

Review of the thesis by Dr. Sachin Trivedi “*Clinical use of neopterin, a laboratory biomarker of immune activation, in the assessment of prognosis, monitoring response to therapy and complications in cancer patients*”

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The topic of the submitted dissertation seems to be up to date. In his thesis encompassing 98 pages Dr. Trivedi focuses on urinary neopterin as a biomarker of inflammatory response in patients with cancer. The topic of inflammatory biomarkers is currently of great interest in medical oncology. After a comprehensive introduction to the topic of the thesis, the author introduces his own results on neopterin in two cohorts of cancer patients, patients with metastatic colorectal carcinoma treated with cetuximab and patients with cervical carcinoma treated with chemoradiation. These investigations have been published in international peer-reviewed journals with impact factor. Neopterin is, despite interesting data, not widely used to monitor the course of disease and therapy in cancer patients. This justifies why Dr. Trivedi makes an extensive review of the published literature of the topic. The methodology of neopterin determination and statistical analysis are adequate. The thesis brings new scientific information. Urinary neopterin concentrations during the course of chemoradiation of cervical cancer have not been, to the best of my knowledge, studied before. Prognostic significance of urinary neopterin in metastatic colorectal carcinoma patients treated with cetuximab has also not been previously studied. The data on these two

topics can therefore be considered priority observations. The results are certainly interesting for the clinician and relevant for the practice of medical oncology. I consider this thesis as having fulfilled its goal.

The language style and range of the dissertation seem to be adequate to the requirements. There have been just minor inaccuracies as far as some of the specific terms were used. The enclosed literature review has been representative and up to date

In the course of the defense I would like to ask following questions:

1. Neopterin is a non-specific biomarker of immune activation and increased neopterin concentrations are encountered also in a number of non-neoplastic conditions. To the opinion of the author, does this interfere with the utility of neopterin as prognostic biomarker?
2. What is known about the correlation of neopterin with other biomarkers of inflammatory response, e.g. CRP? What could be the advantages and disadvantages of neopterin as a biomarker?
3. Currently antibodies targeting immune checkpoints have entered the therapy of cancer. Could neopterin represent a predictive biomarker in this setting?
4. The same group reported a significant increase of neopterin after chemoradiation in patients with head and neck cancer and rectal carcinoma. Why was not the same trend evident in patients with cervical carcinoma?

To my opinion the present thesis meets all requirements stipulated by the law for a Ph.D. thesis. The author should be allowed to defend the thesis, and, after successful defense, the Ph.D. degree should be bestowed on him.

The expert opinion has been elaborated by:

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