Author’s response to reviews

Title: Neoadjuvant docetaxel, cisplatin and ifosfamide (ITP) combination chemotherapy for treating penile squamous cell carcinoma patients with terminal lymph node metastasis

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1. The definition of fixed inguinal nodes is not sufficiently defined. Whilst I accept that it is also not well defined in the TMN clinical nodal stage, it should be clearer in this paper. Correlation with the CT appearances of the size and number of enlarged lymph nodes would be helpful. There may well be patients who would have been pathologically pN2 and who would have a better outcome than the group with extra capsular spread and therefore pN3.

Revised as follows: All of the patients in this study had fixed inguinal lymph node metastasis which specific manifestations included palpation of inguinal region with fixed masses, CT or PET-CT showed enlarged and fused lymph nodes which had rough and irregular margins and invaded the surrounding femoral vessels and Inguinal skin.

2. There was significant variation in the number of neo-adjuvant cycles. There is no explanation as to why, apart from the one patient who progressed early.

Revised as follows: After two cycles of chemotherapy, the four patient's condition was stable, and then two cycles of chemotherapy were carried out. Three patients completed only one cycle because of disease progression (n=2) and toxicity (n=1). Twelve patients completed two cycles and because of the good therapeutic effect, operations were carried out subsequently.
3. I do not agree with the conclusion that ITP is effective in a neo-adjuvant setting. The authors have not presented any evidence to conclude that. It has simply been shown that responders to ITP do better than the non-responders, who ultimately had different treatment and that is has acceptable tolerability. The authors have not shown any benefit over surgery alone.

Revised as follows: In conclusion, according to our preliminary study, neoadjuvant docetaxel, cisplatin and ifosfamide chemotherapy gave 63% (12/19) of patients who were diagnosed with stage n3 penile cancer the chance of radical resection of metastases, and their OS and PFS were significantly higher than those who could not be operated on and the therapeutic dose, toxic and side effects are acceptable in the Chinese Han population. Therefore, neoadjuvant ITP chemotherapy in the treatment of stage T3 penile cancer patients may have cheerful prospects in the Chinese Han population.

Reviewer 2 (Reviewer 2): PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: Overall Impression; This study aims to determine the efficacy of neo-adjuvant chemotherapy for SCC of Penile cancer. Even though this has been proven in a prospective phase 2 study, the present study is conducted on a racially different population (Chinese Han). For studying a rare cancer, the authors have to be applauded. The retrospective nature and small sample size may hinder the generalizability of the study. Additionally, the difference in follow-up clinical treatments (LND or Chemotherapy) of responders and non-responders of neo-adjuvant chemotherapy may introduce a selection bias when comparing the two groups in aspects of survival. The authors do mention the limitations of the study in the discussion.

Revised as follows: Because of the low incidence of penile cancer, our study lacks randomized controls, which requires us to accumulate more clinical data over the long term. We have modified many grammar and structural errors and hope to interpret artical better.