Reviewer’s report

Title: Angiogenesis in Cancer of Unknown Primary: Clinicopathological study of CD34, VEGF and TSP-1.

Version: 1 Date: 31 January 2005

Reviewer: Kostas Papazisis

Reviewer’s report:

This is a well-documented study from a group that has already published interesting papers on the field. Expression of angiogenetic and anti-angiogenetic factors is of great interest in this (probably heterogeneous) group of tumors that have a bad prognosis. First it may help us understand the biology of CUP as to whether there are fundamental differences in angiogenesis between CUP and metastatic carcinoma of known primary. More important, the near to absolute overexpression of VEGF in these cases may prompt some clinical trials using novel anti-VEGF treatments, as the authors comment.

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Major Compulsory Revisions
None

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Minor Essential Revisions
1) Introduction, paragraph #3: A small addition of a justification of the study would benefit the manuscript.
For example: "Up to now, there have been no useful prognostic factors other than the classic pathologic and/or laboratory criteria (Culline S et al, J Clin Onc 2002). Immunohistochemical detection of various factors (van de Wouw AJ, Anticancer Res 2004) have not added any prognostic value. Furthermore, as new therapies targeting angiogenesis are emerging (Ferrara N, Oncologist 2004), expression of crucial angiogenesis factors that can be therapeutically targeted is of great interest for the oncologists that deal with CUP. We were prompt to..."
2) Introduction: Please refer to the paper by van de Wouw et al, Anticancer Res 2004, 24, 297. They have studied expression of CD34 and VEGF-A in CUP
3) Table 3, typing error: 59 microvessels/mm2
4) Table 4, typing error: Please correct second line on VEGF expression. If the groups are: Low (<4) and High (>=3), then they overlap!

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Discretionary Revisions
1) Patients and methods, subgroup definition, page 4, 1st line: Please add a reference for the criteria of favorable prognosis (Cross-reference nu 2 [Pavlidis N et al, Eur J Cancer 2003] would be ok)
2) Replace "splachnic" with "visceral" throughout

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

I declare that I have no competing interests.