Increased mean corpuscular volume as a predictor of response during bevacizumab treatment

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SUMMARY
Background: Remission during sunitinib (a multikinase inhibitor and antiangiogenic drug) treatment correlates with appearance of macrocytosis. There are some suggestions that bevacizumab, an antiangiogenic drug, may result in macrocytosis as well. There are no published data available on the influence of bevacizumab on macrocytosis. This paper attempted to answer the question: does bevacizumab induce macrocytosis being a predictor of the response?

Methods: Between August 2008 and August 2011, 53 patients (29 male and 24 female) were treated with bevacizumab in the combination with chemotherapy at the Oncological Department, University Hospital in Krakow, Poland. Efficacy of bevacizumab was assessed on the basis of the computer tomography scans performed every 3 months within the period of 12 months. Concurrently, mean corpuscular volume (MCV) was evaluated and correlated to the response of the treatment.

Results: The percentage increase of MCV compared to baseline at 3, 6, 9 and 12 months was 3.7%, 9.2%, 8.7% and 11.8% respectively. The mean value of baseline MCV was 85.3 fl. The mean value of MCV at 3, 6, 9 and 12 months was 90.5 fl, 93 fl, 91.8 fl and 93.1 fl respectively. Macrocytosis did not occur in our study but an increase of MCV was observed within bevacizumab therapy. It was closely related to the response of the treatment. It seems that an increase of MCV can be a predictive agent of bevacizumab response.

Conclusion: Bevacizumab does not induce macrocytosis. Increased MCV after treatment with bevacizumab is related to the treatment response. MCV can be a predictor of the response during bevacizumab treatment. A small number of the observed patients requires further investigations.

Key words: Antibodies, Monoclonal; Humanized; Erythrocyte Indices; Antiangioplastic Agents; Treatment Outcome

INTRODUCTION
Bevacizumab is a humanized monoclonal antibody binding and neutralizing all isoforms of vascular endothelial growth factor (VEGF). VEGF is the most powerful pro-angiogenic factor. Multikinase inhibitor – sunitinib is the next antiangiogenic drug. Remission in the course of treatment with sunitinib correlates with appearance of macrocytosis (1). Mean corpuscular volume (MCV) changes from 82 to 92 fl. Macrocytosis was defined as mean corpuscular volume above 100 fl (2). The aim of our study was to evaluate the correlation between bevacizumab response and MCV serum level. The study was based on the assumption that both sunitinib and bevacizumab are the antiangiogenic agents and may have similar predictor factors.

MATERIAL AND METHODS
Fifty-three patients (29 male and 24 female) were treated with bevacizumab in the combination with chemotherapy at the Oncological Department, University Hospital in Krakow, Poland in the period from August 2008 to August 2011. Bevacizumab was administered intravenously every 2 or 3 weeks with chemotherapy. Doses of bevacizumab ranged from 5-15 mg/kg of a body mass.

Efficiency of bevacizumab was assessed on the basis of the CT scans performed after 3, 6, 9 and 12 months of treatment. Response to the treatment was estimated according to RECIST scale. A small number of the observed patients requires further investigations.

3 months during the period of 12 months. The correlation between the response to the treatment and MCV was estimated every 3 months.

RESULTS
Seven patients (13.2%) among 53 treated with bevacizumab were excluded from the analysis due to missing data on MCV and 1 patient (1.9%) was excluded because of his premature death. Finally, 45 patients treated with bevacizumab in the combination with chemotherapy were evaluated. The patients’ mean age was 55 years.

Table 1 shows patients baseline characteristics. MCV was evaluated every 3 months during the period of 12 months. Gradual increase of mean corpuscular volume in comparison to baseline value was observed. Table 2 shows an increase of mean corpuscular volume within bevacizumab therapy. In the control CT scans performed at 3, 6, 9 and 12 months of bevacizumab treatment, progression of the disease was revealed in 28 patients (62.3%) and stabilization in 6 patients (13.3%). Further 6 patients (13.3%) have confirmed treatment with bevacizumab until now. The next 5 patients (11.1%) discontinued treatment due to toxicity. Reasons for completion of the treatment with bevacizumab are presented in Table 3.
A few data on the correlation between response to some tyrosine kinase inhibitors (imatinib, sunitinib) and macrocytosis occurrence have been published so far (1, 6-8). In case of other tyrosine kinase inhibitors such as: sorafenib and erlotinib – macrocytosis does not occur (7, 8). The probability of macrocytosis increases with the duration of treatment. Macrocyclotis develops at average after 3 cycles, which usually means 17 weeks of therapy with sunitinib (1). Macrocytosis was diagnosed regardless the type of neoplasm when sunitinib was used (1, 6-8). Sunitinib-induced macrocytosis is reversible with drug discontinuation (7). Macrocytosis seems to be a predictive factor for response to the therapy. Bevacizumab-humanized monoclonal antibody is an antiangiogenic drug partly similar to sunitinib. Insufifient data does not explain the presence of macrocytosis / increased MCV and potential correlation with the results of bevacizumab treatment. In the presented study, macrocytosis did not occur during bevacizumab therapy. But, an increase of mean corpuscular volume was demonstrated. It was closely related to the response to the treatment with bevacizumab. It seems that an increasing mean corpuscular volume can be a predictive factor of bevacizumab response. However, considering heterogeneity of the sample (37% of the patients received concurrently capcitabine which causes macrocytosis) and a small number of patients enrolled to the analysis, further investigations with numerous patients are recommended.

CONCLUSIONS

Bevacizumab does not induce macrocytosis. Increased MCV after treatment with bevacizumab is related to the treatment response. Increased MCV can be a predictor of the response during bevacizumab treatment. A small number of the observed patients requires further investigations.

Conflict of interest

We declare no conflicts of interest.

REFERENCES