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

R.P. Marques 1,2, A.R. Godinho 3, P. Heudtlass 3, H.L. Pais 4, A. Quintela 4, J.P. Lopes da Cruz 1, A.P. Martins 2
1. Centro Hospitalar Universitário de Lisboa Norte – Hospital de Santa Maria, Pharmacy Department, Lisboa, Portugal; 2. Faculty of Pharmacy of the University of Lisbon, Pharmacoepidemiology Department, Lisboa, Portugal; 3. Centre for Health Evaluation and Research, Epidemiology Department, Lisboa, Portugal; 4. Centro Hospitalar Universitário de Lisboa Norte – Hospital de Santa Maria, Medical Oncology Department, Lisboa, Portugal

Contact Information: Rui Pedro Marques, PharmD, PhD: rui.p.marques@chln.min-saude.pt

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 main retrospective cohort study, in order to compare real-world clinical outcomes from both antibodies;
- 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:
- Effectiveness outcomes: response rates, progression-free survival (PFS) and overall survival (OS);
- 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).

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 compared 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).

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.