36 patients were analyzed, out of which 91% were males, median age 68 years, CT74 86%, CPS 72.2%, GOJ 77.8%, Gastric 22%, Grade 2/3 94% of total 80.6% patients completed all 4 cycles of neoadjuvant FLOT and 88.9% patients underwent surgery (all R0). Median interval between last dose of chemo and surgery was 7 weeks. A total of 52.8% patients completed all 4 cycles of adjuvant FLOT. Treatment was delayed due to COVID-19 in 11%.

Results: Median followup was 16.3 mths. 1 year DFS was 66.3% and OS was 91.4%. Pathologic CR (TRG 1) was seen in 2.8% patients. 3 patients died due to postop complications. Most common grade 3 toxicities were oral mucositis (6%), diarrhea (6%), neutropenia (8.3%) SFU cardiotoxicity noted in 5.6%.

Table: 1389P

| TRG (Mandar) | Frequency | Percent |
|-------------|-----------|---------|
| 1(complete regression) | 1 | 2.8 |
| 2(residual cancer cells) | 4 | 11.1 |
| 3(increased no. of cancer cells/fibrosis still predominates) | 13 | 36.1 |
| 4(residual cancer outgrowing fibrosis) | 10 | 27.8 |
| 5(absence of regressive changes) | 4 | 11.1 |

Conclusions: In our subset of patients, treatment delivery, surgery rates and toxicity profile were comparable to the seminal FLOT4 trial. Our histological responses are lower with pathCR in only 2.8% (vs 16%) patients, with most having TRG 3. The survival rates are better but a longer followup is required.

Evaluation of event-free survival as a trial-level surrogate for overall survival for patients with gastric and gastroesophageal junction adenocarcinoma in neoadjuvant/ adjuvant settings

J. Xie1, A. Valderrama1, L. Yin1, S. Zhang2, C-S. Shih3, C. Gu4, P. Bhagia5, Z. Wainberg6

1Economic, Financial, and Strategy Consulting, Analysis Group, Inc., Los Angeles, CA, USA; 2Center for Observational and Real World Evidence (CORE), Merck & Co., Inc., Kenilworth, NJ, USA; 3Economic, Financial, and Strategy Consulting, Analysis Group, Los Angeles, CA, USA; 4Economic and Data Sciences, Merck & Co., Inc., Kenilworth, NJ, USA; 5 Oncology, Merck & Co., Inc., Kenilworth, NJ, USA; 6Oncology, Merck and Co., Inc., Rahway, NJ, USA; 7Medicine, Hematology and Oncology, Ronald Reagan UCLA Medical Center, Los Angeles, CA, USA

Background: Overall survival (OS) is the standard endpoint in oncology trials but often requires prolonged follow-up. Event-free survival (EFS) is a well-accepted endpoint in early-stage oncology trials and a common surrogate endpoint for OS in neoadjuvant and adjuvant cancer therapy. This study aims to evaluate the trial-level association between EFS and OS for patients with gastric or gastroesophageal junction (GEJ) adenocarcinoma in neoadjuvant/adjuvant settings.

Methods: A systematic literature review was conducted in December 2020 to identify randomized clinical trials (RCTs) of a neoadjuvant therapy (i.e. an adjuvant therapy) in gastric or GEJ adenocarcinoma. Full-text articles with no publication date restriction and conference abstracts from 2018 were reviewed. Though the terminology used for EFS varied, the definitions for events were similar across studies, including disease progression, local or distant recurrence, and death. Treatment effects on EFS and OS were measured as hazard ratios (HRs) between a pair of randomized arms. A weighted linear regression of log(HR) of OS on log(HR) of EFS was performed. The coefficient of determination (R²) and the associated 95% confidence interval (CI) were used to measure the association between the treatment effects on EFS and OS. Sensitivity analyses (SAs) were conducted to assess the association in the RCTs that included a mixed population of patients with esophageal, gastric or GEJ adenocarcinoma, evaluated both neoadjuvant and adjuvant chemotherapy, or measured EFS and OS from neoadjuvant therapy initiation.

Results: The study included 18 comparisons from 17 RCTs. The primary analysis indicated that log(HR) of EFS was a significant predictor of log(HR) of OS with an estimated coefficient of 0.72 (p < 0.001) and R² = 0.75 (95% CI, 0.49-0.95). In the SAs, R² ranged from 0.76 to 0.89. The strongest association was observed in a subgroup of RCTs that measured EFS and OS from neoadjuvant therapy initiation (R² = 0.89, 95% CI, 0.66-0.98).

Conclusions: The findings suggest that EFS is a good surrogate for OS in gastric or GEJ adenocarcinoma in neoadjuvant/adjuvant settings.