Stotz M, Gerger A, Eisner F, Szkandera J, Loibner H, L Ress A, Kornprat P, A Zoughbi W, Seggewies FS, Lackner C, Stojakovic T, Samonigg H, Hoefler G, Pichler M (2013) Increased neutrophil-lymphocyte ratio is a poor prognostic factor in patients with primary operable and inoperable pancreatic cancer. *Br J Cancer* **109**: 416–421.

Szkandera J, Absenger G, Liegl-Atzwanger B, Pichler M, Stotz M, Samonigg H, Glehr M, Zacherl M, Stojakovic T, Gerger A, Leithner A (2013) Elevated preoperative neutrophil/lymphocyte ratio is associated with poor prognosis in soft-tissue sarcoma patients. *Br J Cancer* **108**: 1677–1683.

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Reply: Comment on 'A derived neutrophil to lymphocyte ratio predicts clinical outcome in stage II and III colon cancer patients'

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We would like to thank Balta *et al* (2013) for their valuable comments and suggestions on our study 'A derived neutrophil to lymphocyte ratio predicts clinical outcome in stage II and III colon cancer patients'. The results of our study show that the derived neutrophil to lymphocyte ratio (dNLR; absolute count of neutrophils divided by the absolute white cell count minus the absolute count of neutrophils) and the neutrophil to lymphocyte ratio (NLR) are independent prognostic markers for time to recurrence and overall survival in patients with stage II and III colon cancer (Absenger *et al*, 2013). In contrast to many other previously proposed biomarkers, the dNLR and NLR are relatively cheap and easily determinable laboratory parameters, which would allow a widespread clinical use.

Recent data indicate that inflammation plays a critical role in the pathogenesis and progression of cancer. Systemic inflammatory response to tumours causes changes in the haematological components. The dNLR and NLR have recently been shown to negatively influence the clinical outcome in various cancer entities, including kidney cancer, soft-tissue sarcoma, pancreatic cancer and colon cancer (Procter *et al*, 2012; Absenger *et al*, 2013; Stotz *et al*, 2013; Szkandera *et al*, 2013; Pichler *et al*, 2013a). In most studies including our study, however, major potential confounding factors, such as local or systemic infection, ischaemia, acute coronary syndrome, metabolic syndrome, diabetes mellitus and renal or hepatic dysfunction, that might affect the neutrophil and lymphocyte counts have not been taken into account (Tamhane *et al*, 2008; Azab *et al*, 2012; Buyukkaya *et al*, 2012; Biyik *et al*, 2013; Gary *et al*, 2013). As the preoperative white blood cell count was obtained within 3 days before surgery in our study, at least local or systemic infections or inflammatory diseases could be relatively reliable excluded. However, we absolutely agree with Balta *et al* (2013) that a combination of multiple serum inflammatory biomarkers such as dNLR, NLR, CRP, fibrinogen, platelet to lymphocyte ratio and all possible confounding factors should be included in further studies, preferentially in prospective trials (Shiu *et al*, 2008; Demirkol *et al*, 2013; Son *et al*, 2013; Pichler *et al*, 2013b).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Absenger G, Szkandera J, Pichler M, Stotz M, Arminger F, Weissmueller M, Schaberl-Moser R, Samonigg H, Stojakovic T, Gerger A (2013) A derived neutrophil to lymphocyte ratio predicts clinical outcome in stage II and III colon cancer patients. *Br J Cancer* **109**: 395–400.

Azab B, Daoud J, Naeem FB, Nasr R, Ross J, Ghimire P, Siddiqui A, Azzi N, Rihana N, Abdallah M, Azzi N, Patel P, Kleiner M, El-Sayegh S (2012) Neutrophil-to-lymphocyte ratio as a predictor of worsening renal function in diabetic patients (3-year follow-up study). *Ren Fail* **34**: 571–576.

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Balta S, Demirkol S, Unlu M, Arslan Z, Celik T (2013) Comment on 'A derived neutrophil to lymphocyte ratio predicts clinical outcome in stage II and III colon cancer patients'. *Br J Cancer;* **109**(12): 3125–3126.

Biyik M, Ucar R, Solak Y, Gungor G, Polat I, Gaipov A, Cakir OO, Ataseven H, Demir A, Turk S, Polat H (2013) Blood neutrophil-to-lymphocyte ratio independently predicts survival in patients with liver cirrhosis. *Eur J Gastroenterol Hepatol* **25**: 435–441.

Buyukkaya E, Karakas MF, Karakas E, Akçay AB, Kurt M, Tanboga IH, Sen N (2012) Correlation of neutrophil to lymphocyte ratio with the presence and severity of metabolic syndrome. *Clin Appl Thromb Hemost* doi:10.1177/1076029612459675.

Demirkol S, Balta S, Celik T, Arslan Z, Unlu M, Cakar M, Kucuk U, Demirbas S, Iyisoy A, Yokusoglu M (2013) Assessment of the relationship between red cell distribution width and cardiac syndrome X. *Kardiol Pol* **71**: 480–484.

Gary T, Pichler M, Belaj K, Hafner F, Gerger A, Froehlich H, Eller P, Pilger E, Brodmann M (2013) Neutrophil-to-lymphocyte ratio and its association with critical limb ischemia in PAOD patients. *PLoS One* **8**: e56745.

Pichler M, Hutterer GC, Stoeckigt C, Chromecki TF, Stojakovic T, Golbeck S, Eberhard K, Gerger A, Mannweiler S, Pummer K, Zigeuner R (2013a) Validation of the pre-treatment neutrophil-lymphocyte ratio as a prognostic factor in a large European cohort of renal cell carcinoma patients. *Br J Cancer* **108**: 901–907.

Pichler M, Hutterer GC, Stojakovic T, Mannweiler S, Pummer K, Zigeuner R (2013b) High plasma fibrinogen level represents an independent negative prognostic factor regarding cancer-specific, metastasis-free, as well as overall survival in a European cohort of non-metastatic renal cell carcinoma patients. *Br J Cancer* **109**: 1123–1129.

Proctor MJ, McMillan DC, Morrison DS, Fletcher CD, Horgan PG, Clarke SJ (2012) A derived neutrophil to lymphocyte ratio predicts survival in patients with cancer. *Br J Cancer* **107**: 695–699.

Shiu YC, Lin JK, Huang CJ, Jiang JK, Wang LW, Huang HC, Yang SH (2008) Is C-reactive protein a prognostic factor of colorectal cancer? *Dis Colon Rectum* **51**: 443–449.

Son HJ, Park JW, Chang HJ, Kim DY, Kim BC, Kim SY, Park SC, Choi HS, Oh JH (2013) Preoperative Plasma Hyperfibrinogenemia is Predictive of Poor Prognosis in Patients with Nonmetastatic Colon Cancer. *Ann Surg Oncol* **20**: 2908–2913.

Stotz M, Gerger A, Eisner F, Szkandera J, Loibner H, L Ress A, Kornprat P, A Zoughbi W, Seggewies FS, Lackner C, Stojakovic T, Samonigg H, Hoefler G, Pichler M (2013) Increased neutrophil-lymphocyte ratio is a poor prognostic factor in patients with primary operable and inoperable pancreatic cancer. *Br J Cancer* **109**: 416–421.

Szkandera J, Absenger G, Liegl-Atzwanger B, Pichler M, Stotz M, Samonigg H, Glehr M, Zacherl M, Stojakovic T, Gerger A, Leithner A (2013) Elevated preoperative neutrophil/lymphocyte ratio is associated with poor prognosis in soft-tissue sarcoma patients. *Br J Cancer* **4**: 1–7.

Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS (2008) Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol* **102**: 653–657.

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Comment on 'Histopathologic evaluation of liver metastases from colorectal cancer in patients treated with FOLFOXIRI plus bevacizumab'

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Sir,

We read with interest the article by Loupakis *et al* (2013) entitled 'Histopathologic evaluation of liver metastases from colorectal cancer in patients treated with FOLFOXIRI plus bevacizumab' published in the June 2013 issue of the *British Journal of Cancer*. This paper clearly underlines the positive impact of FOLFOXIRI plus bevacizumab, on the extent of both tumour regression and necrosis, in resected liver metastases from colorectal cancer (CRC). The authors conclude that the addition of bevacizumab leads to a high 'histopathologic activity' as compared

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