The Role of SGLT-2 Inhibitors in the Management of Patients with Type 2 Diabetes

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• Speaker/speakers bureau: Amylin, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Merck, Novo Nordisk
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Please complete the questionnaire/evaluation form
Case Presentation

- 48-year-old African American man with 12 month history of type 2 diabetes
- Hypertension for past 6 years treated with lisinopril 10 mg daily
  - Most recent blood pressure was 138/84 mm Hg
- Increased LDL-C treated with simvastatin 40 mg qd;
  - Most recent LDL-C 98 mg/dL
- Diabetes treated with lifestyle intervention (increased physical activity, medical nutritional therapy) and metformin 1000 mg bid
  - Weight 240 pounds, height 6’ (BMI = 32.5)
- A1C = 7.5 %
Natural History of T2D and β-cell Function

Ominous Octet

- Islet beta cell: Impaired insulin secretion
- Islet alpha cell: Increased glucagon secretion
- Increased hepatic glucose production
- Decreased incretin effect
- Neurotransmitter dysfunction
- Increased lipolysis
- Increased glucose reabsorption
- Decreased glucose uptake

Adapted from DeFronzo, R. Diabetes. 2009;58:783.
# ABCs of Type 2 Diabetes: AACE/ACE 2011 and ADA 2011

<table>
<thead>
<tr>
<th>Target Treatment Goals</th>
<th>AACE/ACE 2011</th>
<th>ADA 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A1C</strong></td>
<td>≤ 6.5%</td>
<td>&lt; 7.0%</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>&lt;130/80 mm Hg</td>
<td>&lt;130/80 mm Hg</td>
</tr>
</tbody>
</table>
| **Cholesterol (lipids)** | • LDL-C < 100 mg/dL (< 70 mg/dL for patients with diabetes and coronary artery disease)  
• HDL-C > 40 mg/dL in men; > 50 mg/dL in women  
• Triglycerides <150 mg/dL | • LDL-C < 100 mg/dL (< 70 mg/dL for patients with diabetes and coronary artery disease)  
• HDL-C > 40 mg/dL in men; > 50 mg/dL in women;  
• Triglycerides < 150 mg/dL |


## Glycemic Control Recommendations for Type 2 Diabetes: AACE/ACE 2011 and ADA 2011

<table>
<thead>
<tr>
<th>Target Treatment Goals</th>
<th>AACE/ACE 2011</th>
<th>ADA 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>≤ 6.5%</td>
<td>&lt; 7.0%</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>Fasting plasma glucose: &lt; 110 mg/dL</td>
<td>Preprandial capillary plasma glucose: 70 – 130 mg/dL</td>
</tr>
<tr>
<td>Postprandial glucose</td>
<td>2-hr postprandial glucose: &lt; 140 mg/dL</td>
<td>Peak postprandial capillary plasma glucose: &lt; 180 mg/dL</td>
</tr>
</tbody>
</table>


ADA/AHA/ACC Consensus Recommendations From ACCORD, ADVANCE, & VA Diabetes Trials

• A1C goal for non-pregnant adults in general = < 7.0%
  – Lowering A1C to ≈7.0% has been shown to reduce microvascular and neuropathic complications
• For selected individual patients, lower A1C goals may be recommended if goal can be achieved without significant hypoglycemia or other adverse events, eg, patients with
  – Short duration of diabetes
  – Long life expectancy
  – No significant cardiovascular disease
• For some patients, less stringent A1C goals may be appropriate, eg, patients with
  – History of severe hypoglycemia
  – Limited life expectancy
  – Advanced microvascular or macrovascular complications
  – Extensive co-morbid conditions
  – Long-standing diabetes where goals have not been achieved despite optimal Rx

Challenges in Type 2 Diabetes

• Large number of patients
  – Diabetes affects 25.8 million people (8.3% of the US population)
    • DIAGNOSED- 18.8 million people
    • UNDIAGNOSED- 7.0 million people
    • PREDIABETES – 79 million people
• Progressive worsening of insulin secretory deficit requiring increased number of antihyperglycemic medications over time
• Risk for hypoglycemia with some therapies
• Risk for weight gain with some therapies
• Difficulty controlling postprandial glucose and glucose fluctuations
• Preventing and managing complications and co-morbidities
• Difficulty attaining and sustaining optimal long-term glycemic control

Diabetes HealthSense provides easy access to resources to help you live well and meet your goals—whether you have diabetes or are at risk for the disease.

Live well. Eat healthy. Be active. It’s not easy, but it’s worth it.

Use the options on the left to find resources to help you get started.

Managing Type 2 Diabetes
Sonya has changed her family’s eating and activity habits to help manage her diabetes—and to prevent the disease in her daughters.

Selected Resources
Need help getting started, or feeling overwhelmed? Take a look at some of the resources below to help you get on the right track:

- Cope with Stress and Emotions
  - My Action Plan to Solve a Problem
  - New Health Partnerships
  - Diabetes TLC

- Be Active
  - Active at Any Size
  - Get Fit on Route 66
  - Exercise & Physical Activity: Your Everyday Guide from the National Institute on Aging

- Eat Healthy
  - A Healthier You
  - Journey to Control

- Manage Your Weight
  - Small Steps. Big Rewards. Your GAME PLAN to Prevent Type 2 Diabetes: Eating Healthy
ADA/EASD Writing Goup Consensus Algorithm

**STEP 1**

*At diagnosis: Lifestyle + metformin*

If A1c ≥ 7%

**STEP 2**

**Tier 1:** Well-validated core therapies*

- Lifestyle + metformin + sulfonylurea†
- Lifestyle + metformin + basal insulin

**Tier 2:** Less-well-validated therapies*

- Lifestyle + metformin + GLP-1 agonist
- Lifestyle + metformin + pioglitazone

**STEP 3**

Lifestyle + metformin + intensive insulin

*Validation based on clinical trials and clinical judgment
†Sulfonylureas other than glybenclamide (glyburide) or chlorpropamide

AACE/ACE Diabetes Algorithm for Glycemic Control

### Summary of Key Benefits and Risks of Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Metformin</th>
<th>DPP-4 Inhibitor</th>
<th>GLP-1 Agonist</th>
<th>Sulfonylurea</th>
<th>Glinide</th>
<th>TZD</th>
<th>Colesevelam</th>
<th>AGI</th>
<th>Insulin</th>
<th>Pramlintide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefits</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPG - lowering</td>
<td>Mild</td>
<td>Moderate</td>
<td>Moderate to Marked</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate to Marked</td>
<td>Moderate to Marked</td>
<td></td>
</tr>
<tr>
<td>FPG - lowering</td>
<td>Moderate</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Neutra</td>
<td>Moderate to Marked</td>
<td>Mild</td>
</tr>
<tr>
<td>Nonalcoholic fatty liver disease (NAFLD)</td>
<td>Mild</td>
<td>Neutral</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutra</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>Risks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutra</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
</tr>
<tr>
<td>GI Symptoms</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutra</td>
<td>Moderate</td>
<td>Neutral</td>
</tr>
<tr>
<td>Risk of use with renal insufficiency</td>
<td>Severe</td>
<td>Reduce Dosage</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Mild</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
</tr>
<tr>
<td>Contraindicated if liver failure or predisposition to lactic acidosis</td>
<td>Severe</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutra</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>Heart failure/Edema</td>
<td>Contra-indicated in CHF</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Mild/Moderate</td>
<td>Neutral</td>
<td>Neutra</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>Weight Gain</td>
<td>Benefit</td>
<td>Neutral</td>
<td>Benefit</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutra</td>
<td>Mild to Moderate</td>
<td>Benefit</td>
</tr>
<tr>
<td>Fractures</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
<tr>
<td>Drug-Drug Interactions</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
</tbody>
</table>

Unmet Needs With Conventional Antihyperglycemic Therapies

• Many therapies are associated with weight gain
• Insulin and non incretin oral insulin secretagogue therapies are associated with significant risk for hypoglycemia
• Other AEs with some therapies include GI side effects and edema
• Many therapies fail to adequately control postprandial hyperglycemia
• Therapies often fail to maintain long-term glycemic control

The Kidneys Play an Important Role in Glucose Control

Normal Renal Glucose Physiology

- 180 g of glucose is filtered each day
- Virtually all glucose reabsorbed in the proximal tubules & reenters the circulation
- SGLT2 reabsorbs about 90% of the glucose
- SGLT1 reabsorbs about 10% of the glucose

Targeting the Kidney

Renal Glucose Transport

Rationale for SGLT2 Inhibitors

• Mutation in SGLT2 transporter linked to hereditary renal glycosuria, a relatively benign condition in humans

• Selective SGLT2 inhibitors have a novel & unique mechanism of action reducing blood glucose levels by increasing renal excretion of glucose

• Decreased glycemia will decrease glucose toxicity leading to further improvements in glucose control

• Selective SGLT2 inhibition, would also cause urine loss of the calories from glucose, potentially leading to weight loss

SGLT2 Inhibitors in Phase 3 Development

- Dapagliflozin
- Canagliflozin
- Empagliflozin
- Ipragliflozin
- Tofogliflozin
Empagliflozin: Change in A1C

Randomized, double-blind, 12 week trial comparing empagliflozin and open-label metformin

*P < 0.001 vs. placebo
†500 mg BID for four weeks, then 1000 mg BID or the maximum tolerate dose

Empagliflozin: Change in Plasma Glucose in the Fasting State

Randomized, double-blind, 12 week trial comparing empagliflozin and open-label metformin

*P<.001 vs. placebo
†500 mg BID for four weeks, then 1000 mg BID or the maximum tolerate dose

Empagliflozin Safety Summary

• In Phase 2b study
  - Reported adverse events were comparable among treatment groups
  - Most frequently reported AEs
    • Frequent urination, thirst, and nasopharyngitis
  - Urinary tract infection frequency was low (1.2%) and comparable to placebo (1.2%) and metformin (1.2%)
  - Incidence of genital infection was low: mycosis (0.8%) and pruritis (1.2%) with Empagliflozin versus none with metformin or placebo
  - Rates of hypoglycemia were similar between groups

BRIGHTEN Trial: Ipragliflozin

Phase 3, Double-blind, Placebo-controlled Study-16 weeks (n=129)

- Ipragliflozin treatment group 50mg QD (n=62)
  - Ipragliflozin achieved a mean decrease of 1.23% in A1c compared with placebo (p<0.001)
  - FPG was reduced by 45.8mg/dL compared with placebo (p<0.001)
  - Total body weight was reduced by 1.47kg compared with placebo (p<0.001)
  - Similar adverse events occurring in about half the patients in both cohorts.
  - 1 case if hypoglycemia and 2 cases of genital infections in ipragliflozin group

Canagliflozin

Metformin + Canagliflozin Dose-Ranging Study

Mean Baseline A1C (%)

- 7.71
- 8.01
- 7.81
- 7.57
- 7.70
- 7.71
- 7.62

ΔA1C (%)

-0.79%
-0.76%
-0.70%
-0.92%
-0.95%
-0.74%

PBO
50 mg
100 mg
200 mg
300 mg
300 mg BID
SITA 100 mg


*P <0.001 vs. placebo calculated using LS means
Canagliflozin

SGLT2 Inhibition for Type 2 Diabetes: Metformin + Canagliflozin Dose-Ranging Study

Mean Baseline Weight (kg)

<table>
<thead>
<tr>
<th>Group</th>
<th>Weight (kg)</th>
<th>Body Weight Change from Baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO</td>
<td>85.5</td>
<td>-1.10%</td>
</tr>
<tr>
<td>50 mg</td>
<td>87.5</td>
<td>-2.30%</td>
</tr>
<tr>
<td>100 mg</td>
<td>87.7</td>
<td>-2.60%</td>
</tr>
<tr>
<td>200 mg</td>
<td>87.7</td>
<td>-2.70%</td>
</tr>
<tr>
<td>300 mg</td>
<td>87.8</td>
<td>-3.40%</td>
</tr>
<tr>
<td>SITA 100 mg</td>
<td>86.3</td>
<td>-3.40%</td>
</tr>
<tr>
<td>SITA 300 mg</td>
<td>87</td>
<td>-0.60%</td>
</tr>
</tbody>
</table>

*P <0.001 vs. placebo calculated using LS means

Canagliflozin Trials

• Symptomatic genital infections in 3-8% canagliflozin arms
  – 2% placebo
  – 2% SITA
• Urinary tract infections in 3-9% canagliflozin arms
  – 6% placebo
  – 2% SITA
• Hypoglycemia in 0-6% canagliflozin arms
  – 2% placebo
  – 5% SITA

Changes from Baseline in A1C in Phase 3 Dapagliflozin Studies

Changes from Baseline in Fasting Plasma Glucose in Phase 3 Dapagliflozin Studies

Changes from Baseline in Body Weight in Phase 3 Dapagliflozin Studies

Dapagliflozin* vs. Glipizide as Add-on Therapy to Metformin: 1 year

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Change in A1c</th>
<th>≥ 1 Hypoglycemic Episode</th>
<th>Change in Total Body Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin + Metformin (n=315)</td>
<td>-0.52% (-0.6, -0.44)</td>
<td>3.5%</td>
<td>-3.2 kg (-3.56, -2.87)</td>
</tr>
<tr>
<td>Glipizide + metformin (n=309)</td>
<td>-0.52% (-0.6, -0.44)</td>
<td>40.8%</td>
<td>+ 1.4 kg (1.09, 1.78)</td>
</tr>
</tbody>
</table>

Urinary tract infection: 10.8% for dapagliflozin; 6.4% for glipizide
Genital infection: 12.3% for dapagliflozin; 2.7% for glipizide


*The FDA has not approved this medication for use.
Dapagliflozin* vs. Glipizide as Add-on Therapy to Metformin: 2 Years

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Change in A1c</th>
<th>≥ 1 Hypoglycemic Episode</th>
<th>Change in Total Body Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin + Metformin (n=315)</td>
<td>-0.32% (-0.42, -0.21)</td>
<td>4.2%</td>
<td>-3.70 kg (-4.16, -3.24)</td>
</tr>
<tr>
<td>Glipizide + metformin (n=309)</td>
<td>-0.14% (-0.25, -0.03)</td>
<td>45.8%</td>
<td>+ 1.36 (0.88, 1.84)</td>
</tr>
</tbody>
</table>

Urinary tract infection: 13.5% for dapagliflozin; 9.1% for glipizide
Genital infection: 14.8% for dapagliflozin; 2.9% for glipizide


*The FDA has not approved this medication for use.
Dapagliflozin as Add-on to Metformin: 2 Year Extension Study

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>DAPA 2.5mg</th>
<th>DAPA 5mg</th>
<th>DAPA 10mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ from BL (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1c, %</td>
<td>0.2 (0.11)</td>
<td>-0.48 (-.1)</td>
<td>-0.58 (0.1)</td>
<td>-0.78 (0.09)</td>
</tr>
<tr>
<td>FPG, mg/dl</td>
<td>-10.4 (3.6)</td>
<td>-19.3 (3.2)</td>
<td>-26.5 (2.8)</td>
<td>-24.5 (2.7)</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>-0.7 (0.5)</td>
<td>-2.2 (0.5)</td>
<td>-3.4 (0.4)</td>
<td>-2.8 (0.4)</td>
</tr>
<tr>
<td>% Pts with ≥ 1 hypoglycemic event</td>
<td>5.8</td>
<td>3.6</td>
<td>5.1</td>
<td>5.2</td>
</tr>
</tbody>
</table>

- Events suggestive of urinary tract infection
  - Dapagliflozin 2.5 mg: 8.0%, 5 mg: 8.8%, 10 mg: 13.3%
  - Placebo: 8.0%

- Events suggestive of genital infection
  - Dapagliflozin 2.5 mg: 11.7%, 5 mg: 14.6%, 10 mg: 12.6%
  - Placebo: 5.1%

- Events primarily mild or moderate in intensity and responded to standard treatment

Dapagliflozin, Metformin XR, or Both as Initial Therapy

Change in A1C

Change in FPG

Change in Body Weight

## SGLT2 Inhibitors Added to Metformin: Effects on Blood Pressure and Lipids

- SBP and DBP reductions of -9.3 and -5.1 mm Hg, respectively, reported for monotherapy with 300 mg canagliflozin
- Increased HDL cholesterol (≈ 4%-6%) and decreased TG (≈ 1%-6%) reported with dapagliflozin

### Table: Blood Pressure Reductions with SGLT2 Inhibitors

<table>
<thead>
<tr>
<th>Agent/Study</th>
<th>Δ SBP (mm Hg)</th>
<th>Δ DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin¹</td>
<td>-4.3</td>
<td>-1.6</td>
</tr>
<tr>
<td>(Titrated dose, 52 weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dapagliflozin²</td>
<td>-5.1</td>
<td>-1.8</td>
</tr>
<tr>
<td>(10 mg, 24 weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Empagliflozin³</td>
<td>≈ -6</td>
<td>NR</td>
</tr>
<tr>
<td>(10 mg, 12 weeks)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Genital Infections: SGLT2 Inhibitors With Metformin

<table>
<thead>
<tr>
<th>Agent</th>
<th>Genital Infections (% of Participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPA (24 wk)</td>
<td>DAPA: 8-13</td>
</tr>
<tr>
<td></td>
<td>PBO: 5</td>
</tr>
<tr>
<td>DAPA (102 wk)</td>
<td>DAPA: 12-15</td>
</tr>
<tr>
<td></td>
<td>PBO: 5</td>
</tr>
<tr>
<td>DAPA (52 wk)</td>
<td>DAPA: 12</td>
</tr>
<tr>
<td></td>
<td>GLIP: 3</td>
</tr>
</tbody>
</table>

- Most events mild to moderate
  - Most resolved with conventional intervention
  - Rarely led to study discontinuation


\(^a\) One discontinuation.
\(^b\) One severe and 3 led to discontinuation in DAPA group.
Occurrence of signs and symptoms suggestive of urinary tract infection was similar across treatments.

Reports indicate that urinary tract infections\(^1,^3\):
- Were generally mild to moderate and not recurrent
- Responded to standard treatments
- Rarely led to discontinuation

---

**Agent** | **Urinary Tract Infections (% of Participants)**
---|---
DAPA (24 wk) | DAPA: 4-8 | PBO: 8
DAPA (102 wk)\(^a\) | DAPA: 8-13 | PBO: 8
DAPA (52 wk)\(^b\) | DAPA: 11\(^b\) | GLIP: 6

---

\(^a\) One discontinuation.

\(^b\) \(P < .05\) for DAPA vs GLIM based on post hoc analysis.

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Potential SGLT2 Safety Considerations?

- **Evidence Demonstrates**
  - Urinary tract/genital infections

- **Questions**
  - Intravascular volume depletion due to osmotic diuresis
  - Nephrotoxicity (AGEs)
  - Hepatotoxicity
  - Drug-drug interactions
  - Breast and bladder cancer

- **Evidence Does Not Demonstrate**
  - Electrolyte imbalance ($Na^+$, $K^+$, $Ca^{++}$, $PO_4$)
  - Increased risk for hypoglycemia
  - Nocturia
Safety: Malignancies

• Bladder cancer incidence rate:
  – 0.16% patients (n=5,478) treated with dapagliflozin vs 0.03% patients (n=3,156) in placebo group (p = 0.15)

• Breast cancer incidence rate:
  – 0.4% patients (n=2,223) treated with dapagliflozin vs 0.09% patients (n=1,053) in placebo group (p = 0.27)

Case Presentation 1

• 48-year-old African American man with 12 month history of type 2 diabetes

• Hypertension for past 6 years treated with Lisinopril 10 mg daily;
  – most recent blood pressure was 138/84 mm Hg

• Increased LDL-C treated with simvastatin 40 mg qd;
  – most recent LDL-C 98 mg/dL

• Diabetes treated with metformin 1000 mg bid and lifestyle intervention (increased physical activity, medical nutritional therapy)
  – Weight 240 pounds, height 6’ (BMI = 32.5)

• A1C = 7.5 %
Case Presentation 2

• 64-year-old Latina with 8 year history of type 2 diabetes
• Hypertension for past 6 years treated with Olmesartan 10 mg and HCTZ 12 mg daily
  – most recent blood pressure was 142/86 mm Hg
• Increased LDL-C treated with simvastatin 40 mg qd;
  – most recent LDL-C 98 mg/dL
• Diabetes treated with metformin XR 1500 mg QD; insulin glargine 30 U QHS and lifestyle intervention (increased physical activity, medical nutritional therapy)
  – Weight 160 pounds, height 5’ 2” (BMI = 29.3)
• A1C = 7.5 %; FPG 160 mg/dL
Perspectives on SGLT2 Inhibition

• Potential advantages
  – Novel and unique MOA
  – Insulin Independence
  – Weight loss (75g urine glucose = 300kcal/day)
  – Low risk of hypoglycemia
  – Blood pressure lowering

• Concerns
  – Fungal genital infections
  – Bacterial urinary tract infections
  – Reduced efficacy in patients with significant CKD
  – Polyuria
  – Electrolyte disturbances
  – Malignancies