Reviewer’s report

Title: Neo-adjuvant treatment of adenocarcinoma and squamous cell carcinoma of the cervix results in significantly different pathological complete response rates.

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Reviewer: Tomasz Banas

Reviewer's report:

The authors Couvreur et al. present a well conducted study on treatment of cervical cancer. The manuscript presents a retrospective analysis of a cohort of 179 patients finally included in the study who were treated by all currently available therapeutic modalities due to cervical cancer showing final treatment results. This is a very interesting, well-designed and well-conducted research that meets the scope of BMC Cancer and presenting a novel results and view in treatment of cervical adenocarcinoma and squamous cell carcinoma. A few comments that should be addressed are provided below:

1. Abstract should contain brief information about all study groups and treatment modalities not only focus on NA-CRT group although results in NA-CRT are the core and novel finding.

2. The statement: "To date, management of cervical cancer is independent of its histological subtype but merely guided by staging at diagnosis" revalidated as is based on NCCN guideline from 2015 and current guidelines include Version 1.2019 - August 2018. Additionally in an everyday clinical practice women with cervical adenocarcinomas in low clinical stages are more likely to be treated with radical surgery compared to RT or CRT compared to cervical squamous cell carcinoma due to increased risk of adnexal metastases and/or lymph node involvement. Therefore this issue needs elucidating according to current guidelines and state-of-art.

3. In the Material and method section the Authors write: "The patient cohort was classified according to histological type and FIGO stage: adenocarcinoma (AC) including adenosquamous subtypes (n= 36) versus squamous cell carcinoma (SCC; n= 143)" while in the Results is written: "Thirty-six out of 205 patients were excluded due to various reasons, including metastatic disease at diagnosis, treatment for recurrent (and not primary) disease and histological types other than AC and SCC." A cohort of 179 women was included (36+143) according to the Material and method section while 205-36 is 169 - this discrepancy needed elucidating and recruiting process should be clearly described in the Material and methods including numbers and reasons for patients exclusions. Statement "due to various reasons" is not enough for high-quality research.
4. Repainting information from the Materials and methods in the Result section (eg. Data of 179 cervical cancer patients were analyzed, of which 36 were AC and 146 were SCC.) should be avoided.

5. The Authors say that: "Mean tumor size was significantly larger for SCC (4.3 cm) than AC (3.3 cm) (p=0.03); ACs were more often stage IB1 (50% versus 25% for SCC; p=0.01) and well differentiated (41% versus 7% in SCC; p=0.001). Squamous cell carcinomas were more often moderately differentiated than AC (48% versus 25% resp.; p=0.02)." and that "The treatment regimens were not significantly different between AC and SCC (table 2). 14/36 (39%) AC and 70/143 (49%) SCC patients were treated with NA-CRT intent respectively (NA-CRT group)." This issue should be discussed (perhaps in the context of the comment no 2) how to explain lack of differences in the treatment modalities while the study groups differed significantly in clinic-pathological features. Such a discussion might be very interesting and improve the overall quality of the manuscript. By the way the issues concerning pCR and locoregional control in AC and SCC were very detailly disused by the Authors.

6. "The 5y OS rate for early AC and SCC was 100% and 89.4% (p=0.40) respectively." How early and advanced AC and SCC are defined according to the Authors (ie. Stage I and II vs. III+?)?

7. As in NA-CRT AC numbers are low did the Authors used Yeates correction for chi-square tests as presented results: "Seventy-seven patients treated with NA-CRT intent were operated upon. A pCR was obtained in 7% (1/14) and 42% (27/63) of the AC and SCC patients respectively (p=0.02). This difference remained statistically significant when all non-operated tumors (n=7, all SCC) were considered as incomplete pathological response: 7% (1/14) versus 39% (27/70) pCR for AC and SCC respectively (p=0.02)." may differed if corrected for low number group. Statistical consultation may be required to resolve this issue.

8. P-value should preferably be presented as 0.000 (3 digits after the decimal)

9. In the Discussion presenting results should be avoided ie. "Table 3 shows the results of studies reporting on survival differences between AC and SCC [3, 4, 6-8, 30-34]."

The limitation of this study were detailly discussed and its retrospective character and low number of women with AC as well as single-center localization do not decrease its value. In my opinion further prospective studies should be designed to confirm this interesting and novel
findings. Overall, the work appears to be of high quality and provides a novel insight to the field of cervical cancer research.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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