- Hi, my name is Rupert Bauersachs, I'm director of vascular medicine at the Clinic Darmstadt in Germany.

1. What is the VOYAGER PAD Trial and what does it aim to address?

Well, the background that we have in patients with peripheral arterial disease is that we know now that after those patients undergo lower extremity revascularization they have a very high risk to develop acute limb ischaemia (ALI) and, and this is not the end of the story but subsequently they develop more complications and especially limb complications and unfortunately, until now, there hadn't been any large prospective randomised trial to look on how to improve that outcome.

1. What was the study design, patient population and endpoints?

So, VOYAGER PAD was a randomised controlled double-blind trial comparing rivaroxaban 2.5 mg twice daily with placebo in 6,564 patients with symptomatic PAD that had undergone infrainguinal lower extremity revascularization within the last 10 days. Clopidogrel was allowed according to the investigator's discretion up to six months and the present analysis looks not only at first events, but this analysis looked at the totality of vascular events, including the primary endpoint, which was a composite of major adverse limb events, was a composite of acute limb ischaemia, amputation of a major [Inaudible], myocardial infarction, ischaemic stroke and cardiovascular death and it added the need for lower extremity revascularization and also for venous thromboembolism. So, the patient population that was studied in VOYAGER PAD was the typical population of patients with peripheral arterial disease. So, they had a high percentage of hypertension of more than 80%, they have hypercholesterolemia in about 60%, unfortunately and that's also typical, more than 30% of the patients were still smoking. A fifth of the patients had impaired renal function and of course, about one third had coronary artery disease and the majority were well treated with the best medical background treatment. 80% had a statin, more than 60% had ERBs, and more than 50% of the patients also receive clopidogrel right after the intervention or the surgery and that was at the discretion of the investigator. It is interesting to compare the baseline characteristics of those patients that had no vascular event during the study, to those patients that had one event or that had multiple events. So those 4,263 patients that had no event differed in those with multiple events, that those with multiple events had more underlying comorbidities. Also, they had undergone more complex revascularization and those with multiple events were less likely to be randomised to rivaroxaban and they received clopidogrel in a higher percentage.

1. What are the key findings to date?

I think a key message from the VOYAGER PAD study is that the event rate in the placebo group was very high after three years, it was 19.9% of the primary endpoint. So, this is a very high rate that occurred on top of best medical background treatment. But if we now look at total events, including lower extremity revascularization and venous thromboembolism, we find that the event rate is even higher. So more than a third of the patients suffered at least one of those events within the three years and the event rate was 88% within three years. So, 88.4 events occurred in a hundred patients with placebo, as compared to 75.9 events per a hundred patients receiving rivaroxaban. Rivaroxaban not only reduce the first event but also the second, the third, and so-on events, with a total reduction of 342 events. Now, if we would've looked only at the first event, we would've missed nearly more than 80% of the benefit.

1. What conclusions can be made and what are the implications on practice?

So, we observed a very high event rate of 88.4 per a hundred patients in three years in the placebo group and 75.9 events per a hundred patients in the rivaroxaban group. So, a very high event rate and more than a third of the patients suffered from one limb event and so, it is very important to not only look at the first event, but also total events, and it is clear that we have to do anything which is possible to reduce that high complication rate in PAD patients undergoing lower extremity revascularization and it's also important that in this trial and in future trials, we not only look at MACE events but also limb events in PAD patients. Rivaroxaban should be used as an agentive treatment in patients undergoing lower extremity revascularization to improve that high complication rate.

1. What are the next steps?

I think it is important that in the future we perform trials in this highly vulnerable population with PAD, especially after lower extremity revascularization. And that we also look at limb events, and not only MACE events and try everything to reduce the total burden of disease in those patients.