Retrospective comparison efficacy and toxicity FOLFIRI plus aflibercept or bevacizumab in patients with metastatic colorectal cancer: results of the multicenter observational study

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Introduction:

The aim of this study was to compare FOLFIRI with aflibercept or bevacizumab efficacy and toxicity in the 2nd line chemotherapy (CT) in patients (pts) with metastatic colorectal cancer (mCRC).

Methods:

We analyzed prospective database of pts with mCRC in 18 cancer clinics in Russia who received FOLFIRI with aflibercept or bevacizumab in the 2nd line CT. The primary endpoints were progression free survival (PFS) and objective response rate (ORR). A multivariate regression analysis was performed with the SPSS v.20 software package.

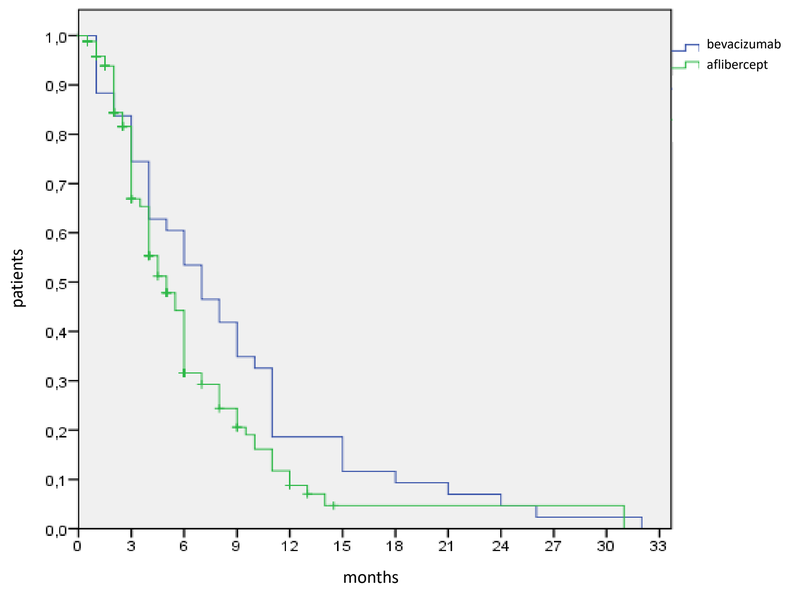
Results: The study included 271 pts (81 in bevacizumab group and 190 in aflibercept group). There were no differences between groups by age, sex, number of organs with metastases, localization of metastases, mRAS (43% vs 42%), synchronous metastases (72% vs 67%), adjuvant CT (17% vs 8%), comorbidities and concomitant therapy. ORR was achieved in 15 (18.5%) pts with bevacizumab and in 39 (20.5%) pts with aflibercept (p=0.4) (Tab.1).

Tab.1. Patient's characteristics

Factors	Bevacizumab	Aflibercept
female	39 (48%)	93 (49%)
T4	30 (37%)	68 (36%)
N1-2	48 (59%)	108 (57%)
Synchronous metastases	58 (72%)	128 (67%)
Adjuvant chemotherapy	14 (17%)	1 (8%)
Liver metastases	64 (79%)	142 (76%)
Lung metastases	27 (33%)	72 (39%)
Bone metastases	6 (7%)	9 (5%)
m*RAS* or m*BRAF*	35 (43%)	80 (42%)

Median PFS was 5 months (95%CI 3.8-6.1) in aflibercept group and 7 months (95% CI 5.7-8.3) in bevacizumab group (HR 1.4, 95%CI 0.99-2.1, p=0.04) (Graph. 1). Cox regression analysis didn't show any statistical difference between treatment groups in term of PFS after adjusted by age and mRAS (HR 1.3, 95%CI 0.9-1.9, p=0.2) (Tab.2) .

Graph.1. Progression free survival



Tab.2. Cox regression analysis

Factor	p	HR	95,0% CI for HR	
			low	high
wt*RAS* and wt*BRAF*	0.01	0.8	0.7	0.9
age	0.5	1.0	0.9	1.0
Bevacizumab vs aflibercept	0.2	1.3	0.9	1.9

Adverse events (AEs) were reported in 216 (79.7%) pts. There were nonsignificant differences between treatment groups in terms of overall toxicities (58% vs 72%, p=0.1), Gr1-2 (54% vs 61%, p=0.6), Gd3-4 (20% vs 22%, p=0.4). Among Gd3-4 nonhematologic AEs arterial hypertension (2 vs 9.5%), and diarrhea (0 vs 5.4%) were often seen in pts with aflibercept. The thrombosis was associated with bevacizumab only (10% vs 1.8%, p=0.015) (Tab.3).

Tab.3. Adverse events

Adverse events	Bevacizumab		Aflibercept	
	1-2 gr.	3-4 gr.	1-2 gr.	3-4 gr.
neutropenia	7 (14%)	4 (8%)	21 (12.5%)	12 (7%)
febrile neutropenia	-	0	-	1 (1%)
thrombocytopenia	1 (2%)	0	9 (5%)	0
anemia	1 (2%)	0	7 (4%)	0
diarrhea	7 (14%)	0	22 (13%)	9 (5.4%)
stomatitis	0	0	5 (3%)	0
asthenia	10 (20%)	1 (2%)	15 (9%)	1 (1%)
nausea	10 (20%)	0	29 (17%)	0
vomiting	4 (8%)	0	8 (5%)	0
arterial hypertension	8 (16%)	1 (2%)	45 (27%)	16 (9.5%)
liver toxicity	2 (4%)	1 (2%)	1 (1%)	1 (1%)
thrombosis	5 (10%)	0	3 (1.8%)	0

Conclusion:

There were no statistical differences in terms of ORR and PFS between bevacizumab or aflibercept plus FOLFIRI in 2nd line treatment in pts with mCRC. AEs were more often seen in aflibercept group except of thrombosis.