Author's response to reviews

Title: Efficacy and safety of a booster dose of influenza vaccination in solid organ transplant recipients: TRANSGRIPE 1-2, study protocol for a multicentre, randomized, controlled clinical trial.

Authors:

- Juliana Martinez-Atienza (jumarati@gmail.com)
- Clara M Rosso Fernández (claram.rosso.sspa@juntadeandalucia.es)
- Cristina Roca (cristinaroca85@gmail.com)
- Teresa A Aydillo (teresa.aydillo@gmail.com)
- Joan Gavalda (gavaldasantapau@gmail.com)
- Asunción Moreno (amoreno@clinic.ub.es)
- Jose M Montejo (josemiquelmontejo@hotmail.com)
- Julian De la Torre (julian.torre.sspa@juntadeandalucia.es)
- Carmen Fariñas (mirfac@humv.es)
- Jesus Fortun (fortunabete@gmail.com)
- Jordi Carratala (jcarratala@bellvitgehospital.cat)
- Patricia Muñoz (pmunoz@micro.hggm.es)
- Marino Blanes-Julia (blanes@ono.es)
- Alejandro Suárez Benjumea (suarezbenjumea@gmail.com)
- Francisco López Medrano (flmedrano@yahoo.es)
- Pilar Perez Romero (mperez-ibis@us.es)
- Elisa Cordero Matia (mariae.cordero.sspa@juntadeandalucia.es)
- TRANSGRIPE 1-2 study group (transgripe@gmail.com)

Version: 5  Date: 20 June 2014

Author's response to reviews: see over
21st October 2013  
Doug Altman  
Trials Editorial Team  
University of Oxford, UK  

Dear Dr. Altman;  

Thank you for your comments and for those of the reviewers regarding our recently submitted manuscript reference number MS: 1715597979122432. On behalf of all the authors, please find enclosed the revised manuscript of the study protocol entitled: “Efficacy and safety of a booster dose of influenza vaccination in solid organ transplant recipients: TRANSGRIPE 1-2, study protocol for a multicentre, randomized, controlled clinical trial”. As suggested we have reviewed and taken into account the reviewer’s and editorial concerns and we have modified the paper, taking into account these comments. A point-by-point response to the reviews follows.  

In the abstract the study is described as non-inferiority, but I think that this is a typo? Elsewhere the trial is referred to as non-commercial, perhaps that is what is meant here? The methods describe a superiority trial. If non-commercial is what is meant a better phrase may be “publicly funded”? Whatever you decide the non-inferiority needs removed.  

To answer the reviewer concern the word “non-commercial” refers to that this is an academic clinical trial not funded by pharmaceutical or biotechnology companies for commercial purposes. Thus it was funded by public-good agencies. As suggested by the reviewer it has been changed for publicly funded clinical trials and non-inferiority trial has been removed.  

The standard of English requires slight improvement. For example the statistical analysis section is written in a mixture of past and future tense.  

As suggested, English has been reviewed and improved; we have made some corrections to the statistical analysis section.  

You may want to justify the decision to use LOCF for missing data given its known shortcomings in most situations.  

The use of LOCF was a mistake in the description of statistical methods for this article as it was not included in the original protocol submitted to EC and RA. However we agree in including a short explanation regarding data missing treatment: we have optimized the design and conduct of the trial to minimize the amount of drop-outs and missing data. The analysis will be performed on the ITT population and missing data will be handled by imputing missingness to failure.  

Discretionary  
I was unsure what the phrase "reference hospital" meant, but that could just mean that it is used outside of the UK to mean tertiary care? Perhaps "referral hospital" would be clearer.
The term has been changed to referral hospital, meaning large hospitals that provide tertiary care and full complement of health care services.

Discretionary
There is a slight error in your sample size section, 462/0.9 is would 514 rounded up to even number to adjust for 10% drop-out but fortunately this has little impact on the sample size required.

No changes were done in the sample size calculation as it was the submitted to Ethics committees and Regulatory Agency approving the study.

The error in sample size calculation has been corrected in the manuscript.

Intention-to-treat and per-protocol should have hyphens.

As suggested the corrections have been made.

Please include the date your study was registered with your trial registration number at the end of your Abstract.

As suggested the dates of study registration in clinicaltrials.gov as well as in EudraCT have been included.

Please move your ethical approval statement to the Methods section. If you do not wish to include this here, please include the list as an additional file and refer to this in the Methods section.

Following the reviewer’s suggestion the statement about ethical approval and the names of all the ethical bodies that approved the study in the hospitals involved, have been moved to the Methods section.

Please ensure that all authors on the author list are mentioned in the Authors’ Contributions section.

The following authors have been removed from the title page but they continue to be included as authors as part of TRANSGRIPE 1-2 study group.


All the remaining authors listed have contributed substantially in the conception and design of the study, and all are thus included in the authors’ contribution section.

This manuscript reports an original work and it has not been published and is not under consideration for publication elsewhere. All the authors have read the manuscript and approved the submission. The authors declare no conflict of interests. Please address correspondence to the author signing this letter.

We look forward to hearing from you.
Sincerely,

Clara M. Rosso Fernández, Ph.D. and M.D.
Virgen del Rocío University Hospital
Avda. Manuel Siurot s/n
41013 Seville (SPAIN)
Phone: +34 955 013414
Fax: +34 954 232992
Email: claram.rosso.sspa@juntadeandalucia.es