

## **Transcript from Video Interview with Professor Paul Valensi**

### **Accompanies publication of primary results from the IMPROVE™ study**

Valensi P, Benroubi M, Borzi B et al. Initiating insulin therapy with, or switching existing insulin therapy to, biphasic insulin aspart 30/70 (NovoMix® 30) in routine care: safety and effectiveness in patients with type 2 diabetes in the IMPROVE™ observational study. *Int J Clin Pract* 2009;63(3):522-31.

#### **Interviewer - Wendy Barnaby**

Hello and welcome to the *International Journal of Clinical Practice* Editor's Choice interview. Today we will be hearing from Professor Paul Valensi, professor of Nutrition and a Diabetologist at the Jean Verdier Hospital at Paris-Nord University. We will be discussing an article he has co-authored in the March issue of the journal on biphasic insulin analogue therapy for patients with type 2 diabetes [1]. And before we start, I would like to thank Novo Nordisk for supporting the video cast with an educational grant.

#### **Interviewer - Wendy Barnaby**

So welcome to you Professor Valensi. First of all can you tell me the conclusion of the study?

#### **Interviewee - Paul Valensi**

The most important conclusions of the IMPROVE™ study are threefold. The first one is that NovoMix® 30, a biphasic insulin analogue is very efficient as to blood glucose control, that's the first point. The second one is that the rate of hypoglycaemic events in particular major hypoglycaemic events decreases during the study. And the third point is that patients expressed an improvement in their satisfaction about their blood glucose control and also they felt less tired, and they worried less about their diabetic complications.

#### **Interviewer - Wendy Barnaby**

Now this was an observational study, not a random control trial in which there are about 58,000 people taking part. You had three subgroups of patients, didn't you?

#### **Interviewee - Paul Valensi**

We had three subpopulations, we can say that. In every case, there were type 2 diabetic patients. Some of them were coming from no previous antidiabetic therapy, some others were coming from oral antidiabetic treatment and the third subgroup were coming from previous insulin therapy, but the most important group was in fact this one coming from oral antidiabetic treatment.

**Interviewer - Wendy Barnaby**

Why was that?

**Interviewee - Paul Valensi**

Because it's usually the case, I can say worldwide. Most of the diabetic patients are first treated by lifestyle advice and secondarily by oral antidiabetic drugs and finally by insulin therapy, but indeed when we see, as a figure of these patients, in particular coming from no insulin therapy, they were poorly controlled. So what we were expecting was an improvement, a marked decrease in HbA<sub>1c</sub> levels when using insulin, in particular NovoMix® 30.

**Interviewer - Wendy Barnaby**

And that's what you found?

**Interviewee - Paul Valensi**

We found indeed a wonderful improvement in glycaemic control as expressed by HbA<sub>1c</sub> levels. The mean decrease in HbA<sub>1c</sub> in the overall diabetic population was about 2.1%; at baselines they were very poorly controlled, mean HbA<sub>1c</sub> level 9.4%. So a marked improvement in HbA<sub>1c</sub> which resulted from a decrease in fasting blood glucose and also as expected from the decrease in the postprandial blood glucose.

**Interviewer - Wendy Barnaby**

And did each subgroup show improvement in the three factors that you mentioned?

**Interviewee - Paul Valensi**

We found an improvement in the overall population that was the first analysis. And also we looked for the improvement in every subgroup and it was the case; every subgroup improved dramatically their HbA<sub>1c</sub> levels.

**Interviewer - Wendy Barnaby**

So what is it about this sort of insulin that gives such good control?

**Interviewee - Paul Valensi**

So what we tested was NovoMix® 30, which is a premix formulation of an insulin analogue. This premix formulation comprises 30% rapid-acting soluble aspart insulin analogue and 70% intermediate acting protaminated aspart insulin analogue. So we have one part which is devoted to improve, to decrease fasting blood glucose, which is the intermediate-acting fraction and the rapid-acting fraction which acts to decrease postprandial increment.

**Interviewer - Wendy Barnaby**

Now the study drew on 12 countries, patients in Asia, in Europe, Canada, the Gulf states — why is it so important to have such a mixture of countries taking part?

**Interviewee - Paul Valensi**

Of course, we can expect the same kind of results, whatever this insulin is tested or proposed to our patients. But in most controlled clinical trials we have such a study performed only in western countries for instance, or the study is performed only in Asia for instance, and here we have performed a study in several continents, in a lot of countries and a huge number of diabetic patients. We had included more than 58,000 type 2 diabetic patients. All of them were insulin requiring and we wanted to confirm in this observational setting what has been seen in randomized controlled trials performed in such continents. So were willing when we were building this study, we were willing to confirm and extend what was seen from randomized controlled trials. And we wanted to confirm it in several countries, several continents and that was the case. We can see the same improvement, the same satisfaction expressed by the patients; the same decrease in the rate of hypos or whatever, the patients are living.

**Interviewer - Wendy Barnaby**

You said that the patients all expressed improved satisfaction with their treatment, but I wonder if some of this might not be a study effect, perhaps there was psychological reasons taking part in the study, perhaps having more of the doctor's attention than usual that might have made them more pleased with their treatment rather than the effect of the insulin itself.

**Interviewee - Paul Valensi**

We may not exclude the psychological influence on the results. We are in a study, but we are in an observational study. So what we did was to ask the physicians to prescribe insulin as I would have done in routine clinical practice and we wanted to be the closest to the routine clinical practice and not to change this practice. Of course, we also provided more information to the physicians about NovoMix® 30, when we were starting the study. We also reminded him/her about the importance of lifestyle advice to their patients. Would have they done more, a bit more than in routine clinical practice, we cannot exclude it completely. So there may be some study effect in these results. But I don't think really that this study effect was so important, probably not so important and this is now confirmed in a huge population of patients. So I think really that the results are reliable.

**Interviewer - Wendy Barnaby**

Now, you yourself have said that observational studies like this one do have shortcomings. So do you think it was really useful? I mean a cynic might say that Novo has simply funded this study in order to promote its brand of insulin.

**Interviewee - Paul Valensi**

This study is certainly important. In randomized controlled studies, we recruit patients on precise selection criteria. We have inclusion criteria and we have exclusion criteria. In this observational study, we had not any of these criteria; the only inclusion criterion was a type 2 diabetic patient who needs to be treated by insulin. And we wanted to see how the physicians prescribe or initiate NovoMix® 30 therapy in such patients in routine clinical practice. So it is interesting to confirm what was seen in controlled trials. We have the same figures; it's the same results which show safety and effectiveness of this insulin in type 2 diabetic patients. Another very important result is that we had here, baseline patients who were very poorly controlled as to blood glucose levels and they were finally insulin treated probably too late. So this study showed the importance of starting earlier probably insulin therapy in many many type 2s.

**Interviewer - Wendy Barnaby**

So, do you think that that's the most important thing that clinicians should take away from this study that they should begin insulin treatment early?

**Interviewee - Paul Valensi**

I think this is one of the most important messages, not wait too long before starting insulin. Of course, we have now lot of interesting oral antidiabetic drugs and we can combine these treatments, but after a few months or very few years we have to consider the necessity to start on insulin and not to wait too long time, during that time complications, long-term complications are occurring and what we saw in the IMPROVE™ study is a very high rate of micro and macro vascular complications in this population.

**Interviewer - Wendy Barnaby**

So, you would hope to avoid that in the future if a clinician began early with this sort of insulin.

**Interviewee - Paul Valensi**

We know from very important controlled studies performed in type 2 and in type 1 diabetes that controlling tightly glycaemic parameters is able to prevent micro and also macro vascular complications. So we have to offer this opportunity to all of our patients and in many cases this consists of insulin therapy.

**Interviewer - Wendy Barnaby**

Now I know that you've got a lot of other data to analyze as a result of this study. Can you tell us about any other conclusions; I know that you've got another paper in press, for example?

**Interviewee - Paul Valensi**

Yes, at this moment we have a paper in press regarding the subgroup of patients who were previously on biphasic human insulin and were switched to NovoMix® 30 during the study [2]. So

we've got some interesting results. HbA<sub>1c</sub> decreased quite significantly in means around 2% and this resulted from a decrease in fasting and postprandial glucose. Interestingly, there was also a decrease in major hypoglycaemic events. And the second kind of information is, in practice how to make this switch? And in fact, of course, physicians did as they did usually and they had patients who made a unit-for-unit switch or others who started on NovoMix® 30 with a slightly higher dose or a slightly lower dose. And what we saw finally is that the best results in terms of HbA<sub>1c</sub> decrease was in this subgroup of patients who made this unit-for-unit switch. So the recommendations could be very simple to keep in mind. Make this switch unit-for-unit and of course you may, if needed adjust this dose, weeks later and we may expect doing that, a very interesting improvement.

**Interviewer - Wendy Barnaby**

Well, thank you very much indeed Professor Valensi. And that's it from us. We've been discussing Professor Valensi's article in the March issue of the *IJCP*. Thank you too for being with us. We hope you will join us again.

**References**

1. Valensi P, Benroubi M, Borzi B et al. Initiating insulin therapy with, or switching existing insulin therapy to, biphasic insulin aspart 30/70 (NovoMix® 30) in routine care: safety and effectiveness in patients with type 2 diabetes in the IMPROVE™ observational study. *Int J Clin Pract* 2009;63(3):522-31.
2. Shah S, Benroubi M, Borzi V et al. Safety and effectiveness of biphasic insulin aspart 30/70 (NovoMix® 30) when switching from human premix insulin in patients with type 2 diabetes: subgroup analysis from the 6-month IMPROVE™ observational study. *Int J Clin Pract* 2009;63 In Press. DOI: 10.1111/j.1742-1241.2009.02012.x