Reviewer’s report

Title: Renal failure during chemotherapy: renal biopsy for assessing subacute nephrotoxicity of pemetrexed

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Reviewer: Martin Früh

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In general renal problems are frequent and important in NSCLC patients receiving chemotherapy. Frequently these are older patients with comorbidities and poly-medications, which all however in this case did not seem to be the case. Pemetrexed is a very widely used agent in this population and renal monitoring seems adequate. Thus the case per se is relevant. I however have several issues that need to be clarified:

English needs to be checked by a native speaker. Just to name a few sentences: Page 2: Loss of chance due to impossibility… (what chance? of treatment benefit?). Reversibility of acute renal events determines following strategy.. (meaning this may hamper administration of further anti-neoplastic therapy?). All drugs often have to resume in acute renal failure (do you mean discontinued?). Page 5: alliviation of cisplatin (do you mean discontinuation?) and so forth...

Oncological background seems to be missing somehow: Pemetrexed is not NEW.. this should be cancelled throughout the manuscript. TNM Staging can not be III, if pleural metastases?: Cisplatin pemetrexed and avastin is typically NOT given together with radiotherapy (at least outside of a clinical trial). Dose of avastin seems strange: either 7.5 or 15 mg/kg??

Avastin has a long half live and typically causes hypertension, which may has contributed to the worsening renal function? in addition there was proteinuria, which is a typical side effect of bevacizumab.. These points were not explained or discussed. Moreover, typically, pemetrexed is halted if clearance decreases below 45 ml/min. Was this done? When were the last infusions given in relation to the decreasing renal function and what was the clearance on that day? It seemed that clearance was 36 ml/min in November but therapy hasn t been stopped until december? Were there any other nephrotoxic contributors such as CT with contrast imaging or NSAIDS?

Lastly, what would be the consequence of a renal biopsy in such a patient? Would one recommend it? Even if the time intervall of renal defiency and chemotherapy is suggestive of a therapy related cause?

Are the methods appropriate and well described?
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