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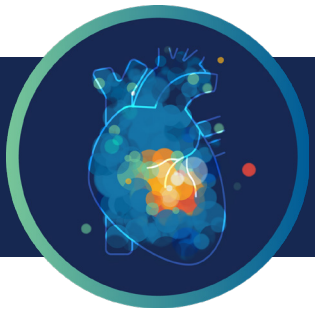
EXPERT INSIGHTS: Q&A WITH DR. KALPA DE SILVA



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How would you sum up the key points from the ORBITA-2 trial in plain language to a patient in your clinic?

ORBITA-2 was a trial that randomly assigned patients with chest pain in keeping with angina to on-going medical treatment with tablets who underwent a placebo procedure versus those who underwent stent implantation (percutaneous coronary intervention – PCI) to one of their heart arteries. The findings suggested that in patients who are symptomatic with angina a stenting procedure is an effective means of reducing/ameliorating these symptoms, and is likely to be better than tablet treatment alone.

ORBITA-2 studied a predominantly male white Caucasian cohort with physiologically significant single vessel coronary artery disease. Can or should the results of the trial be extrapolated to encompass an all comers stable angina population with single or multivessel coronary artery disease given this demographic and anatomical context?

The trial mainly included single vessel disease (81%), although 19% of the study group had two or more territories that had a reduced blood supply to the heart. So whilst the majority of the patients had single vessel narrowing there is no signal that the results do not relate to multi-vessel coronary disease in those with stable angina symptoms. In real-world clinical practice one could postulate that iterative reduction of ischaemic burden with PCI to each significantly diseased vessel would further improve angina burden and improve quality of life further. However, the trial was not designed to answer the question of the utility of PCI vs placebo in multi-vessel disease and therefore this cannot be extrapolated directly from this study.

On a more general note, how can we improve and optimally enrich the gender and ethnic diversity of cardiovascular clinical trials?

There are likely to be many approaches that need to be taken to improve diversity within clinical trials.

1. The institutions involved should be geographically distinct and represent a broader range of demographics and socio-economic scales. This would lead to a broader group of patients being approached and therefore involved in future work. This may mean broadening the pool of research centres beyond those that have historically undertaken this work.
2. The diversity amongst the trial principal investigators is also a key component of increasing awareness about the lack of diversity within the trial groups. A more diverse research group is likely to lead to a more diverse research population.
3. Education about the value of research to different societal groups is important in empowering people and populations about the part they can play individually and collectively in medical research.

It is unclear why a 12-week blinded follow-up phase was specifically chosen for the study design. Would there have been any added value in extending follow-up to 6 months or 1 year?

As PCI procedures in stable coronary disease are unlikely to have a mortality reduction compared to optimal medical therapies further follow-up is unlikely to change the outcome of the study, although extended follow-up is always helpful to define the durability of the intervention that has been carried out. A one-year time point to show the quality of life differences between the two groups would be helpful.

Subjects may have deliberately (or subconsciously) reduced the frequency and/or intensity of their daily activities in response to complete cessation of their pre-existing anti-anginal therapy. This information is not recorded by the Seattle Angina Questionnaire nor was it recorded by the smartphone angina symptom score during the trial. This is speculative of course, but could this have affected the study outcomes?

This is the case for any trial investigating symptoms in conjunction with coronary artery disease. It is difficult to a) account for the clinical relevance/ importance of this and b) know its impact on the trial results. In theory, this may have had a bearing on the trial result but the trial was undertaken in a meticulous, randomized placebo-controlled fashion to minimize the effects of inherent biases present in clinical research.

Do you think the introduction of a smartphone-based angina symptom score inadvertently introduced a volunteer or self-selection bias to the trial?

The inference is that the patient population maybe one that is not au fait with smartphones and therefore from certain age groups and/or demographics. I am less convinced this is the case. All approached would have had the opportunity to familiarize themselves with the smartphone app and therefore I do not believe this added a source of bias to the trial design or results.

Will ORBITA-2 change your clinical practice?

Whilst the results will not personally change my practice, they will allow me to have a more detailed discussion with patients who suffer from angina. Historic data has shown that angina (particularly low-grade symptoms) can be well and safely treated with medications. However, there has been a wealth of observational and registry data supporting the use of PCI procedures to reduce angina symptoms and more frequently leading to complete amelioration of symptoms. ORBITA-2 reaffirms this. If I have a patient who has high grade symptoms or is intolerant to medical therapies then a PCI procedure, depending on anatomic considerations, is an excellent treatment option.