SAFETY AND EFFECTIVENESS OF BEVACIZUMAB IN COMBINATION WITH CHEMOTHERAPY IN PATIENTS WITH METASTATIC COLORECTAL CANCER: UPDATED RESULTS FROM A LARGE CZECH OBSERVATIONAL REGISTRY


Background
- We have already reported our experience from the Czech Specific Therapeutic Programme, the initial part of a large Czech community-based observational registry monitoring safety and efficacy of bevacizumab in combination with standard chemotherapy for patients with metastatic colorectal cancer (mCRC).
- We also reported the updated results from the whole registry (6530) of patients treated with bevacizumab across all lines in 2009 and in the 1st setting (lost 394).
- As one-quarter of enrolled patients were ≥65 years of age, important decisions related to intensity of chemotherapy treatment and use of biosimilars had to be taken (Figure 1). Hence, we focused on possible differences between the two age groups (<65 years and ≥65 years) in efficacy and safety.

Methods
- Data from 1618 unselected patients with mCRC who received bevacizumab plus chemotherapy between Oct 2005 and Oct 2009 were collected from 22 centers.
- Chemotherapy regime choice was at the physicians’ discretion.
- Patients received bevacizumab 5 mg/kg every 3 or 7.5 mg/kg every 3 weeks depending on the chemotherapy regime.
- Patients were followed-up until death or loss to follow-up.
- Data were reported every 3 months including disease status per oncologist assessment.
- Both overall (OS) and progression-free survival (PFS) times were assessed using standard Kaplan-Meier methodology.

Results
- Median follow-up time in all patients was 58 months and median follow-up for 1st-line was 77 months. Safety data are available for 1658 patients. 1914 patients were treated with bevacizumab within the 1st setting; efficacy results were obtained from 2300 patients for PFS, and from 1244 patients for OS.
- 5 patients with invalid birth date were excluded from some analyses.
- First-line treatment was completed in 896 patients, 565 patients are still on treatment, and data for 133 patients are missing (Figure 2).
- The most frequent chemotherapy regimens included Capecitabine (478 patients; 34%), FOLFOX 4 (444 patients; 33%), FOLFIRI (141 patients; 10%) and XELIRI (92 patients; 7%). Figure 3 shows a comparison between the two age groups.
- Median treatment duration was 24 weeks (Figure 4).

Conclusions
- Efficacy and safety of bevacizumab plus chemotherapy in the Czech population based on clinical registry data appear to be consistent with those observed in other observational trials.
- Bevacizumab is effective in the elderly population (≥65 years), and no differences in efficacy were identified between the two age groups (<65 years and ≥65 years). Bevacizumab is well tolerated within the 65 years age group and is similar to that of the <65 year age group.

References
- Berry SR, et al. ASCO GI2008; Abst #350.
- Ackland SP, et al. ASCO GI2008; Abst #463.
- Berioldi S, et al. ASCO GI2008; Abst #1104.

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Figure 1. Patients’ age (1st-line mCRC)

Figure 2. Gender and treatment status (1st-line patients, N=1290)

Figure 3. Type of chemotherapy regimen (1st-line patients, N=1394)

Figure 4. Duration of bevacizumab treatment (1st-line, in patients with bevacizumab treatment termination)

Figure 5. PFS by age (1st-line patients)

Figure 6. Overall survival by age (1st-line patients)

Figure 7. Adverse reactions by age related to bevacizumab treatment (all patients)

Figure 8. Adverse reactions by age related to bevacizumab treatment (all patients)

Safety
- Adverse events (AEs) considered to be related to bevacizumab were reported in 162 patients (<65 years [72.0%]). AEs included hypertension (60 patients; 3.6%), proteinuria (28 patients; 1.7%), arterial thromboembolic event (TE; 8 patients; 0.5%), venous TE (31 patients; 1.9%; 2 deaths), diarrhea (4 patients; 0.2%), bleeding (6 patients; 0.4%), vomiting (5 patients; 0.3%), GIT perforation (5 patients; 0.2%), and other (25 patients; 1.5%).
- Grade 3/4 AEs considered to be related to bevacizumab were reported in 53 patients (65 years [67.9%]). Grade 3/4 AEs included hypertension (21 patients; 1.3%), proteinuria (1 pt; 0.1%), arterial TE (4 patients; 0.2%), venous TE (8 patients; 0.5%; 2 deaths), diarrhea (1 patient; 0.2%), bleeding (4 pt; 0.2%), vomiting (6 pt; 0.4%), GIT perforation (2 pt; 0.1%), and other (12 patients; 0.7%).
- Comparison between the two age groups is described in Figures 7 and 8.

Figure 8. Adverse reactions by age related to bevacizumab treatment (all patients)