

Dear Sir /madam,

I submit a revised version of my editorial commentary entitled: “Large cell neuroendocrine carcinoma (LCNEC) of the ovary: A pathologic entity in search of clinical identity” for publication at the World Journal of Clinical Oncology (manuscript #8204).

All the comments and questions of reviewers have been taken into consideration. Specifically regarding Reviewer 1 general comments:

1. I have presented the points of concern and re-emphasized the fact that LCNEC presents similarly to epithelial ovarian cancers in a closing remark.
2. I have added a proposition for research in an added concluded paragraph. I also note that the commentary as a whole contains a balance of facts and personal views. I must also emphasize that the discussion on pathogenesis and trans-differentiation that draws attention to the similarities of neuroendocrine differentiation with the phenomenon of EMT is original.
3. I have presented my point of view that ovarian LCNEC is a pathologic entity that lacks a clinical identity, lacking clinical characteristics to clearly discern it from epithelial ovarian carcinomas. Nevertheless the diagnosis is worth making because of possible treatment implications that were described in the article (page 4). I have further restated these points in a conclusion paragraph added.
4. A concluded paragraph has been added as per the reviewer’s recommendation.

Regarding Reviewer 1 questions:

1. The proposed distinction in the title between pathology and clinic is re-emphasized in the text.
2. Reference 12 (13 in the revised manuscript because of the addition of a reference) was restored.
3. The debate on prognostic distinction of LCNEC compared with epithelial ovarian cancer is mentioned.
4. The point raised by the reviewer was added in a phrase in the 1st paragraph with an appropriate reference (ref. 2).

5. A discussion of LCNEC of the prostate as it pertains to the pathogenesis of LCNEC in general has been added.

Regarding Reviewer 2 comment, I have added a table (instead of a figure) summarizing the main characteristics of LCNEC of the ovary.

Thank you for your consideration.

Sincerely,

Ioannis A. Voutsadakis, M.D., Ph.D.

Editorial board member, World Journal of Gastrointestinal Oncology
and World Journal of Experimental Medicine