Transcript: ACT Outpatient Trial Results

**Dr. Sanjit S. Jolly**: I'm here to talk about the ACT, both outpatient and inpatient COVID-19 treatment trials.

I'm going to take you back to the spring of 2020 and we were a group of cardiology researchers who, in fact, all our trials had stopped and we pivoted to try to really do a COVID-19 treatment trial. We were hearing horror stories from Italy and we came together and we designed a series of trials: an outpatient trial to really prevent hospitalization and death as well as an inpatient trial to reduce the need for mechanical ventilation, high flow oxygen and mortality.

The predominant mechanisms were both inflammation and thrombosis. And so we tried to target both those mechanisms with therapies. In the outpatient's, we used a two by two factorial design of aspirin versus control as well as colchicine versus control. And there had been promising data from colchicine in the COLCORONA trial.

We randomized about 3,500 patients in the outpatient's with symptomatic COVID-19 who were not hospitalized, who were at home. And we randomized them to aspirin versus control and colchicine versus control. And what we found was, in fact, colchicine did not reduce the incidence of hospitalization or death in outpatients and aspirin did not reduce the incidence of thrombosis, hospitalization or death in outpatients with COVID-19.

Now, moving on to the inpatient trial. In inpatients with COVID-19, the mortality is very high and we randomize patients to a loading dose of colchicine followed by a twice daily regimen and this is a regimen that's been shown in other trials to reduce IL-6, which, of course, is related to tocilizumab and the benefit observed there.

We also use rivaroxaban, 2.5 milligrams twice daily and a low dose aspirin in a two by two factorial design, randomized.

 What we found for the primary outcome of death: need for high flow oxygen, invasive mechanical ventilation. In fact, there was no difference. Mortality was very high. It was about 20% for these patients, but colchicine did not reduce this.

In terms of aspirin and rivaroxaban, we found a similar finding. In fact, no difference for the primary outcome of major thrombosis: high flow oxygen, need from invasive mechanical ventilation or death. And so really entirely neutral.

We did find that intensified anticoagulation did increase bleeding. We then went back to literature and did an updated meta-analysis of all the available trials of colchicine versus control and hospitalized patients and found no difference in mortality or difference in the primary outcome of the trial.

So it's very, very clear that colchicine, on a background of steroids, most of our patients, about 90%, were on steroids, did not seem to reduce hard clinical outcomes in COVID-19.

In terms of intensified anticoagulation, the story's a little bit different there. When you look at the meta-analysis of all the available trials, there is a 40% reduction in the incidence of venous thromboembolism when you intensify anticoagulation, but that 40% reduction in VTE does not translate into reduction in mortality and there's, in fact, no reduction in mortality.

In conclusion, how does this take us forward? Well, colchicine clearly should not be used either in outpatients or inpatients with COVID-19 for the treatment to reduce hospitalization, mortality or other outcomes.

In terms of anticoagulation, we did not observe a benefit for low dose aspirin and low dose rivaroxaban. However, the totality of the data suggests that an intensifying anticoagulation may reduce VTE. However, it actually has no impact on mortality.

And I think really, this is really closing the chapter because there's been a number of trials looking at anticoagulation and it does not impact mortality.

I'd like to thank you for this opportunity to present on the ACT trials. Thank you.