Glucose-lowering medication in type 2 diabetes: overall approach.

**FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)**

**INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF**

**CONSIDER INDEPENDENTLY OF BASELINE A1C OR INDIVIDUALIZED A1C TARGET**

**ASCVD PREDOMINATES**

- Established ASCVD
- Indicators of high ASCVD risk (age ≥ 65 years with coronary, carotid, or lower extremity arterial stenosis ≥ 50%, or LVH)

**HF OR CKD PREDOMINATES**

- Particularly HFREF
- CKD: Specifically eGFR 30-60 mL/min/1.73 m² or UACR > 30 mg/g, particularly UACR > 300 mg/g

**PREFERABLY GLP-1 RA with proven CV benefit**

- OR
- SGLT2i with proven CV benefit if eGFR adequate

- If SGLT2i not tolerated or contraindicated or if eGFR less than adequate add GLP-1 RA with proven CV benefit

**IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW**

**COMPPELLING NEED TO MINIMIZE HYPOGLYCEMIA**

| DPP-4 | GLP-1 RA | SGLT2i
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- Avoid TZD in the setting of HF
- Choose agents demonstrating CV safety
- For patients on a GLP-1 RA, consider adding SGLT2i or basal insulin
- DPP-4i if not on GLP-1 RA
- T2D
- SUL

**IF A1C above target**

- Continue with addition of other agents as outlined above

**COMPPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS**

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<th>SGLT2i</th>
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- Consider addition of SUL or basal insulin
- Choose agent in setting with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia

**IF A1C above target**

- Consider multiple therapy regimens, or SGLT2i and GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

**COST IS A MAJOR ISSUE**

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<th>T2D</th>
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- Insulin therapy basal insulin with lowest acquisition cost
- Consider DPP-4i or SGLT2i with lowest acquisition cost

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1. Proven CV benefit means it has label indication of reducing CV events
2. Be aware that GLP1R/GP inhibits varies by region and individual with regard to residual level of CVR or initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CV progression in CVD patients. Carinafoz has primary renal outcome data from CANVAS-3. Dapagliflozin has primary renal failure outcome data from CANVAS-HF
4. Dapagliflozin or canagliflozin have demonstrated CV safety
5. Low dose may be better tolerated though less well studied for CV safety
6. Cholesterol-lowering medication is sometimes considered in addition to GLP1R inhibitors
7. Degludec or U100 can be used for basal insulin
8. SGLT2i are preferred in patients with proteinuria
9. Weight loss is an important component of type 2 diabetes management
10. Combination therapy is often necessary in real-world practice

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