Plenary Lecture 1

Chairperson

Jeong Taek Woo
Kyung Hee University, Korea

Speaker

Michael A. Nauck
Ruhr-University Bochum, Germany

Michael A. Nauck

Ruhr-University Bochum, Germany

Education

Period	Affiliation	Position
– **1975-1980**	University Freiburg	M.S
– **1973-1975**	Heinrich Heine University Düsseldorf	M.S

Affiliations / Experience

Period	Affiliation	Position
– **2015-Present**	Head of Clinical Research, Ruhr-University Bochum, St. Josef-Hospital	Research Position
– **2000-2015**	Diabetes Centre Bad Lauterberg	Head Physician
– **1993-2000**	Ruhr-University Bochum, Knappschafts-Krankenhaus	Consultant
– **1981-1993**	University Göttingen, Gastroenterology and Endocrinology	Physician in Training
– **1980-1981**	University Göttingen, Biochemisty	Scientist

Committee Memberships

- ADA/EASD Guideline Writing Group
- Working Group (ADA/EASD/Diabetes UK/ Endocrine Society) Diabetes Remission

Publications

- Drucker DJ, Nauck MA. The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. *Lancet*. 368:1696-705
- Nauck M, Stöckmann F, Ebert R, Creutzfeldt W. Reduced incretin effect in Type 2 (non-insulin-dependent) diabetes. *Diabetologia*. 29:46-54
- Nauck MA, Heimesaat MM, Ørskov C, Holst JJ, Ebert R, Creutzfeldt W. Preserved incretin activity of glucagon-like peptide 1 [7-36 amide] but not of synthetic human gastric inhibitory polypeptide in patients with type-2 diabetes mellitus. J Clin Invest. 91(1):301-7
- Nauck MA, Kleine N, Ørskov C, Holst JJ, Willms B, Creutzfeldt W. Normalization of fasting hyperglycaemia by exogenous glucagon-like peptide 1 (7-36 amide) in type 2 (non-insulin-dependent) diabetic patients. *Diabetologia*. 36(8):741-4
- Nauck MA, Müller TD. Incretin hormones and type 2 diabetes. *Diabetologia*

Plenary Lecture 1

GLP-1 Based Therapy of Obesity

Michael A. Nauck (Ruhr-University Bochum, Germany)

Glucagon-like peptide-1 is an insulinotropic gut hormone produced in entero-endocrine L-cells predominantly found in the distal small and large intestines. In 1993, this incretin hormone was discovered to lower plasma glucose in subjects with type 2 diabetes, and this was the basis for using GLP-1 receptor agonists for the therapy of type 2 diabetes. In 1992, µg amounts of GLP-1, when administered intracerebroventricularly, reduced energy intake in rodents. In 1998, appetite and ad libitum energy intake in healthy human subjects were reduced while receiving an intravenous infusion of GLP-1. In clinical trials in type 2 diabetes patients, body weight was consistently lowered, by 1-2 kg with exenatide b.i.d. and liraglutide, but now by 5-10 kg with semaglutide (selective GLP-1 receptor agonist) and tizepatide (a GIP/GLP-1 dual receptor agonist). Weight loss with the same agents is greater in non-diabetic obese subjects, and they are approved for the treatment of obesity in the absence of diabetes mellitus.

GLP-1 receptor agonists like liraglutide and semaglutide specifically enter small areas of the brain, which are equipped with GLP-1 receptors and are involved in the regulation of energy balance (intake and expenditure), like the arcuate nucleus in the hypothalamus. GLP-1 receptors are found on anorexigenic POMC/CART neurons, and inhibit orexigenic Agouti-related peptide/NPY neurons, with projections to the brain stem.

Weight loss in response to GLP-1 RA therapy in non-diabetic subjects probably is greater, because there is no reduction in HbA1c, such that there is no reduction in glucosuria (energy loss through urinary excretion).

Since the main (or even only) effect of GLP-1 receptor agonists is the reduction in food (energy) intake due to reduced appetite and increased satiety, weight lost as the consequence of GLP-1 RA therapy will be regained after discontinuing treatment. There is substantial inter-individual variability regarding the extent of weight loss, such that some subjects lose a lot, and others very little body weight, which we cannot predict.

Obesity associated medical problems can meaningfully be addressed by GLP-1 RA treatment: Cardiovascular events are reduced in obese subjects with pre-existing CV disease (semaglutide, SELECT), and symptoms of obstructive apnoea syndrome can be improved (tirzepatide).

In most countries, medications inducing body weight reduction are not reimbursed by health insurance companies, such that patients will have to pay out of their own pockets. The impressive weight-reducing effectiveness with proven medical benefits for well-defined subgroups will spark a discussion leading to the characterization of sub-populations, in whom there is a clearly positive benefit/risk relationship.