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| **Supplementary Table S2.** Compliance with REMARK guidelines |
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| **Introduction** |   |
|   | Marker analyzed is HOXB9. |
|   | Objectives; to determine whether HOXB9 is predictive for benefit from bevacizumab-containing first-line chemotherapeutic treatment. |
|   | Hypotheses; HOXB9 positivity is associated with poor response to bevacizumab treatment. |
| **Materials and Methods** |   |
|  - Patients  | Metastatic colorectal cancer patients treated or not with a bevacizumab-containing first-line chemotherapeutic regimen. |
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|  - Specimen characteristics | Paraffin-embedded tissue from biopsies specimens obtained at the diagnosis of metastatic colorectal cancer with at least 80% of tumor cellularity. |
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|  - Assay method  | IHC analysis was assessed evaluating nuclear positivity and staining intensity (- negative, + weak, ++ moderate, +++ intense). IHC analysis was performed blinded to the study endpoint. Detailed protocol described in Materials and Methods section. |
|  - Study design  | Retrospective analysis of paraffin-embedded samples from patients treated or not with a bevacizumab-containing first-line chemotherapeutic regimen collected between October 2004 and July 2015. The median follow-up was 23.7 months. |
|   | Clinical end-point, progression free survival (PFS). |
|   | Sample size determined by the availability of tissue. |
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|  - Statistical methods  | Survival curves of patients in each treatment arm stratified according to HOXB9 levels were drawn by Kaplan-Meier estimates and compared by log rank test. |
|   | Multivariate analysis of PFS, with stepwise variable selection, was conducted by Cox’s proportional hazard regression model to assess the independent predictive value of HOXB9. |
|   | Relationship between HOXB9 expression and clinic-pathological characteristics was examined using the χ2 method for linear trend. |
| **Results** |   |
|  - Data  | Patient’s characteristics reported in supplementary Table S1. |
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|  - Analysis and presentation | Univariate and multivariate analyses results reported in Table 1.  |
|   | Correlation between HOXB9 expression and clinic-pathologic characteristic displayed in supplementary Table S3. |
|   | Kaplan–Meier survival curves for effect of HOXB9 expression on progression free survival in Figure 5. |
| **Discussion**  |   |
|   | HOXB9 had no prognostic value in patients treated with a first-line chemotherapeutic regimen non-containing bevacizumab. However, patients affected by an HOXB9-negative tumor had a significantly longer PFS compared with those with an HOXB9-positive tumor if treated with a first-line regimen containing bevacizumab. Study limited by sample size and by retrospective analysis. |