### Hypoglycemia

Drugs that lower blood glucose come with various levels of evidence regarding their balance of benefits and tolerability.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Death / findings</th>
<th>Risk of HF</th>
<th>Risk of * complications between agents have not been done so one is left to evaluate each drug for its relative advantages &amp; disadvantages.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td></td>
<td></td>
<td><strong>A1C</strong></td>
</tr>
<tr>
<td>TZDs</td>
<td></td>
<td></td>
<td><strong>A1C</strong></td>
</tr>
</tbody>
</table>

#### Major trials to support findings/ Outcomes*

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Risk of Death / Major CVⅠ</th>
<th>Risk of Hypoglycemia</th>
<th>Risk of HF /Edema</th>
<th>Effect on GI tolerance</th>
<th>Cost</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKPDS-33,34,80 (ADOPT)</td>
<td>in obese, in mortality &amp; obesity, in M (UKPDS-34)</td>
<td>? less risk with MR formulation</td>
<td>1st line in HF with eGFR &gt;30 mL/min (DCLE18)</td>
<td>Start low &amp; titrate</td>
<td><strong>A1</strong></td>
<td>May have to hold or reduce in acute illness/FHF, renal dysfx (? lactacidosis), may ↓ B12</td>
</tr>
</tbody>
</table>

**Antihyperglycemic Diabetes Agents in T2DM: Outcomes Comparison Summary Table**

<table>
<thead>
<tr>
<th>Generic/BRAND</th>
<th>Sulfonylureas</th>
<th>DPP4 Inhibitors</th>
<th>GLP1 Agonists ***</th>
<th>SGLT2 Inhibitors ***</th>
<th>Intensity</th>
<th>Insulin in T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Advantage**: see page 39
- **Neutral**: see page 39
- **Disadvantage**: see page 39
- **Unknown/Ongoing**: see page 39

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Individual approach considering balance of potential benefits & harms. Over-aggressive pursuit of targets can ↑ mortality.
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>GLP1 Agonists</th>
<th>SGLT2 Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major trial(s) to support findings/Outcomes</strong></td>
<td></td>
<td><strong>CANVAS</strong>&lt;br&gt; Homozygous 42 / 3.4 yr&lt;br&gt; DECLARE-TIMI 55 / 5.2 yr&lt;br&gt; DAPA-HF 7906 / 1.19 yrs&lt;br&gt; EMPA-REG 9702 / 3.1 yr</td>
</tr>
<tr>
<td><strong>↓ Risk of Major CV - MACE</strong></td>
<td><strong>LEADER</strong>&lt;br&gt; GLP1&lt;br&gt; 77% risk reduction&lt;br&gt;</td>
<td><strong>GLP1</strong>&lt;br&gt; GLP1&lt;br&gt; Non-inferior to Placebo&lt;br&gt; 3.8% vs 4.8%&lt;br&gt; HR: 0.79 (0.57-1.11)&lt;br&gt; Many trial limitations, e.g. short&lt;br&gt;</td>
</tr>
<tr>
<td><strong>↓ Risk of All-Death</strong></td>
<td></td>
<td><strong>HR</strong>: 0.97 (0.86-1.10)&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Less Renal Disease (composite: surrogate)</strong></td>
<td></td>
<td><strong>HR</strong>: 0.87 (0.74-1.01)&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Effect on AIC</strong></td>
<td></td>
<td><strong>HR</strong>: 0.83 (0.68-1.02)&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Weight (loss vs natual vs gain)</strong></td>
<td></td>
<td><strong>HR</strong>: 0.93 (0.79-1.12)&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Less Risk of Hypoglycemia</strong></td>
<td></td>
<td><strong>HR</strong>: 0.77 (0.63-1.01)&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Effect on GI &amp; D/C due to Tolerability</strong></td>
<td></td>
<td>**D/C due to AE 6% vs 9%&lt;br&gt; NNH=36/4 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>? AE Concerns Associated with Class</strong></td>
<td></td>
<td>**D/C due to AE 12% vs 13%;&lt;br&gt; NNH=7/0.6 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Cost – 1 month</strong></td>
<td></td>
<td>**D/C due to AE 8% vs 15%;&lt;br&gt; NNH=6/0.8 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td>**D/C due to AE 11.6% vs 14%;&lt;br&gt; NNH=20/0.4 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Practical / Clinical Considerations</strong></td>
<td></td>
<td>**D/C due to AE 6.8% vs 6.3%;&lt;br&gt; NNH=24/0.4 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Time Tested</strong></td>
<td></td>
<td>**D/C due to AE 11.6% vs 6.5%;&lt;br&gt; NNH=20/0.4 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Convenience</strong></td>
<td></td>
<td>**D/C due to AE 7.7% vs 6.3%;&lt;br&gt; NNH=20/0.4 yrs&lt;br&gt;</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td>**D/C due to AE 7.7% vs 6.3%;&lt;br&gt; NNH=20/0.4 yrs&lt;br&gt;</td>
</tr>
</tbody>
</table>

*Drugs that lower blood glucose come with various levels of evidence regarding their balance of benefits & harms. This chart relies predominantly on current evidence, especially from randomized controlled trials that have evaluated patient oriented outcomes.

Direct comparisons between agents have not been done so one is left to evaluate each drug for its relative advantages & disadvantages. **AIC will vary depending on dose, combinations & initial AIC.

See full version of this ANTI-HYPERGLYCEMIC DIABETES AGENTS: Outcomes Comparison Summary Table online for additional notes: http://www.nuffield.ca/files/uploads/documents/Diabetes-Agents-Outcomes-Comparison-Summary-Table.pdf

**What should doctors and patients be aware of when choosing a GLP-1 agonist or SGLT2 inhibitor?**

- **GLP1 Agonists**
  - **REWARD**
    - Lower risk group; e.g. 21% had past CVD; others higher risk.
    - Renal: macroalbuminuria, eGFR decline 30%, chronic renal replacement tx
  - **LEADER**
    - High risk group
  - **SUSTAIN-6**
    - High risk group: 83% had established CVD, CKD or both
  - **PIONEER 6**
    - MF: 77%, insulin 60%; Smaller, shorter trial; SAE leading to lower discontinuation rate in tx group, 2.6% vs 3%
    - Higher risk group: CVD or CKD 84.7%

- **SGLT2 Inhibitors**
  - **CANVAS**
    - High risk group: 66% had established/hx of CVD [1° outcome if no CV disease history, HR= 0.98 (0.74-1.3)]
  - **DECLARE-TIMI**
    - High risk group: >40% had atherosclerotic CVD; 33% CAD, 6% PAD, 7.6% cerebrovascular dx, 10% HF
  - **DAPA-HF**
    - Both patients with and without diabetes studied; similar benefit in both groups.
  - **EMPAT-REG**
    - High risk group: 100% had established CVD. Patients had not received glucose-lowering agents for >12 weeks

Studies have not evaluated whether findings are generalizable to people with new onset type 2 diabetes, or those at average or lower CV risk.
Death/MACE (MACE: Major adverse cardiovascular event)

1. Drug manufacturers must establish CV safety (one-sided upper boundary of 95% CI ≤ 1.3) vs comparator (typically placebo) in a RCT for all new agents in ↑ CV risk patients; 1 FDA
2. Metformin vs conventional diet; obese ≥120% BW & small sample n=775; ↓ all-cause mortality NNT 14/10.7 yr, and ↓ MI NNT=14/10.7 yr. 2 UKPDS-34 10 yr observational follow-up ↓ all-cause mortality NNT=14/20 yr, and ↓ MI NNT=16/20 yr. 3 UKPDS-80
3. Intensive Hba1c target (included glitazide) vs standard Hba1c target; MACE 10% vs 16% p=NS; all-cause mortality 8.9% vs 9.6% p=NS. 4 ADVANCE
4. Intensive therapy (chlorpropamide, glipizide/5A, glibenclamide or insulin) vs conventional diet; all-cause mortality 17.9% vs 18.9% p=NS, MI 14.7% vs 17.4% p=NS, and stroke 5.6% vs 5% p=NS. 5 UKPDS-33 10 yr observational follow-up ↓ all-cause mortality NNT=29/~20 yr, and ↓ MI NNT=36/~20 yr. 6 UKPDS-80
5. SU (2nd or 3rd generation) vs control (diet, placebo, other antihyperglycemic); all-cause mortality OR 1.12 (0.96-1.3), I2=0%, CV mortality OR 1.12 (0.87-1.42, I2=12%), MI OR 0.92 (0.76-1.12, I2=NR), stroke OR 1.16 (0.81-1.66, I2=NR). 6
6. Metformin vs glitazide; Chinese, small sample n=304, & medically undertreated ↓ MACE NNT=10/5 yr. 7 SPREAD-DIMCAD
7. Pioglitazone vs placebo; T2DM & high CV risk; ↓ MACE NNT=50/2.9 yr, 8 PROACTIVE insulin resistance & recent TIA/stroke; ↓ MACE RR=36/4.8 yr. 9 IRIS
8. Rosiglitazone vs placebo; ↑ MACE 2.9% vs 2.1% p=0.08 (NS), trial stopped 5 mons early. 10 DREAM ↑ MI NNT=167 & CV death 0.87% vs 0.39% p=0.06. 10 Rosiglitazone vs glyburide ↑ MACE NNH 63/4 yr. 12 ADOPT
9. Acarbose vs placebo; impaired glucose tolerance; ↓ MACE NNT=40/3.3 yr. 13 STOP-NIDDM Acarbose vs placebo; coronary heart disease (Chinese) HR 0.98 95% CI, 0.86-1.0, p=0.73. 13 ACE
10. Saxagliptin vs placebo; MACE 7.3% vs 7.2%, non-inferior (p<0.001), but not superior (p=0.99). 14 SAVOR-TIMI 53 Alogliptin vs placebo; MACE 11.3% vs 11.8%, non-inferior (p<0.001), but not superior (p=0.32). 15 EXAMINE Alinaeglaptin vs placebo; MACE 9.6% vs 9.6%, non-inferior (p<0.001), but not superior (p=0.65). 16 TECOS Meta-analysis (SAVOR-TIMI 53, EXAMINE, TECOS) MACE RR 0.99 (95% CI, 0.93-1.06, I2=0%). 17
11. Linagliptin vs placebo; MACE 12.4% vs 12.1% non-inferior (p<0.001), but not superior (p=0.74). 18 CARMELINA Linagliptin vs glimepiride: MACE 11.8% vs 12% non-inferior (p<0.001) but not superior. 19 CARDIO2019
12. Liagliptin vs placebo; MACE 13% vs 14.9%, superior (p=0.01, NNT=53/3.8 yr), but results neutral in North America subgroup; ↓ CV death NNT=77/3.8 yr and ↓ all-cause mortality NNT 72/3.8 yr. 19 LEADER Semaglutide SC weekly vs placebo; MACE superior; (nephropathy was better; however, retinopathy complications were worse). 20 SUSTAIN6
13. Lixisenatide vs placebo (post-ASC) MACE 13.4% vs 13.2%, non-inferior (p<0.001), not superior (p=0.83). 21 ELIKA
14. Intensive insulin vs standard insulin; T1DM population; ~11 yr observational follow up ↓ MACE NNT=23/~7 yr. 32 DCT, 33 EDIC
15. Rosiglitazone: ↓ 2.9 kg/4 yr 1 ADOPT
16. Sulfonylureas: ↑ 1.6 kg/4 yr 1 ADOPT
17. Pioglitazone: ↑ 3.6 kg/3 yr 2 PROACTIVE
18. Acarbose: ↑ 1.15 kg/3 yr 3 STOP-NIDDM
19. Repaglinide: ↑ 0.7 kg/4 yr 4 STOP-NIDDM
20. Sitagliptin: ↑ 0.4 kg/2.1 year (similar to placebo) 8 SAVOR-TIMI 53
21. Saxagliptin ↓ 0.4 kg/2.1 year (similar to placebo) 8
22. Albiglutide: ↓ 0.4 kg/12 weeks 6
23. Sitagliptin ↓ ≤ 0.5 kg/12 weeks 10
24. GLP1 agonists
25. Exenatide ↓ 2.8 kg/24-52 weeks 11
26. Liraglutide ↓ 2.3 kg/3.8 yr 12 LEADER
27. Dulaglutide ↓ 1.3-3 kg/5-52 weeks 13
28. SGLT2 inhibitors 14
29. Canagliflozin ↓ 2.8-4 kg/5-12 weeks 15, 16 CANTATA-M
30. Dapagliflozin ↓ 2 kg/12-52 weeks 17
14. Exenatide extended release vs placebo (~70% CVD, ~30% primary prevention); MACE 11.4% vs 12.2% over median 3.2 yr, non-inferior (p<0.001), but not superior (p=0.06). 22 DISOL Dulaglutide 23 CV trial ongoing, estimated completed 2018. 23 REMIND Albiglutide CV trial ongoing, estimated completed 2018. 24 SEMIGlumal PO CV trial semaglutide vs placebo: MACE, non-inferior; ↓ all-cause death 1.4%, vs 2.8% 2nd endpoint 2019. 25 PIONEER-4 15. Empagliflozin vs placebo; MACE 10.5% vs 12.1%, superior (p=0.04, NNT=63/3.1 yr); ↓ CV death NNT=46/3.1 yr and ↓ all-cause mortality NNT 39/3.1 yr. 25 EMPA-REG Canagliflozin vs placebo; MACE 26.9/1000tpyrs (2.7%/yr) vs 31.5/1000tpyrs (3.15%/yr), superior (p=0.02, NNT=220/yr), f/u duration 3.6yr, no significant difference in components of primary composite or death; ↑ MACE in 1st 30 days (n=13 vs n=1, p=NS, non-dose related); ↓ MACE (NS) after 30 days (HR 0.89, 95% CI 0.64, 1.25); numeric imbalance not present in non-CNANS trials. 26,27,28 CANVAS Dapagliflozin vs placebo; MACE 8.8% vs 9.4% p<0.001 non-inferior, but not superior p=0.17; ↓ CV death & HF hospitalization combo outcome. 28 16. Ertugliflozin CV trial ongoing, estimated completed 2019. 29 VERTIS CV Sotagliflozin CV trial ongoing, estimated completed 2022. 30 SCORE 17. Basal insulin (glargine) vs standard care; all-cause mortality 15.2% vs 15.4% p=NS, MI 5.4% vs 5.2% p=NS, and stroke 5.3 vs 5.1% p=NS. 30 ORIGIN 18. Basal insulin vs basal/bolus insulin; small sample n=152; CV mortality 3.8% vs 6.7% p=NS, MACE 20% vs 32% p=NS. 31 HF/Edema- cont’d 29 Repaglinide vs rosiglitazone; peripheral edema 0% vs 3.2%, p=NS. 9 30 Saxagliptin vs placebo; ↑ hospitalization for HF NNH=143/2.1 yr; however, subgroup without a history of HF at baseline ↑ hospitalization for HF NNH=147/2.1 yr, subgroup eGFR <60 ml/min ↑ hospitalization for HF NNH=68/2.1 yr & no difference from 12 months on (HR 1.05, 95% CI 0.81-1.35). 10,11 SAVOR-TIMI 53 Alogliptin vs placebo; hospitalization for HF 3.9% vs 3.3% p=0.02; subgroup without a history of HF at baseline ↑ hospitalization for HF NNH=111/1.5 yr. 12,13 EXAMINE Sitagliptin vs placebo; hospitalization for HF 3.1% vs 3.1% p=0.98; and neutral results when adjusted for baseline HF (HR 1.00, 95% CI 0.83-1.20 [unpublished data]). 14,15 TECOS Meta-analysis (SAVOR-TIMI 53, EXAMINE, TECON) HF admission RR 1.12 (95% CI, 1.00-1.25, I²=42%). 16 FDA warnings for both saxagliptin & albiglutide. 17 Linagliptin vs placebo; hospitalization for heart failure 6.0% vs 6.5% for an absolute incidence rate difference of –0.27 (95% CI, –0.82 to 0.28), with no significant difference between the 2 treatment groups (HR, 0.90; 95% CI, 0.74-1.08; P = .26). CARMELINA 31 Linagliptin vs placebo; hospitalization for HF 4.7% vs 5.3% p=0.14. 18 LEADER Lixisenatide vs placebo; hospitalization for HF: 4.0% vs 4.2% p=0.75. 15 ELIXA 32. Empagliflozin vs placebo; hospitalization for HF: 2.7% vs 4.1% p=0.002. 20 EMPA-REG Empagliflozin in HF patients (regardless of diabetes status) ongoing trial estimated to be complete 2020 IMPEROR-Reduced & Preserved Canagliflozin vs placebo; hospitalization for HF: 5.5/1000tpyrs (0.55%/yr) vs 8.7/1000tpyrs (0.87%/yr) (HR 0.67, 95% CI 0.52-0.87) follow up 3.6yr but exploratory. 27,28 CANVAS Dapagliflozin vs placebo; hospitalization for HF: 2.5%/1000 patient year vs 3.3%/1000 patient year HR:0.73 (95% CI 0.61-0.88) but exploratory. 28 DECLARE Dapagliflozin 10mg po once daily vs placebo; composite primary outcome: worsening HF (hospitalization or urgent visit resulting in IV therapy for heart failure) or CV death: 16.3% vs 21.2% p<0.001. DAPA-HF 33 Basal insulin (glargine) vs standard care; hospitalization for HF 4.9% vs 5.5% p=NS. 21 ORIGIN 34. Basal insulin vs basal/bolus insulin; small sample n=152; HF 1.3% vs 5.3% p=NS. 22 ArchInternMed1997 Other/Additional Trials Recently Published 35. Pioglitazone & Rosiglitazone FDA +/-: Health Canada warnings/label changes: • ↑ Fractures?; pioglitazone vs placebo 5.1% vs 2.5%, calculated p=0.005 ↑ Fractures? NNH=38/2.9 yr (unpublished). 24,25 PREVLECT pioglitazone vs MF ↑ Fractures NNH=224/4 yr, rosiglitazone vs glyburide ↑ Fractures NNH=17/4 yr. 8 ADAPT Post marketing data: pioglitazone exposure in women associated 0.8 excess fractures (distal upper and lower limbs)/100 patient-years vs comparator treated group. 8 No ↑ risk in males. 8,9 • empagliflozin ↓ 1.5-2.3 kg/3.1 yr 18 EMPA-REG 10. Insulin • intensive therapy vs standard therapy; avg weight ↑ 3.5 kg vs 0.4 kg/3.5 yr; weight ↑ 10 kg 28% vs 14% p<0.001. 19 ACCORD • Note: detemir -1.27 to -0.8 kg vs NPH (glargine no difference vs NPH) 20 35. Pioglitazone vs placebo: ↑ hospitalization for HF NHH=50/2.9 yr (not adjudicated), ↑ edema (without HF) NHH=8/2.9 yr 5 PROACTIVE 36 Rosiglitazone +metformin or SU vs control; ↑ hospitalization for HF or death NHH=69/5.5 yr. 6 RECORD Rosiglitazone placebo: ↑ HF NNT=250/3 yr. 7 DREAM 37 Acarbose vs placebo; impaired glucose tolerance; HF 0% vs 0.3% p=NS. STOP-NIDDM Other-continued • or sitagliptin/metformin of which n=58 cases were hospitalized (n=4 cases admitted to the ICU), n=2 cases of hemorrhagic or necrotizing pancreatitis. Listed adverse event for other agents (e.g., irinotecan) in product monograph. 41 40 Incretin agents (DPP-4 inhibitors and GLP1 agonists) ?↑ pancreatic cancer: n=13 pancreatic cancer cases suspected of being associated with all incretin-based therapies (July 31, 2014). 24,28 38 Liraglutide: ↑ thyroid C-cell tumor (including medullary thyroid carcinoma) in animal studies (both genders, dose-dependent, and treatment-duration-dependent). 29 37 ↑ Gl (nausea, diarrhea, vomiting) AE with long acting agents30,31; ↑ GLA: tosaptoglute once weekly 59% vs exenatide BID 35% (clinical development of tosaptoglute has been stopped). 32 ↑ GLA: Exenatide once weekly 28% vs exenatide BID 48%, albiglutide alone weekly 29.8% vs liraglutide daily 52%, exenatide once 19.1% vs liraglutide daily 44.5%; kid 29,31; HARMONY 5,3; DURATION 6; Neutral GI: dulaglutide once weekly 39.4% vs sitagliptin/metformin of which n=96 cases required hospitalization (n=22 cases required ICU admission), n=15 cases required hospitalization or e- 30 days worsening NYHA class) 3.9% vs 4.1% p=NS. A7 STOP-NIDDM Other trials. 37 38 39 40 41 42,43 May 2017 FDA: canagliflozin -increased risk of leg and foot amputations. https://www.fda.gov/Drugs/DrugSafety/ucm537507.htm#source=go-dev---&utm_medium=email&utm_source=go-dev
• ↑ diabetic macular edema: retrospective cohort, TZD users vs nonusers ↑ macular edema 1 year follow up AOR 2.3 (1.5-3.6) & 10 year follow up HR 2.3 (1.7-3.0).10 Cross-section of ACCORD ↑ macular edema AOR 0.97 (0.67-1.40).11 Note: only rosiglitazone has a warning.12

36. Piog: ↑ bladder cancer; France, retrospective observational cohort pioglitazone exposure vs other diabetic agent HR 1.22 (1.03-1.43), pioglitazone exposure cumulative dose > 28 000 mg vs other diabetic agent HR 1.75 (1.22-2.5), pioglitazone exposure cumulative dose > 12 months vs other diabetic agent HR 1.28 (1.09-1.51).13 US, prospective observational cohort (5 yr interim analysis) pioglitazone exposure vs never exposed HR 1.2 (0.9-1.5), pioglitazone exposure >12 months vs never exposed HR 1.4 (0.9-2.1), & pioglitazone exposure > 12 months vs never exposed HR 1.4 (1.03-2.0).14 FDA calculated pioglitazone >12 months associated 27.5 excess cases of bladder cancer /100 000 person-yrs vs never exposed.15 16

38. Rosiglitazone FDA +/- Health Canada warnings/label changes: restricted access- in Canada (SK-EDS) due to ↑ CV events- see MACE/mortality.17 21

39. DPP-4 inhibitors FDA +/- Health Canada warnings/label changes:
• ↑ HF risk with saxagliptin and alogliptin (see above).10, 11 SAVOR-TIMI 53, EXAMINE, & Tecos (n=36,395) demonstrated ↑ acute pancreatitis OR 1.79 (1.13-2.82) and ARI of 0.13% vs placebo.24 US case control study; incretin agent (exenatide or sitagliptin) within 30 days OR 2.24 (95% CI, 1.36-3.68).25 FDA: n=30 cases of pancreatitis with exenatide of which n=21 cases hospitalized, n=3 cases reported positive rechallenge.26 FDA: n=88 cases of pancreatitis with sitagliptin

44. ↑UTI; SGLT2 inhibitor vs placebo: OR 1.34 (1.03-1.74, P=0.05), vs active agent: OR 1.42 (1.06-1.9, P=0.25); however recent real world surveillance data suggests this may not be an issue.47 48

45. Dapagliflozin: ↑ bladder/breast cancer; approved by FDA 2014 (rejected in 2012 due to bladder & bladder cancer concerns). Dapagliflozin vs control; bladder cancer: n=10 cases vs n=1 case & breast cancer: n=12 cases vs n= 3 cases (up to 2013).

46. Canagliflozin 100mg once daily vs placebo: ↑ primary composite outcome of ESKD, doubling of Scr & renal or CV death: 11.1% vs 15.5% = 0.00001.49 Evidence


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References:

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