

## Peer Review File

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### Reviewer A

**Comment 1** article is out of focus

Reply 1

I have changed the title of article to reflect the contents

**Comment 2** style is amateur

Reply 2

This article has been reviewed by Prof I O Ellis who is a world authority on breast cancers and has over 500 international published articles to his credit. He has made few changes to improve the article.

**Comment 3** the only relevant line for the title are lines 284-291

Reply 3

This has been changed by the new title and improved content of the paper.

**Comment 4** the author uses informal language "i have treid" , "please figur 1 "- this should be corrected

Reply 4

This has been corrected

**Comment 5** line 108"I present the following article in accordance with the Narrative Review reporting checklist"

Reply 5

This line has been removed

**Comment 6** lines 113-117 are inappropriate for methods use

Reply 6

Amended

**Comment 7** 1 125-128 "Stage 3 & 4 patients are candidates for chemotherapy, radiotherapy, targeted therapy and immunotherapy. Every effort is made to identify actionable mutations/translocations in tumour cells as chemotherapy and radiotherapy treatments

128 are the last option for our patients" this is not correct for stage 3.

Reply 7

On line 144 I have added Patients with Stage I, II & IIIa disease are candidates for surgical intervention

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### Reviewer B

**Comment 1** The review article is in fact hard to summarize, as it highlights different aspects in the title, abstract and in the main manuscript body. The title promises an outlook on the prognostic impact of different neoadjuvant regimens in lung cancer, the abstract describes the treatment of lung cancer in general and the role of pathologists in general, and the main manuscript body tries to focus on assessing histomorphological changes after neoadjuvant therapy. Here, the author first includes different regression grading options in other tumors (gastrointestinal, breast and ovarian cancer), but falls short of giving an objective and in-depth description of how the topic is handled or best-practice recommendations. Rather, the author focuses on personal experience and hand picks some regression grading scores – unfortunately almost always without properly describing them with their proper definition, e.g. right in the beginning on page 4/5, TRG 1-5 is not defined, we don't get to know what is meant by it.

**Reply 1:** The title of article has been changed to match the contents of this article.

**Comment 2** This shortcoming also holds true for the review of pathological response after neoadjuvant therapy in lung cancer. One whole paragraph is dedicated to the study by Zens et al, which introduces important aspects into the discussion on the topic, but should be set in the context of current practice (I recommend to cite the IASLC recommendations for regression grading in lung cancer, published in JTO).

**Reply 2** I have added summary of article IASLC, please see line 281-288. This article has been added to the list of references (Ref 20).

**Comment 3** Recent papers on lymph node regression should be added.

**Reply 3** I have added an article on lymph node regression. Please see lines 289-291. A new reference has been added (Ref 21).

**Comment 4** The following paragraph on apoptosis and necroptosis is also a bit out of focus, as it is not possible to differentiate between those on a histopathological basis – and if so, this should be included. It is also not possible to differentiate between histomorphological changes after neoadjuvant chemotherapy and immunotherapy – but this is suggested in the article. Again, irPRC should be defined.

**Reply 4** I have added comments related to cell death and signaling pathways, line 356 -360 in discussion. This should address the first part. I have also explained irPRC in detail on by adding a new paragraph, Line 330-334.

**Comment 5** It is not clear to me why liquid biopsies are added in the article on assessing post-neoadjuvant therapy effects.

**Reply 5** I have commented that liquid biopsies are useful in assessing response to various treatments and predicting recurrence of treated lung cancer.

**Comment 6** Lastly, there are multiple errors in the article “e.g. page 8 stage 111”, and the two sentences where this is mentioned are the same ones only with different percentage numbers? This is not clear to me.

Reply 6 These have been corrected

**Comment 7** English language needs significant improvement.

Reply 7 Prof I O Ellis, Breast expert in our department has read the article and has made changes to improve the English language.

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Reviewer C

In general, the text is considerably revised and improved compared with the first version.

**1. Discussion:**

- Line 127-128 - *“If regional lymph nodes show disease activity, attempts are made to obtain tissue for diagnosis and molecular testing.”*

This sentence should be revised as in the absence of lymph node involvement too, tissue is obtained and molecular testing is performed.

**Response:** I have added -In addition if, to make it accurate, please see line 126.

- As the review is on pathological response after neoadjuvant treatment in lung cancer, pathologic response details for gastroesophageal, tubo-ovarian, gastrointestinal, breast tumors and melanomas should be shortened to 1-2 paragraphs and subtopics should be deleted.

**Response:** I have removed the subtopics, please see lines 154, 171, 179, 186 and 208.

**2. Another figure can be added on one of the following or whatever the author chooses:**

- An algorithm for proposed pathological approach,
- Different pathological changes after different neoadjuvant treatments
- **Response:** Two figures for the paper are attached with this e-mail response. None of these are post immune therapy. We dont get information on the therapy given before surgery and that is the message being given in this article.

**3. Edition and correction of the text:**

- There are many typographic and grammatical errors (unnecessary capital letters, missing letters or words in some sentences, etc.). These should be checked and corrected carefully.
- There are several sentences to be revised to make them clearly understood.
- **Response:** I have made corrections, please see lines 85, 111, 115, 126, 156, 257, 267, 280, 290, 374. I have also added text to make subject easi