Actotalk In Tabriz

Sept, 2021

ACTOVERCO

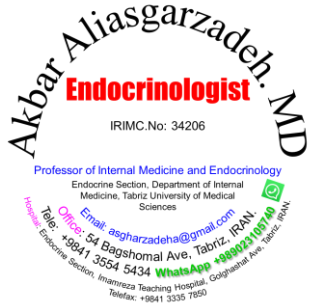
Together for a healthy future

VERCO

a healthy future

بنام خدا

ACTOtalk
Sharing Best Practices



ACTOtalk
Sharing Best Practices

ACTOVERCO
Together for a healthy future

Case (1)

- 52 y/o man
- Truck driver (12 h/day)
- Middle income
- First visit to the Clinic
- CC: Frequent urination and excessive thirst
- **PMHx:**
  - Confirmed T2DM family history on both sides
  - Sedentary life style
- **PE:**
  - BW: 85.5 kg
  - BH: 185 cm
  - BMI: 26.2
  - Thyroid exam.: Normal
  - Cardiovascular exam.: Normal
  - Lung hearing: Normal
  - Peripheral pulses are full and symmetrical

Lab Tests

Lab Test
HbA1c: 9.1%; FBS: 185 mg/dL, 2hPPBS: 310 mg/dL
Cr: 0.7 mg/dL
TSH: Normal
LFT: Normal
TG: 147 mg/dL , Chol: 177 mg/dL, HDL: 46 mg/dL , LDL: 102 mg/dL
U/A Albumin: Negative

A1C Goal of Therapy

Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	**<7.0%** More or less stringent glycemic goals may be appropriate for individual patients. CGM may be used to assess glycemic target. Goals should be **individualized** based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations
Preprandial capillary plasma glucose	**80–130 mg/dL** More or less stringent glycemic goals may be appropriate for individual patients. CGM may be used to assess glycemic target. Goals should be **individualized** based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations
Peak postprandial capillary plasma glucose Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.	**<180 mg/dL** More or less stringent glycemic goals may be appropriate for individual patients. CGM may be used to assess glycemic target. Goals should be **individualized** based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations

Which one is better for the start?

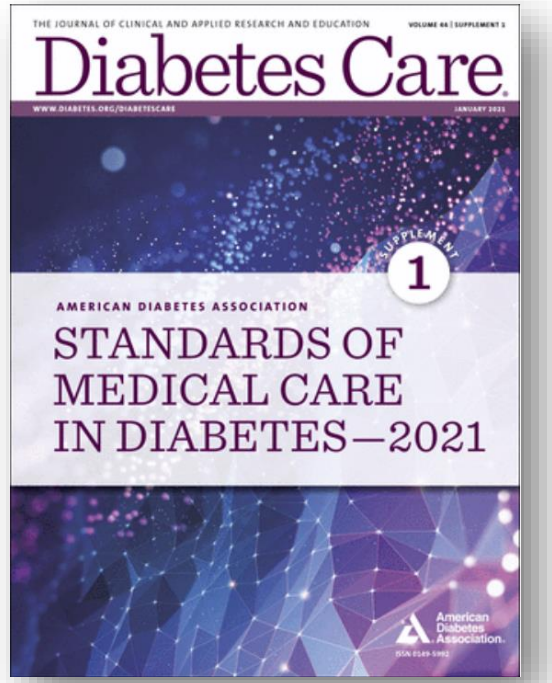
Along side of life style modification (calorie restriction and increasing physical activity):

1. **Start Metformin 500 mg BD then increase to 1000 mg BD**
2. **Start with Metformin 1000 mg BD then add Sitagliptin (Glysta) 100 mg or change to Metformin/Sitagliptin (Sigomet) (1000/50) BD**
3. **Start Sigomet (500/50) BD then increase to Sigomet (1000/50) BD**
4. **Start with Sigomet (1000/50) BD then add 1000 mg Metformin in the evening**
5. **Start with Metformin 500 mg BD and Liraglutide**
6. **Start with Metformin 1000 mg BD then add Pioglitazone**
7. **Start with Glibenclamide 5 mg/day**
8. **Start with Gliclazide MR (Glicover) 30 mg/day then increase the dose or add Metformin**
9. **Start with Liraglutide**
10. **Start with Metformin 500 mg BD and Empagliflozin 10 mg/day then increase Metformin dose**
11. **Other options?**

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes—2021*

American Diabetes Association

Diabetes Care 2021;44(Suppl. 1):S111–S124 | https://doi.org/10.2337/dc21-S009



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, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

NO

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

+ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age >55 years with coronary, carotid, or lower-extremity artery stenosis or LVH)

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification required or patient is unable to tolerate GLP-1 RA and/or SGIT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-I RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- Dpp-4i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

+HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6,7]

1.Proven CVD benefit means it has label indication of reducing CVD events
2.Low dose may be better tolerated though less well studied for CVD effects
3.Degludec or U-IOO glargine have demonstrated CVD safety
4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to DPP-4i
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8. Refer to Section 11 : Microvascular Complications and Foot Care
9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
11. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and DPP-4i are relatively cheaper.

+CKD

DKD and Albuminuria[8]

NO

PREFERABLY SGLT2i with primary evidence of CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOT[5,6,8]

OR

GLP-1RA with proven CVD benefit if SGIT2i not tolerated or contraindicated

For patients with T2D and CKD[5] (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
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COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i **OR** DPP-4i **OR** GLP-1 RA

if HbA_{1c} above target

Continue with addition of other agents as outlined above

if HbA_{1c} above target

Consider the addition of SU[4] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[9]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/ OR

- GLP-1 RA with good efficacy for weight loss[10]
- SGLT2i[2]

if HbA_{1c} above target

- SGLT2i[2]
- GLP-1 RA with good efficacy for weight loss[10]

if HbA_{1c} above target

If quadruple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

•SU[4] •TZD[2] •Basal insulin

COST IS A MAJOR ISSUE[11,12]

- SU[4]
- TZD[12]

if HbA_{1c} above target

- TZD[12]
- SU[4]

if HbA_{1c} above target

Insulin therapy basal insulin with lowest acquisition cost

OR

Consider other therapies based on cost

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

چرخه تصمیم گیری برای مدیریت هیپرگلیسمی بیمار محور در دیابت نوع ۲

ویژگی های اصلی بیمار را ارزیابی کنید

•شیوه زندگی فعلی
•بیماری ها ی همراه نظیر بیماری قلبی عروقی آترواسک
کلیه و نارسایی قلب
•ویژگی های بالینی، به عنوان مثال، سن، HbA1c، و
•مسائلی مانند انگیزه و افسردگی
•زمینه فرهنگی و اجتماعی و اقتصادی

فاکتورهای خاصی که انتخاب شیوه درمان را تحت تاثیر قرار میدهد را در نظر بگیرید

• هدف فردی HbA1c
• تاثیر درمان بر وزن و هیپوگلیسمی
• طیف اثرات جانبی دارو
• پیچیدگی رژیم درمانی، یعنی دفعات و روش مصرف
• شیوه درمانی را انتخاب کنید تا بیشترین امکان به دست آوردن پایبندی و پایداری در ادامه درمان را فراهم سازد.
• هزینه و امکان در دسترس بودن دارو را ارزیابی کنید.

طراحی شیوه درمان با لحاظ نظر بیمار و/یا مراق

• شامل یک بیمار (و خانواده / مراقب یا پرستار) آموزش دیده و آگاه خواهد بود.

• ترجیحات بیمار را دنبال می کند

• مشاوره موثر شامل مصاحبه انگیزشی، تنظیم هدف و تصمیم گیری مشترک خواهد بود.
• بیمار را توانمند می سازد.

• دسترسی به DSMES (آموزش مدیریت بیماری خویشتن در دیابت و پشتیبانی مستمر) تضمین می کند.

مرور دوره ای مجدد رویه درمان تایید آن در صورت

ان
ی تغییرات لازم در رویه درمان
شدن تغییرات توافق شده درمانی به صورت زمان بندی شده به
تفاوتی به روند درمان
ی یک یا دو بار در سال فرآیند چرخه تصمیم گیری بازنگری شده

نظارت و پشتیبانی مستمر شامل موارد زیر خواهد بود:

•دستیابی به احساس درونی تندرستی
• قابلیت تحمل داروهای مصرفی را ارزیابی کنید
• وضعیت گلیسمی را پایش کنید
•با ارزیابی مواردی نظیر اندازه گیری خانگی قند خون (SMBG)،
وزن، شمارش تعداد قدم های پیموده شده، HbA1C، فشار خون،
چربی های خون بازخوردهای تشویقی به بیمار بدهید(بیوفیدبک)

دیریت درمان طراحی شده

قادر به دستیابی به اهداف درمان نمی شوند معمولا تا
فتی دیده می شود باید حداقل هر ۳ ماه یکبار ویزیت
غلب مطلوبتر است فواصل ویزیت ها کمتر باشد تا برنامه
DSM) پیاده شود.

-قابل اندازه گیری Measurable
-قابل دستیابی Achievable
-واقع بینانه Realistic
-زمان بندی شده Time limited باشد.

ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self- Monitored Blood Glucose


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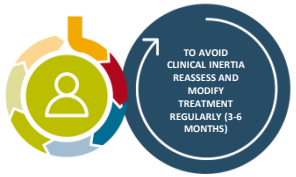

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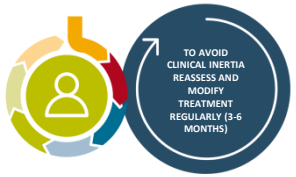

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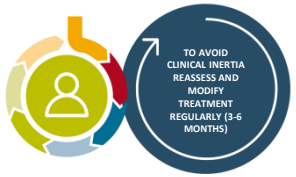

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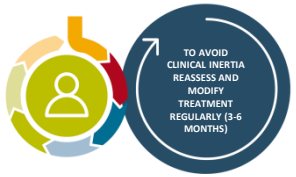

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IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

- COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA
- COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS
- COST IS A MAJOR ISSUE[11,12]

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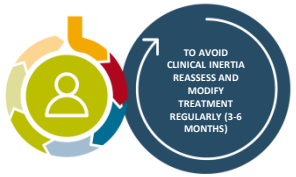

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EITHER/OR

GLP-1 RA with proven CVD benefit[1]

SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification required or patient is unable to tolerate GLP-1 RA and/or SGIT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-I RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
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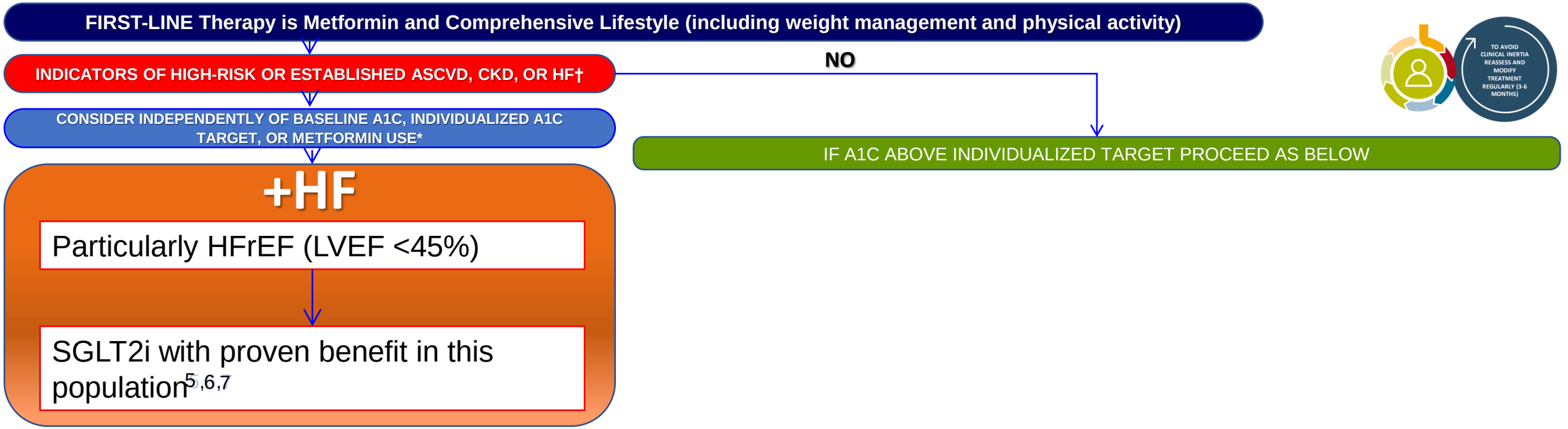

5.Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use

6.Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data

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+CKD

DKD and Albuminuria[8]

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PREFERABLY SGLT2i with primary evidence of CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOT[5,6]

OR

GLP-1 RA with proven CVD benefit if SGIT2i not tolerated or contraindicated

For patients with T2D and CKD (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

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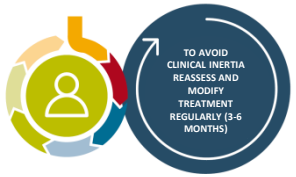

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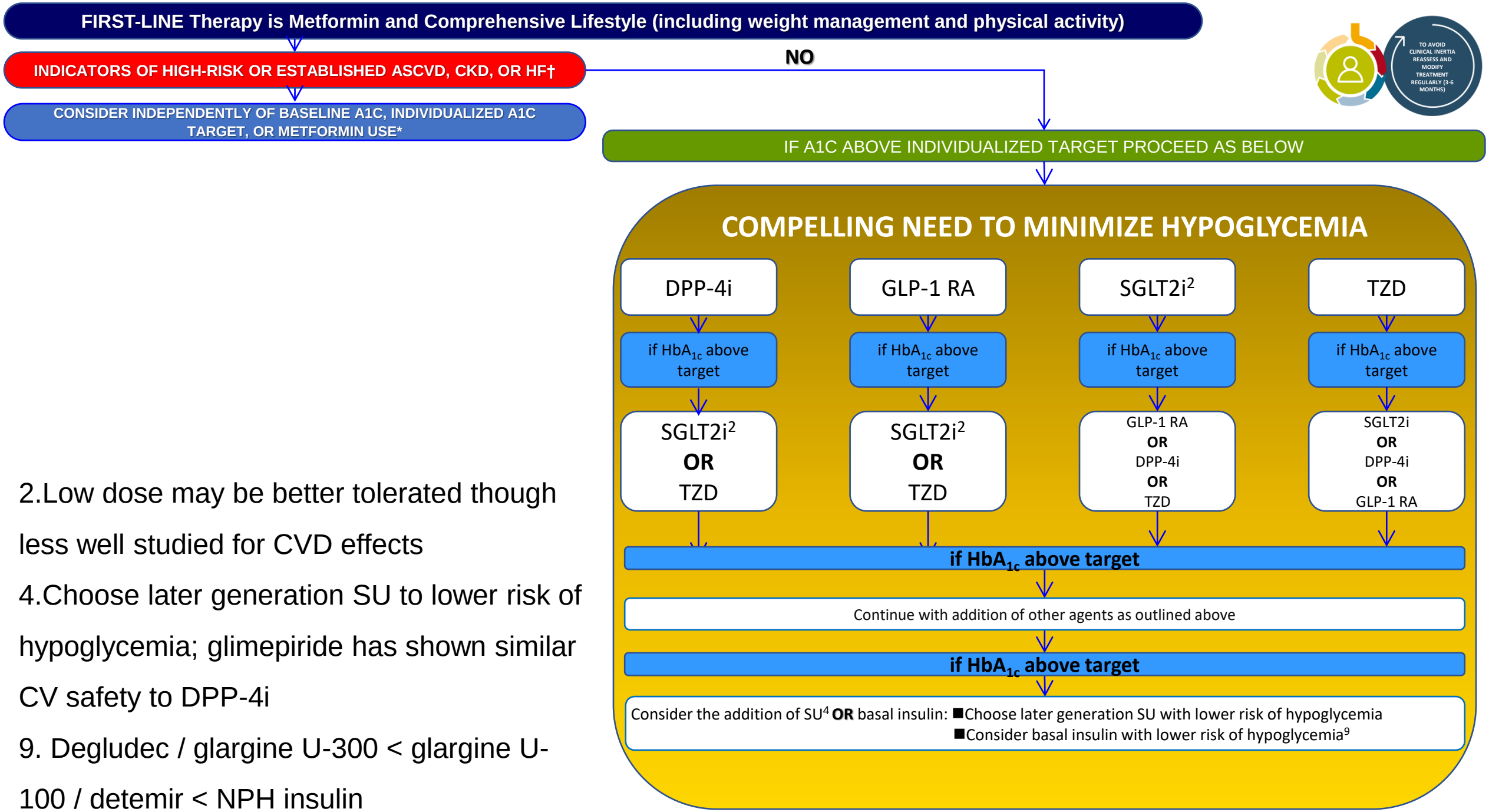

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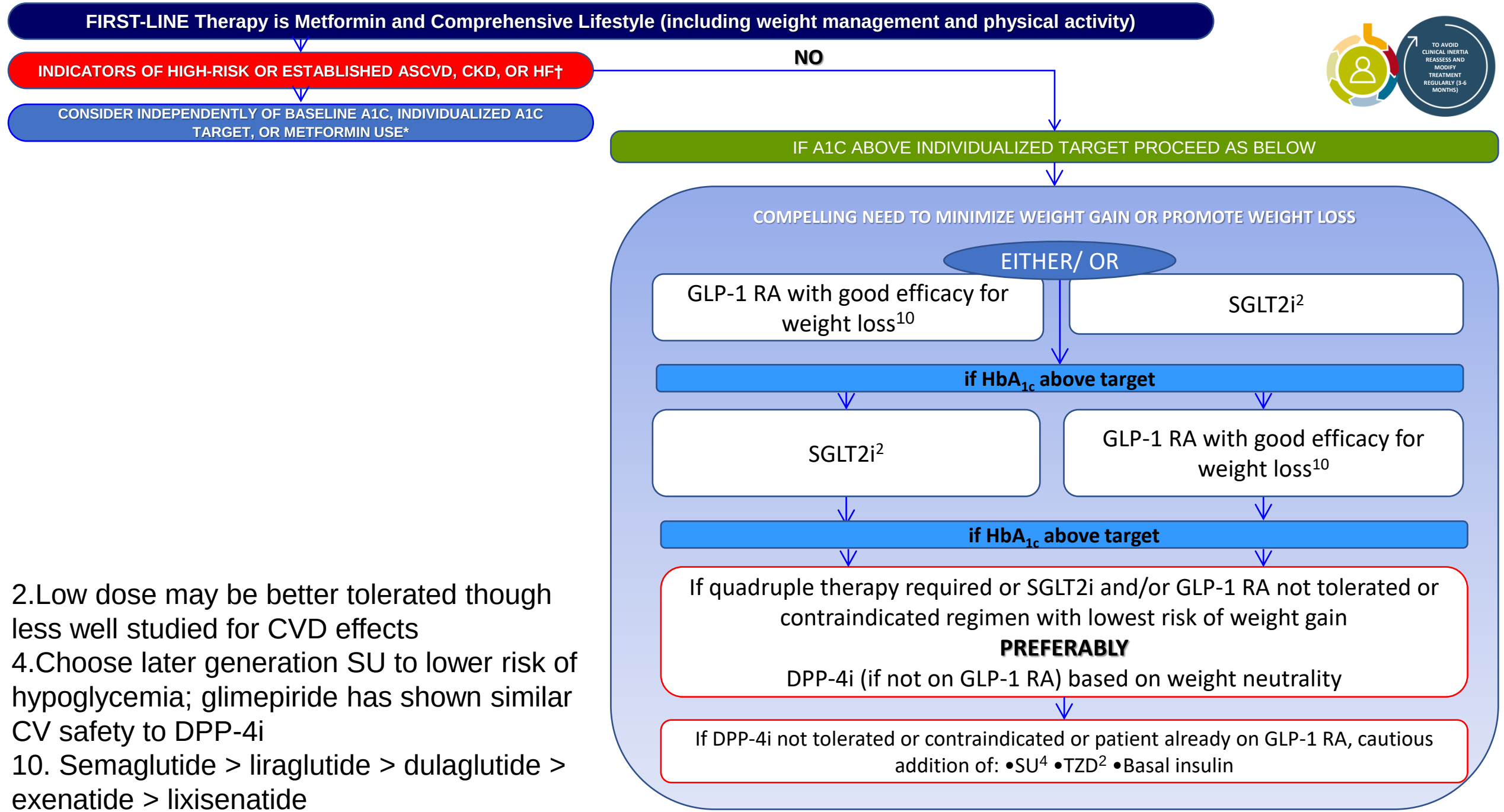

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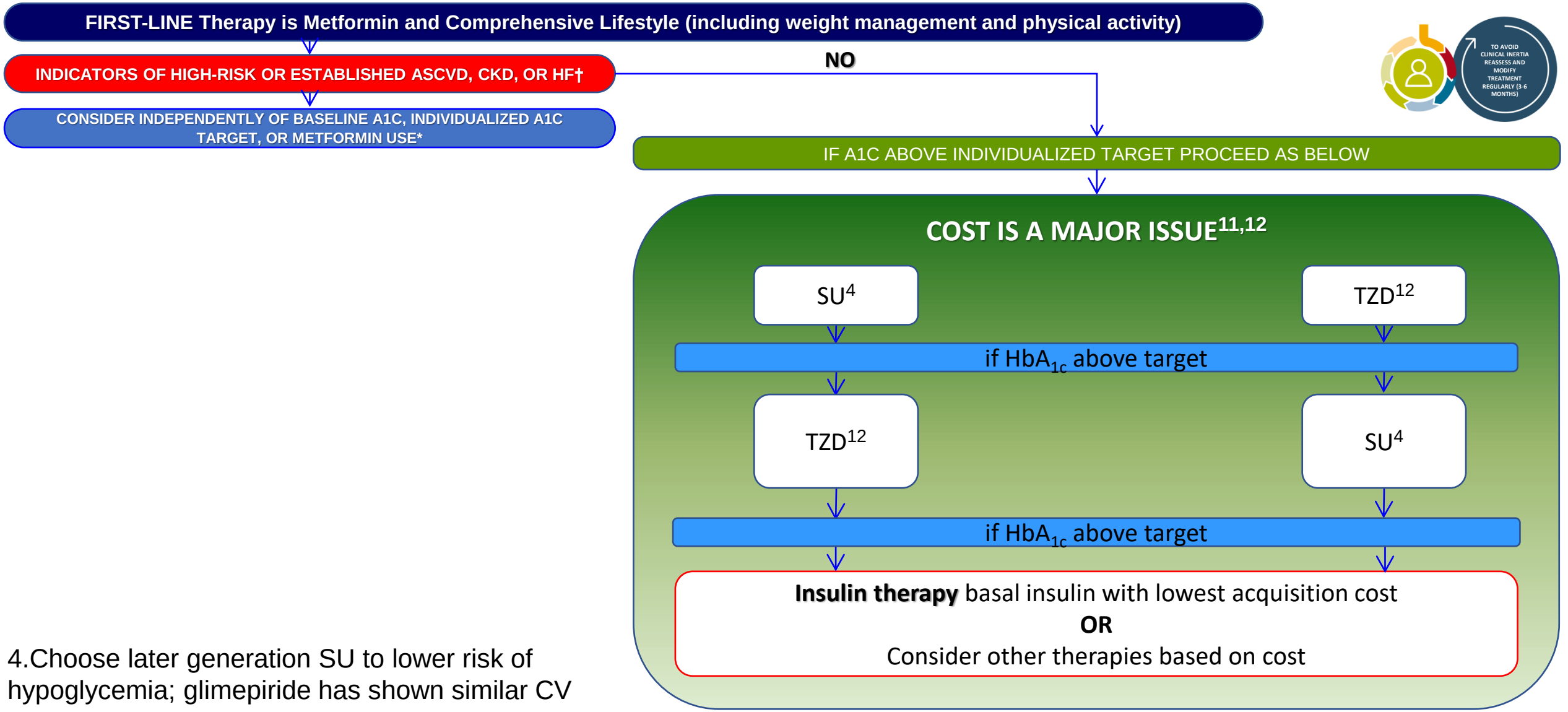

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For patients with T2D and CKD[5] (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

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- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,7]

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i **OR** DPP-4i **OR** GLP-1 RA

if HbA_{1c} above target

Continue with addition of other agents as outlined above

if HbA_{1c} above target

Consider the addition of SU[4] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[9]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

EITHER/ OR

- GLP-1 RA with good efficacy for weight loss[10]
- SGLT2i[2]

if HbA_{1c} above target

- SGLT2i[2]
- GLP-1 RA with good efficacy for weight loss[10]

if HbA_{1c} above target

If quadruple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

•SU[4] •TZD[2] •Basal insulin

COST IS A MAJOR ISSUE[11,12]

- SU[4]
- TZD[12]

if HbA_{1c} above target

- TZD[12]
- SU[4]

if HbA_{1c} above target

Insulin therapy basal insulin with lowest acquisition cost

OR

Consider other therapies based on cost

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

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, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE*

NO

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

+ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age >55 years with coronary, carotid, or lower-extremity artery stenosis or LVH)

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification required or patient is unable to tolerate GLP-1 RA and/or SGIT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-I RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- **Dpp-4**i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

+HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6,7]

1.Proven CVD benefit means it has label indication of reducing CVD events
2.Low dose may be better tolerated though less well studied for CVD effects
3.Degludec or U-IOO glargine have demonstrated CVD safety
4.Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar CV safety to **DPP-4i**
5.Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
6.Empagliflozin, canagliflozin, and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin and dapagliflozin have primary renal outcome data. Dapagliflozin and empagliflozin have primary heart failure outcome data
7. Proven benefit means it has label indication of reducing heart failure in this population
8. Refer to Section 11 : Microvascular Complications and Foot Care
9. Degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
10. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
11. If no specific comorbidities (i.e., no established CVD, low risk of hypoglycemia, and lower priority to avoid weight gain or no weight-related comorbidities)
12. Consider country- and region-specific cost of drugs. In some countries TZDs are relatively more expensive and **DPP-4i** are relatively cheaper.

+CKD

DKD and Albuminuria[8]

NO

PREFERABLY SGLT2i with primary evidence of CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOT[5,6,8]

OR

GLP-1RA with proven CVD benefit if SGIT2i not tolerated or contraindicated

For patients with T2D and CKD[5] (e.g., eGFR <60 mL/min/1.73m^2) and thus at increased risk Of cardiovascular events

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,7]

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target	if HbA_{1c} above target
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** **DPP-4i** **OR** TZD	SGLT2i **OR** **DPP-4i** **OR** GLP-1 RA

if HbA_{1c} above target

Continue with addition of other agents as outlined above

if HbA_{1c} above target

Consider the addition of SU[4] **OR** basal insulin:
- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[9]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

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If quadruple therapy required or SGLT2i and/or GLP-1 RA not tolerated or contraindicated regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If **DPP-4i** not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

•SU[4] •TZD[2] •Basal insulin

COST IS A MAJOR ISSUE[11,12]

- SU[4]
- TZD[12]

if HbA_{1c} above target

- TZD[12]
- SU[4]

if HbA_{1c} above target

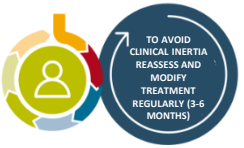
Insulin therapy basal insulin with lowest acquisition cost

OR

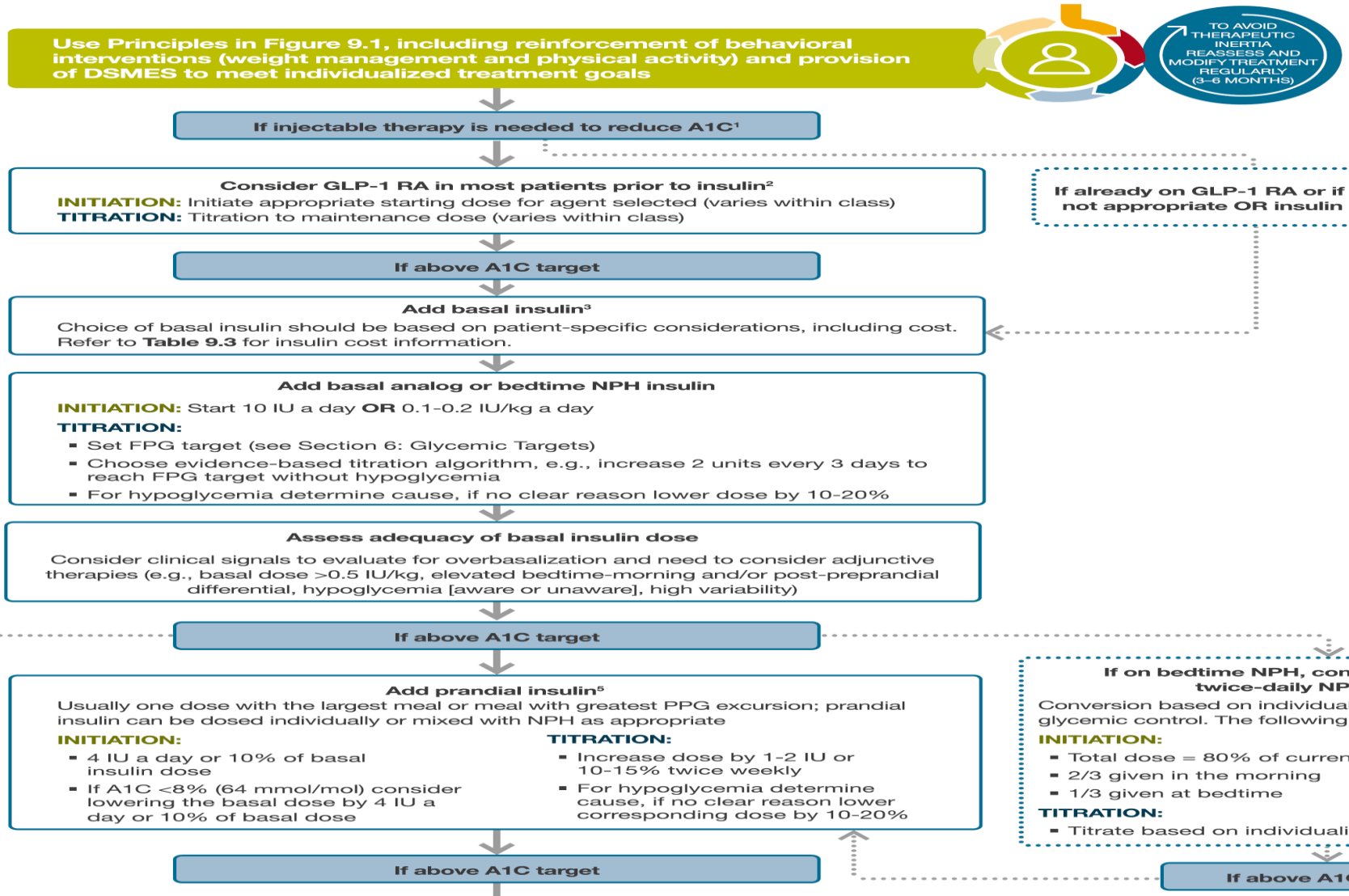
Consider other therapies based on cost

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

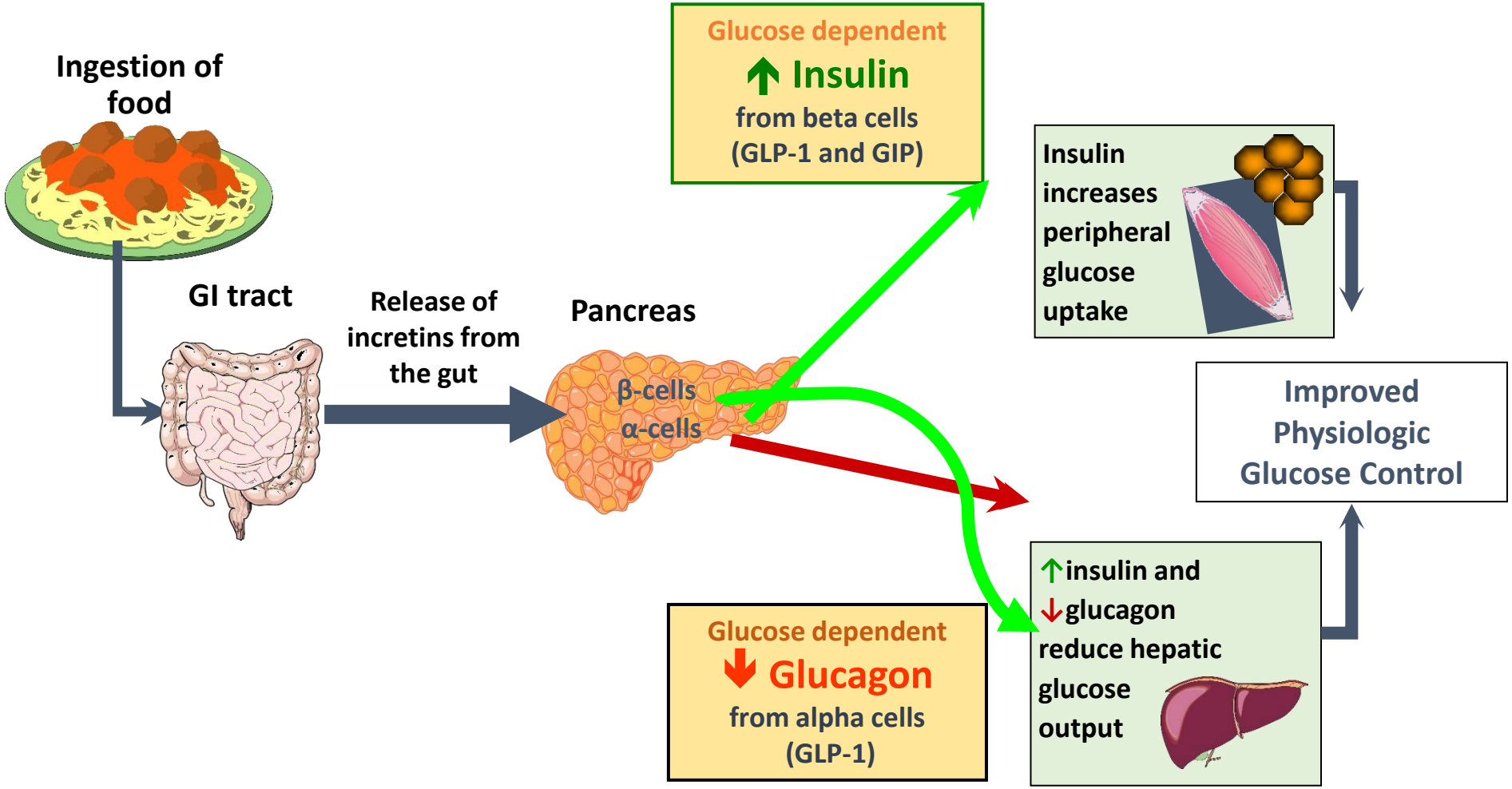
*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.



Intensifying to injectable therapies


Use Principles in Figure 9.1, including reinforcement of behavioral interventions (weight management and physical activity) and provision of DSMES to meet individualized treatment goals
TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)
If injectable therapy is needed to reduce A1C[1]
Consider GLP-1 RA in most patients prior to insulin[2]
INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Titration to maintenance dose (varies within class)
If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred
If above A1C target
Add basal insulin[3]
Choice of basal insulin should be based on patient-specific considerations, including cost. Refer to Table 9.3 for insulin cost information.
Add basal analog or bedtime NPH insulin
INITIATION: Start 10 IU a day OR 0.1–0.2 IU/kg a day
TITRATION:
Set FPG target (see Section 6: Glycemic Targets)
Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG target without hypoglycemia
For hypoglycemia determine cause, if no clear reason lower dose by 10–20%
Assess adequacy of basal insulin dose
Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose >0.5 IU/kg, elevated bedtime-morning and/or post-preprandial differential, hypoglycemia [aware or unaware], high variability)
If above A1C target
Consider GLP-1 RA if not already in regimen
For addition of GLP-1 RA, consider lowering insulin dose dependent on current glycemic assessment and patient factors
Add prandial insulin[5]
Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate
INITIATION:
4 IU a day or 10% of basal insulin dose
If A1C <8% (64 mmol/mol) consider lowering the basal dose by 4 IU a day or 10% of basal dose
TITRATION:
Increase dose by 1–2 IU or 10–15% twice weekly
For hypoglycemia determine cause, if no clear reason lower corresponding dose by 10–20%
If on bedtime NPH, consider converting to twice-daily NPH regimen
Conversion based on individual needs and current glycemic control. The following is one possible approach:
INITIATION:
Total dose = 80% of current bedtime NPH dose
2/3 given in the morning
1/3 given at bedtime
TITRATION:
Titrate based on individualized needs
If above A1C target
If above A1C target
Stepwise additional injections of prandial insulin
(i.e., two, then three additional injections)
Proceed to full basal-bolus regimen
(i.e., basal insulin and prandial insulin with each meal)
Consider self-mixed/split insulin regimen
Can adjust NPH and short/rapid-acting insulins separately
INITIATION:
Total NPH dose = 80% of current NPH dose
2/3 given before breakfast
1/3 given before dinner
Add 4 IU of short/rapid-acting insulin to each injection or 10% of reduced NPH dose
TITRATION:
Titrate each component of the regimen based on individualized needs
Consider twice daily premix insulin regimen
INITIATION:
Usually unit per unit at the same total insulin dose, but may require adjustment to individual needs
TITRATION:
Titrate based on individualized needs

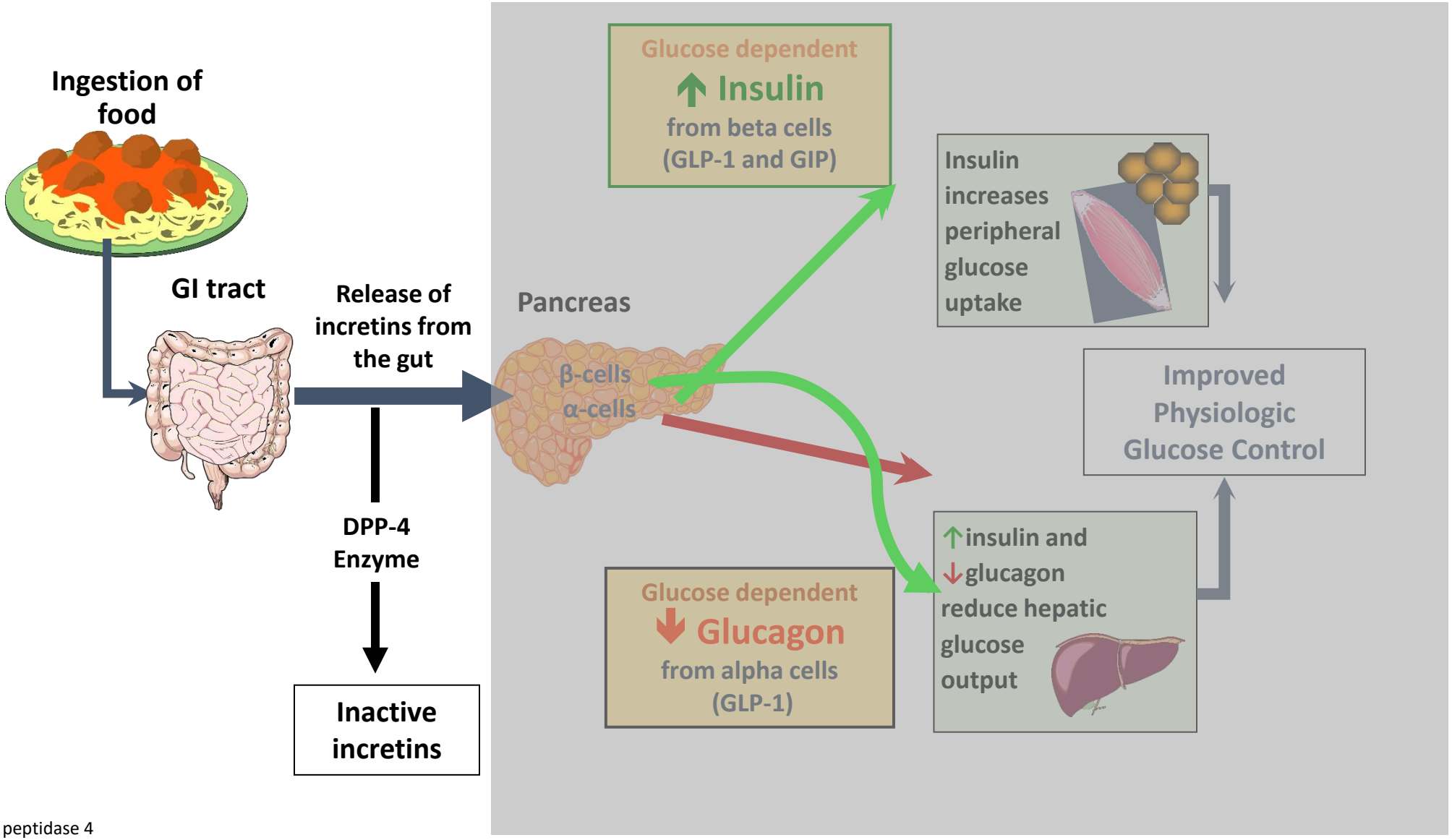
DPP-4 Inhibitors Improve Glucose Control by Increasing Incretin Levels in Type 2 Diabetes[1-4]



DPP-4 = dipeptidyl peptidase 4

1-Endocrinology. 2004 ;145(6):2653-9. 2- Lancet. 2002 ;359(9309):824-30; 3-Curr Diab Rep. 2003;3(5):365-72; 4-Buse JB et al. In *Williams Textbook of Endocrinology*. 10th ed., 2003:1427–1483.

DPP-4 Inhibitors Improve Glucose Control by Increasing Incretin Levels in Type 2 Diabetes[1-4]



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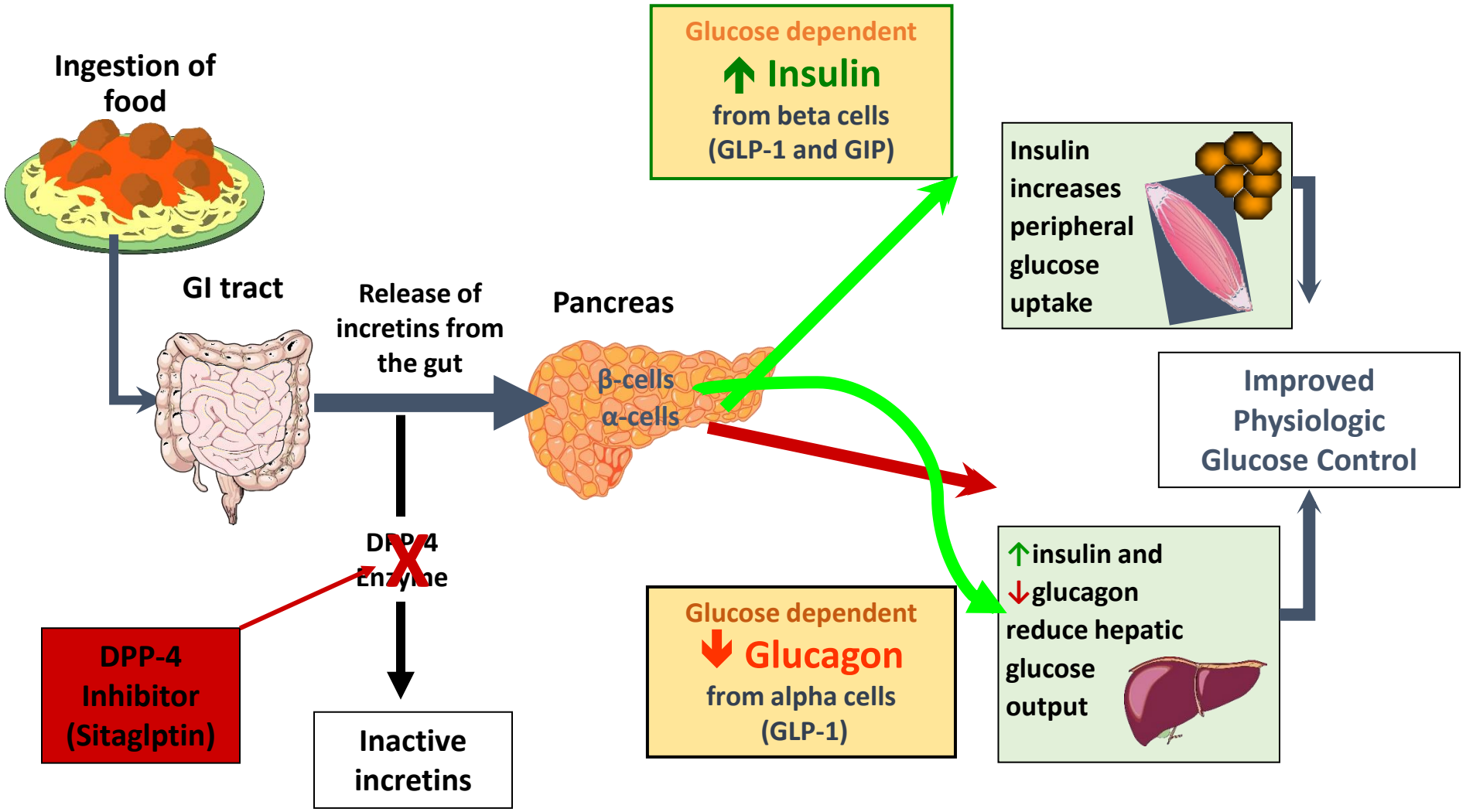

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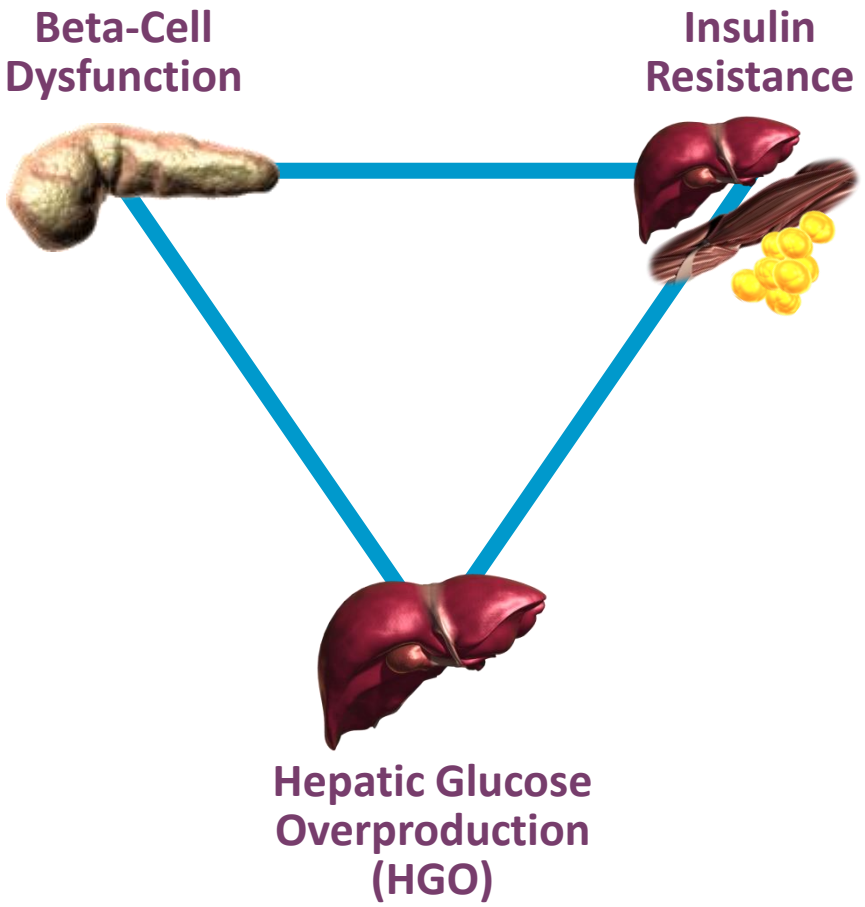
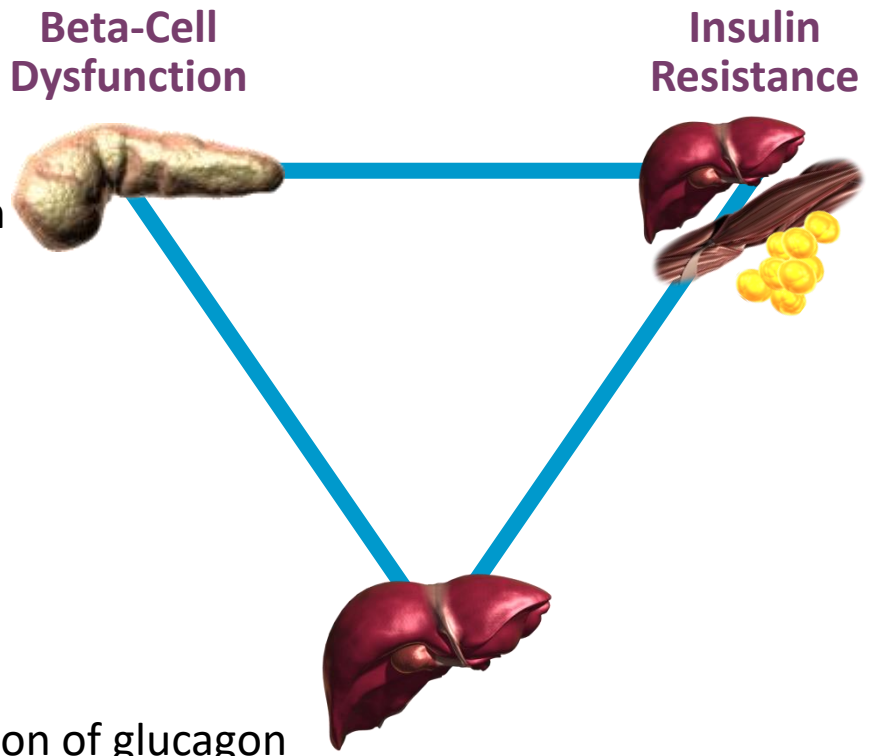
Sitagliptin and Metformin Target the Core Metabolic Defects of Type 2 Diabetes



1. Diabetes Care; 2006;29(12):2632–2637. 2- Data on file. 3- *Diabetes Care*. 1998;21(8):1301–1305. 4- *Ann Intern Med*. 2002;137(1):25–33. 5- *J Clin Invest*. 2001;108(8):1167–1174.

Sitagliptin Target the Core Metabolic Defects of Type 2 Diabetes

Sitagliptin
improves beta-cell function
increases insulin synthesis
and release.[1]



Sitagliptin
reduces HGO
through suppression of glucagon
from alpha cells.[2]

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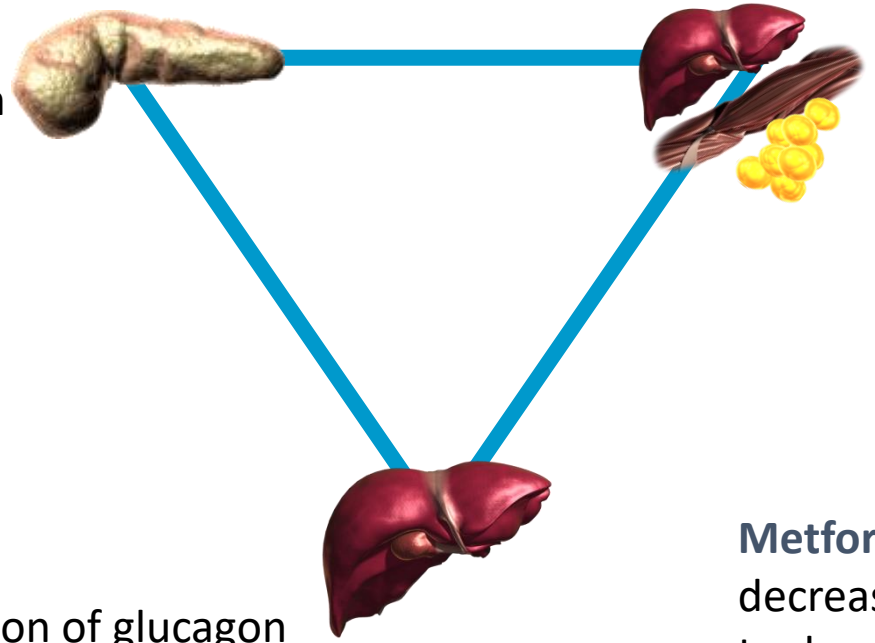
Sitagliptin and Metformin Target the Core Metabolic Defects of Type 2 Diabetes

Beta-Cell Dysfunction

Sitagliptin
improves beta-cell function
increases insulin synthesis
and release.[1]



Insulin Resistance

Metformin
insulin- sensitizing [3–5]
(Liver, Muscle, fat)

Sitagliptin
reduces HGO
through suppression of glucagon
from alpha cells.[2]

Hepatic Glucose Overproduction (HGO)

Metformin
decreases HGO by targeting the liver
to decrease gluconeogenesis and
glycogenolysis.[4]

1. Diabetes Care; 2006;29(12):2632–2637. 2- Data on file. 3- *Diabetes Care*. 1998;21(8):1301–1305. 4- *Ann Intern Med.* 2002;137(1):25–33. 5- *J Clin Invest.* 2001;108(8):1167–1174.

Diabetes Obes Metab. 2015 March ; 17(3): 268–275. doi:10.1111/dom.12417.

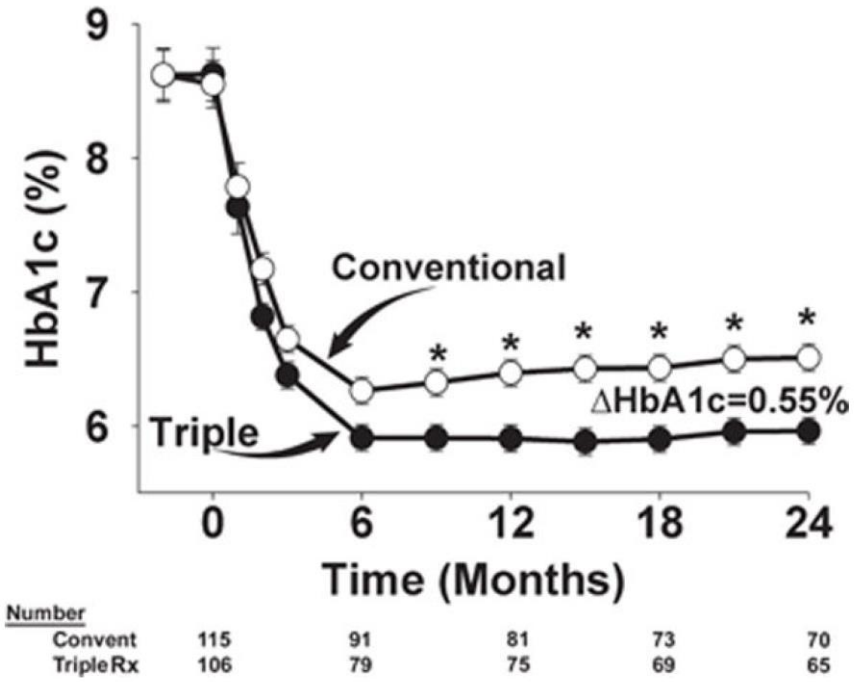
Initial combination therapy with metformin, pioglitazone and exenatide is more effective than sequential add-on therapy in subjects with new-onset diabetes. Results from the Efficacy and Durability of Initial Combination Therapy for Type 2 Diabetes (EDICT): a randomized trial

M. A. Abdul-Ghani[1], **C. Puckett**[1], **C. Triplitt**[1], **D. Maggs**[2], **J. Adams**[1], **E. Cersosimo**[1], and **R. A DeFronzo**[1]

[1]Diabetes Division, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

[2]GI Dynamics, Lexington, MA, USA

Conclusion—The results of this exploratory study show that combination therapy with metformin/pioglitazone/exenatide in patients with newly diagnosed T2DM is more effective and results in fewer hypoglycaemic events than sequential add-on therapy with metformin, sulfonylurea and then basal insulin.



Time-related change in glycated haemoglobin (HbA1c) in participants receiving conventional (convent) therapy and initial triple combination (Rx) therapy during the 24-month follow-up period. *$p < 0.01$.

THE LANCET

Articles

Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial

David R Matthews, Päivi M Paldánius, Pieter Proot, YannTong Chiang, Michael Stumvoll, Stefano Del Prato, for the VERIFY study group

Interpretation

Early intervention with a combination therapy of vildagliptin plus metformin provides greater and durable long-term benefits compared with the current standard-of-care initial metformin monotherapy for patients with newly diagnosed type 2 diabetes.

Which one is better for the start?

Along side of life style modification (calorie restriction and increasing physical activity):

1. **Start Metformin 500 mg BD then increase to 1000 mg BD**
2. **Start with Metformin 1000 mg BD then add Sitagliptin (Glysta) 100 mg or change to Metformin/Sitagliptin (Sigomet) (1000/50) BD**
3. **Start Sigomet (500/50) BD then increase to Sigomet (1000/50) BD**
4. **Start with Sigomet (1000/50) BD then add 1000 mg Metformin in the evening**
5. **Start with Metformin 500 mg BD and Liraglutide**
6. **Start with Metformin 1000 mg BD then add Pioglitazone**
7. **Start with Glibenclamide 5 mg/day**
8. **Start with Gliclazide MR (Glicover) 30 mg/day then increase the dose or add Metformin**
9. **Start with Liraglutide**
10. **Start with Metformin 500 mg BD and Empagliflozin 10 mg/day then increase Metformin dose**
11. **Other options?**

{special}

THANKS

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