

**Title: ESC 23: Day 3 Wrap-Up with Dr Alasnag and Dr Al-Shaibi**

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## **Dr Mirvat Alasnag**

"Well, hello everybody from Amsterdam again, and this is day three of the ESC Congress, and with me again is Dr. Khaled Al-Shaibi to go over a wrap-up of today's late-breaking trials. We're going to cover the ILLUMIEN IV trial, the OCTAVIUS trial, the OCTOBER trial, and of course, the meta-analysis that was presented by Dr. Gregg Stone. So I'm going to turn over to you, Dr. Khalid, you're going to cover the ILLUMIEN trial which stirred some conversations today during the conference.

## **Dr Khalid Al-Shaibi**

It did indeed. Well, as you all know, the ILLUMIEN set of trials I through III established that OCT is superior to angiography as far as getting better results, as far as minimal stent area, better stent expansion, reducing malapposition, reducing dissections, a lot of good things. And OCT clearly did that far better than angiography. But what remained unanswered was did these better results we get by using OCT translate to better clinical outcomes. And this was the whole point behind ILLUMIEN IV.

So, ILLUMIEN IV randomized high-risk patients with undergoing PCI to either an OCT-based PCI strategy or an angiography-based strategy. The primary endpoint, there were two. There was an imaging endpoint which was essentially minimal stent area and this was again powered for superiority and there was a clinical endpoint which was target vessel failure. And target vessel failure included cardiac death, target vessel myocardial infarction, and ischemia-driven target vessel revascularization. There was also a safety endpoint that looked at sub-acute stent thrombosis.

Now just under 2500 patients were randomized around 1200 to OCT and 1200 to angio. And the follow-up period was two years. Now the primary imaging endpoint, which was minimal stent area was achieved for superiority with a minimum of stent area of 5.7 in the OCT group and 5.3 in the angio group with the p-value of 0.01.

Now, as far as the clinical endpoint, and this was really the whole reason why the study was performed was the reduction in target vessel failure. This was unfortunately not met with the OCT. Target vessel failure occurred in 7.4% and in the angio group 8.2% with a p-value of 0.045. If we then look at the secondary endpoints which included the components of the TVF, cardiac death, target vessel MI, and cardiac and ischemia-driven TLR. All again, unfortunately did not reach statistical significance, although for cardiac death and for target vessel myocardial infarction, they were numerically lower in the ACT group but didn't quite reach statistical significance. While for ischemia-driven TLR, there was absolutely no difference there.

As far as the safety endpoint, and this is an interesting one here. There was a clear and statistical reduction in subacute stent thrombosis in the OCT arm, so it seemed to be beneficial there. The final conclusion was that oct-guided percutaneous coronary intervention leads to a larger minimal stent area but did not reduce two-year rates of target vessel failure compared to the angiography-guided PCI. But again, I think we need to interpret this in the broader context of all studies that we've done that looked at intracoronary imaging compared to angio and the meta-analysis that you're going to discuss a little later.

## **Dr Mirvat Alasnag**

Absolutely. So I think before we say a single study is going to change the guidelines, we need to look at the totality of evidence and that's what we'll hopefully go through today.

So OCTAVIUS is the next one that I want to go over. And this was an investigator-initiated prospective multicenter trial that was actually conducted in Korea. And it was an open-label, very pragmatic trial with the purpose of having all comers and just having patients represented from acute coronary syndrome to chronic coronary syndromes to different anatomies. Now, about 2008 patients were enrolled in this trial. They were randomized one-to-one where oct guided PCI compared with IVUS guided PCI. The average age of patients that were enrolled was about 64.7 years and women were only

21.6%. But interestingly, only 33% were diabetic and the majority, 76% were chronic coronary syndromes. Acute coronary syndrome was only 23%.

The primary endpoint here was a composite of death from cardiac cause target vessel myocardial infarction and ischemia-driven target vessel revascularization at one year. Now this was powered for non-inferiority. So at one year the primary endpoint occurred in 2.5% of the OCT arm and 3.1% of the IVUS arm. And in terms of the safety endpoint, the incidence of contrast-induced nephropathy was similar between OCT and IVUS, 1.4 and 1.5 respectively. And the incidence of major complications was actually lower in the OCT arm 2.2 versus 3.7, with a p-value of 0.48. And interestingly, the total PCI time was shorter in the OCT group, 46 minutes compared with 48 minutes. And again the p-value was significant.

But overall the investigators conclude that among patients undergoing PCI, OCT-guided PCI was non-inferior. This was a non-inferiority design, non-inferior to IVUS guidance with respect to composite of death, cardiac from cardiac causes target vessel revascularisation and ischemia-driven revascularisation at twelve months, which takes me to the next trial, the OCTOBER trial, which was probably more complex patient population. Want to tell us about that?

## **Dr Khalid Al-Shaibi**

Well, the OCTOBER trial is interesting. This looked at patients with complex bifurcations and randomized them to either an oct guided strategy or the conventional angiographic-guided strategy. The primary endpoint was major adverse cardiac events. This was a composite of cardiac death, target vessel, MI and ischemia-driven TLR. The secondary endpoints were all-cause mortality, cardiac death, target lesion, myocardial infarction and ischemia-driven TLR. The trial included just over 1200 patients, 600 patients randomized to each shard. The primary endpoint, which was major adverse cardiac events at two years, occurred in 10.1% of the OCT guided arm and 14% of the angio-guided arm. That's a relative risk reduction of 30% if you use OCT guidance in treating these complex bifurcations. And the p-value here was significant at 0.35.

As far as the clinical endpoints, at two years, they were numerically lower for all components of the primary endpoint, but did not reach statistical significance as the trial was really not powered for this. But just to give you a flavor of the numbers, all-cause death was 2.4% in the OCT arm compared to 4% in the angio arm. For target vessel MI, it was 7.8% in the OCT group, 8.5 in the angio group and for ischemia-driven TLR, it was 3% in the OCT group and 5% in the angio group. There was no apparent differences in procedural safety, but the volume of contrast, obviously, and actually the time for the procedure was longer in the OCT-treated arms.

So the conclusion of the authors here was that PCI guided by OCT reduces adverse cardiac events in patients with bifurcation lesions.

### **Dr Mirvat Alasnag**

Yeah, that was interesting. And they did use oct multiple times to check wire position lesions, stent deployments, and so on. What was the type of lesions that were done or the strategy that was adopted?

### **Dr Khalid Al-Shaibi**

In the majority of these cases, the strategy was equal between both and the two most commonly used strategies were provisional strategy and a DK crush strategy. But they were equally divided among the two groups.

### **Dr Mirvat Alasnag**

Yeah, which takes us to the meta-analysis that Gregg Stone presented today and actually really helped us put everything into perspective and perhaps that's what we need when reconsidering the guidelines that were just elaborated, actually.

So a number of trials have actually looked at intravascular ultrasound compared with angiography. We don't have as much data with optical coherence tomography. Nevertheless, I think it is important in this meta-analysis, what they did is they looked at the overall effects of intravascular imaging, be it IVUS or oct compared with

angiography. They looked at IVUS compared with angiography, they looked at OCT compared with angiography and then also IVUS compared with OCT. And it incorporated about 20 randomized trials with over 12,400 patients enrolled, both with chronic coronary syndrome and acute coronary syndrome. And the conventional endpoints were analyzed here. Over 7000 patients were randomly allocated to the intravascular ultrasound group and over 5000 in the angiography only group in this meta analysis. And they looked at it between six months and outcomes between six months and five years.

So in terms of intravascular imaging, not unexpectedly, in terms of IVUS and OCT-guided PCI, the results showed a definite reduction in the primary composite outcome of target lesion failure by 31% compared with those who had angiography guided PCI only angiography guided PCI. Now, with respect to the secondary outcomes, intravascular imaging guidance showed a reduction in cardiac death by 46%, target vessel MI by 20%, TVR 29%, and stent thrombosis by 52% compared with angiography and all. So these are very significant findings. There were also statistically significant reductions in all-cause death, all-cause MI, target vessel revascularization, and so on.

So this analysis did not include the OCTAVIUS trial, which was presented today. But Davide Cappodanno provided a very elegant commentary on this meta-analysis, and he actually included the OCTAVIUS, which even after including the numbers, just don't pan out to give us what we need. And really, he helped us put it very well into perspective. There is evidence that supports from clinical trials and the meta-analyses that support IVUS, and it's very consistent in showing substantial reductions in cardiac events. Now, IVUS and OCT really should not be seen as competitive technologies, but rather complementary technologies, and any intracoronary imaging is better than none.

Now, the remaining question now is whether the optimal candidates in IVUS and OCT and the strategic timing of doing the intracoronary imaging. We just went over the complex PCI with the OCTOBER, but we know that DK crush eight, I believe, is still recruiting at this time, and the intracoronary imaging portion of that is going to be very complex. So I think these are still areas that we need to iron out in the field.

## **Dr Khalid Al-Shaibi**

I think the bottom line here is imaging whether it's IVUS or OCT will provide superior results to angio only.

## **Dr Mirvat Alasnag**

There are a couple of other trials that we're not going to go into depth on because the main hype at ESC today has been the intracoronary imaging trials. But two important trials that I think we can't have the day go by without us just at least telling you about them. Dr. Al-Shaibi, you want to start with the well, there was a MULTISTARS-AMI trial.

## **Dr Khalid Al-Shaibi**

We all know that in patients who present with STEMI, complete revascularization is indicated, and the guidelines tell us so. But it's unclear as to whether it makes a difference whether this is done during the reference index hospitalization or whether this can be done at a later date within the first 40 to five days, as was done in the complete trial. And this study, randomized patients to immediate in-hospital complete revascularization versus deferred revascularization and the primary endpoint was all-cause death, non-fatal MI stroke and unplanned ischemia-driven TLR. And to cut a long story short, the result was positive for both non-inferiority and superiority. An immediate complete revascularization during the index hospitalization was superior to and definitely not inferior to a deferred strategy.

## **Dr Mirvat Alasnag**

And that's certainly something to take into consideration with multivessel disease. And the last one is not really my area of specialty, but we're all seeing it and there's a lot of discussion about it. And it's patients who have amyloid cardiomyopathy. There are several drugs that are now available. The one that was presented today is the ATTR-tribute trial. It was a very strongly positive trial, and it really looked at acoramidis. I'm not even sure I'm pronouncing it correctly. And they really looked at some very hard endpoints, but they also looked at surrogate endpoints, such as BNP Hospitalizations.

And there was a significant reduction in all of those in patients who received the appropriate drug doses. So thank you everybody, for tuning in on day three. And stay tuned for tomorrow as well on day four.”