

## CERTIFICATE OF BIOSTATISTICS

3 April 2020

To whom it may concern

Title of Study: HER2 positive rates in invasive lobular breast carcinoma: the Singapore experience

This letter is to certify that the statistical methods and techniques mentioned are appropriate for the research.

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CIRB Ref: **2019/2419**

14 March 2020

Dr Wong Fuh Yong  
Department of Radiation Oncology  
National Cancer Centre

Dear Dr Wong

**RENEWAL OF SINGHEALTH CENTRALISED INSTITUTIONAL REVIEW BOARD (CIRB) APPROVAL**

**Protocol Title: (2012/093/A) Outcomes Research in Breast Cancer Care**

We are pleased to inform you that the SingHealth CIRB A has reviewed and approved the renewal of IRB approval for the study to be conducted in Changi General Hospital, KK Women's and Children's Hospital, National Cancer Centre, National Heart Centre, Singapore General Hospital and Sengkang General Hospital.

Please note that annual IRB renewal is required and the review is based on the Study Renewal Report submitted. It is the Principal Investigator's responsibility to submit a Study Renewal Report for the study at least two months before the expiry date of the study for renewal of IRB approval. This approval is valid till **13 March 2021**.

The document reviewed is:

- Study Renewal Report Form dated 12 Mar 2020

The SingHealth CIRB operates in accordance with the ICH Guideline for Good Clinical Practices, and with the applicable regulatory requirement(s).

Yours sincerely,

Prof Ho Lai Yun  
Chairman  
SingHealth Centralised Institutional Review Board A

cc: Institution Representative, CGH  
Head, Department of General Surgery, CGH  
A/Prof Tan Su Ming, Site PI, CGH

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National Cancer Centre Singapore • National Dental Centre Singapore • National Heart Centre Singapore  
National Neuroscience Institute • Singapore National Eye Centre • SingHealth Community Hospitals • SingHealth Polyclinics

- cc: Institution Representative, KKH  
Head, Department of Breast, KKH  
Dr Lim Swee Ho, Site PI, KKH
- cc: Institution Representative, NCC  
Head, Department of Radiation Oncology, NCC
- cc: Institution Representative, NHC  
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Dr Ng Choon Ta, Site PI, NHC
- cc: Institution Representative, SGH  
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Dr Lim Sue Zann, Site PI, SGH
- cc: Institution Representative, SKH  
Head, Department of Surgery, SKH  
A/Prof (Adj) Benita Tan Kiat Tee, Site PI, SKH

*This submission is reviewed online. No signature is required.*

## STROBE Statement

	Item No	Recommendation	Reported on Page
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6-7; Figure 1
		(b) For matched studies, give matching criteria and number of exposed and unexposed	6-7; Figure 14-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-8
		(b) Describe any methods used to examine subgroups and interactions	6-8
		(c) Explain how missing data were addressed	6-8
		(d) If applicable, explain how loss to follow-up was addressed	6-8
		(e) Describe any sensitivity analyses	6-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8; Table 1
		(b) Give reasons for non-participation at each stage	8-9
		(c) Consider use of a flow diagram	N.A.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8-9
		(c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	8-9

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(b) Report category boundaries when continuous variables were categorized	8-9
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N.A.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N.A.