EMERGING PERSPECTIVES AND NEW PARADIGMS IN DIABETES MANAGEMENT

Focus on the Role of the Kidney in Glucose Homeostasis: A Diabetes, World Experts’ Forum Analyzes Practice-Changing Advances in Diabetes Management

A Global, FAQ-Driven, Multi-Lingual, Multimedia Web-Based Initiative Addressing Novel Mechanisms of Action and Therapeutic Approaches to Glycemic Regulation in T2D: Translating Scientific Advances in Renal-Mediated Glucose Homeostasis to the Front Lines of Clinical Practice for T2D

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Question # 1:
Can you outline new mechanisms of action involving SGLT2 inhibitors and their impact on glucose homeostasis?

Question # 2:
Can you illuminate the role of the kidney in glucose homeostasis, both in normal individuals and those with T2D, and its role to other glycemic-regulating systems in patients with diabetes?

Question # 3:
Exactly which glucose-transporting mechanisms in the kidney are being targeted with agents such as dapagliflozin to improve glycemic control in T2D?

Question # 4:
What are the clinical implications of employing SGLT2-linked mechanisms to shift the glucose reabsorption threshold to the left in order to improve glycemic control and achieve ADA target goals?

Question # 5:
Which of the available oral antidiabetic agents (OADs) have been shown to improve attainment of ADA and AACE target goals for T2D?

Question # 6:
What do you anticipate would be a reasonable sequencing strategy for deploying currently available oral agents in combination with SGLT2 inhibitors such as dapagliflozin in T2D?

Question # 7:
What do we still need to know about SGLT2 inhibitors to deploy them as foundation agents in T2D?

Professor Markolf Hanefeld, MD, PHD
Centre for Clinical Studies,
Dresden Technical University
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Question # 8:
Are SGLT2 inhibitors such as dapagliflozin most likely to be effective in T2D patient with high, moderate, or low levels of HbA1c elevation? Or is their efficacy independent of glycemic status?

Question # 9:
Can you provide an overview of the scope of disease burden for T2D and the implications for intervention?

Question # 10:
Is there a scientific and/or medical rationale for using glucosuric agents affecting the SGLT2 system, as opposed to other currently available approached to achieve glycemic control in T2D?

Question # 11:
Based on the available clinical trial results, what are the possible implications for weight loss with dapagliflozin?

Question # 12:
What are the possible pleiotropic effects of SGLT2 inhibitors such as dapagliflozin on weight, blood pressure, and atherogenesis in patients with T2D?

Question # 13:
What integrated, multifactorial interventions in patients with T2D are likely to produce reductions in macrovascular thrombotic disease end points?

Question # 14:
Is there an evidence-based rationale for using SGLT2 inhibitors such as dapagliflozin in T2D, and what are the effects likely to be on HbA1c levels? (German)
**Question # 15:** What are the effects of SGLT2 inhibitors on weight gain in the setting of T2D? (German)

**Professor Krzysztof Strojek, MD**
Department of Internal Diseases, Diabetology, and Nephrology
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Katowice, Poland

**Question # 16:** What therapeutic strategies have been shown to be effective for reducing the risk of microvascular and/or macrovascular disease in T2D?

**Question # 17:** Can you explain the underlying pathophysiology of dysglycemic syndromes? And specifically, the role of the kidney in maintaining glucose homeostasis?

**Question # 18:** With respect to selecting potential patients with T2D who are good candidates for SGLT2-mediated intervention for glycemic control, does the underlying HbA1c level play a role in patient selection?

**Question # 19:** What is the distribution in the body of sodium-glucose coupled transporters such as the SGLTs and what role do they play in glucose homeostasis?

**Question # 20:** What multifactorial strategies have been shown to be effective for thrombovascular risk reduction in T2D?

**Question # 21:** Based on the clinical trials and animal studies conducted thus far, what do you believe is the likely role of SGLT2 inhibitors as therapeutic modalities for T2D?

**Vincent Woo, MD**
Endocrinology Section
Department of Internal Medicine
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**Question # 22:** What is the scope of disease burden associated with T2D?

**Question # 23:** What are the current glycemic (HbA1c) target goals recommended by the ADA and AACE for patients with T2D?

**Question # 24:** Which patient subgroups with T2D are likely to be the most responsive to agents that inhibit SGLT2 transport system?

**Question # 25:** Are there any significant safety issues and/or adverse side effects that we need to consider when thinking about SGLT2 inhibitors?

**Question # 26:** What is the likely role of SGLT2-inhibiting agents such as dapagliflozin, and how are such agents likely to fit into the sequencing strategies and treatment algorithms for T2D?

**Question # 27:** What is the basic mechanism of action involving SGLT2 inhibitors and why does this action have an impact on glucose homeostasis?

**Lawrence A. Leiter, MD, FRCP(C), FACP**
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Clinical Nutrition and Risk Factor Modification Centre
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**Question # 28:** How do you perceive the likely benefit-risk equation for SGLT2 inhibitors based on the clinical trial data we have thus far, and how do you think it will compare to other agents currently used on the T2D toolkit?

**Question # 29:** What emerging agents with novel mechanisms of action are likely to provide complementary therapies for patients with T2D?

**Clifford J. Bailey, PhD, FRCP, FRCPath**
UK Diabetes Research
Aston Pharmacy School
School of Life and Health Sciences Triangle
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Birmingham, UK

**Question # 30:** What are the most important current challenges for cardiovascular risk reduction in patients with T2D?

**Question # 31:** What specific metabolic interfaces and risk factors should be addressed to optimize cardiovascular risk reduction in patients with T2D?

**Question # 32:** Can you clarify the role of glucose lowering and HbA1c target goal attainment as a strategy for lowering risk of microvascular disease in diabetes?

**Question # 33:** How much glucose lowering is enough? How much is too much? And should diabetic patients be risk-stratified as far as the intensity of glycemic regulation?

**Question # 34:** Based on the data from clinical trials with SGLT2 inhibitors, what is the expected incidence of hypoglycemia, and how does the risk of hypoglycemia with these agents compare to the risk associated with other oral anti-diabetic agents (OADs)?

**Question # 35:** What is the potential advantage of kidney-mediated pathways, including inhibition of SGLT2 pathways with agents such a dapagliflozin for achieving glycemic control in T2D?
Question # 39: What is the importance of the role of the kidney in glucose homeostasis and what are the implications of renal-mediated metabolic interfaces for glycemic control in normal individuals and those with T2D?

Question # 40: How might SGLT2 inhibition with agents such as dapagliflozin play a foundation or adjucive role in HA1c target goal attainment in patients with T2D?

Question # 41: Can you compare and contrast the different SGLT transporters in the body and which ones are of special relevance in patients with T2D?

Question # 42: Is there a clinical rationale for the use of SGLT2 inhibitors for T2D and how do their mechanisms of action help achieve ADA and AACE target goals for HA1c?

Question # 43: Do the studies suggest a role for these agents as monotherapy in T2D or as complementary agents in combination with other OADs; how should these agents be sequenced?

Question # 44: How does the presence of renal disease affect the action, efficacy and/or side effects of agents working through SGLT2 inhibition? And are certain levels of GFR incompatible with these agents?

Question # 45: What is the role of glucose lowering and HA1c target goal attainment as a strategy for lowering risk of microvascular disease in diabetes?

Question # 46: Based on current clinical trial data, which patients with T2D will make good candidates for SGLT2-mediated intervention for glycemic control, and does the underlying HA1c level play a role in patient selection?

Question # 47: What do we still need to know about the SGLT2 inhibitors and their likely role in the management paradigm for T2D?

Question # 48: What do we still need to know to connect the dots in the association between microalalbuminuria and cardiovascular risk?

Question # 49: What therapeutic strategies have been shown to be effective for reducing the risk of microvascular and/or macrovascular disease in T2D?

Question # 50: What sequencing strategies do you think will likely emerge for deploying currently available oral agents in combination with SGLT2 inhibitors such as dapagliflozin for patients with T2D?

Question # 51: What are the most pressing challenges in the area of cardiovascular risk reduction for diabetes?

Question # 52: What specific multifactorial modalities, if any, have been shown to be valuable for CV risk reduction in T2D? And what is on the horizon?

Question # 53: What will we still need to know about glucose regulation in patients with T2D?

Question # 54: Can you clarify the role of glucose lowering and HA1c target goal attainment as a strategy for lowering risk of microvascular disease in diabetes? How much glucose lowering is enough? How much is too much? And should diabetic patients be risk-stratified as far as the intensity of glycemic regulation?

Question # 55: What sequencing strategies do you think will likely emerge for deploying currently available oral agents in combination with SGLT2 inhibitors such as dapagliflozin for patients with T2D? (German)

Question # 56: What do we still need to know about glucose regulation in patients with T2D? (German)

Question # 57: What advances are being made in the area of SGLT2 inhibition that may offer new therapeutic strategies for optimizing target goal attainment in T2D, and how do these agents work?

Question # 58: What are the mechanisms underlying SGLT2 inhibition, and what are the potential clinical implications of shifting the glucose reabsorption excretion curve to the left?

Question # 59: What therapeutic strategies have been shown to be safe and effective for achieving ADA, AACE, and EASD target goals?

Question # 60: Based on clinical trials evaluating dapagliflozin, what are the effects of SGLT2 inhibitors on weight gain in patients with T2D?

Question # 61: Based on clinical trials evaluating dapagliflozin, what are the effects of SGLT2 inhibitors on weight gain in patients with T2D? (German)

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Question # 63: What are the mechanisms underlying SGLT2 inhibition, and what are the potential clinical implications of shifting the glucose reabsorption excretion curve to the left? (German)

Question # 64: Based on clinical trials evaluating dapagliflozin, what are the effects of SGLT2 inhibitors on weight gain in patients with T2D? (German)
Question # 65: What are the direct and indirect effects of SGLT2 inhibitors on such cardiometabolic biomarkers as glucose, HbA1c levels, lipid levels, and other established and surrogate markers of vascular disease?

Question # 66: What effects might SGLT2 inhibitors such as dapagliflozin have on insulin resistance, obesity, blood pressure, and other vasculopathic processes that are involved in atherogenesis in the setting of T2D?

Question # 67: What is the relationship between insulin resistance and macrovascular disease?

Question # 68: What is the precise mechanism by which SGLT2 inhibitors regulate glucose homeostasis?

Question # 69: What therapeutic strategies have been shown to be effective for reducing the risk of microvascular disease in T2D, and what role are glucosuric agents likely to play in combination with these established interventions?

Question # 70: What sequencing strategies do you think will likely emerge for deploying currently available oral agents in combination with SGLT2 inhibitors such as dapagliflozin for patients with T2D?

Question # 71: What therapeutic strategies have been shown to be effective for reducing the risk of microvascular disease in T2D?

Question # 72: Is there an evidence basis for using SGLT2 inhibitors as monotherapeutic agents or as adjuncts to established glycemic-regulating agents?

Question # 73: How might SGLT2 inhibition with agents such as dapagliflozin play a foundation or adjunctive role in HbA1c target goal attainment in patients with T2D?

Question # 74: Do the studies suggest a role for SGLT2 inhibitors as monotherapy in T2D or as complementary agents in combination with other OADs; how should these agents be sequenced?

Question # 75: Which patients with T2D do you feel are optimal candidates for treatment with SGLT2 inhibitors? Treatment naïve? Patients on metformin? Others?

Question # 76: What are the most important current challenges for cardiovascular risk reduction in patients with T2D?

Question # 77: How might SGLT2 inhibition with agents such as dapagliflozin play a foundation or adjunctive role in HbA1c target goal attainment in patients with T2D? (French)

Question # 78: Do the studies suggest a role for SGLT2 inhibitors as monotherapy in T2D or as complementary agents in combination with other OADs; how should these agents be sequenced? (French)

Question # 79: Which patients with T2D do you feel are optimal candidates for treatment with SGLT2 inhibitors? Treatment naïve? Patients on metformin? Others? (French)

Question # 80: What effects might SGLT2 inhibitors such as dapagliflozin have on insulin resistance, obesity, blood pressure, and other vasculopathic processes that are involved in atherogenesis in the setting of T2D? (French)

Question # 81: What do we know about the relationship between T2D and atherosclerosis?

Question # 82: What mechanisms are involved in mitigating progression or inducing regression of atherogenesis in patients with T2D?

Question # 83: What mechanisms are involved in mitigating progression or inducing regression of atherogenesis in patients with T2D? (Italian)

Question # 84: What do we know about the relationship between T2D and atherosclerosis? And what specific metabolic interfaces and risk factors should be addressed to optimize cardiovascular risk reduction? (Italian)