

Genomic assays for lobular breast carcinoma

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Handling editor:

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1st Editorial decision

24-Jul-2022

Ref.: Ms. No. JCTRes-D-22-00058

Genomic assays in lobular carcinoma of the breast: A literature review.

Journal of Clinical and Translational Research

Dear Dr Göker,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Aug 23, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: This is a very interesting review on invasive lobular carcinoma (ILC), worth publishing.

However there is a number of necessary revisions to improve quality of the paper, including the RS categorization which creates confusion and multiple corrections and update of the references.

Major revisions:

- 1) Page 5, line 9: this categorization [low-risk (LR, score 1-10), intermediate risk (IR, score 11-25) or high-risk (HR, score >26)] used by the authors, is referring to "prediction of Chemo benefit and is not the official one of "prognostication" (Low <18, InterM 18-30, High >30). As all studies reviewed in this paper used the later (apart from TAILORx and RxPONDER) it should be replaced to avoid confusion; using different "versions" of RS in multiple instances of the review, creates a major problem.
- 2) There are multiple corrections needed across all manuscript in regards to references (missing or wrong references, some outdated)
- 3) The "Discussion" sounds like an extensive "summary" of the review. Needs to be shorten and avoid repeating the reviewed papers again
- 4) Although referred to in text, "Blueprint" (page 17, line 32), it is not explained what it is
- 5) Page 15, line 35: "Lobsig" is the first gene signature with a primary focus on prognostication of ILC patients and should be presented earlier in the text and not only refer to in the Discussion

Minor revisions:

- 1) Page 5, line 28: Replace reference of presentation with paper publication: RxPONDER, published on December 1, 2021, at NEJM.org.
- 2) Page 5, line 34: RSs for the randomised groups are missing;
- 3) Page 5, line 34: "with RS ≤ 25 " should be added in the statement about post-M patients.
- 5) Page 5, line 60: how does it come to include HER2-positive ILCs? OncotypeDX is only applicable in ER/PR positive HER2-negative cancers.
- 6) Page 7, line 35: compared to what ??? (missing)
- 7) Page 7, line 54: the Table 1 title should be modified (chemo benefit according to age and RS)
- 8) Page 8, Table2: it should be mentioned what cut-offs were used in the rest of the series reported here
- 9) Page 8, line 37: ref 33 is wrong (it is TAILORx trial and not a paper on Mammprint)
- 10) Page 9, Table 3: this table is difficult to read and rather confusing
- 11) Page 10, Table 4: as EPclin involves LN status in the calculation algorithm, I am not sure about the value of this table
- 12) Page 11, 1st paragraph: it has to be mentioned how ROR score is calculated (including T-size)
- 13) Page 11, line 53: word missing: ... it predicts the benefit of extended
- 14) Page 12, line 30: missing: what are these % corresponding to?
- 15) Page 13, lines 19-20: rephrase

16) Corrections in referenses:
ref 23: vol, pages is missing
ref 32: journal, year, pages etc is missing
ref 65: is missing from the list of refs
ref to RxPONDER publication is missing

Authors' response

Reviewer #1: This is a very interesting review on invasive lobular carcinoma (ILC), worth publishing.

However there is a number of nessesary revisions to improve quality of the paper, including the RS categorization which creates confussion and multiple corrections and update of the referrences.

Major revisions:

1) Page 5, line 9: this categorization [low-risk (LR, score 1-10), intermediate risk (IR, score 11-25) or high-risk (HR, score >26)] used by the authors, is refering to "prediction of Chemo benefit and is not the official one of "prognostication" (Low <18, InterM 18-30, High >30). As all studies reviewed in this paper used the later (apart from TAILORx and RxPONDER) it should be replaced to avoid confusion; using different "versions" of RS in multiple instances of the review, creates a major problem.

The cutoffs are replaced in the text.

2) There are multiple corrections needed across all manuscript in regards to referrences (missing or wrong referrences, some outdated),

I checked all the referrences, deleted the outdated ones.

3) The "Discussion" sounds like an extensive "summary" of the review. Needs to be shorten and avoid repeating the reviewed papers again

DONE in text

4) Although refered to in text, "Blueprint" (page 17, line 32), it is not explained what it is **it is a molecular subtyping assay using the combined expression of 80 genes to categorize tumors as Luminal-, HER2- or Basal-type. But In this review imakes little sense to mention this, no consequence for ILC, so I deleted this sentence.**

5) Page 15, line 35: "Lobsig" is the first gene signature with a primary focus on prognostification of ILC patients and should be presented earlier in the text and not only referd to in the Discussion

DONE in text

Minor revisions:

1) Page 5, line 28: Replace referense of presentation with paper publication: RxPONDER, published on December 1, 2021, at [NEJM.org](https://www.nejm.org).

DONE

2) Page 5, line 34: RSs for the randomised groups are missing.

DONE

3) Page 5, line 34:"with RS ≤ 25 " should be added in the statement about post-M patients.

DONE

5) Page 5, line 60: how does it come to include HER2-positive ILCs? OncotypeDX is only applicable in ER/PR positive HER2-negative cancers.

All cases sent for Oncotype Dx testing were HER-2 negative tumors in this cohort of 135 patients. I deleted HER2 in the text to avoid confusion.

6) Page 7, line 35: compared to what ??? (missing)

DONE, compared to ductal Ca

7) Page 7, line 54: the Table 1 title should be modified (chemo benefit according to age and RS)

DONE

8) Page 8, Table2: it should be mentioned what cut-offs were used in the rest of the series reported here

The cut-offs are reported under the table.

9) Page 8, line 37: ref 33 is wrong (it is TAILORx trial and not a paper on Mammaprint)

DONE, reference is replaced

10) Page 9, Table 3: this table is difficult to read and rather confusing

Only two studies, I simplified the table by omitting some text!

11) Page 10, Table 4: as EPclin involves LN status in the calculation algorithm, I am not sure about the value of this table

I simplified the table, only results in lobular and ductalca are mentioned

12) Page 11, 1st paragraph: it has to be mentioned how ROR score is calculated (including T-size)

DONE in text

13) Page 11, line 53: word missing: ... it predicts the benefit of extended

DONE

14) Page 12, line 30: missing: what are these % corresponding to?

It corresponds to the percentage of histologic subtype (lobular vs ductal) in this cohort of 2554 LN negative breast cancers. (80.7% IDC; 13.7% ILC; 2.6% mixed; 2.9% other)

15) Page 13, lines 19-20: rephrase: **DONE**

16) Corrections in referenses:

ref 23: vol, pages is missing: **DONE**

ref 32: journal, year, pages etc is missing: **DONE**

ref 65: is missing from the list of refs: **It was the same reference as Iorfida et al.**

ref to RxPONDER publication is missing: **DONE**

2nd Editorial decision

21-Aug-2022

Ref.: Ms. No. JCTRes-D-22-00058R1

Genomic assays in lobular carcinoma of the breast: A literature review.

Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Sep 20, 2022.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

I have received your manuscript at the Journal of Clinical and Translational Research. Thank you for submitting your revised paper.

I have gone through the manuscript and noted excessive spelling/grammatical errors. These need to be resolved before we can proceed with the publication.

The editorial board therefore kindly requests that you to have a preferably native speaker go through the paper and polish the language in accordance with academic standards.

Please understand that this has always been the responsibility of the authors, as advertised clearly in our author guidelines (<https://www.jctres.com/en/author-guidelines/>).

Publishing properly written papers is a putative standard in science. We have worked hard to maintain a level of excellence with the journal in every respect so that we can serve past, present, and future contributors with a stamp of high quality and impeccable reputation.

If you do not manage to undertake the task yourself or get a colleague to help you, please contract a third-party language editor. Alternatively, contact the journal (m.heger@jctres.com) so that we can try to engage a paid language editing service. JCTR has dedicated language editors who undertake a deep dive in terms of content and language editing that is in accordance with the journal's standards.

Thank you for understanding and kindest regards,

Michal Heger
Editor

3rd Editorial decision
01-Oct-2022

Ref.: Ms. No. JCTRes-D-22-00058R2
Genomic assays in lobular carcinoma of the breast: A literature review.
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: