P-52 Overall survival with cetuximab every 2 weeks vs standard once-weekly administration schedule for first-line treatment of RAS wild-type metastatic colorectal cancer in patients with left- and right-sided primary tumor location

S. Kasper[1], A. Cheng[2], M. Rouyer[3], C. Foch[4], F. Lamy[4], R. Esser[4], M. Batech[4], C. Wong[5], A. Zhang[6], T. Brodowicz[7], C. Zielinski[8]

[1]Medical Oncology, University Hospital Essen Westdeutsches Tumorzentrum, Essen, Germany; [2]National Taiwan University Hospital, Taipei, Taiwan; [3]INSERM CIC1401, Bordeaux PharmacoEpi, University of Bordeaux, Bordeaux, France; [4]Merck KGaA, Darmstadt, Germany; [5]Cytel Singapore Pte. Ltd, Singapore, Singapore; [6]Merck Serono, Shanghai, China; [7]Department of Medical Oncology, Internal Medicine 1, General Hospital - Medical University of Vienna, Vienna, Austria; [8]Oncology, Comprehensive Cancer Center, Vienna General Hospital and Medical University of Vienna, Vienna, Austria

Background: In patients with RAS wild-type metastatic colorectal cancer (mCRC) receiving first-line treatment with cetuximab in combination with chemotherapy, the noninferiority of the off-label schedule of cetuximab 500 mg/m^2 every 2 weeks (q2w) vs the approved schedule of cetuximab at an initial dose of 400 mg/m^2 followed by weekly doses of 250 mg/m^2 (q1w) was demonstrated in a pooled analysis of patient-level data from 2 noninterventional cohort studies (EREBUS, ERBITAG) and 3 clinical trials (CEBIFOX, CECOG/CORE 1.2.002, APEC) (Kasper et al. Eur J Cancer. 2021;144:291-301). However, primary tumor sidedness was not available at the time of final main analysis and was thus not considered. Tumor sidedness has now been collected from all studies except CECOG/CORE 1.2.002, and subgroup analyses have been conducted by tumor sidedness (left/right).

Methods: The main analysis was repeated in subgroups of patients with left- and right-sided primary tumors. Differences in baseline characteristics were accounted for with inverse probability of treatment weighting (IPTW) based on propensity scores specific to each subgroup. As in the main analysis, baseline covariates included in the propensity score were selected based on their association with outcome (ie, $P < 0.20$ in a univariate model). Overall survival (OS) and progression-free survival (PFS) were assessed via Cox proportional hazards regression after IPTW.

Results: In total, 830 (79%) and 227 (21%) patients presented with left- and right-sided primary tumors, respectively. As expected, patients with right-sided primary tumors had lower frequencies of favorable prognostic factors such as liver-limited metastases (left subgroup: q1w, 45%; q2w, 40%; right subgroup: q1w, 35%; q2w, 35%) and higher frequencies of unfavorable prognostic factors such as peritoneal carcinomatoses (left subgroup: q1w, 12%; q2w, 9%; right subgroup: q1w, 35%; q2w, 32%). After IPTW, baseline confounders included in the propensity score were well balanced between administration schedules. In the left subgroup, the median OS time after IPTW was 26.78 months (95% CI, 23.59-31.84) for the q1w cohort and 31.70 months (27.86-34.60) for the q2w cohort. In the right subgroup, the median OS time was 11.63 months (10.22-16.62) for the q1w cohort and 18.23 months (14.00-22.14) for the q2w cohort. The hazard ratios (HRs) (95% CI) for OS after IPTW were 0.754 (0.622-0.913) in the left subgroup and 0.754 (0.545-1.041) in the right subgroup. These results were consistent with the main analysis (HR after IPTW of 0.827 [0.715-0.956]). Also consistent with the main analysis, no major differences were found in PFS between administration schedules after IPTW in the left (HR, 0.927; 95% CI, 0.786-1.094) and right subgroups (0.813; 0.597-1.108).

Conclusions: Patients with right-sided primary tumors had a shorter median OS time vs patients with left-sided primary tumors. These subgroup analyses support the conclusion of noninferiority in OS for cetuximab q2w vs q1w in the first-line treatment of RAS wild-type mCRC in combination with chemotherapy among patients with left- and right-sided primary tumors.

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P-53 Prognostic factors for relapse in resected gastroenteropancreatic neuroendocrine neoplasms: A systematic review and meta-analysis

R. Broadbent[1], R. Wheatley[1], S. Stajer[2], T. Jacobs[3], A. Lamarca[1], R. Hubner[1], J. Valle[1], E. Amir[2], M. McNamara[1]

[1]University of Manchester / The Christie NHS Foundation Trust, Manchester, United Kingdom; [2]The Princess Margaret Cancer Centre, Toronto, Canada; [3]The Christie NHS Foundation Trust, Manchester, United Kingdom

Background: Gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs) are a rare, heterogeneous group of malignancies. Potential cure can be achieved through surgical resection, but only 42-57% achieve 5-year disease-free survival. Here, the factors associated with relapse following potentially-curative resection of GEP-NENs are investigated, using a systematic review and meta-analysis.

Methods: A systematic search of MEDLINE, EMBASE, Web of Science, BIOSIS, CENTRAL, Cochrane Library, and abstracts from ESMO and ASCO was performed and last updated July 2020. Prospective and retrospective studies reporting factors associated with relapse in patients with GEP-NENs following resection of a primary tumour, including concurrent resection of a metastatic site were included. Papers not reporting the proportion of patients with tumour grades 1-3 were excluded. Only variables which were reported by at least 3 studies were included in the meta-analysis. Hazard Ratios (HR) for Relapse-Free Survival (RFS) or Overall Survival (OS) were weighted using generic inverse variance and pooled using random effects modelling.

Results: Of 729 studies identified initially; 96 were eligible for inclusion in the meta-analysis (17,698 patients); 83 studies (14,801 patients) included pancreatic NENs only, the remaining 13 studies reported on mixed primary site or non-pancreatic NENs. For the entire cohort, on multivariable analysis, vascular resection performed [HR 2.25 (95% confidence interval (CI) 1.29-3.90), p=0.004], M1 disease [HR 2.53 (95%CI 1.22-5.23), p=0.01], tumour size >20mm [HR 2.39 (95%CI 1.68-3.40), p 5% [HR 3.78 (95% CI 2.12-6.76), p 20mm [HR 5.32 (95%CI 1.64-17.25), p=0.005], grade 2 [HR 4.48 (95% CI 2.89-6.94), p < 0.001], R1 resection [HR 2.97 (95%CI 1.47-6.02), p=0.002], microvascular invasion [HR 2.60 (95%CI 1.01-6.75), p=0.049], perineural invasion [HR 2.48 (95%CI 1.17-5.25), p=0.02] and any lymph node positivity [HR 3.67 (95%CI 2.44-5.52), p < 0.001]. When studies reporting on mixed primary site or non-pancreatic NENs were analysed independently, lymph node positivity [HR 2.21 (95%CI 1.58-3.08), p < 0.001], grade 2 [HR 5.80 (95% CI 3.35-10.04), p < 0.001] lymphovascular invasion [HR 4.90 (95% CI 1.39-17.26), p=0.01], R1 resection [HR 2.40 (95% CI 1.36-4.22), p=0.002] were prognostic for worse RFS in the univariable analysis. For these studies, pooling of multivariable data was possible only for lymph node positivity [HR 3.54 (95% CI 1.07-11.77), p=0.04]. Few OS data were available for pooling; in univariable analysis (entire cohort), grade 2 disease [HR 5.17 (95%CI 1.58-16.93), p=0.007] was prognostic for worse OS, while R1 resection was not [HR 1.89 (95%CI 0.82-4.39), p=0.14).

Conclusions: This is one of the largest meta-analyses to identify pathological tumour characteristics which are prognostic for RFS and OS following resection of GEP-NENs. The majority of included studies reported on pancreatic NENs, which may introduce bias; however, the results will inform selection and stratification criteria for future adjuvant trials.

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P-54 Higher muscle mass is associated with better response to concurrent neoadjuvant chemoradiotherapy in rectal cancer patients

K. Zhelev[1], Z. Zahariev[1], N. Conev[2], I. Donev[3]

[1]MHAT Uni Hospital, Panagyurishte, Bulgaria; [2]Medical University of Varna, Varna, Bulgaria; [3]Hospital Nadezhda, Sofia, Bulgaria

Background: Sarcopenia (low muscle mass) is an emerging syndrome associated with poor outcome in cancer patients. We investigated the relationship between skeletal muscle index (SMI), psoas muscle index (PMI), and neoadjuvant rectal score (NAR) in a group of patients with locally advanced rectal adenocarcinoma, treated with neoadjuvant concurrent chemoradiotherapy (nCCRT) with capecitabine and surgery.

Methods: Patients with locally advanced lower and middle rectal adenocarcinoma (n = 91) in Stage II and III disease were retrospectively analyzed between 2016 and 2019. All patients were treated with nCCRT with capecitabine and after 6-8 weeks surgery. SMI and PMI were calculated at L3 position on computed tomography (CT) before to start with nCCRT and on CT after surgery. NAR score was developed as a composite short-term endpoint for clinical trials involving neoadjuvant therapy for rectal cancer and can predict response of the treatment. NAR score was defined as [5pN - 3 (cT - pT) + 12]2/9.61.