This article is a CME certified activity. To earn credit for this activity visit: http://cme.medscape.com/viewarticle/709649

From MedscapeCME Diabetes & Endocrinology

What Happened at the European Association for the Study of Diabetes (EASD) 45th Annual Meeting? An Update on Insulin Therapy CME

Jay S. Skyler, MD, MACP; Stefano Del Prato; Hannele Yki-Jarvinen, MD, PhD; Hans-Ulrich Häring, MD

CME Released: 10/05/2009; Valid for credit through 10/05/2010

Jay S. Skyler, MD, MACP: Hello, I'm Jay Skyler from the Diabetes Research Institute at the University of Miami Miller School of Medicine, and I'd like to welcome you to our CME Spotlight entitled, "What Happened at the EASD 45th Annual Meeting?" The EASD is the European Association for the Study of Diabetes, and we're going to be particularly focusing on an update on insulin therapy. I'm pleased to be joined today by 3 world-renowned experts in diabetes. To my right is Prof. Stefano Del Prato, Professor of Endocrinology from the University of Pisa in Italy; next is Prof. Hannele Yki-Jarvinen, Professor of Medicine at the Division of Diabetes in the University of Helsinki in Finland; and finally Prof. Hans-Ulrich Häring, Professor of Medicine at the University of Tubingen in Germany. Welcome, folks. Hope you've had an enjoyable meeting here in Vienna. Before we begin, please take a moment to complete the 2-question pretest. This will help us measure the effectiveness of this continuing education activity. The activity will address these questions within our presentation.

Now let's turn to our panel. What I'd like to do is ask each of you what you really thought was the most important thing about insulin that occurred at this meeting. Hans, why don't we start with you?

Professor Dr. Hans-Ulrich Häring, MD: To me the most important thing was the discussion about insulin and cancer in general. I think we have learned a lot about the general risk of insulin therapy and cancer risk, and I think this is a topic which should be discussed.

Dr. Skyler: So tell us your thoughts on that.

Prof. Dr. Häring: The issue which was discussed was the question of whether insulin therapy, in particular therapy with insulin analogs, has a different outcome with respect to cancer progression. This is a topic which has been discussed for a while, not only for insulin analogs but rather in more general terms -- the question of whether cancer and metabolism has an interrelation. If so, what is the interrelation of cancer and metabolism; what is the impact of body weight on cancer progression and insulin resistance, which is frequently found in obese individuals; and what is the impact of physical activity on cancer progression? What we want to look at is the whole picture of our type 2 diabetes-risk patient and evaluate how diabetes and/or diabetes therapy can potentially be connected to progression of cancer. Here at this meeting I was particularly impressed that more and more epidemiologic data are now being discussed. The data have been discussed in a very specific way addressing mode of insulin therapy but also mode of diabetes therapy in general, including the connection to cancer progression. We learned here at the meeting 2 important things: (1) insulin therapy in general might be connected to some increased incidences of certain forms of cancer; and (2) that the standard of therapy for these patients, namely metformin, might have the opposite effect. These, for me, are the 2 most important new messages which have to be weighed against each other; and in particular, the potential of metformin to have specific effects on cancer progression is very important information.

Dr. Skyler: Do either one of you, Stefano or Hannele, want to comment on this particular issue since it was such a hot issue here at this meeting.

Hannele Yki-Jarvinen, MD, PhD: I would say that for me, this discussion of insulin diabetes and cancer was also the most interesting, and I was particularly surprised to see that in obese subjects, the cancer risk that was increased the most was hepatocellular carcinoma, or cancer in the liver. That piece of information I also heard last week in a liver meeting by liver doctors, who were very concerned that obesity, the prevalence of fatty liver, and also inflamed liver increases the incidence of hepatocellular carcinoma. But some of these patients also get liver cancer, so that was worrying news confirmed at this meeting. I wasn't so convinced that it was insulin therapy that is associated with an increased risk for cancer. I became convinced that, in general, diabetes, obesity, and hyperinsulinemia (which is a marker of insulin resistance) were associated with an increased risk for cancer. What was not mentioned -- but what I thought about -- was that when you successfully treat with insulin, you improve insulin sensitivity and reduce insulin resistance, and that might have a beneficial effect; but in the types of analysis that we were shown yesterday [at the 45th Annual Meeting of the EASD], it is very difficult to control for all of the confounding variables which are associated -- for example, with prolonged insulin therapy. We saw numbers showing that you have an increased incidence of cancer once you've been on insulin for 15 years, but obviously when we get older there are multiple things that happen. Cancer becomes more prevalent as you age, but there are also many lifestyle factors that might be involved, and those patients are generally more sick who are put on insulin, so it's very difficult to control for all of that. The insulin therapy may be just a marker of something unrelated going on, so I wasn't convinced that insulin itself is bad for any patient.

Dr. Skyler: Sort of what you're saying about how hyperinsulinemia is a marker of insulin resistance reminds me of the story 30 years ago when hyperinsulinemia was first associated with coronary disease and everybody said that insulin caused heart disease. In fact it's insulin resistance that causes the heart disease, and the hyperinsulinemia is really marking that. Maybe this is the same story all over again.

Professor Stefano Del Prato: I think, Jay, that we're just at the beginning of the story. Maybe this idea that diabetes is associated with cancer has been around for a long time but never received specific attention. I think this is the right time and we will see more information emerge. What would be very important is to understand how this can dissect the potential mitogenic effect of insulin vs the presence of insulin resistance. It's actually pretty interesting -- the fact that insulin sensitizers like metformin or thiazolidinediones (TZDs) are associated with a reduction in cancer risk in diabetic individuals. I think there are several aspects that we need to understand and to explore. So I wouldn't really focus the attention just on the insulin therapy. The insulin therapy has probably been the trigger for opening up a new venue of research that will probably help us to understand better and maybe also will help us come up with a better solution for our patients.

Dr. Skyler: I'm concerned about the newspaper headlines this past June, when the first series of articles appeared in *Diabetologia* [1-4] -- they came out in the United States, at least -- saying that insulin glargine causes cancer, which is dramatically different than what it really says in the articles. In fact, with careful analyses that were subsequently added to that, there is really no evidence for supporting that statement. It was really a completely unsubstantiated statement, and even the implication that there was a mechanism for that (which some people have raised), being that glargine in some tissue culture lines of cancer cells may be more mitogenic, is probably not relevant because they're looking at the intact glargine molecule and glargine actually gets cleaved. The arginines at the end get cleaved off prior to it entering the circulation and so it circulates as A21 glycine, which has a decreased binding affinity, not an increased binding to receptors with an increased mitogenic potential. So the putative mechanism that has been used to say that this might be relevant actually doesn't exist, and I think that's important to clarify.

Dr. Yki-Jarvinen: May I comment? You presented data comparing glargine and neutral protamine Hagedorn (NPH), a study which addressed diabetic retinopathy where the result was entirely negative in that there was no difference between the 2 insulins.[5] Retinopathy has been the disease which has been particularly thought to be induced by growth factors such as IGF-1 (insulin-like growth factor-1), and to me, that piece of evidence is quite convincing, at least the idea that one mechanism doesn't play a role because you would have seen it already. And something to perhaps add to the interpretation of these very complicated data you presented yesterday is in regard to the first study from Germany,[1] which was really supported by the insurance companies, in making the decision of whether

analogs should be reimbursed or not. I think one very important parameter that was missing in the German study was one that suggested that a higher insulin dose was associated with a greater risk for cancer, but if you don't consider or adjust for the dose, glargine was found to be associated with a significantly lower risk for cancer.

Dr. Skyler: This was the only study in which there was a significant decrease in the risk for cancer with glargine.

Dr. Yki-Jarvinen: Yes. So then if you do this adjustment for the insulin dose, if we think about who the patients are who would have a big dose, they would be the obese patients; but there were no weight data in this German study, so they completely ignored the impact of obesity on cancer. We heard in the first sessions how convincing the data are that obesity is also associated with an increased risk for cancer, so not having reported BMI (or body mass index) or weight at all in the German study makes it quite worthless in my view, and it's very unfortunate that this adjustment, which would have said that they considered the insulin dose by including obesity in the equation, was not done. Unfortunately, that news made it through the headlines and not the fact that there was actually a lower risk for cancer with insulin glargine use.

Dr. Skyler: The dose analysis in that study has been totally criticized by really expert people, including Stuart Pocock, who is probably one of the 2 or 3 leading statisticians in the world. He wrote an editorial in *The Lancet* saying that that was a totally flawed analysis and that was the only bit of evidence that created a problem there.[6] Hans, you have to live in Germany under all of this. Tell us your view.

Prof Dr. Häring: Before discussing more of these studies, I would like to comment on the so-called preclinical evidence for increased risk for cancer with insulin analogs in general. I think there is a very clear procedure in how the preclinical studies are addressed, and this was done in a very systematic way for all insulin analogs in the last 12 years. There's always the rule that you use isolated cells or isolated receptors to generate a hypothesis and to understand the mechanism. Then the logical next step is to always test this hypothesis in animal models because it's common knowledge today that you can't discuss the behavior of an isolated cancer cell. It's the cancer cell in the environment of the stroma and in the environment of the whole body, so in order to ask whether you can extrapolate a hypothesis, you always have to conduct controlled studies in animals, and this was done. In the case of the famous SP-10 analog, which has an increased infinity to the insulin receptor A, the animals showed in vivo tumors, so in a way the hypothesis generated in the in vitro system was verified. In the case of glargine, there was a hypothesis based on in vitro data, and this hypothesis was not verified in 2-year animal toxicology studies published 10 years ago. This was part of the registration process. So in fact, if you follow this, there is no preclinical evidence for a hypothesis which could be tested in humans. I think this is something which was a little bit confused yesterday in the discussions -- how can you use preclinical information; because there's a very clear procedure on how to test your hypothesis. And as you said, this is just one reason why there may be no preclinical hypothesis at all. The other reason is that we now know that glargine is degraded very rapidly in the circulation. In the famous paper written about all of these analogs 10 years ago by Peter Kurtzhals, this degradation product is described,[7] and it's described as having a lower affinity to the IGF receptor. So to summarize, for the preclinical data, there is no hypothesis and this is very clear. I think preclinical data should not be included in the discussion nor included in the evidence with human data because there is, according to the rules, an interpretation of in vitro data that there is no hypothesis. I think this is important because this is used again and again as an argument.

Dr. Skyler: So Stefano, the bottom line on this: Would you change the way you use insulin therapy as a consequence of any of this at all?

Prof. Del Prato: Jay, rather than ask me, you should ask the regulatory agency. As far as I know, the European Agency didn't make any change at all and actually recommended not to switch treatment But for a patient who may have read the scandalistic headlines in the newspaper, they should go to their doctor and speak with them. But a physician should feel confident because of all the reasons that have been discussed here; and for the time being, there is no specific reason to be afraid of using a glargine for treating diabetic individuals.

Dr. Skyler: Or any insulin.

Prof. Del Prato: Or any insulin, of course or any insulin. During the symposium yesterday, a comparison between insulin analogs was also mentioned, and for the number of patients following the randomized clinical trials, there was no difference between the glargine and other insulins, such as detemir.

Dr. Yki-Jarvinen: If I may comment, in Finland we have for almost 20 years used the combination of basal insulin and metformin, and I just became convinced yesterday that we have chosen the right regimen because metformin seemed to be at least not harmful in terms of increasing cancer risk, and may even be beneficial.

Dr. Skyler: You've done it for 20 years. The ancients again have taken the best ideas, right? So Stefano, I would like to ask you, if we move beyond cancer, what you found in terms of insulin that was most interesting at this meeting.

Prof. Del Prato: First of all, I've always been impressed that in spite of the fact that insulin has been around now for almost a century that there is still a flourishing number of studies on insulin.

Dr. Skyler: Isn't that amazing?

Prof. Del Prato: It is amazing. That means that we still have to learn a lot. That's because of new preparations of insulin, but also because strategies for the treatment of diabetes is changing both for type 1 and even more for type 2 diabetes, so it's really interesting to see how diabetologists are trying to get the best out of the use of insulin. There are a couple of things that interested me. There is this idea that insulin treatment may increase body weight, may worsen insulin resistance to some extent, and because of the insulin resistance, may worsen lipid profile or some cardiovascular risk factors. And there were 2 abstracts, one from Dr. P. Dandona[8] and the other from Dr. J. Rosenstock,[9] in which insulin treatment added to oral agents was compared with oral agents added with TZDs (glitazones), so they are considered to be, particularly pioglitazone, a good way to reduce HbA1c and also to improve the lipid profile. It turned out that insulin treatment was associated with an improvement in glycemic control but an even better improvement in the lipid profile. I think that this may also make a physician confident that if insulin is used in a proper manner, it can be very powerful in improving glycemic control but it can also have good effects in terms of cardiovascular risk factors, for instance the lipid profile.

Dr. Skyler: Hannele, you've written about TZDs extensively. Wonderful review a few years ago in *The New England Journal*.[10] How do you react to what Stefano is talking about here?

Dr. Yki-Jarvinen: Well, the TZDs do increase body weight, and I think the mechanism of action of TZDs is very complicated compared with insulin after all, because it is a transcription factor agonist, which really affects the transcription of many genes. Although not presented at this meeting, I think it's important to remember that insulin is still the only agent in addition to sulfonylureas and metformin that has been shown to reduce the incidence of complications in the UKPDS (UK Prospective Diabetes Study) 20-year follow-up study,[11] and that such data are not available for the TZDs. I think there is a place for TZD treatment in certain individuals, perhaps particularly those who have an inflamed liver, but not for the garden-variety typical type 2 patient without some special reason. Insulin therapy, as mentioned earlier, has been shown to improve insulin sensitivity in at least 15 studies, so we know very well that insulin therapy is also an insulin sensitizer but it very frequently is forgotten that this is the case.

Dr. Skyler: You said "a couple of strategies," Stefano; what was the other strategy that you were particular interested in?

Prof. Del Prato: There was also a big discussion during this meeting on how type 2 diabetes is a progressive disease. It's progressive because of the nature of the disease but also in terms of the progression of the treatment that we have to implement. We know that most of our patients will end up with a basal-bolus insulin treatment at the end of the day; however, I think that we probably need to have an intermediate strategy to gain compliance of the

patients with a proper basal-bolus strategy. There is a paper suggesting an intermediate step towards the basal-bolus strategy, called the basal-plus strategy.[12] That means that you may be able, after implementing an effective basal insulin strategy, to identify the highest peak of glucose after a meal in those individuals and then add just 1 single shot of the short-acting insulin. It has been shown that this can be quite effective. It is, of course, not the final solution, but it may allow patients to gain more confidence with the treatment and to also gain control over timing to help achieve good glycemic control. We actually have been contributing to this approach and the results have been quite interesting: There is a very low rate of hypoglycemia and very little change in body weight.

Dr. Skyler: Yes, it's interesting, Stefano. I know you've contributed to this, and you've mentioned very carefully that it makes it easier for the patient to begin to implement insulin that way, but I would have thought that you, who have been interested in postprandial glucose control, would want to see glucose control after all meals and not just after 1 meal.

Prof. Del Prato: Yes, you're perfectly right. This may be a regional issue. If you come to Italy, we tend to skip breakfast so we don't have much of a peak after the breakfast. And most people are used to having a very light lunch and having a larger meal at dinner, so you can come up with a really major peak at the time of 1 of the 3 meals.

Dr. Skyler: Particularly with pasta.

Prof. Del Prato: Exactly. And what we have done in the study that we completed[12] was, during titration of the basal insulin, to monitor the glucose profile through the day to try to identify the meal with the highest peak. It's not that you just go and pick up the one meal you like the most or the one meal that you are most more comfortable with, but to potentially identify the meal with the largest glucose score and to tackle that first. In doing that, it's interesting, because not only can you reduce the fasting plasma glucose because of the basal insulin initiation, but you can also flatten down the curve during the day because you are really hitting the highest peak after a meal. As I was saying, this is not the final solution but it's a way to proceed toward a more effective basal-bolus approach.

Dr. Skyler: I think one of the things it does, particularly if you're using it in the evening meal, is that it gets the pre-bedtime glucose under better control so that the basal insulin overnight can truly be a basal insulin and not be forced to also lower glucose but rather just keep it constant. Hannele, you look like you want to get in on this.

Dr. Yki-Jarvinen: Well, I am still waiting for the study which will compare this basal-plus regimen with a properly titrated basal and oral agent strategy. There was the 4T study[13] that was published and also a few others, but what they tend to show is that once you have more prandial shots, you have a much higher risk for hypoglycemia without any benefits, which cannot be explained by improved glycemic control. And what bothers me with this basal-plus concept is that although it may be okay, a controlled study where you would continue the basal insulin and titrate it properly is something that I would like to see amongst all these studies. It still hasn't been done because just adding 1 shot doesn't mean that titrating the other properly will give you the same result. For example, there is this abstract which I thought of bringing up. The title is "Baseline HbA1c predicts the likelihood of reaching the 7% HbA1c," which is generally our target, with structured titration of add-on insulin glargine; this is a large analysis with 2300 patients.[14] This is over a 24-week time period in which this was performed, and I know from our old studies over the years that in 24 weeks in people who really need big insulin doses, you are not able to fully titrate. You don't even reach in 24 weeks the maximum dose or the dose that's required to actually control fasting glycemia, so it doesn't come as a surprise that the baseline A1c reaches7% in 24 weeks. Again, titrating longer may get you there to a similar A1c goal with no risk for increased hypoglycemia, as you have consistently seen in the studies where you add all of these prandial insulins. Also, there was a new study that was presented at this meeting which showed that comparing just 1 shot of glargine vs 2 shots of detemir, the patients were much happier when they had the 1 shot,[15] so the more shots usually decreases the compliance. I think we need a study which rigorously continues to titrate the basal insulin, keeping the pills, and then another study where you would add the 1 dinner injection or use some of the other alternatives that we have for controlling postprandial glucose nowadays.

Prof. Del Prato: I think that you're right, because the patients we have been adding the shots of prandial insulin to were patients who achieved a fasting plasma glucose lower than 120 mg/dL. But I agree with you that we need to evolve more and to have more comparisons before we can really know. I think it's a way to try to get new strategies for those people who are failing at a certain time to properly titrate with the basal insulins.

Dr. Yki-Jarvinen: I think it's important to define what you mean by "achieving a fasting blood glucose of less than 120 mg/dL." We generally aim at more stringent values; we want to have a value of 100 mg/dL to really push the HbA1c down. And then if the fasting glucose measurement is done just a couple of times before the patient comes to the next visit, they generally may try to perhaps be a little bit better. But when you actually measure, for example, glucose at home all the time, you can see in your computer all the glucose measurements over the past 2 months, and then you see that the mean is 100 mg/dL, or at least lower than 110 mg/dL. This makes a big difference on the A1c because at a level of 120 mg/dL you may end up with an HbA1c of maybe 7.5%, but when you go to 110 mg/dL you start to get closer to 7%, so it's quite important.

Dr. Skyler: Hans?

Prof. Dr. Häring: I would like to touch again on a topic that Hannele has mentioned, which I think is a very important topic, and where Hannele was a pioneer in the way of helping us understand the role of the inflamed fatty liver and how to treat this condition. I think the data are piling up to show that the question of whether your fatty liver has a tendency to react in a way of microinflammation is probably very important for the overall long-term perspective. It's a very important issue that needs more studies which address the question of which therapeutic schemes are efficiently targeting this particular issue. As Hannele already said, so far the TZDs are the strongest agents that act on this, but it's clear that we have all of the other adverse characteristics of TZDs, so I think it's very important in the future to look at other regimens that efficiently address this issue. So far at this meeting here I didn't see anything new in this direction. Did you see anything?

Dr. Yki-Jarvinen: I know that there is a big study that is going to be presented at The Liver Meeting in Boston, October 30-November 3, 2009, but it seems that at this diabetes meeting, perhaps there's a little bit of a disappointment this year in the program -- that although there is such a big interest in nonalcoholic steatohepatitis and what is happening with the liver in patients with diabetes, that was not addressed so much this time. We have had more data on GLP-1-based therapies and this quite interesting symposium on diabetes and cancer.

Dr. Skyler: I really thank all of you for being with me for this program, and I want to thank MedscapeCME and our viewers for participating in this activity. We'd like you now to proceed to the online CME test, clicking on the "earn CME credit" link on the page. Thanks again for being with us. We've appreciated it and we're enjoying Vienna.

Supported by an independent educational grant from sanofi-aventis.

This article is a CME certified activity. To earn credit for this activity visit: http://cme.medscape.com/viewarticle/709649

References

1. Hemkens LG, Grouven U, Bender R, et al. Risk of malignancies in patients with diabetes treated with human insulin or insulin analogues: a cohort study. Diabetologia. 2009;52:1732-1744. Abstract
2. Jonasson JM, Ljung R, Talbäck M, Haglund B, Gudbjörnsdòttir, Steineck G. Insulin glargine use and short-term incidence of malignancies--a population-based follow-up study in Sweden. Diabetologia. 2009;52:1745-1754. Abstract
3. Colhoun HM; SDRN Epidemiology Group. Use of insulin glargine and cancer incidence in Scotland: A study from the Scottish Diabetes Research Network Epidemiology Group. Diabetologia. 2009;52:1755-1765. Abstract

4. Currie CJ, Poole CD, Gale EA. The influence of glucose-lowering therapies on cancer risk in type 2 diabetes. Diabetologia. 2009;52:1766-1777. Abstract
5. Rosenstock J, Fonseca V, McGill JB, et al. Similar progression of diabetic retinopathy with insulin glargine and neutral protamine Hagedorn (NPH) insulin in patients with type 2 diabetes: a long-term, randomised, open-label study. Diabetologia. 2009;52:1778-1788. Abstract
6. Pocock SJ, Smeeth L. Insulin glargine and malignancy: an unwarranted alarm. Lancet. 2009;374:511-513. Abstract
7. Kurtzhals P, Schäffer L, Sørensen A, et al. Correlations of receptor binding and metabolic and mitogenic potencies of insulin analogs designed for clinical use. Diabetes. 2000;49:999-1005. Abstract
8. Dandona P, Rosenberg N, Hollander P, Rosenstock J, Meneghini L. Effects of insulin glargine vs thiazolinediones on glycaemic and lipid variables in type 2 diabetes mellitus: the impact of obesity. Program and abstracts of the 45th Annual Meeting of the European Association for the Study of Diabetes; September 29-October 2, 2009. Vienna, Austria. Abstract 895.
9. Rosenstock J, Rosenberg N, Riddle M, Meneghini L, Chaudhuri A. The impact of age and disease duration on glycemic control and lipid profile: insulin glargine vs thiazolidinediones in type 2 diabetes. Program and abstracts of the American Diabetes Association 69th Scientific Sessions; June 5-9, 2009; New Orleans, Louisiana. Poster 2094-PO.
10. Yki-Järvinen H. Thiazolidinediones. N Engl J Med. 2004;351:1106-1118. Abstract
11. U.K. Prospective Diabetes Group: Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352:837-853. Abstract
12. Nicolucci A, Del Prato S, Vespasiani G. Optimizing basal-plus insulin therapy in type 2 diabetes (T2D): impact on patient (Pt) quality of life (QoL) and treatment satisfaction (TS) -- the ELEONOR study. Program and abstracts of the American Diabetes Association 69th Scientific Sessions; June 5-9, 2009; New Orleans, Louisiana. Poster 550-P.
13. McMahon GT and Dluhy RG. Intention to treat -- initiating insulin and the 4-T study. N Engl J Med. 2007;357:1759-1761. Abstract
14. Zhou R, Vlajnic A, Riddle M, Orloff D, Rosenstock J. Baseline HbA1c predicts the likelihood of reaching the 7.0% HbA1c target with structured titration of add-on insulin glargine: patient-level analysis of 12 studies in type 2 diabetes mellitus. Program and abstracts of the 45th Annual Meeting of the European Association for the Study of Diabetes; September 29-October 2, 2009. Vienna, Austria. Abstract 893.
15. Swinnen SGH, Dain MP, Aronson R, et al. Once-daily insulin glargine requires a significantly lower dose than insulin detemir twice daily to achieve good glycaemic control in patients with type 2 diabetes failing oral therapy. Program and abstracts of the 45th Annual Meeting of the European Association for the Study of Diabetes; September 29-October 2, 2009. Vienna, Austria. Abstract 966.

Authors and Disclosures

As an organization accredited by the ACCME, MedscapeCME requires everyone who is in a position to control the content of an education activity to disclose all relevant financial relationships with any commercial interest. The ACCME defines "relevant financial relationships" as financial relationships in any amount, occurring within the past 12 months, including financial relationships of a spouse or life partner, that could create a conflict of interest.

MedscapeCME encourages Authors to identify investigational products or off-label uses of products regulated by the US Food and Drug Administration, at first mention and where appropriate in the content.

Moderator(s)

Jay S. Skyler, MD

Professor of Medicine, University of Miami, Miami, Florida

Disclosure: Jay S. Skyler, MD, has disclosed the following relevant financial relationships:
Served as an advisor or consultant to: BD Technologies; Ideal Life; Johnson & Johnson Pharmaceutical Research & Development, L.L.C.; MannKind Corporation; Medingo Ltd.; Merck Serono; Novo Nordisk; Patton Medical Devices, LP; Salutria; sanofi-aventis; Tethys Bioscience, Inc.; Teva Neuroscience, Inc.; Valeritas, LLC
Served as a speaker or a member of a speakers bureau for: Eli Lilly and Company; Novo Nordisk; sanofi-aventis
Received grants for clinical research from: Bayhill Therapeutics; Halozyme Therapeutics; Osiris Therapeutics, Inc.
Owns stock, stock options, or bonds from: Amylin Pharmaceuticals, Inc.; DexCom Corporation; MannKind Corporation; Medingo Ltd.; Moerae Matrix, Inc.; Patton Medical Devices, LP; Tandem Diabetes Care, Inc.; Tethys Bioscience, Inc.
Served on board of directors: Amylin Pharmaceuticals, Inc.; DexCom Corporation; Moerae Matrix, Inc.

Panelists(s)

Stefano Del Prato

Professor of Endocrinology, University of Pisa - Ospedale casa cello, Pisa, Italy; Director, Ospedale casa cello, Pisa, Italy

Disclosure: Stefano Del Prato has disclosed the following relevant financial relationships:
Served on an advisory panel for: Novartis Pharmaceuticals Corporation; Merck & Co., Inc.; Roche; Roche Diagnostics Corporation; Pfizer Inc.; Eli Lilly and Company; Amylin Pharmaceuticals, Inc.; MannKind Corporation; Boehringer Ingelheim Pharmaceuticals, Inc.; Bristol-Myers Squibb Company
Received grants for clinical research from: Merck & Co., Inc.; sanofi-aventis
Served on the speakers bureau for: GlaxoSmithKline; sanofi-aventis

Hannele Yki Jarvinen, MD, PhD

Professor, Department of Medicine, Division of Diabetes, University of Helsinki, Helsinki, Finland; Helsinki University Central Hospital, Helsinki, Finland

Disclosure: Hannele Yki-Jarvinen, MD, PhD, has disclosed the following relevant financial relationships:
Served as an advisor or consultant to: AstraZeneca Pharmaceuticals LP; MSD Pharmaceuticals; sanofi-aventis; Bristol-Myers Squibb Company
Served as a speaker or a member of a speakers bureau for: MSD Pharmaceuticals; sanofi-aventis; Eli Lilly and Company

Hans-Ulrich Haring, MD

Professor, Department of Internal Medicine IV, University of Tubingen, Baden-Wurttemberg, Germany

Disclosure: Hans-Ulrich Haring, MD, has disclosed the following relevant financial relationships:
Served as an advisor or consultant to: MSD Pharmaceuticals; Novo Nordisk; Nycomed; sanofi-aventis
Received grants for clinical research from: Novo Nordisk; sanofi-aventis

Editor(s)

Anne G. Le, PharmD, RPh

Scientific Director, MedscapeCME

Disclosure: Anne G. Le, PharmD, RPh, has disclosed no relevant financial relationships.

This article is a CME certified activity. To earn credit for this activity visit: http://cme.medscape.com/viewarticle/709649

CME Information

CME Released: 10/05/2009; Valid for credit through 10/05/2010

Target Audience

This activity is intended for diabetologists, endocrinologists, primary care physicians, certified diabetes educators, and other healthcare professionals who care for patients with type 2 diabetes.

Goal

The goal of this activity is to provide expert insight on the clinical relevance of new data presented at the 45th Annual Meeting of the European Association for the Study of Diabetes (EASD) on insulin therapy.

Learning Objectives

Upon completion of this activity, participants will be able to:

- Compare and contrast the safety and efficacy of insulin analogs, including rapid-acting analog insulin, on the basis of new data presented at the 45th Annual Meeting of the European Association for the Study of Diabetes (EASD)
- Discuss the impact of insulin therapy on glycemic control and metabolic profiles and strategies to optimize basal plus insulin therapy in patients with type 2 diabetes

- Analyze and interpret recent data in regard to diabetes, diabetes therapy, and risk for cancer, and discuss how to present these data to patients and other clinicians

Credits Available

Physicians - maximum of 0.50 *AMA PRA Category 1 Credit(s)™*

All other healthcare professionals completing continuing education credit for this activity will be issued a certificate of participation.

Physicians should only claim credit commensurate with the extent of their participation in the activity.

Accreditation Statements

For Physicians

MedscapeCME is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

MedscapeCME designates this educational activity for a maximum of 0.5 ***AMA PRA Category 1 Credit(s)™*** . Physicians should only claim credit commensurate with the extent of their participation in the activity.

Contact This Provider

For questions regarding the content of this activity, contact the accredited provider for this CME/CE activity noted above. For technical assistance, contact CME@medscape.net

Instructions for Participation and Credit

There are no fees for participating in or receiving credit for this online educational activity. For information on applicability and acceptance of continuing education credit for this activity, please consult your professional licensing board.

This activity is designed to be completed within the time designated on the title page; physicians should claim only those credits that reflect the time actually spent in the activity. To successfully earn credit, participants must complete the activity online during the valid credit period that is noted on the title page.

Follow these steps to earn CME/CE credit*:

1. Read the target audience, learning objectives, and author disclosures.
2. Study the educational content online or printed out.
3. Online, choose the best answer to each test question. To receive a certificate, you must receive a passing score as designated at the top of the test. MedscapeCME encourages you to complete the Activity Evaluation to provide feedback for future programming.

You may now view or print the certificate from your CME/CE Tracker. You may print the certificate but you cannot alter it. Credits will be tallied in your CME/CE Tracker and archived for 6 years; at any point within this time period you can print out the tally as well as the certificates by accessing "Edit Your Profile" at the top of your Medscape homepage.

*The credit that you receive is based on your user profile.

Hardware/Software Requirements

MedscapeCME is accessible using the following browsers: Internet Explorer 6.x or higher, Firefox 2.x or higher, Safari 2.x or higher. Certain educational activities may require additional software to view multimedia, presentation or printable versions of their content. These activities will be marked as such and will provide links to the required software. That software may be: Macromedia Flash, Adobe Acrobat, or Microsoft PowerPoint.

This activity is supported by an independent educational grant from