P-90 First-line anti-EGFR agents (panitumumab or cetuximab) plus chemotherapy in patients with metastatic colorectal cancer: Onco-colon Turkey study subgroup analysis

A. Isıkdogan[1], H. Turk[2], C. Bilir[3], M. Şendur[4], B. Karabulut[5], M. Artac[6], I. Cicin[7], C. Geredeli[8], A. Alacacioglu[9], U. Kefeli[10], H. Harputluoglu[11], O. Bozkurt[12], E. Cubukcu[13], D. Tural[14], A. Sakin[15], T. Cil[16], F. Dane[17], D. Çevik[18], Ç. Arslan[19], N. Karadurmus[20], M. Gumus[21], S. Yalcin[22]

[1]Dicle University Hospital, Diyarbakir, Turkey; [2]Bezmialem Vakif University Hospital, Istanbul, Turkey; [3]Sakarya University Medical School, Sakarya, Turkey; [4]Ankara Yildirim Beyazıt University, Faculty of Medicine, and Ankara City Hospital, Ankara, Turkey; [5]Ege University, Tulay Aktas Oncology Hospital, Izmir, Turkey; [6]Necmettin Erbakan University, Meram Medical School, Konya, Turkey, Konya, Turkey; [7]Trakya University, School of Medicine, Edirne, Turkey; [8]SBU Cemil Tascioglu Sehir Hospital, Istanbul, Turkey; [9]Katip Celebi University, Ataturk Research and Training Hospital, Izmir, Turkey, Izmir, Turkey; [10]School of Medicine, Kocaeli University, Kocaeli, Turkey; [11]Inonu University Turgut Ozal Medical Center, Malatya, Turkey; [12]Erciyes University School of Medicine, Kayseri, Turkey; [13]Uludag University Hospital, Bursa, Turkey; [14]SBU Bakirkoy Sadi Konuk Hospital, Istanbul, Turkey; [15]Van Yuzuncu Yıl Univesity Hospital, Istanbul/ FATİH, Turkey; [16]SBU Adana SUAM, Adana, Turkey; [17]Marmara University, Istanbul, Turkey; [18]Amgen Turkey, Turkey, Istanbul, Turkey; [19]Izmir Ekonomi University Medicalpark Hospital, Izmir, Turkey; [20]SBU Gulhane Medical Faculty, Ankara, Turkey; [21]Istanbul Medeniyet Universitesi, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey; [22]Hacettepe Universitesi, Ankara, Turkey

Background: The guidelines support the use of the epidermal growth factor receptor (EGFR) inhibitors panitumumab or cetuximab for the treatment of metastatic colorectal cancer (mCRC) on significant clinical benefits in patients with wild-type RAS. We assessed the efficacy and toxicity of panitumumab versus cetuximab in Onco-Colon Turkey registry patients.

Methods: Patients with wild-type RAS mCRC treated with fluorouracil-oxaliplatin- and irinotecan-based chemotherapies in first-line setting were evaluated to either panitumumab or cetuximab including combinations. The efficacy of cetuximab vs panitumumab on overall survival (OS) and progression-free survival (PFS) and safety profile when combined with chemotherapy regimen was compared retrospectively.

Results: From January 2016 to March 2019, 1065 patients were recorded in Onco-Colon Turkey Registry, and 316 (47.4%) and 351(52.6%) patients were received the panitumumab and cetuximab as anti-EGFR treatment in first-line setting, respectively. The panitumumab was used more commonly with a combination regimen containing oxaliplatin (74.9%), while the cetuximab was used more in contingency with a combination regimen containing irinotecan (50.4%) (p=0.000). The median PFS was 11.6 months in the panitumumab arm and 11.0 months in the cetuximab arm, (p=0.270), and median OS was 26.5 and 27.6 months (p = 0.726), respectively. The overall response rate was 58.4% in panitumumab arm and 51.4% in cetuximab arm (p=0.138). The incidence of acneiform rash and thrombocytopenia was higher in the panitumumab arm (p=0.011 and 0.045) and the incidence of nausea/vomiting was higher in the cetuximab arm (p=0.013).

Conclusions: Our findings show that panitumumab is similar to cetuximab and that these agents provide equal progression-free and overall survival benefit in this population of patients with wild-type RAS. Both agents had toxicity profiles that were to be expected.

Legal entity responsible for the study: The author.

Funding: Amgen.

Disclosures: M. Artac: Honoraria (self): Amgen; Travel / Accommodation / Expenses: Amgen. D. Çevik: Full / Part-time employment: Amgen. N. Karadurmus: Honoraria (Institution): Novartis, Roche, MSD. S. Yalcin: Honoraria (self): Pfizer, Merck Serono, Gen ilac, Amgen, Novartis, Abbott, Natera; Advisory / Consultancy: Pfizer, Merck Serono, Amgen, Abbott; Speaker Bureau / Expert testimony: Gen ilac, Eczacibasiıı, Amgen, Merck Serono, Roche, Abbott; Travel / Accommodation / Expenses: Gen ilac, Amgen, Roche. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.180

P-91 Quality of life (QoL)-based end-points for patients with advanced pancreatic ductal adenocarcinoma (aPDAC): Results from the PanDA prospective observational study

A. Lamarca[1], L. Carnie[1], D. Shah[1], K. Vaughan[2], Z. Kapacee[1], L. McCallum[3], M. Abraham[1], A. Backen[1], L. Gillespie[1], M. McNamara[4], R. Hubner[1], J. Valle[4]

[1]The Christie National Health Service Foundation Trust, Manchester, United Kingdom; [2]The University of Manchester, Manchester, United Kingdom; [3]Pancreatic Cancer UK, London, United Kingdom; [4]The University of Manchester/The Christie National Health Service Foundation Trust, Manchester, United Kingdom

Background: Adequate design of clinical trials using QoL-based primary-end points to assess benefit derived from supportive interventions such as exercise, nutrition or complementary therapies is challenging in PDAC due to a lack of available data describing baseline QoL and changes over time for this patient population.

Methods: PanDA was a prospective observational study of prevalence, assessment and treatment of pancreatic exocrine insufficiency in patients with aPDAC (NCT03616431). QoL data using the EORTC QlQ-C30 and QLQ-PAN26 questionnaires were collected for the follow-up cohort at baseline (BSL), week6 (W6) and month3 (M3). This post-hoc analysis included patients with aPDAC and explored the mean and standard deviation (SD) of the Physical Functioning Scale (PhFS) at BSL, W6, M3) and mean (SD) intra-patient changes over time (W6-BSL and M3-BSL). Subgroup analysis by stage (locally-advanced vs metastatic) was also performed. Percentage of patients evaluable at each time point was reported. Descriptive statistical analysis was performed (Stata v.17).

Results: Of 37 patients recruited into the follow-up cohort, 32 met eligibility criteria for this post hoc analysis. Thirty (93.8%), 17 (53.1%; all had paired BSL data) and 13 (40.6%; all had paired BSL data) patients were evaluable with PhFS data available at BSL, W6 and M3, respectively. PhFS (mean (SD); number of observations) did not vary over time when all patients were analysed together (BSL: 76.17(26.46);30) (W6: 79.18(12.74);17) (M3: 74.46(16.76);13). Intra-patient mean changes at W6 (-6.59(15.13);17) or M3 (-5.46(24.82);13). Subgroup analysis identified that changes in W6 were more marked in patients with metastatic disease (-12.14(15.54);7) compared to locally advanced (-2.70(14.32);10).

Conclusions: Changes on PhFS over time were likely impacted by selection bias. Intra-patient mean changes at W6 or M3 seemed more reliable to be utilised as primary-end point and sample size calculation in future clinical trials. Subgroup analysis identified that changes in W6 were more marked in patients with metastatic Intra-patient changes rather than pooled results may be more reliable when designing clinical trials with QoL-based primary end-points in aPDAC. W6 assessment may be most informative, as waiting until M3 may compromise the power of the study due to significant drop out.

Legal entity responsible for the study: The Christie NHS Foundation Trust.

Funding: Ms Lindsay Carnie was funded by Pancreatic Cancer UK Fellowship (Clinical Pioneer Award 2015) and Neuroendocrine Cancer UK, formerly known as the NET Patient Foundation. Dr Kate Vaughan is funded by Cancer Research UK [Funder reference: C2930/A25234, University of Manchester reference: R120976] Authors would like to acknowledge that patient advocate groups [Pancreatic Cancer UK and Neuroendocrine Cancer UK (formerly known as the NET Patient Foundation)] were involved in the development of this study protocol. Dr Angela Lamarca has received funding from European Society for Medical Oncology (ESMO) Fellowship Programme, Pancreatic Cancer Research Fund, Spanish Society of Medical Oncology (SEOM) Fellowship Programme, American Society of Clinical Oncology (ASCO) Conquer Cancer Foundation Young Investigator Award and The Christie Charity. Dr Zainul Abedin Kapacee was funded by The Christie Charity.

Disclosures: A. Lamarca: Advisory / Consultancy: Advisory and consultancy honoraria from EISAI, Nutricia Ipsen, QED, Roche, Servier, Boston Scientific, Albireo Pharma, AstraZeneca, Boehringer Ingelheim and GENFIT. ; Speaker Bureau / Expert testimony: Speaker honoraria from Merck, Pfizer, Ipsen, Incyte, AAA, QED, Servier, Astra Zeneca and EISAI. ; Research grant / Funding (self): Member of the Knowledge Network and NETConnect Initiatives funded by Ipsen. Roche; Travel / Accommodation / Expenses: Travel and educational support from Ipsen, Pfizer, Bayer, AAA, SirtEx, Novartis, Mylan and Delcath. R. Hubner: Advisory / Consultancy: BeiGene. J. Valle: Advisory / Consultancy: AstraZeneca. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.181

P-92 Real-life experience with maintenance chemotherapy plus biologics after the first-line treatment of RAS wild-type metastatic colon cancer (mCRC): A multicenter Onco-Colon Turkey study

M. Artac[1], E. Cubukcu[2], O. Bozkurt[3], A. Bilici[4], S. Celik[5], M. Ozcelik[6], B. Oven[7], E. Simsek[8], C. Geredeli[9], M. Karaca[10], T. Cil[11], H. Harputluoglu[12], M. Şendur[13], H. Turk[14], U. Kefeli[15], A. Alacacioglu[16], D. Tural[17], A. Sakin[18], N. Karadurmus[19], D. Çevik[20], F. Dane[21], M. Gumus[22]

[1]Necmettin Erbakan University, Meram Medical School, Konya, Turkey, Konya, Turkey; [2]Uludag University Hospital, Bursa, Turkey; [3]Erciyes University School Of Medicine, Kayseri, Turkey; [4]Medipol University Hospital, Istanbul, Turkey, Istanbul, Turkey; [5]Istanbul Oncology Hospital, Istanbul, Turkey; [6]SBU Umraniye Research and Training Hospital, Istanbul/ FATİH, Turkey; [7]Bahcesehir University Goztepe Medical Park Hospital, Istanbul, Turkey; [8]Haydarpasa Research and training Hospital, Istanbul, Turkey; [9]SBU Cemil Tascioglu Sehir Hospital, Istanbul, Turkey; [10]Health Sciences University, Antalya Education and Research Hospital, Department of Medical Oncology, Antalya, Turkey, Antalya, Turkey; [11]SBU Adana SUAM, Adana, Turkey; [12]Inonu University Turgut Ozal Medical Center, Malatya, Turkey; [13]Ankara Yildirim Beyazıt University, Faculty of Medicine, and Ankara City Hospital, Ankara, Turkey; [14]Bezmialem Vakif University Hospital, Istanbul, Turkey; [15]School of Medicine, Kocaeli University, Kocaeli, Turkey; [16]Katip Celebi University, Ataturk Research and Training Hospital, Izmir, Turkey, Izmir, Turkey; [17]SBU Bakirkoy Sadi Konuk Hospital, Istanbul, Turkey; [18]Van Yuzuncu Yıl Univesity Hospital, Istanbul/FATİH, Turkey; [19]SBU Gulhane Medical Faculty, Ankara, Turkey; [20]Amgen Turkey, Turkey, Istanbul, Turkey; [21]Marmara University, Istanbul, Turkey; [22]Istanbul Medeniyet Universitesi, Goztepe Prof. Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

Background: Randomized clinical trials showed that maintenance chemotherapy plus biologics in patients with mCRC could increase the progression free survival (PFS) without any advantage for overall survival (OS). Our aim was to study the real-life experience (onco-colon registry Turkey) of maintenance chemotherapy with antiEGFR or antiVEGF mAbs after the standart firstline doublet chemotherapy backbone in RAS wild-type mCRC patients.

Methods: This multicenter, retrospective study aimed to evaluate clinicians' attitude and post-induction therapies in patients with RAS wild-type mCRC treated with doublet chemotherapy as a first-line regimen plus anti-EGFR or anti-VEGF who did not experience disease progression within the first 6 months during the first series of therapy. The safety and effectiveness of these strategies were evaluated at 28 centers. Progression-free survival (PFS), overall survival (OS), adverse events, and objective response rate (ORR) were compared in groups receiving anti-EGFR and anti-VEGF-based therapy as first-line therapy.

Results: Among 1065 patients with RAS wild-type mCRC treated with doublet plus anti-EGFR or anti-VEGF as a first-line regimen from January 2016 to March 2019, 665 eligible patients with no progression within the first 6 months were included in the current analysis. The median follow-up was 25 months (6-59) and the median age was 60 (17-85), and 35% of the patients were female. The rate of maintenance therapy was 37.7% in those who received anti-VEGF-based therapy as initial therapy, and 29.2% in patients who received anti-EGFR-based therapy (p=0.036). There was no significant difference between the groups receiving panitumumab and cetuximab in terms of transition to maintenance therapy in the group receiving anti-EGFR treatment, 28.3%, 30.1%, respectively (p=0.685). Of these patients, 151 (22.7%) patients were fluoropyrimidine (5FU/LV /capecitabine) + biologic combination, 42 (6.3%) patients were anti-EGFR or anti-VEGF (single agent), and 18 (2.7%) patients were single-agent fluoropyrimidine (5FU) /LV /capecitabine), and 454 (68.3%) patients continued induction therapy without switching to maintenance therapy until disease progression, unacceptable toxicity, patient judgment, or completion of planned therapy. The median PFS values of the cohorts who continued to receive 5FU/LV + anti-EGFR / VEGF, anti-EGFR/VEGF single agent, 5FU/LV single agent, and combination therapy without maintenance therapy were found as 16.8, 14.3, 15.8, and 11.8 months, respectively ($p < 0.001$). The median overall survival values of the cohorts were determined as 35.5, 44.5, 38.9 and 28.3 months, respectively ($p < 0.001$). There was no difference between groups in ORR (p=0.057).

Conclusions: In a "real life" setting, among the treatment strategies following the anti-EGFR/VEGF-based doublet first-line induction regimen in RAS wild-type mCRC patients, the combination of 5FU/LV + biologic as maintenance therapy emerges as the most widely adopted and effective regimen with survival advantage.

Legal entity responsible for the study: The author.

Funding: Amgen.

Disclosures: M. Artac: Honoraria (self): Amgen; Travel / Accommodation / Expenses: Amgen. N. Karadurmus: Honoraria (Institution): Novartis, Roche, MSD. D. Çevik: Full / Part-time employment: Amgen. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.182

P-93 The role of combined treatment of metastatic colorectal cancer in patients with liver metastases

A. Popov[1], D. Gridnev[1], A. Gritskevich[1], M. Trandofilov[2], D. Islamova[1], V. Makarov[1], E. Vozny[3]

[1]A.V. Vishnevsky National Medical Research Center of Surgery, Moscow, Russia; [2]Federal State Budgetary Educational Institution of Higher Education "A.I. Evdokimov Moscow State Universyty of Medicine and Dentistry" of the Ministry of Helthcare of the Russian Federation, Moscow, Russia; [3]Moscow State Budgetary Healthcare Institution "D.D. Pletnev`s City Hospital" Moscow City Health Department, Moscow, Russia

Background: Combined treatment for patients with metastatic colorectal cancer(mCRC) offers better long-term outcomes and chemotherapy can increase the rate of hepatic resectability for patients with initially inoperable disease.

Methods: The analysis included 132 patients diagnosed with mCRC having metastases in the liver treated from 2015 to 2021. Of these, 62 (47%) were men and 70 (53%) women. The average age of the patients was 63 years. At the beginning of the treatment, the overall condition of all patients met ECOG 0-1points. Primary metastatic CRC had 93 (71%) patients. A total of 39 (29%) patients were diagnosed with advanced disease. Localization of the primary tumor in 25 patients (18.9%) was in the right part of the large intestine and 107 (81.1%) in the left part of the colon. At the time of the sample, metastases were detected only in the liver in 73 patients (55.3%). In the remaining 59(44.7%) other organs were affected besides the liver. Various types of surgical treatment of metastases in the liver received 42 (31.8%) patients. The decision on the choice of chemotherapy was made by the attending physician on the basis of the recommendations of NCCN and RUSSCO, taking into account the molecular genetic characteristics of the tumor. The decision to apply and choose the method of surgical treatment was taken in conjunction with the surgeon.

Results: From the general population of patients receiving complex therapy, 2 groups were identified, between which a comparison was made. The first group(group A) was 42 (31.8%) patients who received some surgical treatment of the liver. The second group (group B) included 90 (68.2%) patients, who for some reason or another, did not receive any surgical treatment. The groups are fairly homogeneous in their characteristics. The median overall survival (OS) ingroup A was 43.1 months, and in group B, 26.3 months. A similar trend continued in subgroup analysis. The calculation of the PFS was complicated by the fact that surgical operations were given at different stages of complex treatment. Three-year survival in group A was approximately 51%, and in group B, 29%. "Five-year" survival (In those patients who were observed from the start of the study for all 5 years) in group A was 19 %, and in group B, 8,5%.

Conclusions: The inclusion of modern surgical techniques in the complex therapy of metastatic colorectal cancer, if possible, at any stage, can significantly increase the life expectancy of patients.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.183

P-94 Circulating-tumour DNA (ctDNA) detection using an ultra-sensitive next generation sequencing (NGS)-based assay in patients with resected colorectal cancer (CRC) in the phase III ASCOLT trial

D. Day[1], A. Starus[2], O. Sieber[3], D. Prasse[4], A. Lamik[4], J. Fredebohm[4], J. Simes[5], F. Day[6], M. Jeffery[7], R. Zielinski[8], M. Singh[9], G. Chong[10], S. Li[3], D. Mouradov[3], J. Chia[11], R. Ali[12], H. Toh[11], F. Jones[2], E. Segelov[1]

[1]Department of Oncology, Monash Health and Department of Medicine, Monash University, Melbourne, Australia; [2]Sysmex Inostics Inc., Baltimore, United States; [3]Walter and Eliza Hall Institute, Melbourne, Australia; [4]Sysmex Inostics GmbH, Hamburg, Germany; [5]University of Sydney NHMRC Clinical Trials Centre, Sydney, Australia; [6]Calvary Mater Newcastle, Newcastle, Australia; [7]Christchurch Hospital, Christchurch, New Zealand; [8]Orange Health Service, Orange, Australia; [9]Barwon Health Andrew Love Cancer Centre, Geelong, Australia; [10]Ballarat Regional Integrated Cancer Centre, Ballarat, Australia; [11]Division of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore; [12]Public Health Research Centre, New York University, Abu Dhabi, United Arab Emirates

Background: Identification of somatic mutations in ctDNA may detect minimal residual disease (MRD) in patients with curatively treated CRC who may eventually recur. Highly sensitive NGS-based assays are known to have comparable sensitivity to digital PCR approaches, with the added benefit of broader coverage and no requirement for a priori knowledge of tumour-based mutations. The ASpirin for Dukes C and high risk Dukes B COLorecTal cancer trial (ASCOLT, NCT00565708) is a randomised, double-blinded, phase III fully accrued study investigating the benefit and safety of aspirin in the adjuvant setting. In the Australian and New Zealand cohort, serial plasma samples were prospectively collected at study enrolment (within 90 days of completing adjuvant chemotherapy), then at 6 and 12 months, along with baseline tumour tissue. In this pilot, we evaluated the utility of an ultra-sensitive ctDNA NGS assay (SafeSEQ, Sysmex Inostics), comparing plasma and tumour-based sequencing.

Methods: Extracted cell-free DNA (cfDNA, up to 20,000 genomic equivalents [GE, validated maximum DNA input]) was analysed using a SafeSEQ CRC MRD assay that detects mutations in 14 genes relevant in CRC, including AKT1, APC, BRAF, CTNNB1, ERBB3, FBXW7, KRAS, NRAS, PIK3CA, POLE, PPP2R1A, RNF43, SMAD4 and TP53. Tumour sequencing used an amplicon-based NGS 59-gene custom panel. cfDNA results were correlated with tumour sequencing and recurrence data.

Results: Twenty-nine plasma samples (median 3.6 mL, median DNA 71.7 GE/μL) from the first 10 patients were analysed (6 female; median age 65; 2 with high-risk stage II, 8 stage III). All patients had received adjuvant 5-Fluorouracil-based chemotherapy (7 also with oxaliplatin; 1 also with neoadjuvant chemoradiation for rectal cancer). Median follow-up was 59.9 months, with 3 known recurrences (median time to recurrence 23.3 months). Two of 3 patients who experienced recurrence had detectable ctDNA: 1 at the 6-month timepoint and the other at 12 months (negative at 6 months). In relation to the timing of ctDNA positivity, cancer recurrence was detected by CT 16.5 months after (lung metastases) for 1 patient and within 4 weeks (lung and nodal metastases) for the other. Both patients' plasma mutation profiles (KRAS G12V and KRAS G13D/ SMAD4 L540P, respectively) were concordant with their tumour analysis. A third patient experienced disease recurrence 59.2 months after study commencement (peritoneal metastases) but did not have detectable ctDNA at any of the 3 timepoints. CEA did not predict recurrence in any of the 3 patients. Another patient with detectable cfDNA at the 6-month timepoint (TP53 R248W, seen in plasma only, negative at 12 months) has not had a recorded recurrence; analysis of matched peripheral blood mononuclear cells is awaited.

Conclusions: In this pilot cohort of 10 ASCOLT trial patients with high-risk resected CRC following adjuvant chemotherapy, 2 of 3 patients who recurred had early detectable ctDNA using an NGS-based SafeSEQ assay. A third patient with late recurrence did not have detectable ctDNA. Plasma and tumour sequencing results were concordant in 2 of 3 patients with detectable cfDNA. Analyses in the larger cohort (n=368) are underway.

Clinical trial identification: NCT00565708.

Legal entity responsible for the study: Australasian Gastro-Intestinal Trial Group.

Funding: This work is supported by an Australasian Gastro-Intestinal Cancer Trials Group Innovation Grant. D. Day is a recipient of the Royal Australasian College of Physicians Foundation 2022 Basser Research Entry Scholarship.

Disclosures: A. Starus: Full / Part-time employment: Sysmex Inostics, Inc. D. Prasse: Full / Part-time employment: Sysmex Inostics GmbH. A. Lamik: Full / Part-time employment: Sysmex Inostics GmbH. J. Fredebohm: Full / Part-time employment: Sysmex Inostics GmbH. J. Simes: Research grant / Funding (institution): Bayer. S. Li: Research grant / Funding (institution): WEHI, WEHI, WEHI. F. Jones: