449P Randomized phase II study comparing pathological responses of resected colorectal cancer metastases (CRCM) after bevacizumab (BEV) with FOLFOX or FOLFIRI (BEV-ONCO trial)

P. Baldin[1], G. Beniuga[2], A. Jouret-Mourin[1], G. Demolin[3], S. Roland[4], L.A. D'Hondt[5], P. Vergauwe[6], D. Vandaele[7], M. Mailleux[8], I. Sinapi[9], A. De Cuyper[10], N. Bletard[11], B. Massart[11], M. Delos[12], M-L. Castella[13], A. van Maanen[14], J. Carrasco[15], M. van den Eynde[13]

[1]Pathology, Cliniques Universitaires St. Luc - Université Catholique de Louvain, Bruxelles, Belgium; [2]Department of Anatomopathology, Institut de Pathologie et de Génétique, Gosselies, Belgium; [3]Gastroenterology, Clinique CHC MonLégia, Liège, Belgium; [4]Gastroenterology, CHIREC - Hôpital Delta, Auderghem, Belgium; [5]Oncology Department, CHU-UCL-Namur - Site Sainte-Elisabeth, Namur, Belgium; [6]Gastroenterology, AZ Groeninge Hospital, Kortrijk, Belgium; [7]Gastroenterology, CHU de Liège, Liège, Belgium; [8]Medical Oncology, Clinique Saint-Luc Bouge, Namur, Belgium; [9]Medical Oncology, Grand Hopital de Charleroi Site Notre Dame, Charleroi, Belgium; [10]Department of Medical Oncology, Cliniques Universitaires St. Luc - Université Catholique de Louvain, Bruxelles, Belgium; [11]Pathology, Clinique CHC MonLégia, Liège, Belgium; [12]Pathology, CHU-UCL-Namur - Site Sainte-Elisabeth, Namur, Belgium; [13]Department of Digestive Oncology, Cliniques Universitaires St. Luc - Université Catholique de Louvain, Bruxelles, Belgium; [14]Institut Roi Albert II, Cliniques Universitaires St. Luc - Université Catholique de Louvain, Bruxelles, Belgium; [15]Medical Oncology Department, GHdC - Grand Hopital de Charleroi - Site Notre Dame, Charleroi, Belgium

Background: Pathological response (PR) of resected CRCM after preop treatment is a recognized prognostic factor. Retrospective studies reported that BEV + oxaliplatin-based chemotherapy increased PR compared to irinotecan-based chemotherapy. In this trial, we aim to demonstrate that preop BEV + FOLFOX would increase PR.

Methods: BEV-ONCO (NCT01858649) is a multicenter prospective randomized (1/1) phase II trial evaluating PR on resected CRCM after 3 to max 6 cycles of mFOLFOX (ARM A) or FOLFIRI (ARM B) + BEV (5mg/kg/2 weeks). Primary endpoint is the major pathological response rate (MPRR) defined as the % of patients presenting CRCMs with a mean tumor regression grade (TRG) <3. Secondary endpoints include DFS, OS, safety, complete PR, R0 resection rate and liver toxicity comprising sinusoidal obstruction syndrome (SOS) and nodular regenerative hyperplasia (NRH). 54 pts (27 per arm) are needed to detect a difference (alpha=0.05; beta=0.2) of MPRR proportion of 0.40 between treatment arms (two-sided Fisher's Exact test).

Results: Among 65 pts included between 06/2013 and 09/2018, 57 pts (28 ARM A / 29 ARM B) have had CRCM resection. Clinical and treatment characteristics were similar in both treatment arms (median age 60 y-old, 51% male, 33% RAS wt, 98% liver CRCM, 75% synchronous, median 2 CRCM/pt, median of 4 chemo cycles and 3 BEV cycles). 11/28 pts presented 1-month postop surgical complications in ARM A (39%, grade 3-4: 17.9%) and 9/29 pts in ARM B (31%, grade 3-4: 6.9%, p=0.58). MPRR was 32% in ARM A and 21% in ARM B (p=0.38). 4 pts presented complete PR (ARM A/B: 14%/0%, p=0.05). No difference between treatment arms was observed for R0 resection (ARM A/B: 89%/93%, p=0.80), SOS (ARM A/B: 54%/38%, p=0.50), NRH (ARM A/B: 21%/17%, p=0.75), DFS (ARM A/B: HR=1.14, 95%CI:0.58-2.21, p=0.71) and OS (ARM A/B: HR=1.38, 95%CI:0.48-4.00, p=0.55). Pts with PR among all CRCM (Max TRG$\leq$3; 44% of pts) had a lower risk of relapse/death (DFS: HR=0.41, 95% CI=0.20-0.82, p=0.01) and death (OS: HR=0.34, 95%CI=0.10-1.11, p=0.07).

Conclusions: This trial fails to demonstrate any significant difference of PR between BEV with FOLFOX or FOLFIRI but confirms PR as a prognostic factor.

Clinical trial identification: NCT01858649.

Legal entity responsible for the study: The authors.

Funding: Roche Belgium.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.560

450P The impact of late-line treatment on overall survival (OS) from the initiation of first-line chemotherapy (CT) for patients (pts) with metastatic colorectal cancer (mCRC): Updated analysis

T. Kawakami[1], K. Yamazaki[2], H. Go[3], T. Masuishi[4], Y. Kawamoto[5], K. Kato[4], R. Kumanishi[4], K. Sawada[6], H. Shirasu[1], S. Yuki[5], K. Yamamoto[3], T. Yamanaka[3], Y. Komatsu[5], K. Muro[7], H. Yasui[1]

[1]Department of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan; [2]Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Shizuoka, Japan; [3]Biostatistics Department, Yokohama City University Hospital, Yokohama, Japan; [4]Department of Clinical Oncology, Aichi Cancer Center, Nagoya, Japan; [5]Gastroenterology And Hepatology, Hokkaido University Hospital, Sapporo, Japan; [6]Cancer Center, Hokkaido University Hospital, Sapporo, Japan; [7]Department of Clinical Oncology, Aichi Cancer Center, Nagoya, Aichi, Japan

Background: Regorafenib (REGO) and trifluridine/tipiracil (FTD/TPI) as late-line treatment has been available since 2012, however, their impact on the total OS of pts that is measured from the initiation of first-line CT in clinical practice. We previously demonstrated late-line treatment with REGO or FTD/TPI could improve OS, however, the number of events and the follow-up time was insufficient. Thus, we conducted an updated analysis of our study.

Methods: Data cutoff for this updated analysis was Dec 2019 (previously, Sep 2018). We retrospectively collected the data of consecutive mCRC pts who received first-line CT at 3 institutions between Jan 2005 and Sep 2016. We divided the pts into 3 groups according to the availability of drugs at the initiation of first-line CT; pts who initiated between Jan 2005 and Dec 2006 (cohort A), Jan 2007 and Dec 2011 (cohort B), and Jan 2012 and Sep 2016 (cohort C). The primary outcome is to compare OS between cohort A, B and C.

Results: A total of 1,426 pts were analyzed. Pts' characteristics of cohort A (165 pts), B (626 pts) and C (635 pts) were as follows; median age, 62 /63/65 years; ECOG PS $\geq$2, 8.5%/8.8%/8.2%; number of metastatic sites $\geq$2, 63.6%/61.3%/58.1%, respectively. Median OS in cohort A, B, and C, was 18.8, 25.3, and 25.8 M, respectively. Hazard ratio (HR) (95% confidence interval [CI]) for cohort B vs. A was 0.82 (0.68-0.98), for C vs. A was 0.75 (0.62-0.90), and for C vs. B was 0.92 (0.81-1.04), respectively. Multivariate analysis revealed PS $\geq$2, right sided tumors, number of metastatic sites $\geq$2, WBC$\geq$10,000/μL, ALP$\geq$300IU/L, and LDH$\geq$ 400U/L were poor prognostic factors. The adjusted HR (95% CI) for cohort B vs. A was 0.79 (0.66-0.95), cohort C vs. A was 0.76 (0.63-0.91), and cohort C vs. B 0.96 (0.84-1.08) after adjusting for poor prognostic factors above.

Conclusions: This updated analysis showed late-line treatment with REGO or FTD/TPI would contribute to prolong total OS of mCRC.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosure: T. Kawakami: Honoraria (self): Taiho Pharmaceutical; Honoraria (self): Chugai Pharmaceutical; Advisory/Consultancy: Bayer Pharmaceutical; Honoraria (self): Takeda Pharmaceutical. K. Yamazaki: Honoraria (self): Chugai Pharma, Diichi Sankyo, Yakult Honsha, Takeda, Bayer, Merck Serono, Taiho Pharmaceutical, Lilly, Sanofi, Ono Pharmaceutical, MSD, Bristol-Meyers Squibb. T. Masuishi: Honoraria (self): Takeda, Chugai, Merck Bio Pharma, Taiho, Bayer, Lilly Japan, Yakult Honsha, Sanofi; Research grant/Funding (institution): MSD, Daiichi Sankyo, Ono. Y. Kawamoto: Honoraria (self): Taiho Pharmaceutical. S. Yuki: Honoraria (self): Taiho Pharmaceutical; Honoraria (self): Bayer. K. Yamamoto: Honoraria (self): Taiho Pharmaceutical. T. Yamanaka: Honoraria (self): Bayer. Y. Komatsu: Speaker Bureau/Expert testimony: ASAHNippon Kayaku Co.,Ltd. I Kasei Pharma Corporation, Bristol-Myers Squibb Co, Eli Lilly Japan K.K. Mitsubishi Tanabe Pharma Corporation, Nipro Corporation, Ono Pharmaceutical Co., Ltd. Pfizer Japan Inc. Sanofi K.K. Taiho Pharmaceutical Co., Ltd. Takeda ; Honoraria (self): Asahi Kasei Pharma Corporation. Bayer Yakuhin, Ltd Chugai Pharmaceutical Co., Ltd. Daiichi Sankyo Company, Limited. Eli Lilly Japan K.K. Kyowa Kirin Co., Ltd. Merck Biopharma Co., Ltd. Sanofi K.K. Shire Japan K.K. Taiho Pharmaceutical Co., Ltd. Yakult Hons; Research grant/Funding (institution): A2 Healthcare Corp. Astellas Pharma Inc. Bayer Yakuhin, Ltd Daiichi Sankyo Company, Limited Dainippon Sumitomo Pharma Co., Ltd. Eisai Co., Ltd. MSD K.K. NanoCarrier Co., Ltd. Ono Pharmaceutical Co., LTD. Parexel International Corporation. Sanofi-aventis S. K. Muro: Honoraria (self), Research grant/Funding (institution): Ono Pharmaceutical; Honoraria (self), Research grant/Funding (institution): Sanofi; Honoraria (self), Research grant/Funding (institution): Daiichi Sankyo; Research grant/Funding (institution): Parexel International; Research grant/Funding (institution): Shionogi Pharmaceutical; Research grant/Funding (institution): Sumitomo Dainippon Pharma; Research grant/Funding (institution): MSD; Research grant/Funding (institution): Mediscience Planning; Research grant/Funding (institution): Solasia Pharma; Research grant/Funding (institution): Merck Serono; Honoraria (self): Eli Lilly; Honoraria (self): Chugai Pharmaceutical; Honoraria (self): Takeda Pharmaceutical; Honoraria (self): Taiho Pharmaceutical; Honoraria (self): Bristol-Meyers Squibb; Honoraria (self): Bayer. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2020.08.561