

Format for ANSWERING REVIEWERS

June 25, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 10900-review.doc).

Title: Spontaneous Regression of Renal Cell Carcinoma – reality or myth?

Author: Matthias Maruschke, Aristotelis G. Anastasiadis and Oliver W. Hakenberg

Name of Journal: *World Journal of Clinical Urology*

ESPS Manuscript NO: 10900

The manuscript has been improved according to the suggestions of editor and reviewers. All changes are highlighted in the text with blue color.

1. Format has been updated according to the comments of the editor:

A short running title of less than 6 words was created.

Author contributions were added.

An abstract not less than 200 words, key words and a summary less than 100 words were added at the beginning of the manuscript.

The numbers of the references were placed in Arabic numerals according to the citation order in the text and were put in square brackets in superscript at the end of citation content or after the cited author's name.

The references in the reference list were provided with PubMed citation numbers, e.g. PMID and DOI.

The references in Table 2 have been revised according to the specification.

2. Revision has been made according to the suggestions of the reviewer:

- (1) The definition of regression on page 4 at the beginning of the chapter "results" (former page 2, 3rd line from bottom) was modified according to the comment of the reviewer: "Spontaneous regression of a malignant tumor or its metastases has been defined as a partial or total disappearance of disease without any treatment or induced by local treatments or interventions like embolisation of the primary tumor."
- (2) Similarly, the definition on page 7, last paragraph (former page 5, line 7 from bottom) was adapted: "More stringently, spontaneous regression of an RCC or its metastases should be defined as a partial or complete regression of a renal neoplasm which has been histologically confirmed first and then regressed either without treatment or sometimes following an intervention, e.g. cytoreductive nephrectomy."
Additionally, the contribution by Horn and Horn (1971) was worked out even more in the

discussion, page 5, last paragraph, in this context: "A remarkable report is that by Horn and Horn (1971) about the induction of an RCC regression in a patient with metastatic disease after the transfusion plasma from another patient of the same family who had experienced spontaneous regression. The authors suggested "some sort of host resistance" in this case, mainly a plasma-related transfer factor, an interferon-like agent or a kind of cytotoxic antibody or a substance mediating cellular immunity [27]."

- (3) For a better explanation of the role of immunosuppression in cancer development after transplantation an addition was added on page 5, first paragraph, line 4: "As a possible reason some authors postulated a lack of immune-surveillance of virus-transformed cells by strong immunosuppression. That may lead to an increased frequency of viral infections and/or virus-induced malignancies. Nevertheless, other types of malignant tumors, which are not associated with viral infections, are frequently increased in transplant recipients, too, in dependence of the duration of exposure to immunosuppression."
- (4) The reviewer recommended a presentation of a histological verification of regression. This fact still remains a problem as already mentioned in the discussion, page 5, because it is a very rare appearance. The best documented cases were reported by Choi Kang et al. 1986 and Hamid and Poller 1986. Therefore it is not feasible to give a histological presentation of a spontaneous regression in this review. There remains only the reference to the cited historical case reports.
- (5) To emphasize the Pansera's hypothesis more, an explanation has been added on page 6, last paragraph: "This phenomenon of morphological similarities between growing tissues, like embryological and cancer cells has its reasoning in a common origin from a precursor stem cell. Thus, spontaneous regression of RCC may be explained as a kind of re-expression of embryonic features by adult carcinoma."

References and typesetting were corrected.

I believe that the changes made were in an appropriate manner and the manuscript will now be suitable for publication in the *World Journal of Clinical Urology*. Thank you very much in advance for your kind consideration.

Sincerely yours,



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