Title: ESC 23: Day 4 Wrap-Up with Dr Alasnag and Dr Al-Shaibi
Participants: Dr Mirvat Alasnag and Dr Khaled Al-Shaibi
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Dr Mirvat Alasnag

" Hello everybody, and welcome to the final day of ESC 2023 from Amsterdam. This is Mirvat Alasnag and Khaled Al-Shaibi. So, you know, we're winding down and yesterday was a very intense day with a lot of trials that have been presented today. We've selected, really, two trials that we want to cover. One is the OPT-BIRISK and the other one is NITRATE-CIN that Dr. Al-Shaibi will cover for you. So I'm going to start with the OPT-BIRISK.

Now, the OPT-BIRISK study was conducted in China in over 100 centres and it really enrolled patients who had an acute coronary syndrome and underwent PCI with a drug-eluting stent and were on dual antiplatelet therapy that consisted of aspirin and a P2Y12 inhibitor, either Clopidogrel or Ticagrelor. Now, it also stipulated that during the previous six months, these patients were clinically free from any events before enrollment. And then they were enrolled and randomized to an extended dual antiplatelet regimen that consisted of aspirin 100 milligrammes and clopidogrel 75 milligrammes or 75 milligrammes of clopidogrel monotherapy.

Now, note that there was a run-in period where they continued an open-label aspirin regimen for approximately three months and the purpose of that was to exclude any kind of rebound events. They followed up these patients for three, six, nine and twelve months. And then they reported the primary endpoint, which was bleeding BARC two, three or five, and the secondary endpoints, which was major adverse cardiovascular and cerebral vascular events at nine months. And the other secondary endpoints included a composite of cardiac death, myocardial infarction and clinically driven revascularization, and of course, the individual components of this composite.

So ultimately, they ended up enrolling over 7000 patients, about 3800 in each arm, and the mean age was 65, with women enrolled about 41%, which was great. Eventually, they noted that BARC two, three and five bleeding in the groups was actually 2.5% in

those assigned to Clopidogrel monotherapy and 3.3% in the dual antiplatelet therapy arm. In terms of the secondary endpoint, particularly major adverse cardiovascular and cerebral vascular events, the incidence was 2.6% and 3.5% respectively.

So really, in patients who have suffered an acute coronary syndrome and underwent PCI with a drug-eluting stent and were event free for at least six months and received clopidogrel or and ticagrelor during that time, what we see is monotherapy actually had lower bleeding rates and lower ischemic events, meaning cerebral, vascular and coronary events. Now, it's interesting because the investigators, when asked, they really didn't have an explanation other than perhaps the bleeding event in these patients required remedial actions and medications that perhaps rendered them at risk for their ischemia.

And from there I'll turn to you, Dr. Al-Shaibi, for the NITRATE-CIN trial. If you could tell us about that one.

Dr Khaled Al-Shaibi

Well, as we all know, as an interventionalist, patients with renal dysfunction frequently pose a problem and we always worry about contrast-induced nephropathy and the NITRATE-CIN trial essentially examined the efficacy of organic nitrates in preventing CIN in patients at high renal risk who presented with ACS and underwent coronary angiography. Patients were considered at risk for CIN if their EGFR was less than 60 mils per minute. Or they had two of five other criteria. Those criteria being age greater than 70 diabetes, heart failure or reduced ejection fraction less. Than 40% taking renal active drugs, which most of these patients would be in the form of a nasal and ARB. Or had received contrast within the prior week, or had significant chronic liver disease.

So if they had two of those five criteria, you'd also be considered a risk for contrast nephropathy. Now, patients were randomized in a one-to-one fashion to once daily potassium nitrate twelve millimoles or placebo, and the active treatment was given for five days. Now, both groups received standard of care, IV hydration and angiography was undertaken with low osmolar contrast agents. The primary endpoint was the

incidence of cin, the incidence of contrast-induced nephropathy as defined by the kidney disease improving Global Outcomes criteria, which essentially were an increase of 30 milligrammes per deciliter. That's around 325 millimoles per litre. In the first 48 hours. There were three secondary outcomes. They were renal function at three months, the rate of procedural MI and major adverse cardiac events out to one year.

Now, 640 patients were randomized, approximately 320 in each arm. The mean age was around 70. Half of these patients were diabetic, half were nondiabetic and half had chronic kidney disease, as evidenced by EGFR less than 60. The median follow-up was twelve months. If we look at the primary endpoint, active treatment with inorganic nitrate reduced the incidence of contrast-induced nephropathy. It was 9.1% in the active treatment versus 30% in the placebo group. That's a relative risk reduction of over 80% with a highly significant p-value of 0.01. And this difference persisted after adjustment for baseline creatinine and the presence or absence of underlying diabetes.

Now, the secondary endpoints, all three secondary endpoints were also in favour of active treatment with inorganic nitrates. Procedural MI was 2.7% in the active treatment group and 12.5% in the placebo group with a p-value of 0.03. Furthermore, one year MACE was reduced in the active treatment group. It was 9% in the active treatment group and 18% in the placebo group. That's a p-value again of 0.01. And these patients also received active treatment had improved renal function at three months. The conclusion was that inorganic nitrate therapy reduced the incidental contrast-induced nephropathy and subsequent cardiac events in the ensuing one year and preserved renal function.

So I think it was a very interesting study that many of us may be able to take home tomorrow and potentially implement in these patients.

Dr Mirvat Alasnag

Practice changing, actually, yes. Well, that is a wrap from ESC 2023 in Amsterdam. I know for me the guidelines that were elaborated were certainly going to impact my

practice. But I want to turn to you on a final note, Dr Al-Shaibi. What were the most important trials, in your opinion, impactful trials for you as a clinician?

Dr Khaled Al-Shaibi

Well, I think one that's going to change practice almost immediately is the STEP-HFpEF trial, which really has expanded. Now, the use of GLP1 agonists to all patients with obesity and heart failure. I think that's going to be potentially a practice-changing trial. Now, obviously, the trials that created the greatest debate and discussion at ESC this year are the intracoronary imaging trials ILLUMIEN IV, the network meta-analysis presented by Gregg Stone and the OCTOBER Bifurcation trial. So I think those four for me, would be the pick of the crop.

Dr Mirvat Alasnag

Well, thank you for tuning in and we'll see you next year from ESC London. Mark your calendars."