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POSTER DISCUSSIONS

PD-1 The impact of COVID-19 on diagnosis, stage and treatment of esophageal and gastric cancer

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Background: During the COVID-19 pandemic, a profound decrease in the number of cancer diagnoses was observed. For patients with esophagogastric cancer, a diagnostic delay may have resulted in more advanced disease at the time of diagnosis. Also, downscaling of oncological care during COVID-19 may have resulted in postponed or different treatments. Therefore, we aimed to investigate the effects of the COVID-19 pandemic in 2020 on the stage at diagnosis and oncological care of esophagogastric cancer.

Methods: Patients who were diagnosed in 2020 and included in the Netherlands Cancer Registry were allocated to 5 periods that correspond to the severity of the COVID-19 pandemic in the Netherlands. These were compared to patients diagnosed in the same period in the years 2017-2019. The number of diagnoses, tumor characteristics, type of treatment, time until the start of treatment and, in case of resection, the time between neoadjuvant therapy and resection were evaluated for esophageal cancer (EC) and gastric cancer (GC) separately.

Results: The 2020 cohort in the Netherlands consisted of 2388 EC patients and 1429 GC patients. The absolute number of diagnoses decreased most prominently in the months March and April of 2020 for both EC and GC. The total number of EC diagnoses in 2020 decreased significantly compared to 2017-2019 (n=2522, p=0.027), whereas the total number of GC diagnoses did not decrease (n=1442, p=0.270). In the weeks after the first COVID-19 case in the Netherlands and before the COVID-19 lockdown, the percentage of incurable diagnoses increased from 52.5% to 67.7% for GC (p=0.011) and did not increase for EC (33.0% to 40.8%, p = 0.092). The percentage of patients with potentially curable EC receiving neoadjuvant chemoradiotherapy with resection decreased from 35.0% in 2017-2019 to 27.4% in 2020 (p < 0.001), whereas the percentage of patients receiving neoadjuvant chemoradiation without resection increased from 9.5% in 2017-2019 to 13.9% in 2020 (p < 0.001). The percentage of patients receiving definitive chemoradiation did not change significantly (p=0.119). For GC patients, no significant changes in type of treatment were found. The time between neoadjuvant chemotherapy and gastric resection decreased in 2020 with four days (p=0.006), while the time between neoadjuvant therapy and esophageal resection increased with 5 days (p=0.005). For both tumor types, the time between diagnosis and start of treatment was significantly shorter for patients diagnosed during and after the COVID-19 lockdown.

Conclusions: We found a significant decrease in the number of EC diagnoses in 2020 and a shift in the type of treatment in potentially curable EC patients, with fewer resections being performed. Yet, it is unclear whether this is the result of the COVID-19 pandemic or due to an ongoing trial which implements watchful waiting after chemoradiotherapy. The oncological care for GC patients did not change during the COVID-19 pandemic. The shorter time between diagnosis and start of treatment may have been the result of a sense of urgency, since it was unknown in what way COVID-19 might affect the continuity of care in the upcoming future.

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PD-2 EMERGE: A multi-centre, non-randomised, single-arm phase II study investigating domatinostat plus avelumab in patients with previously treated advanced mismatch repair-proficient oesophagogastric and colorectal adenocarcinoma

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Background: Mismatch repair proficient (MMRp) oesophagogastric (OG) and colorectal cancers (CRC) respond less frequently to checkpoint inhibition. Epigenetic modulation of tumours using HDAC inhibitors can increase the chance of response to immunotherapy. We previously reported dose escalation (EMERGE phase IIA) and the established recommended phase II dose (RP2D) of domatinostat (selective class I HDAC inhibitor) 200mg BID continuously plus avelumab 10mg/kg q2w.

Methods: Patients with MMRp advanced OG and CRC who received at least one prior line of chemotherapy were enrolled in two cohorts. Patients were treated with a two-week domatinostat prime (orally) followed by combination domatinostat and avelumab from cycle 2 onwards. The trial was conducted using a Simon two-stage optimal design. The primary endpoint was best objective response rate (ORR) 6 months from initiation of combination treatment by RECIST 1.1. A secondary end point was disease control rate (DCR) during the same period. The total accrual target was 29 in the CRC cohort and 34 patients in the OG cohort, with interim analysis due to take place once 10 CRC patients and 9 OG patients had been evaluated for best ORR; ≥ 1 response and ≥ 2 responses were required in the respective cohorts to proceed to stage two.

Results: 21 patients were recruited between January 2020 and October 2021. In the OG cohort 9 patients were treated. 56% patients had received ≥ 2 prior lines of systemic anti-cancer therapy (SACT). The median duration of treatment was 1.8 months (range: 0.9-12.8). The best ORR was 22.2% [95% CI: 2.8, 60.0] (one PR and one CR). The patient with PR had a combined positive score (CPS) of 9, whilst the CPS was unavailable for the patient with CR. At time of data cut off on 25th February 2022, both patients remained on treatment at cycles 28 and 16 respectively. The median CPS for the patients whose disease did not respond to treatment was 12 (range: 0-26). In the CRC cohort, 12 patients were treated; of these, 2 did not receive avelumab and were non-evaluable. In the evaluable CRC population, 90% received ≥ 2 prior lines of SACT. No responses were observed. DCR was 30.0% [95% CI: 6.7, 65.2]. The median duration of treatment was 2 months (range: 1.3-9.0). The most common treatment related adverse events (TRAE) of any grade were fatigue (58%), anaemia (37%) and nausea (32%). There were no grade ≥ 3 TRAEs reported.

Conclusions: For OG adenocarcinoma the ORR of 22.2% met the criteria to expand the stage two recruitment with a favourable safety profile. In CRC there was insufficient signal to progress to stage two.

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