

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	In vitro fertilisation (IVF) versus intracytoplasmic sperm injection (ICSI) in patients without severe male factor infertility: study protocol for the randomised, controlled, multicentre trial INVICSI
AUTHORS	Berntsen, Sine; Nøhr, Bugge; Grøndahl, Marie Louise; Petersen, Morten; Andersen, Lars; Mikkelsen, Anne Lis; Knudsen, Ulla; Prætorius, Lisbeth; Zedeler, Anne; Nielsen, Henriette; Pinborg, Anja; Freiesleben, Nina

VERSION 1 – REVIEW

REVIEWER	Buckett, William McGill University, Obstetrics and Gynecology
REVIEW RETURNED	07-Apr-2021

GENERAL COMMENTS	<p>This is a hugely important question and the study protocol is a brave attempt to answer this question (and is very much needed). It is also encouraging that non-severe MFI cases are included and that teratozoospermia is NOT an exclusion.</p> <p>There are a couple of minor comments:</p> <ol style="list-style-type: none">1. It is unclear exactly when randomization occurs/will occur - is it during or at the start of stimulation (where knowing the ICSI or IVF randomization could affect the decision or timing of collection or cancellation) or once the trigger/collection timing is determined (in my opinion the best time) or after collection (where the number/maturity of oocytes obtained may affect the decision to continue in the study or not). Whichever timing is used should be justified in the text.2. Is rescue ICSI planned or considered in cases of total fertilization failure? Whether it is or not (or only at some centres) should be specified in the text3. Not sure whether other references eg Foong et al 2006 Very small IVF vs ICSI RCT (no difference) or more recent Isikoglu et al 2021 Medium sized sibling oocyte RCT (no diff) should be included or not
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REVIEWER	Anifandis, George University of Thessaly
REVIEW RETURNED	18-Apr-2021

GENERAL COMMENTS	It is a very fine and well designed protocol for investigating the outcome of IVF vs. ICSI in couples with no male factor
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. William Buckett, McGill University

Comments to the Author:

This is a hugely important question and the study protocol is a brave attempt to answer this question (and is very much needed). It is also encouraging that non-severe MFI cases are included and that teratozoospermia is NOT an exclusion.

Response: We are very glad to hear that the reviewer agrees that this is an important research question and that the study is warranted. We thank the reviewer sincerely for the comments provided below which were very useful.

There are a couple of minor comments:

1. It is unclear exactly when randomization occurs/will occur - is it during or at the start of stimulation (where knowing the ICSI or IVF randomization could affect the decision or timing of collection or cancellation) or once the trigger/collection timing is determined (in my opinion the best time) or after collection (where the number/maturity of oocytes obtained may affect the decision to continue in the study or not). Whichever timing is used should be justified in the text.

Response: Thank you for highlighting that the timing of the randomisation was unclear. We have tried to further specify this in the manuscript (please see under the section "Screening, inclusion and consent").

2. Is rescue ICSI planned or considered in cases of total fertilization failure? Whether it is or not (or only at some centres) should be specified in the text.

Response: Thank you for this relevant question. Rescue ICSI is not used which is now specified in the text under the section "Intervention".

3. Not sure whether other references eg Foong et al 2006 Very small IVF vs ICSI RCT (no difference) or more recent Isikoglu et al 2021 Medium sized sibling oocyte RCT (no diff) should be included or not.

Response: These suggestions are indeed very relevant. Thank you for that. We have added both studies as references as we agree that these contribute to the existing evidence in this field.