**Title: ESC 22: PANTHER: P2Y12i Vs Aspirin Monotherapy in Pts with CAD With Prof Valgimigli**

**Participants: Dr Marco Valgimigli**

**Date: 29th August 2022**

**Dr Marco Valgimigli**

"- Hello, my name is Marco Valgimigli. I am a professor of cardiology at the University of the Italian Switzerland and deputy chief of Cardiocentro Ticino Institute in Lugano, Switzerland.

The PANTHER Collaborative Initiative

So, we asked principal investigators of these seven large randomised control studies to provide us the data because we wanted to ask a very critical question. Is aspirin monotherapy the way to go forward in terms of secondary and tertiary prevention in patient with established CAD? That was the unique way to gather huge amount of data. These seven studies gave us as many as 35,000 patients. Not all of them had established CAD, mainly from the old CAPRIE study, so that group of patients have been excluded. We also excluded patients who had an initial DAPT phase a part of the study protocol. And then they had either events or died during the DAPT phase. So, we only focused on patient really started the comparison of aspirin versus P2Y12 inhibitor. And by making this extra selection, the dataset now contains over 25,000 patients who have been allocated either to aspirin or P2Y12 inhibitor which was either clopidogrel or ticagrelor.

Oral P2Y12-I’s as a Potential Alternative to ASA Therapy

While we have seen a huge amount of studies giving us the key information that P2Y12 inhibition is central in the prevention of coronary related adverse events, we've discovered the value of that class of drug for stent thrombosis prevention. And nowadays, in the last 10 years, we have realised that P2Y12 inhibitor is central for secondary prevention irrespective of prior stent implantation. So, I think the key question was is aspirin still as good as P2Y12 inhibitor or perhaps is aspirin already a relatively old drug which can be replaced by more contemporary agents?

Study Design and Qualifying Trials

So, we perform an individual patient data meta-analysis whereby we pre-specified to select all randomised control studies comparing either aspirin or one of the P2Y12 inhibitor in a randomised fashion on centrally adjudicated endpoint. We identified seven studies for the very old CAPRIE to the most recent HOST-EXAM. And actually, these seven studies are providing data for that amount of patient was referring to. So more than 25,000 patients, roughly more than 500 sites recruiting patient in Europe, United States, and South America.

Key Findings

So, the primary point of the study was the composite of CV death, MI, and stroke. And that was significantly reduced by 12% in favour of P2Y12 inhibitor with the number needed to treating the range of 113. We also pre-specified a key safety endpoint, which was any major bleeding, they did not differ from a statistical standpoint despite numerically, were interestingly in favour of P2Y12 inhibitor. However, inside the box of a major bleeding, we did see that there were two type of major bleeding which were significantly reduced by P2Y12 inhibitor. One being GI bleeding complications, and the other one was almost 70% reduction of intracranial bleeding. So, any major bleeding did not differ but the most common one, GI bleeding, and the most concerning one, intracranial bleeding, were indeed significantly reduced. When we look into other secondary endpoint, stroke did not differ, yet there was a borderline reduction in favour of P2Y12 inhibitor, and there was almost 50% reduction for stent thrombosis favouring P2Y12 inhibitor.

Impact on Clinical Practice and Guideline Recommendations

I think these findings are really practice changing and I hope that will be incorporated into new guidelines released. Now, we have been prescribing aspirin with a class recommendation 1A since many years. I think now this is not justifiable anymore, I think we have a slightly better option. Now, you may question the fact that the relative risk difference between aspirin and a P2Y12 inhibitor was not huge, was only 12, 13%. Yet this extra benefit does not come with any extra cost. The bleeding are, if anything, the same or even lower at least some type of bleeding. So I think now, the new class 1 recommendation should be given to P2Y12 inhibitor more than aspirin, and perhaps, leave aspirin as a second-line option.

Unanswered Questions

I think these evidence is solid enough but I'm pretty sure that there will be many in the community who will question the results. So, I think the next step will be hopefully to do a more contemporary and perhaps very large study comparing, again, aspirin and P2Y12 inhibitor. Now, we need to understand whether any P2Y12 inhibitor makes any difference. In our study, there was no heterogeneity with respect to the type of, speaking about clopidogrel and ticagrelor. We would need to have data about prasugrel, and I think that will be an extra important question to be answered, which P2Y12 inhibitor be preferred and in which patients.