An expert interview – managing type 2 diabetes with thiazolidinediones

Dr. Peter WEISSMAN

In a recent interview, diabetes expert, Dr. Peter WEISSMAN, University of Miami School of Medicine, Miami, FL USA, was asked about the management of type 2 diabetes mellitus (T2DM) in general and the role of the thiazolidinediones (TZDs) in particular.

Blood glucose control

The discussion began with the importance of blood glucose control in patients with T2DM. Dr. Weissman said that glycaemic control was of particular importance among the many macrovascular risk factors that need to be controlled in patients with T2DM. While there is a clear relationship between glycaemic control and microvascular disease, as shown by numerous clinical trials, "I believe an equally beneficial role will eventually be shown for the prevention of macrovascular diseases". Whether glycaemic control can be "too good", as suggested by the ACCORD study findings, remains to be seen. However, "I believe that none of the targets for glycaemic control need to be altered at this time", he added.

Rosiglitazone and management of T2DM

"Rosiglitazone is a TZD, a class of drug that conveys multidimensional benefits in patients with T2DM," said Dr. Weissman, discussing the current importance of rosiglitazone as a therapeutic option for the management of patients with T2DM. He explained that a substantial reduction in glycosylated haemoglobin (HbA1c) could be achieved with rosiglitazone, usually 1–2% in the average newly diagnosed patient. Moreover, there is pancreatic beta-cell preservation with TZDs such as rosiglitazone. "In patients who are not at high risk for congestive heart failure, I believe we will eventually see cardiovascular benefits with the TZDs". He pointed out that rosiglitazone was the most extensively studied of any of the oral diabetes drugs, with over 40,000 patient-years of study, giving "a very firm platform on which to place rosiglitazone as a top choice for treating T2DM".

Cardiovascular safety

Asked to comment on the latest clinical evidence on the safety of rosiglitazone, Dr. Weissman said he thought it was time to move on from the issues of the cardiovascular safety of rosiglitazone. "Many people considered that the original meta-analysis by Nissen & Wolski was not a very good study, but it had a large impact because of the considerable media attention that it attracted, perhaps more so than any other single study in recent history". He pointed out that the publication's findings had since been contradicted by the results of "an avalanche" of major large, long-term prospective observational studies showing that rosiglitazone does not increase the risk of myocardial ischaemic or cardiovascular death. These all provide evidence that the original concerns about ischaemic disease were not well founded. More reassuring safety evidence now exists for rosiglitazone than for any drug used to treat diabetes. Physicians can feel confident that, once inappropriate patients have been excluded, the remaining population of T2DM patients are excellent candidates for rosiglitazone and that they can feel extremely confident about the safety of this drug.

Appropriate patients for rosiglitazone (Table)

The discussion then turned towards the most appropriate patients for rosiglitazone treatment, with Dr. Weissman saying that patients who are insulin-resistant and those with early-stage diabetes are the most suitable candidates. "Around 95% of T2DM patients have varying degrees of insulin resistance. Clinically, the most insulin-resistant are those who are the most obese or who have other features associated with insulin resistance, such as acanthosis nigricans or polycystic ovarian disease", he explained. Generally, the

Table. Appropriate patients and potential benefits of rosiglitazone.

Patient characteristics	Potential benefits of rosiglitazone
Early-stage diabetes	Preservation of beta-cell function and mass
Insulin resistance and overweight	The more insulin-resistant the patient, the more likely they are to benefit from a TZD
Poor drug compliance	Fixed-dose-combination oral medication

more insulin-resistant the patient, the more likely they are to benefit from TZDs. Regarding the stage patients are at in the natural history of diabetes, "one of the benefits of TZD therapy is preservation of beta-cell function and mass, so those with earlier stage diabetes will be the best candidates for TZDs, while those with more advanced disease will be less suitable".

Practical benefits of the fixed-dose combination oral drug – Avandamet® (rosiglitazone/metformin HCl)

While talking about fixed-dose combination therapies, Dr. Weissman said that in general they had been shown to be a more effective strategy with regard to patient compliance. "With Avandamet in particular the combination of rosiglitazone and metformin is an extremely good combination for a variety of reasons". He explained that two separate pathophysiological pathways are being addressed with these drugs, so in that sense they complement each other and that neither can cause hypoglycaemia, which is a major concern with some oral agents. "The metformin may offset some of the weight gain tendencies that some patients experience on TZDs and, in a practical sense, the dosing of Avandamet seems somewhat easier to use than the doses that are available with the pioglitazone/metformin combination. Avandamet is particularly good for those patients being considered for early combination therapy, an excellent first choice for those who might not be brought to target with a single agent", Dr. Weissman concluded.