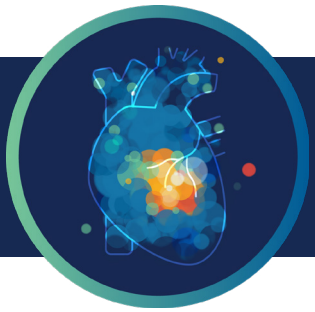
MEDPACE

EXPERT INSIGHTS: Q&A WITH PROF. AMITAVA BANERJEE



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Access the full publication: **Empagliflozin After Acute Myocardial Infarction**

In plain language, how would you summarize the study and its findings to a patient in your heart failure clinic?

Empagliflozin, and drugs like it — known as SGLT2-inhibitors — is a drug proven to reduce the risk of hospitalisation and death in people with heart failure, chronic kidney disease and those with diabetes and a high risk of cardiovascular disease. The EMPACT-MI trial showed that this drug does not provide a benefit in people who have just had a heart attack, even though they are at increased risk of heart failure.

The study employed a "streamlined" design with a predominantly decentralized approach to follow-up visits and the decision to forego central adjudication of endpoint events, relying instead on assessments by site investigators. This may have led to missed adverse events and introducedvariability and potential biases in the evaluation of outcomes. Do you think the results of this study could have been different had the protocol been a more standardized cardiovascular outcomes trial format?

I think the investigators should be applauded for this streamlined design and I have not seen convincing evidence of missed adverse events. It is unlikely to have had different results in the more traditional trial format because the outcomes are well recorded in routine practice. I feel that it is more reflective of, and therefore more relevant to, real world clinical practice.

The median follow-up period of 17.9 months may have potentially been insufficient to capture the long-term benefits or risks associated with empagliflozin use in this population. What are your thoughts on this?

First, the trial follow-up period is comparable with, if not greater than, the SGLT2-inhibitor outcome trials in heart failure, chronic kidney disease and diabetes. Second, the trial follow-up period is comparable with the trials of other well-established therapies which have reduced heart failure admissions and mortality after an acute myocardial infarction. Therefore, I think the follow-up period was likely to be sufficient to pick up any effect of empagliflozin in this context.

Are you concerned that an apparent delay in commencing empagliflozin therapy post acute MI (up to 14 days after the event) might not have been optimal for influencing heart failure outcomes, as earlier intervention may have yielded different results?

No, I am not concerned as I would have expected to see a signal of benefit even in this time-window post-MI.

The enrolled patient cohort were relatively stable and well-treated with guideline-mandated secondary preventative therapy (most of whom received renin-angiotensin system inhibitors and beta-blockers). Do you think this may have diluted the potential effects of empagliflozin, making it harder to demonstrate a significant benefit?

Rather, I think this cohort makes the true relative impact of empagliflozin easier to understand in the context of other established, guideline-recommended therapy.

Like many large cardiovascular outcomes trials before it, EMPACT-MI failed to adequately enrich the study cohort with hitherto underrepresented demographics such as women and ethnically diverse groups. How do we make access to clinical trials for these groups more equitable?

This is the crucial issue. Sadly, we continue to have trials which, at best, do not recruit populations representative of the whole, or even the majority of the global population at risk of cardiovascular disease, and at worst, we provide evidence which may not apply in those groups which are grossly under-represented. There are three things we can do. First, we must have pre-specified targets in trials for under-represented groups so that they are powered to provide results for these patients, and where necessary, we may need specific trials in these under-represented groups. Second, trials must actually recruit and meet these targets for under-represented groups, including women and ethnically diverse groups. This should be as important as, if not more important than, the other stipulations placed upon trials by regulatory authorities. Third, presentation and publication of trial results have to include these groups as part of the main study. Overall, we need a change of culture and a commitment to that change by all stakeholders.