Author’s response to reviews

Title: Reendothelialisation after Synergy stent and Absorb bioresorbable vascular scaffold implantation in acute myocardial infarction: COVER-AMI study

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Reviewer reports:

The comments of the reviewers led us to consider a new analysis of the data set, entrusting this analysis to a second statistician. The results of this analysis were included and highlighted in red in the revised manuscript (text, tables and figures).

We think that this new version presents a serious and sincere analysis of the data and interpretation of the results.

Reviewer #1: I want to congratulate the authors for their completed trial and I only think the manuscript needs minor, but important revision:

1) I would make the aim of the trial more clear and what the current study aims to add to the body of information already available eg. contrasting the information obtained in this trial to that obtained in the trial in reference 4. I would already in the introduction specify the evidence from non-MI patients on the subject rather than in the discussion. In general I encourage the authors to move parts of the discussion to the introduction section.
The objective of our trial has been clarified in the last two sentences of the introduction, and the reference numbers have been amended accordingly (for example, reference 4 became ref. 5).

In our trial, we were interested in the SYNERGY stent: the XIENCE stent, studied in reference 6, has a different design and showed a particularly rapid endothelialisation in preclinical studies.

2) I lack a sample size calculation for the primary outcomes. If none was performed prior to performing the trial, it should be stated as a limitation and added to the discussion that the trial might not have sufficient power to detect a difference not only on the clinical end points but also the non-clinical.

No sample size calculation was performed because this was an exploratory pilot study. Moreover, in the absence of previous data on early reendothelialisation after STEMI, no hypothesis could be formulated on the differences to be expected in strut coverage between the two groups. This has been added as a limitation.

3) The authors state in the result section that: "At 3-month follow-up, the lumen loss was lower in SYNERGY device (0.03 mm [IQR: 0.00 to 0.07 mm] vs. 0.10 mm [IQR: 0.03 to 0.31 mm]; p = 0.096" but in the discussion write "Finally, late loss was not significantly higher in the ABSORB arm (0.10 vs. 0.03 mm in the EES arm; P: 0.096)”. This seems contradictory.

We corrected this mistake. There is a non-significant trend of late loss reduction in the SYNERGY arm, possibly due to a lack of power. Moreover, the p-value in the text and the p-value in the table were not concordant, this was amended in the revised manuscript. The right p-value is p=0.165.

4) The results of the clinical endpoints should be mentioned in the article or as an appendix.

A paragraph dedicated to clinical outcomes was added before the discussion.

5) I would add what kind of participants were included in the Absorb 2 trial.

Absorb 2 trial only included non-MI patients, and limited data are available on the use of ABSORB in STEMI. These points were added in the discussion about the Absorb-2 trial.

6) If there is a pre-published protocol, this should be made available as an appendix (I see the clinical trial registration, but if there is a more detailed protocol?). Any outcomes not reported that were called for in the original protocol should be mentioned with reasoning for failure to report these, if there are any such outcomes. Otherwise, I would state that all outcomes called for in the protocol were reported.
The study protocol was added as an appendix. Outcomes called in the protocol were reported.

7) Lack of blinding should be mentioned as a limitation

Patients were blinded to the allocated treatment. Physicians and analysts blinding was not possible due to the distinctive appearance of ABSORB and EES stent struts. This particular point was addressed in a new paragraph in the study limitations.

8) If there was data available from all participants for all outcomes, this should be mentioned. If data from any participants were missing, this should be mentioned.

All data from all participants were available for clinical, angiographic and OCT analyses.

Reviewer #2: 1. The authors conclusion about the healing profile of Synergy DES compared to BVS is of concern. The incidence of uncovered struts remains the main predictor of stent thrombosis, and in this study Absorb BVS showed better arterial healing than DES in terms of strut coverage and apposition.

We agree with this comment.

2. Mean diameter of implanted stents significantly differed between study groups. In this case all the statistical analysis of quantitative OCT findings both at baseline and 3-month follow-up seems to be biased as well as the summary, based on this analysis. This could be the crucial limitation of this study and it can be recommended to perform propensity score matching or other actions to even the groups in terms of stent diameter.

Propensity score matching is not possible due to the small number of patients. The imbalance in stent’s diameter used in this study is attributable to differences in stent diameter availability between BVS and Synergy stents. In particular, the maximal diameter existing for BVS was 3.5mm, while 4-mm diameter Synergy stents were available. To take this point into account, data analysis for OCT results at cross-section and struts levels were presented both for the whole sample and after exclusion of 5 patients who received 4mm Synergy stents (Table 5).

This point was mentioned in the results section, and developed in the discussion.