#445 A MULTICENTRE, NON-INTERVENTIONAL, POST-AUTHORISATION STUDY TO OBSERVE IN DAILY CLINICAL PRACTICE THE TREATMENT DURATION OF PATIENTS TREATED WITH BEVACIZUMAB IN 1ST LINE mCRC IN BELGIUM.

JC. Goeminne, JM. Vandenbulcke, A.Bols, L. Marcelis, J.Arts, B.Naessens, M.De Man, D. Frijns, J.Decaestecker.

Clinique Sainte Elizabeth, Namur Belgium, CHwapi, Tournai Belgium, AZ St Jan, Brugge Belgium, Chirec Cancer Institute, Bruxelles Belgium , AZ St Lucas, Brugge Belgium, AZ Nikolaas Sint-Niklaas Belgium, OLV, Aalst Belgium, Roche SA/NV Belgium, AZ Delta, Roeselare Belgium.

BACKGROUND

According to the Belgian cancer register of 2012 CRC was the second most frequent cancer in women after breast cancer, representing 12,1% of all female cancer cases, and the third most frequent cancer in men after prostatic and lung cancer, representing 12.6% of all male cancer cases. Bevacizumab became available on the Belgian market as a first-line regimen for mCRC in combination with FOLFIRI, FOLFOX and XELOX at the end of 2008. This real life study aims to complement the knowledge on bevacizumab use in current practice in Belgium.

METHODS

This was a multicentre, non-interventional, post-authorisation study in patients with first line chemotherapy for mCRC, for whom the physician decided to prescribe bevacizumab. Dosing and treatment were at the discretion of the investigator and in accordance with Belgian labelling. The conduct of the study did not influence medical decisions or procedures for individual patients. Twenty Belgian centres were involved in the study to collect data of 200 patients. The primary objective was to observe in daily clinical practice the treatment duration of bevacizumab in first line mCRC. Secondary objectives were to determine the PFS of bevacizumab treatment and to identify the reasons for stopping the bevacizumab treatment.

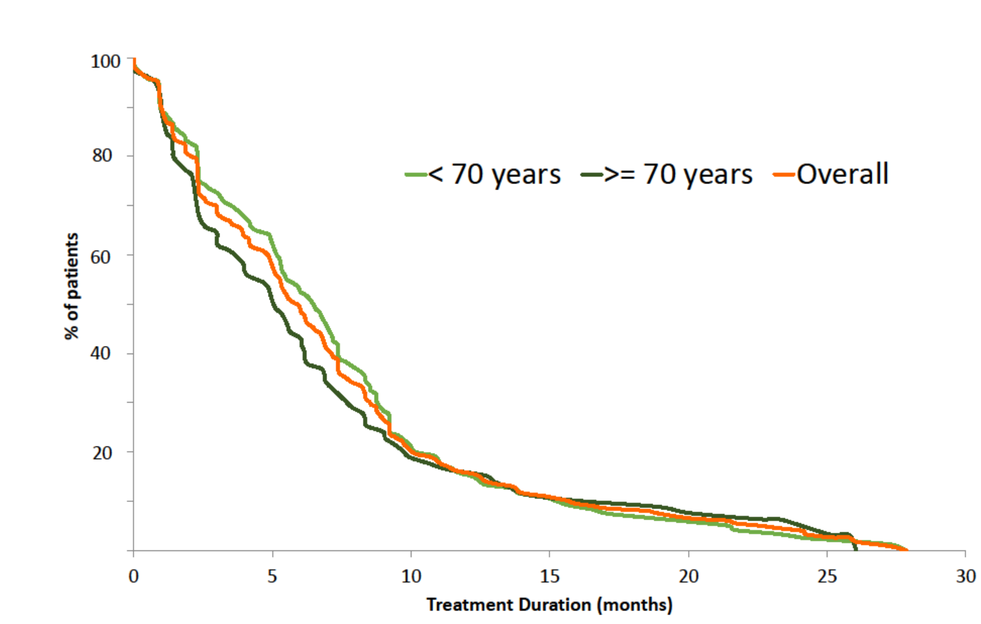
RESULTS

From January 2010 until July 2011, a total of 201 patients were enrolled in the study. 199 patients received bevacizumab. These 199 patients are defined as the Full Analysis Population (FAS). 58.3% of the patients were men, mean age was 66.3 years. Baseline ECOG performance status of 0, 1 or ≥2 was observed in 79 patients (39.7%), 84 patients (42.2%) and 17 patients (8.5%) respectively. 152 (76.4%) patients received FOLFIRI chemotherapy and 39 patients (19.6%) FOLFOX or XELOX chemotherapy. 8 patients began bevacizumab treatment with another chemotherapy combination (4.0%).

Table 1: Demographic characteristics

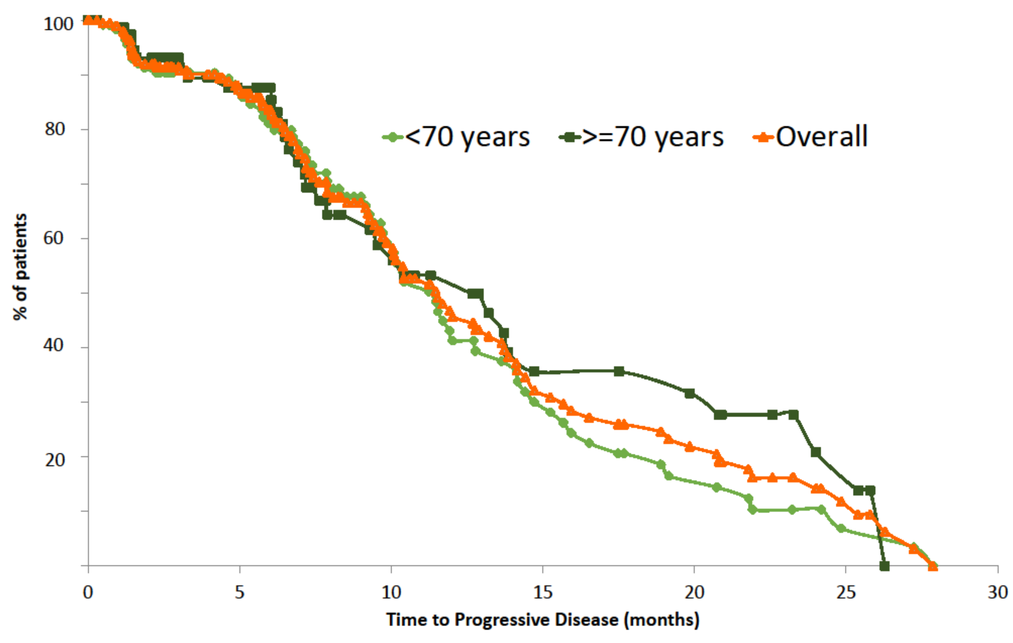
Characteristic n (%)	Overall N=199	FOLFIRI N=152	FOLFOX/XELOX N=39
Mean age at screening (years)	66.3	66.4	65.8
Gender			
Male	116 (58.3)	86 (56.6)	25 (64.1)
Female	83 (41.7)	66 (43.4)	14 (35.9)
Smoking addiction			
Yes	49 (24.6)	36 (23.7)	10 (25.6)
No	117 (58.8)	88 (57.9)	24 (61.5)
Not known	33 (16.6)	28 (18.4)	5 (12.8)
Stage at initial diagnosis			
Stage I	3 (1.5)	3 (2.0)	0 (0.0)
Stage II	22 (11.1)	17 (11.2)	4 (10.2)
Stage III	45 (22.6)	38 (25.0)	6 (15.4)
Stage IV	126 (63.3)	92 (60.5)	28 (71.8)
missing	3 (1.5)	2 (1.3)	1 (2.6)
Adjuvant chemotherapy			
No	126 (63.3)	90 (59.2)	28 (71.8)
Yes	73 (36.7)	62 (40.8)	11 (28.2)
CRC primary location			
Colon Ascending	35 (17.6)	31 (20.4)	4 (10.3)
Colon Descending	12 (6.0)	10 (6.6)	2 (5.1)
Colon Transverse	7 (3.5)	4 (2.6)	3 (7.7)
Colon Sigmoid	75 (37.7)	57 (37.5)	14 (35.9)
Rectum	61 (30.7)	43 (28.3)	15 (38.5)
missing	9 (4.5)	7 (4.6)	1 (2.6)
KRAS mutation status			
wild type	61 (30.7)	42 (27.6)	16 (41.0)
mutant	45 (22.6)	31 (20.4)	12 (30.8)
NK	93 (46.7)	79 (52.0)	11 (28.2)
ECOG performance status at baseline			
0	79 (39.7)	61 (40.1)	16 (41.0)
1	84 (42.2)	67 (44.1)	15 (38.5)
≥2	17 (8.5)	10 (6.6)	6 (15.4)
Not done	19 (9.5)	14 (9.2)	2 (5.1)
Relevant medical history at screening			
Cardiac disorders	27 (13.6)	22 (14.5)	4 (10.3)
Hypertension	88 (44.2)	67 (44.1)	17 (43.6)

Figure 1: Kaplan-Meier graph for treatment duration (N=199)



Overall, the median Kaplan-Meier estimate for treatment duration was 5.95 months (95% CI 5.09-6.80), estimated treatment duration for patients treated with FOLFIRI 6.01 months (95% CI 5.09-6.93), estimated treatment duration for patients treated with FOLFOX/XELOX 4.14 months (95% CI 2.10-6.14). The median Kaplan-Meier estimates for treatment duration were 6.5 months (95% CI 5.26-7.39) for patients <70 years old and 5.09 months (95% CI 3.48-6.24) for patients ≥70 years old. Metastasis in the liver were associated with a higher probability of shorter treatment duration.

Figure 2: Kaplan-Meier graph for Progression Free Survival of bevacizumab treatment in first-line mCRC (N=199)



The median Kaplan-Meier estimate for PFS was 11.53 months (95% CI 9.86-13.73), estimated PFS for the FOLFIRI treated patients 12.78 months (95% CI 9.72-14.42), estimated PFS for the FOLFOX/XELOX treated patients 8.54 months (95% CI 6.21-20.73). The median Kaplan-Meier estimates for PFS were 11.47 months (95% CI 9.72-13.63) for patients <70 years old and 12.68 months (95% CI 7.88-19.84) for patients ≥70 years old.

Table 2: Median Kaplan-Meier estimate for treatment duration and for median PFS

	Overall N=199	FOLFIRI N=152	FOLFOX/XELOX N=39
Estimates for median Treatment duration (months)	5.95 (95% CI 5.09-6.80)	6.01 (95% CI 5.09-6.93)	4.14 (95% CI 2.10-6.14)
Estimates for median PFS (months)	11.53 (95% CI 9.86-13.73)	12.78 (95% CI 9.72-14.42)	8.54 (95% CI 6.21-20.73)

Table 3: Median Kaplan-Meier estimate for treatment duration and for median PFS per age group

	Overall N=199		FOLFIRI N=152		FOLFOXN/XELOX N=39	
	<70 years (N=120)	≥70 years (N=79)	<70 years (N=89)	≥70 years (N=63)	<70 years (N=25)	≥70 years (N=14)
Estimates for median Treatment duration (months)	6.5 (95% CI 5.26-7.39)	5.09 (95% CI 3.48-6.24)	6.70 (95% CI 5.16-7.39)	5.45 (95% CI 3.48-6.80)	5.09 (95% CI 2.37-7.39)	3.24 (95% CI 1.38-6.14)
Estimates for median PFS (months)	11.47 (95% CI 9.72-13.63)	12.68 (95% CI 7.88-19.84)	12.02 (95% CI 9.72-14.72)	13.21 (95% CI 7.88-19.84)	8.54 (95% CI 6.14-15.93)	6.44 (95% CI 4.63-NE)

The main reason for ending bevacizumab treatment was progressive disease 93/199 (46.7%). For patients treated with FOLFIRI, FOLFOX or XELOX these reasons were: progressive disease 87/191 (45.5%), metastasectomy 13/191 (6.8%), unacceptable toxicity 12/191 (6.3%), patient died 9/191 (4.7%), one patient withdrew consent and 1 patient was lost for follow-up. For 68/191 patients, investigators mentioned other reasons. These other reasons were: physician's decision 39/68, toxicity 22/68, 3/68 patients developed another malignancy, for 2/68 patients the other reason was progressive disease and 2/68 patient had to undergo surgery. In table 4 the reasons for ending bevacizumab treatment are pooled with corresponding other reasons.

Table 4: Grouped reasons (reasons and other reasons) for ending bevacizumab treatment in patients treated with FOLFIRI, FOLFOX or XELOX (N=191)

Reason for ending treatment n (%)	FOLFIRI or FOLFOX/XELOX N=191	FOLFIRI N=152	FOLFOX/XELOX N=39
Progressive disease	89 (46.6)	71 (46.7)	18 (46.2)
Physician decision	39 (20.4)	34 (22.4)	5 (12.8)
Unacceptable toxicity	34 (17.8)	26 (17.1)	8 (20.5)
Metastasectomy	13 (6.8)	9 (5.9)	4 (10.3)
Patient died	9 (4.7)	5 (3.3)	4 (10.3)
Other malignancy	3 (1.6)	3 (2.0)	0 (0)
Surgery	2 (1.0)	2 (1.3)	0 (0)
lost for follow up	1 (0.5)	1(0.7)	0 (0)
Patient withdrew consent	1 (0.5)	1(0.7)	0 (0)

Progressive disease was the main reason for ending treatment followed by physician decision in FOLFIRI treated patients and by toxicity in FOLFOX/XELOX treated patients.

Spontaneous Adverse Events related to treatment needed to be reported by the investigators to the drug safety department of Roche SA. No new safety alerts were observed during this study. The toxicity profile confirmed what was known with bevacizumab.

CONCLUSIONS

The observed treatment duration and PFS are in line and even tend to be higher compared to recently published studies like CALGB-80405 and FIRE-3. The most likely reason for stopping bevacizumab treatment was progressive disease.

References: Belgian Cancer Registry - www.kankerregister.org absolute figures 2012.

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Clinical trial information: NCT01089413

Corresponding Authors: JC. Goeminne e-mail: jeancharles.goeminne@cmsenamur.be; J.Decaestecker e-mail: Jochen.Decaestecker@azdelta.be.

Disclosure This study was funded by Roche Belgium sa/nv, Brussels.

ESMO WORLD CONGRESS ON GASTROINTESTINAL CANCER 2015
1-4 JULY 2015 BARCELONA, SPAIN.

WCGC 2015 254--P

Clinical Colon Cancer

Jean-Charles Goeminne

DOI: 10.3252/pso.eu.17wcgc.2015

Poster presented at: ESMO 17th World Congress on Gastrointestinal Cancer 1–4 JULY 2015 BARCELONA, SPAIN