

# Symposium 16

## International Collaboration 2

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### Chairpersons

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**Eun-Jung Rhee**

Sungkyunkwan University, Korea

**Chang Hee Jung**

University of Ulsan, Korea

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### Speakers

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**Jang Won Son**

The Catholic University of Korea, Korea

**Erika Bezerra Parente**

Boehringer Ingelheim, Germany

**W. Timothy Garvey**

University of Alabama at Birmingham, USA

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### Panel Discussion

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**Sunyoung Kim**

Kyung Hee University, Korea

**Ye Seul Yang**

Seoul National University, Korea



## Jang Won Son

The Catholic University of Korea, Korea

### • Education

Period	Affiliation	Position
- 2011	Graduate school, The Chung-Ang University of Korea, Seoul, Korea	Ph.D.
- 2006	Graduate School, The Chung-Ang University of Korea, Seoul, Korea	
- 1995-2001	College of Medicine, The Chung-Ang University of Korea, Seoul, Korea	M.D.

### • Affiliations / Experience

Period	Affiliation	Position
- 2021 -Present	Bucheon Saint Mary Hospital. College of Medicine, The Catholic University of Korea	Professor
- 2017-2018	Karolinska institute, Sweden	Visiting researcher
- 2016-2021	Bucheon Saint Mary Hospital. College of Medicine, The Catholic University of Korea	Associate professor
- 2012-2016	Bucheon Saint Mary Hospital. College of Medicine, The Catholic University of Korea	Assistant professor

### • Publications

- Genetic Determinants of Obesity in Korean Populations: Exploring Genome-wide Associations and Polygenic Risk Scores. Briefings in Bioinformatics 2024 [Epub ahead of print]
- GLP-1 Based Therapies: A New Horizon in Obesity Management. *Endocrinol Metab.* 2024 Apr;39(2):206-221
- An international multidisciplinary consensus statement on MAFLD and the risk of CVD. *Hepatol Int* 17, 773–791 (2023).
- Human Tissue-Engineered Skeletal Muscle: A Tool for Metabolic Research. *Endocrinol Metab.* 2022;37(3):408-414.
- Obesity Fact Sheet in Korea, 2021: Trends in Obesity Prevalence and Obesity-Related Comorbidity Incidence Stratified by Age from 2009 to 2019. *JOMES* 2022;31:169-177

**Symposium 16**

## **The New Wave of Anti-Obesity Drugs: Advances and Challenges**

Jang Won Son (The Catholic University of Korea, Korea)

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Obesity is a significant risk factor for health issues like type 2 diabetes and cardiovascular disease. It often proves resistant to traditional lifestyle interventions, prompting a need for more precise therapeutic strategies. This has led to a focus on signaling pathways and neuroendocrine mechanisms to develop targeted obesity treatments.

Recent developments in obesity management have been revolutionized by introducing novel Glucagon-like peptide-1 (GLP-1) based drugs, such as semaglutide and tirzepatide. These drugs are part of an emerging class of nutrient-stimulated hormone-based therapeutics, acting as incretin mimetics to target G-protein-coupled receptors like GLP-1, glucose-dependent insulinotropic polypeptide (GIP), and Glucagon (GCG). These receptors are vital in regulating body fat and energy balance. The development of multi agonists, including GLP-1-GCG and GIP-GLP-1-GCG receptor agonists, especially with the potential for GCG receptor activation, marks a significant advancement in the field.

In a move to improve patient convenience, semaglutide has been formulated as an orally available tablet with an absorption enhancer, overcoming the need for injections. Despite its lower oral bioavailability and specific intake requirements, this development marks a step forward in drug administration. Additionally, the advent of small molecules such as orforglipron, which can interact with the GLP-1 receptor and offer greater resistance to gastrointestinal breakdown, is a groundbreaking advancement previously deemed unachievable.

In this lecture, I will cover the development and clinical efficacy of various GLP-1-based therapeutics, exploring the challenges and future directions in obesity management.



## Erika Bezerra Parente

Boehringer Ingelheim, Germany

### Education

Period	Affiliation	Position
– 2019-2020	University of Helsinki and Folkhälsan Research Center, Finland	Post Doctoral
– 2005-2009	Faculdade de Medicina da Universidade de São Paulo, Brazil	Ph.D.
– 1995-2000	Faculdade de Medicina da Universidade Federal do Ceará, Brazil	Medical Diploma

### Affiliations / Experience

Period	Affiliation	Position
– 2024-Present	Boehringer-Ingelheim, Germany	Senior Global Medical Advisor
– 2019-Present	University of Helsinki, Finland	Visiting Researcher
– 2020-2023	Folkhälsan Research Center	Senior Researcher
– 2003-2005	Faculdade de Medicina da Universidade de São Paulo, Brazil	Medical Residency in Endocrinology & Metabolism
– 2001-2003	Faculdade de Medicina da Universidade de São Paulo, Brazil	Medical Residency in Internal Medicine

### Committee Memberships

- Sociedade Brasileira de Endocrinologia e Metabologia: Rio de Janeiro, RJ, BR
- Sociedade Brasileira de Diabetes: São Paulo, BR
- European Association for the Study of Diabetes: Dusseldorf, Nordrhein-Westfalen, DE
- Finnish Diabetes Research Society: Helsinki, FI
- European Society of Endocrinology: Bristol, GB

### Publications

- Mutter, S., Parente, E. B., Januszewski, A. S., Simonsen, J. R., Harjutsalo, V., Groop, P.-H., Jenkins, A. J., & Thorn, L. (2024). Insulin sensitivity estimates and their longitudinal association with coronary artery disease in type 1 diabetes. Does it matter? *Cardiovascular Diabetology*, 23, Article 152. <https://doi.org/10.1186/s12933-024-02234-x>
- Lampenius I, Harjutsalo V, Parente EB, Groop PH; FinnDiane Study Group. Associations between alcohol consumption and body fat distribution in type 1 diabetes. *Diabetes Res Clin Pract*. 2023 Oct;204:110891. doi: 10.1016/j.diabres.2023.110891. Epub 2023 Aug 30. PMID: 37657645.
- Lithovius, R., Mutter, S., Parente, E.B. et al. Medication profiling in women with type 1 diabetes highlights the importance of adequate, guideline-based treatment in low-risk groups. *Sci Rep* 13, 17893 (2023). <https://doi.org/10.1038/s41598-023-44695-2>
- Parente EB, Ahola AJ, Kumar A, Lehto M, Groop PH; FinnDiane Study Group. The relationship between FGF23 and body composition according to albuminuria stage in type 1 diabetes. *Diabetes Res Clin Pract*. 2023 Apr;198:110620. doi: 10.1016/j.diabres.2023.110620. Epub 2023 Mar 12. PMID: 36914006.
- Kumar A, Mutter S, Parente EB, Harjutsalo V, Lithovius R, Mathavan S, Lehto M, Hiltunen TP, Kontula KK, Groop PH. L-type calcium channel blocker increases VEGF concentrations in retinal cells and human serum. *PLoS One*. 2023 Apr 13;18(4):e0284364. doi: 10.1371/journal.pone.0284364. PMID: 37053203; PMCID: PMC10101440.

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# Beyond the Weight Metrics, a Deeper Look on Obesity Management with Survodutide: A Dual GCGR/GLP-1R Agonist

Erika Bezerra Parente (Boehringer Ingelheim, Germany)

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Obesity is a disease that goes beyond the weight metrics. The fat deposits in and around key organs contribute to cardio-renal-metabolic (CRM) diseases such as metabolic dysfunction-associated steatohepatitis (MASH), type 2 diabetes, chronic kidney disease and heart failure. CRM diseases are interconnected, and having one of them increases the risk of developing another. Therefore, new treatments are essential for supporting long-term weight management and holistic health improvements for people living with obesity.

Survodutide, is a dual glucagon receptor and GLP-1 receptor agonist that potentially combines the beneficial effects of GLP-1 receptor agonism with a separate mechanism of action on glucagon receptor.

In a Phase 2 trial, including people living with overweight/obesity without type 2 diabetes, the treatment with Survodutide over 46 weeks reduced body weight up to 18.7% and showed reduction on waist circumference and blood pressure. In another Phase 2 trial, including people with type 2 diabetes, Survodutide decreased body weight by up to 8.7% and reduced mean HbA1c of up to 18.38 mmol/mol (1.68%).

In a Phase 2 trial, including people living with MASH (F1–F3), Survodutide met its primary and key secondary endpoint following 48 weeks of treatment vs placebo. Up to 83.0% of participants experienced MASH improvement with no worsening of fibrosis (vs 18.2% placebo).

Across all these Phase 2 trials there have been no unexpected safety concerns. Tolerability is in line with the GLP-1 class and the majority of adverse events were gastrointestinal in nature.

Survodutide chronic weight management Phase 3 trials are ongoing and based on the results from Phase 2 trials it has the potential to offer new treatment option for patients with overweight or obesity and patients with MASH and moderate to advanced fibrosis, targeting two distinct medical conditions that often coexist.

### References

1. le Roux CW, et al. Lancet Diabetes Endocrinol. 2024.
2. Blüher et al. Diabetologia 2024.
3. Sanyal AJ, et al. N Engl J Med 2024.



## W. Timothy Garvey

University of Alabama at Birmingham, USA

### • Education

Period	Affiliation	Position
– 1983-1984	University of California, San Diego, School of Medicine	Clinical and Research Fellow
– 1982-1983	University of Colorado Health Sciences Center	Clinical and Research Fellow
– 1974-1978	St. Louis University School of Medicine, St. Louis, Missouri	M.D.
– 1970-1974	Washington University, St. Louis	B.A.

### • Affiliations / Experience

Period	Affiliation	Position
– 2018-Present	UAB Diabetes Research Center	Director/ PI
– 2018-Present	University of Alabama at Birmingham	Professor
– 2003-Present	Birmingham Veterans Affairs Medical Center Birmingham	Staff Physician and GRECC Investigator
– 2003-2018	Medical University of South Carolina	Adjunct Professor of Medicine
– 1994-2003	Ralph H. Johnson Veterans Affairs Medical Center, Charleston	Staff Physician

### • Committee Memberships

- National Board of Medical Examiners
- American Board of Internal Medicine
- Specialty Board in Endocrinology and Metabolism
- American Board of Obesity Medicine
- American Association of Clinical Endocrinology

### • Publications

- Everett AB, Garvey WT, Fernandez JR, Habegger K, Harper LM, Battarbee AN, Martin SL, Moore BA, Fouts AE, Bahorski J, Chandler-Laney PC. Leptin resistance in children with in utero exposure to maternal obesity and gestational diabetes. *Pediatr Obes* (12):e13081. doi: 10.1111/ijpo.13081. Epub. PMID: 37859518; PMCID: PMC10841866
- Hankosky ER, Wang H, Neff LM, Kan H, Wang F, Ahmad NN, Griffin R, Stefanski A, Garvey WT. Tirzepatide reduces the predicted risk of atherosclerotic cardiovascular disease and improves cardiometabolic risk factors in adults with obesity or overweight: SURMOUNT-1 post hoc analysis. *Diabetes Obes Metab*. 26(1):319-328. doi: 10.1111/dom.15318. Epub. PMID: 37932236
- Kirkman MS, Tripputi M, Krause-Steinrauf H, Bebu I, AbouAssi H, Burch H, Duran-Valdez E, Florez H, Garvey WT, Hsia DS, Salam M, Pop-Busui R; GRADE Research Group. Comparative Effects of Randomized Second-line Therapy for Type 2 Diabetes on a Composite Outcome Incorporating Glycemic Control, Body Weight, and Hypoglycemia: An Analysis of Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE). *Diabetes Care*. dc231332. doi: 10.2337/dc23-1332. Epub ahead of print. PMID: 38194519
- Garvey WT, Cohen RM, Butera NM, Kazemi EJ, Younes N, Rosin SP, Suratt CE, Ahmann A, Hollander PA, Krakoff J, Martin CL, Seaquist E, Steffes MW, Lachin JM; GRADE Research Group. Association of Baseline Factors With Glycemic Outcomes in GRADE: A Comparative Effectiveness Randomized Clinical Trial. *Diabetes Care*. dc231782. doi: 10.2337/dc23-1782. Epub ahead of print. PMID: 38285957
- Howell CR, Zhang L, Mehta T, Wilkinson L, Carson AP, Levitan EB, Cherrington AL, Yi N, Garvey WT. Cardiometabolic Disease Staging and Major Adverse Cardiovascular Event Prediction in Two Prospective Cohorts. *JACC Advances*, In press

**Symposium 16**

## **Adiposity-Based Chronic Disease and an International Consensus on a Complications-Centric Approach to Care**

W. Timothy Garvey (University of Alabama at Birmingham, USA)

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Beginning with the American Association of Clinical Endocrinology (AACE) Obesity Treatment Guidelines in 2016, all subsequent obesity guidelines published internationally have advocated a complications-centric approach to care. The goal of treatment is not the loss of a given amount of weight per se but the loss of sufficient weight to prevent or treat obesity complications and related diseases that are responsible for morbidity, mortality, and impaired quality of life. This is consistent with the diagnostic term Adiposity-Based Chronic Disease (ABCD) recommended by AACE and the European Association for the Study of Obesity (EASO). ABCD is a medically actionable diagnosis that indicates what we are treating (adiposity-based: abnormalities in the mass, distribution, and function of adipose tissue) and why we are treating it (chronic disease: prevention and treatment of complications). Treatment principles of complications-centric care and the pathophysiological and clinical rationale for the term, ABCD will be discussed. In addition, evaluation, disease staging, and treatment recommendations for obesity will be reviewed based on guidelines of multiple professional societies.