IAN ODELL: All right, so the main indication for ECP in scleroderma is for progressive skin disease. So it's not used for involvement of internal organs. And so a patient with early disease, less than two to three years, who has progressive skin involvement despite therapy with a separate immunosuppressive medication would be a good candidate to consider ECP. And so here, we'll review the data, the clinical trial data, that supports its use for scleroderma.

Now, there are three main clinical trials ranging from the earliest one, in 1992, and the most recent one was in the early 2000s. Now, the first one was by Rook et al. It was a multi-center, single-blinded study, and they looked at 79 patients with less than four years of active disease. In this trial, they looked at a skin severity score, so the skin induration, as well as the total amount of skin surface area covered, as well as functional outcomes, such as hand grip and oral aperture, or the ability to open the mouth.

They compared ECP to penicillamine which at the time was also considered to be a potential therapy for scleroderma. And in the side-by-side trial of ECP to penicillamine, they found that 2/3 of patients treated with ECP had a greater than 15% improvement in their skin severity score. Whereas, only 1/3 of patients with penicillamine achieved greater than 15% improvement.

So there's a caveat to this, because in the natural history of scleroderma, after the induration phase, there's an atrophic phase in which a number of patients will improve on their own due to just the natural course of disease. And these trials have had issues because of this spontaneous improvement in a subset of patients. And so this can be seen even in this early data, because both if we look at just the skin severity scores and the mean improvement in skin severity score, both ECP and penicillamine improved about five to six points in their score. And this likely reflects the improvement that would have happened in those patients anyway.

In addition in this trial, with the functional outcomes, ECP really looked the best. So they had improved hand grip and oral aperture. And actually, in this trial, the most impressive data was that they really had good functional outcomes in their skin involvement.

Now, subsequent to this trial there's a very small trial, published in 1999, by [INAUDIBLE] et al in which they enrolled 19 patients and 15 of which had diffused systemic sclerosis. They measured many areas of the body and also did functional outcomes but found no difference. Really, the take home message from this negative study is that it was underpowered to find the results.

But however, given this negative study, there is a subsequent double-blinded, multi-center clinical trial looking at ECP for scleroderma, and in this case, this is [INAUDIBLE] et al. And in this case, they enrolled 64 patients with diffuse systemic sclerosis that had disease for less than two years. They measured outcomes at 6 and 12 months with a skin severity score, the extent of skin involvement, and again the functional outcomes of hand grip and oral aperture.

So in terms of quality, this was the best ECP clinical trial, because not only was it multi-centered, but it is also double-blinded. And in one arm of the study, they treated patients with ECP, but in the other arm of the study, they treated patients with a sham procedure. And what they did in this case was they placed the IV and actually drew blood from the patients into the machine, but they didn't run the ECP procedure on the patients. And so neither the patient nor the investigator knew which arm of the trial that the patient was receiving.

And so then going back to the natural improvement that occurs within some patients the scleroderma, what they found, surprisingly, was that in patients with ECP, they saw improvement from baseline. And this was a statistically-significant improvement by about again five to six points on the severity scale. Now, so that looked great. However, in the sham procedure, they also saw improvement to a little over three points in the skin severity score, so both arms actually saw improvement even with the sham procedure. And one of the problems with this trial is that in the analysis, there was no significant difference by a p-value of 0.05 between patients treated with the ECP compared to patients treated with the sham procedure.

So this data really has to be taken in light, that they didn't hit their p-value. And in further analysis, after the study completed, they determined that they would need probably double the amount of patients that they had to find that statistically-significant improvement in ECP over sham procedure. But if you actually look at the p-values that they had, they had a p-value of 0.12. So what this means is that instead of hitting that 95% probability that ECP was better over a sham, instead their data really shows that the likelihood is 9 out of 10 that ECP is better than sham. So depending on where you draw your statistical significance, I think the data still supports the role of ECP in therapy of scleroderma.