To patients and their families

Cetuximab versus Bevacizumab in Metastatic Colorectal Cancer: A Comparative Effectiveness and Patient-Reported Outcomes Multi-Cohort Study

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Background and importance

Uncertainty exists regarding comparative effectiveness of cetuximab *versus* bevacizumab in metastatic colorectal cancer (mCRC), due to conflicting evidence of previous randomised trials and the absence of Quality of Life (HRQoL) studies.

Aim and objectives

To assess simultaneously clinical effectiveness and patient-reported tolerability of the different targeted treatment options, through:

a) A main retrospective cohort study, in order to compare real-world clinical outcomes from both antibodies;

b) A smaller prospective cohort study for the purpose of measuring patient-reported outcomes (PROs), nested in the main study.

Materials and Methods

Retrospective cohorts were defined by treatment line, and subgroups by (K)RAS status and tumour sidedness. We compared:

a) Effectiveness outcomes: response rates, progression-free survival (PFS) and overall survival (OS);

b) PROs, which were measured prospectively through EORTC disease-specific instruments.

Results

Between 2010 and 2018, 311 mCRC patients were included in overall analysis, of which 44 were further allocated to PROs nested cohorts.

In full analyses, PFS (first-line: HR=0.85; P=0.26; second-line: HR=1.16; P=0.51, OS (first-line: HR=0.83; P=0.26; second-line: HR=0.88; P=0.58), and response rates were similar between treatment arms (Figure 1 A & B, Table 1).

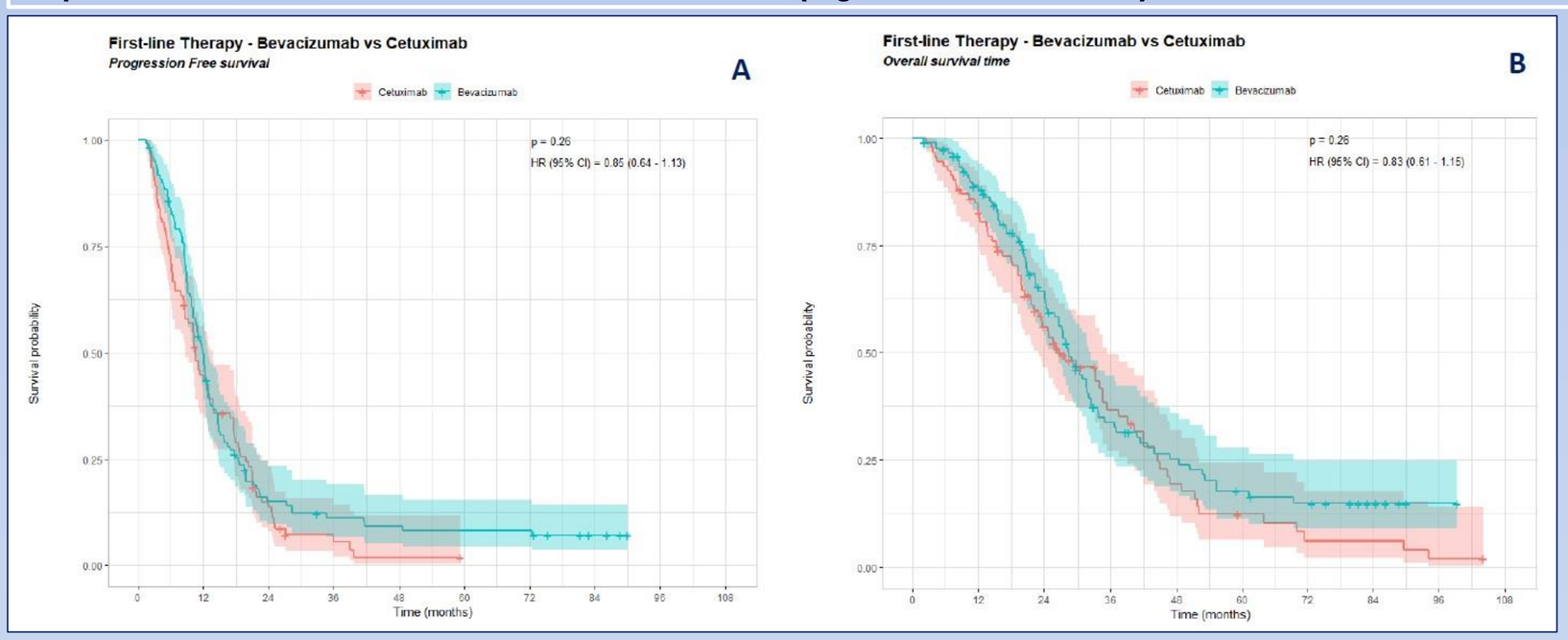

Figure 1 – Kaplan–Meier estimates of PFS (A) and OS (B) of full first-line cohorts, according to treatment group.

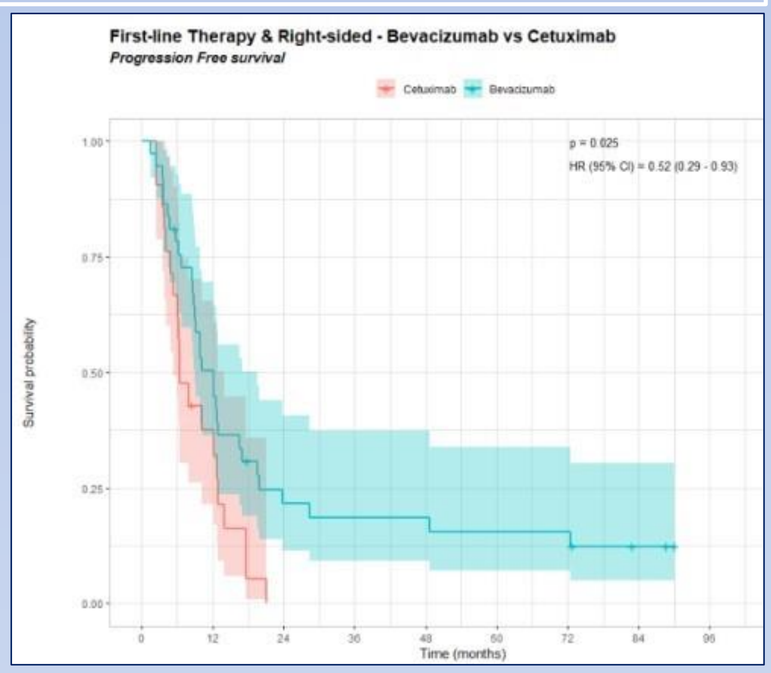

Figure 2 – Kaplan–Meier estimates of PFS for the subgroup of patients with right-sided primary tumour location.

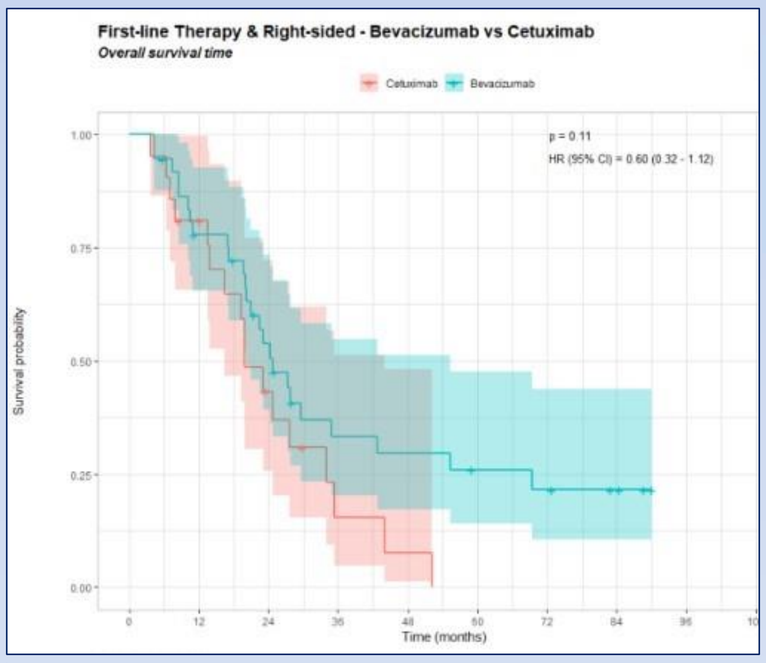

Figure 3 – Kaplan–Meier estimates of OS for the subgroup of patients with right-sided primary tumour location.

	First-line treatment		Second-line treatment		First-line treatment: (K)RASwt subgroup		First-line treatment: Left-sided tumours subgroup		First-line treatment: Right-sided tumours subgroup	
	Bevacizumab (N=121)	Cetuximab (N=93)	Bevacizumab (N=67)	Cetuximab (N=30)	Bevacizumab (N=30)	Cetuximab (N=93)	Bevacizumab (N=83)	Cetuximab (N=72)	Bevacizumab (N=37)	Cetuximab (N=21)
Best response % (n)										
CR	9.9 (12)	9.7 (9)	0.0 (0)	6.7 (2)	13.3 (4)	9.7 (9)	7.2 (6)	9.7 (7)	16.2 (6)	9.5 (2)
PR	42.2 (51)	33.3 (31)	17.9 (12)	10.0 (3)	50.0 (15)	33.3 (31)	41.0 (34)	36.1 (26)	43.2 (16)	23.8 (5)
SD	33.1 (40)	34.4 (32)	47.8 (32)	26.7 (8)	23.3 (7)	34.4 (32)	38.6 (32)	30.6 (22)	21.6 (8)	47.6 (10)
PD	8.3 (10)	20.4 (19)	26.9 (18)	50.0 (15)	6.7 (2)	20.4 (19)	6.0 (5)	20.8 (15)	13.5 (5)	19.0 (4)
Not evaluable	6.6 (8)	2.2 (2)	7.5 (5)	6.7 (2)	6.7 (2)	2.2 (2)	7.2 (6)	2.8 (2)	5.4 (2)	0.0 (0)
Objective response % (n)	55.8 (63)	44.0 (40)	19.4 (12)	17.9 (5)	67.9 (19)	44.0 (40)	51.9 (40)	47.1 (33)	62.9 (22)	33.3 (7)

Table 1 – Response Rates of all analysed cohorts and subgroups.

In subgroup analyses (first-line), we found a survival difference favouring bevacizumab in right-sided tumours (PFS: HR=0.52; P=0.025; OS: HR=0.60; P=0.11; Figures 2 & 3), but not in left-sided or (K)RAS wild-type tumours. Response rates were higher for bevacizumab in patients bearing right-sided primaries (Table 1).

PROs:

- Higher % of patients in cetuximab arm experienced clinically meaningful (≥10%) deterioration of HRQoL comparing to bevacizumab cohort: 53.8% vs 18.2% at 6 weeks and 66.7% vs 12.5% at 12 weeks (Figure 4A);
- Progressively increased scoring on symptom scales in cetuximab cohort during follow-up (Figure 4B).

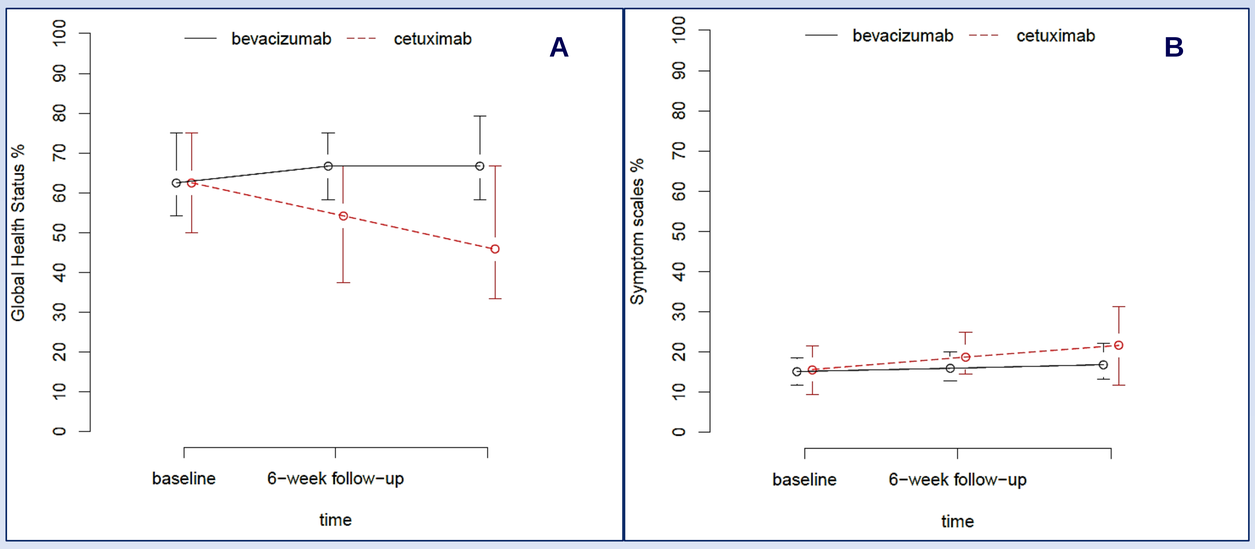

Figure 4 – Global Health Status (A) and Symptom Scales (B) median scores at baseline, 6-week and 12-week follow-up.

Conclusion and Relevance

We found evidence suggesting bevacizumab and cetuximab-containing regimens result in similar clinical effectiveness outcomes in mCRC, except for right-sided tumours, where bevacizumab performed substantially better. Cetuximab led to a progressive negative impact on HRQoL, when compared to baseline and bevacizumab. These findings should be further explored through randomised studies.