1. The authors must clarify definition of the name of HROC57. Is it the name of cell line or resected tissue or both ? What is HROC57 B cell line ?

Primarily HROC57 is the name of the corresponding index patient´s tumor in our bio bank. Subsequently cell line, xenograft model and B cell line are designated as HROC57 cell line, HROC57 xenograft and HROC57 B cell line.

As a standard routine of our tumor characterization protocol, a B cell line of patient`s B cells is established. In the body of the manuscript, we did not elaborate the B cell line establishment and did also not provide data on the B cell line. We only referred to it once as an ideal control for ID testing.

2. The authors must explain why they selected HCT116, which is adenocarcinoma but not NEC, as control in Figure 1 ?

To our knowledge there is no commercially available NEC cell line which could serve as a control for our HROC57 cell line. Therefore, we used our "standard" HCT116 cell line, that we use routinely when we characterize colon carcinoma cell lines.
In addition, our NEC cell line is of colonic provenance, thus a comparison to a colon cancer cell line might be justified. Moreover, many researchers working on colorectal carcinoma might be also interested in HROC57 cell line(s) – and for those, it will be easier to find if HCT116 is mentioned in the manuscript.

3. They should show results of CD26, CD29, CD73, and CD166 in Figure 2.

CD26, CD29, CD73 and CD166 were added to Figure 2.

4. Although they wrote results of immunohistochemistry only in Table 1, they must show those pictures in Figure.

We agree with the reviewer that this information might be worth to be added as supplemental information. However, since these data were obtained in the course of routine pathological assessment of the resection specimen, they are not readily available to us. If finally wished, we could provide such data, but this would definitely require more time. That's why we kindly ask to accept the information given in Table 1 as sufficient to make the point.

5. Discussion is too much long. They should shorten this section.

We did this according to the reviewers' recommendation.

6. They wrote "Actual chemotherapeutic regimen for the treatment of advanced NEC consists of a combination of etoposide and cisplatin but results are very poor" in the first paragraph of Discussion. However, they wrote "HROC57 showed a high sensitivity towards etoposide and cisplatin with a distinct increase of sensitivity after combination of cisplatin and etoposide (Figure 4)". Thus, this cell line might not reflect the nature of NEC.

G3 NEC show a very aggressive biologic behavior, with a rapid tumor growth and early metastatic disease. Therefore, a complete surgical resection of the tumor mass is often unattainable at time of diagnosis. First line therapy consists of a platinum based chemotherapy

with response rates ranging from 42% to 67% and a very low median survival of 15 to 19 months despite this principally good initial response rate (1).
The poor clinical outcome of this tumor entity might rather be consequence of the aggressive biological behavior than due to poor initial response rates. This fact underscores in our opinion the importance of our tumor model for further research. With the before mentioned results in mind, one can assume that G3 NEC tumor cells are likely to quickly develop secondary resistance (upon or under treatment). Which can be best analyzed using patient-derived primary tumor models!

1. Nothing But NET: A Review of Neuroendocrine Tumors and Carcinomas. Oronsky B, Ma PC, Morgensztern D, Carter CA. Neoplasia. 2017 Dec;19(12):991-1002. doi: 10.1016/j.neo.2017.09.002. Epub 2017 Nov 5.