DPP-4 Inhibitors

Their Place in Type 2 Diabetes Treatment

Objectives

- Case
- DPP-4 inhibitors in ADA guideline
- DPP-4 inhibitors Mechanism of Action
- Sitagliptin Efficacy
- Linagliptin Efficacy
- Conclusion

Case

- **Background**
  - A **64** year woman known case of **type 2 diabetes** since **5** years ago
  - Presents with recurrent episodes of **dizziness** and **weakness**
  - Has mild NPDR in ophthalmic examination.
- **Medical History**
  - Radical mastectomy due to **breast cancer** 7 years ago without any complication.
  - The patient is well controlled with regular follow up
- **Social History**
  - Lives alone
- **Physical Exam**
  - BMI: **24** kg/m^2
  - BP: **140/80** mmHg

Lab Summary		
Glycemia	HbA1c	**7.5** %
	FBS	**150** mg/dl
	2 hpp BS	**200** mg/dl
Lipid Profile	Total Chol	**194** mg/dl
	HDL-C	**46** mg/dl
	LDL-C	**120** mg/dl
	TG	**140** mg/dl
Renal Function	UACR	**78** mg/gr
	eGFR	**63** ml/min/1.73m^2
	Cr	**1** mg/dl

Current Medications	**Metfomin 1000 mg/daily**	**ASA 80 mg/daily**
	Glibenclamide 5 mg/BD	
	Atorvastatin 10 mg/daily	

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Case

What Is the Most Appropriate Treatment for Glycemic Control?

A. Maximize metformin therapy plus glibenclamide dose reduction

B. Maximize metformin therapy and switch to sitagliptin 100 mg once daily

C. Maximize metformin therapy and switch to gliclazide MR from glibenclamide

D. Maximize metformin therapy plus pioglitazone

E. Others

Patient History

- **64** Y/O female, **T2DM**, **breast cancer**
- HbA1c: **7.5** %
- FBS: **150** mg/dl
- 2hpp BS: **200** mg/dl
- Total Chol: **194** mg/dl TG: **140** mg/dl
- HDL-C: **46** mg/dl LDL: **120** mg/dl
- eGFR: **63** ml/min/1.73 m^2
- UACR: **78** mg/g Cr: **1** mg/dl
- Medications: **Metformin 1000 mg/daily; Glibenclamide 5mg/BID; Atorvastatin 10 mg/daily; ASA 80 mg/daily**
- BMI: **24** kg/m^2
- BP: **140/80** mmHg

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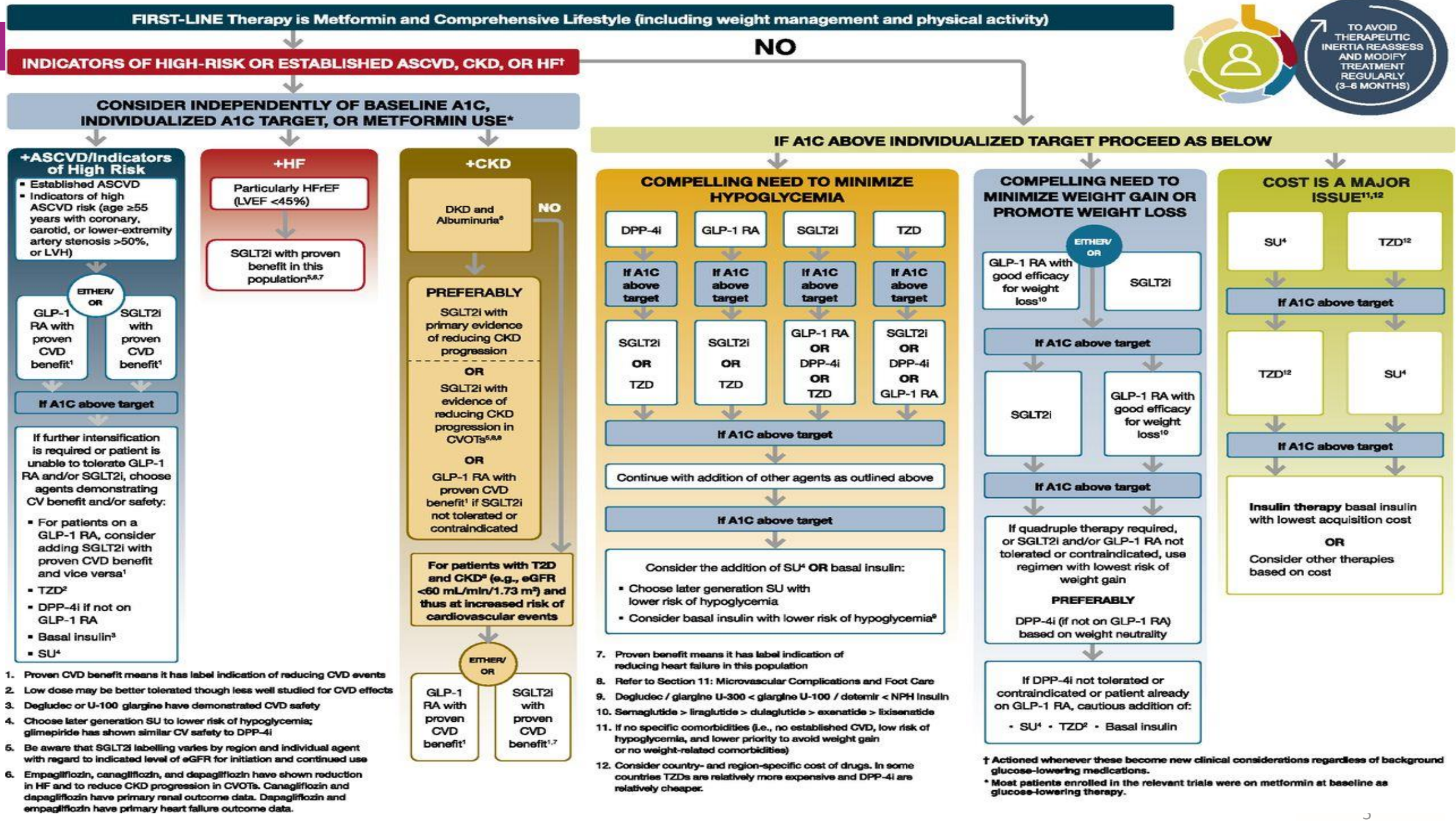
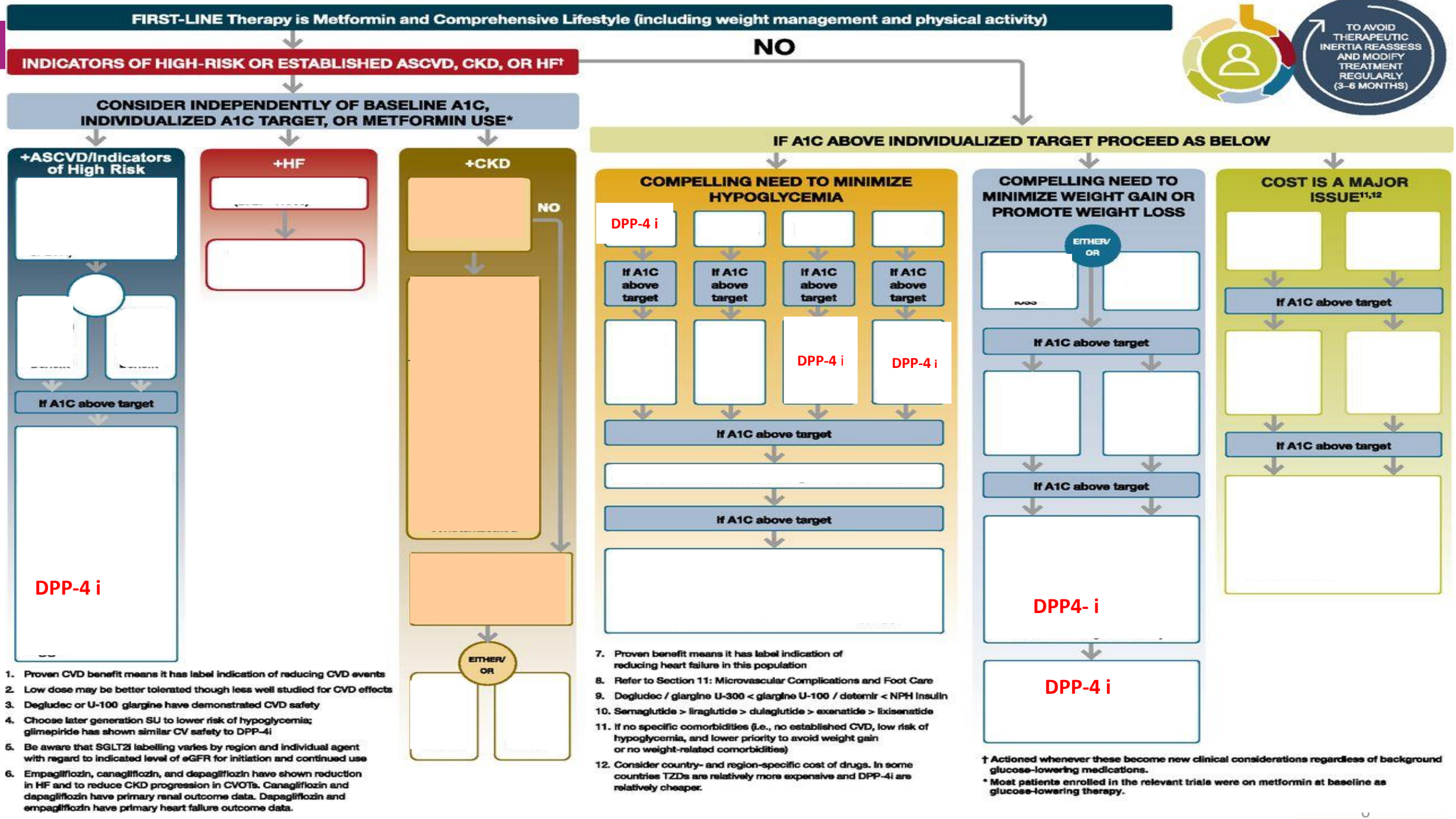


1. Proven CVD benefit means it has label indication of reducing CVD events
2. Low dose may be better tolerated though less well studied for CVD effects
3. Degludec or U-100 glargine have demonstrated CVD safety
4. Choose later generation SU to lower risk of hypoglycemia; glimepiride has shown similar 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.

† 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.

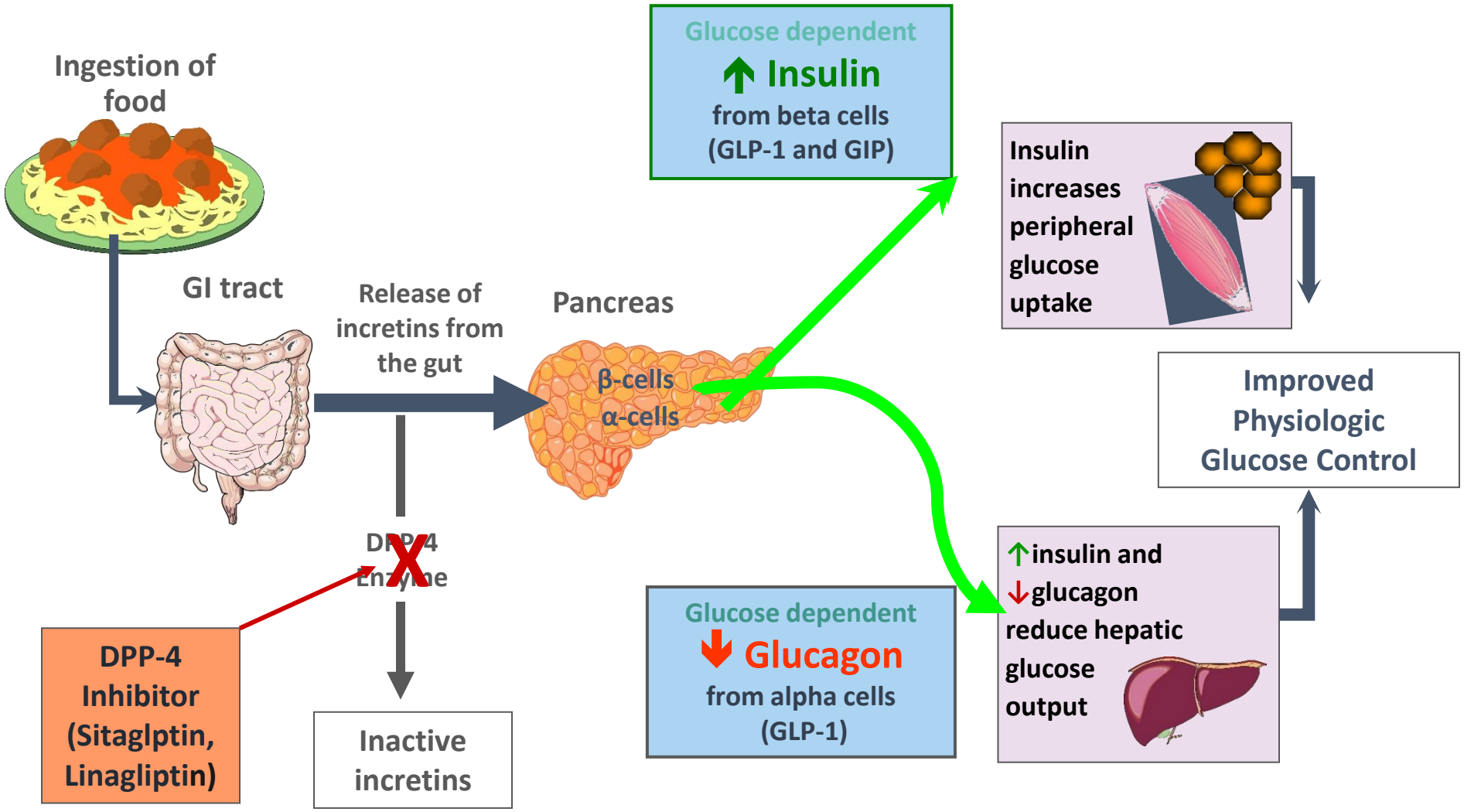
Diabetes Care 2021; 44(Suppl. 1):S111-S124.



Diabetes Care 2021; 44(Suppl. 1):S111-S124.

- **DPP-4 inhibitors Mechanism of Action**

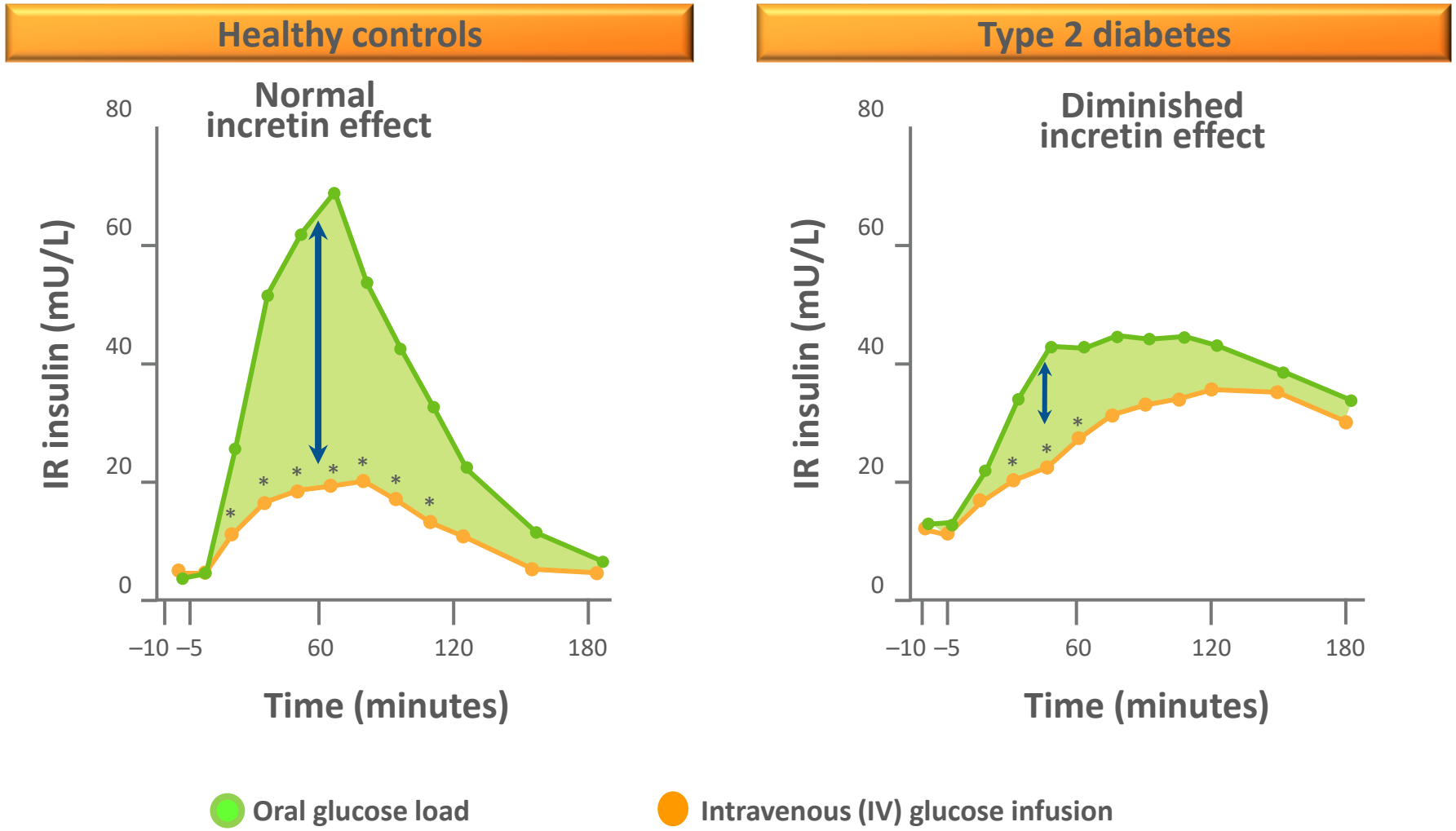
DPP-4 Inhibitors Improve Glucose Control by Increasing Incretin Levels in Type 2 Diabetes[1-4]



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.

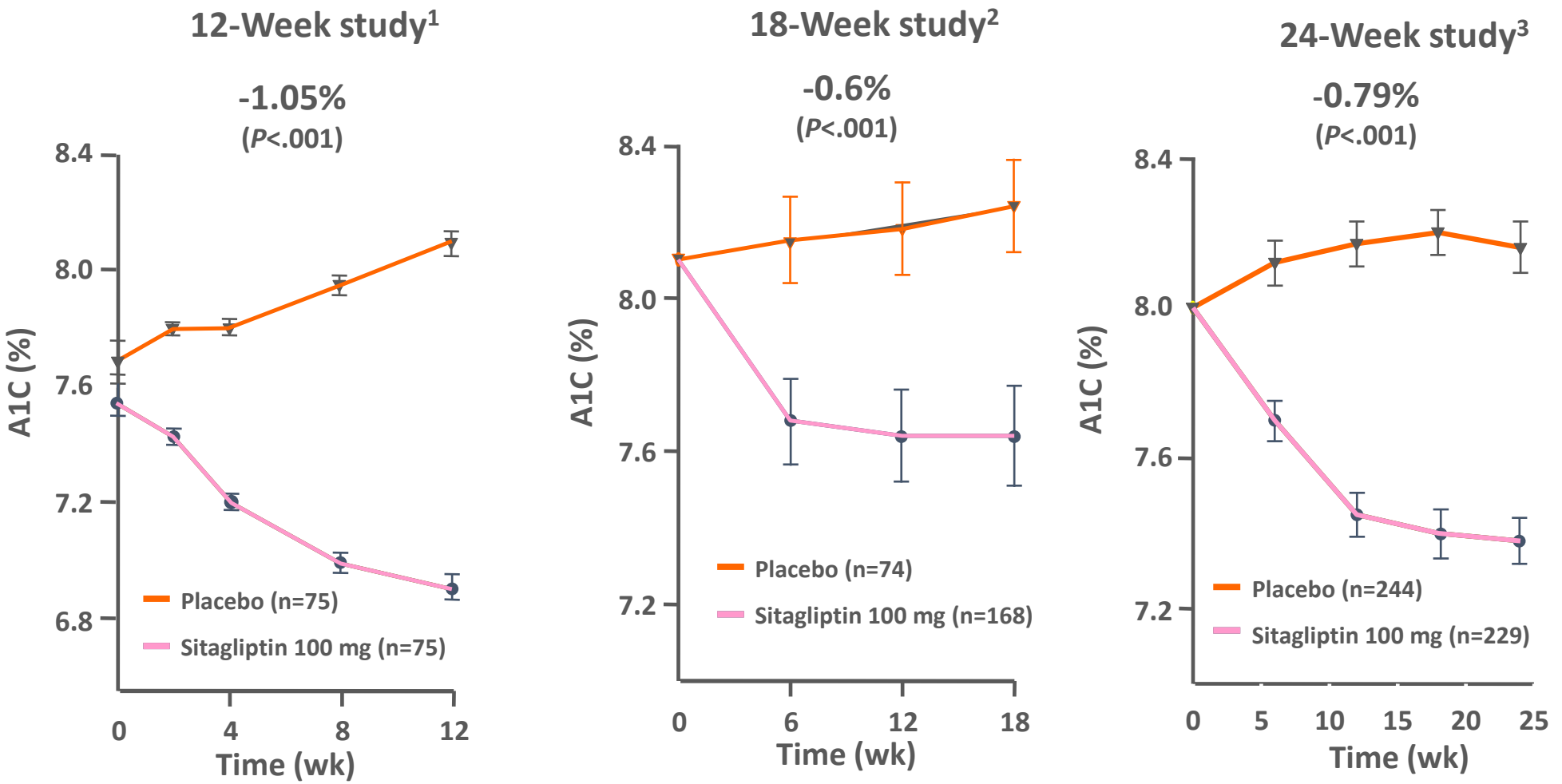
The Effect of Incretins in Type 2 Diabetes and Non-Diabetes[1]



1-Diabetologia. 1986 ;29(1):46-52.
IR: Immunoreactive

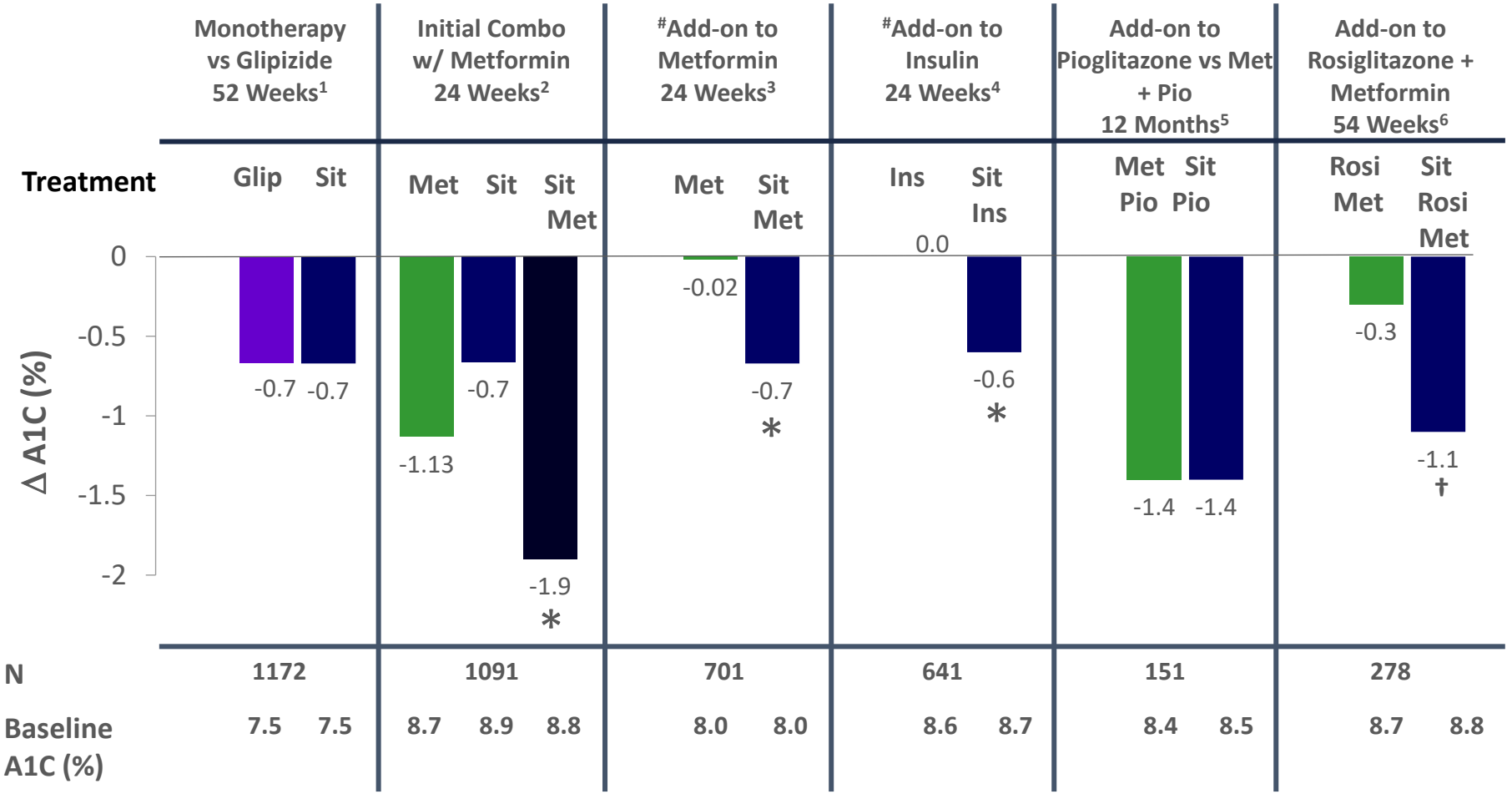
- **Sitagliptin Efficacy**

Sitagliptin Consistently and Significantly Lowers A1C With Once-Daily Dosing in Monotherapy



1. Diabetes Care. 2006;29(12):2632-7. 2- Diabetes Res Clin Pract. 2008 ;79(2):291-8 . 3. Diabetologia. 2006 ;49(11):2564-71.

Glucose Control With Sitagliptin in Different Studies



**P*<0.001 vs active comparator monotherapy. †*P*<0.001 vs active comparator dual therapy. # Compare to placebo. Met: Metformin; Sit= Sitagliptin; Glip=Glipizide; Ins=Insulin; Pio=Pioglitazone, Rosi=Rosiglitazone .

1. Diabetes Obes Metab. 2007 ;9(2):194-205; 2. Diabetes Care. 2007 ;30(8):1979-87. 3. Diabetes Care. 2006;29(12):2638-43.;4. Diabetes Obes Metab. 2010;12(2):167-77.
5. Metabolism. 2010 ;59(6):887-95.; 6. J Diabetes. 2013r;5(1):68-79

EXPERIMENTAL AND THERAPEUTIC MEDICINE 9: 1528-1536, 2015

Efficacy and safety of sitagliptin compared with sulfonylurea therapy in patients with type 2 diabetes showing inadequately controlled glycosylated hemoglobin with metformin monotherapy: A meta-analysis

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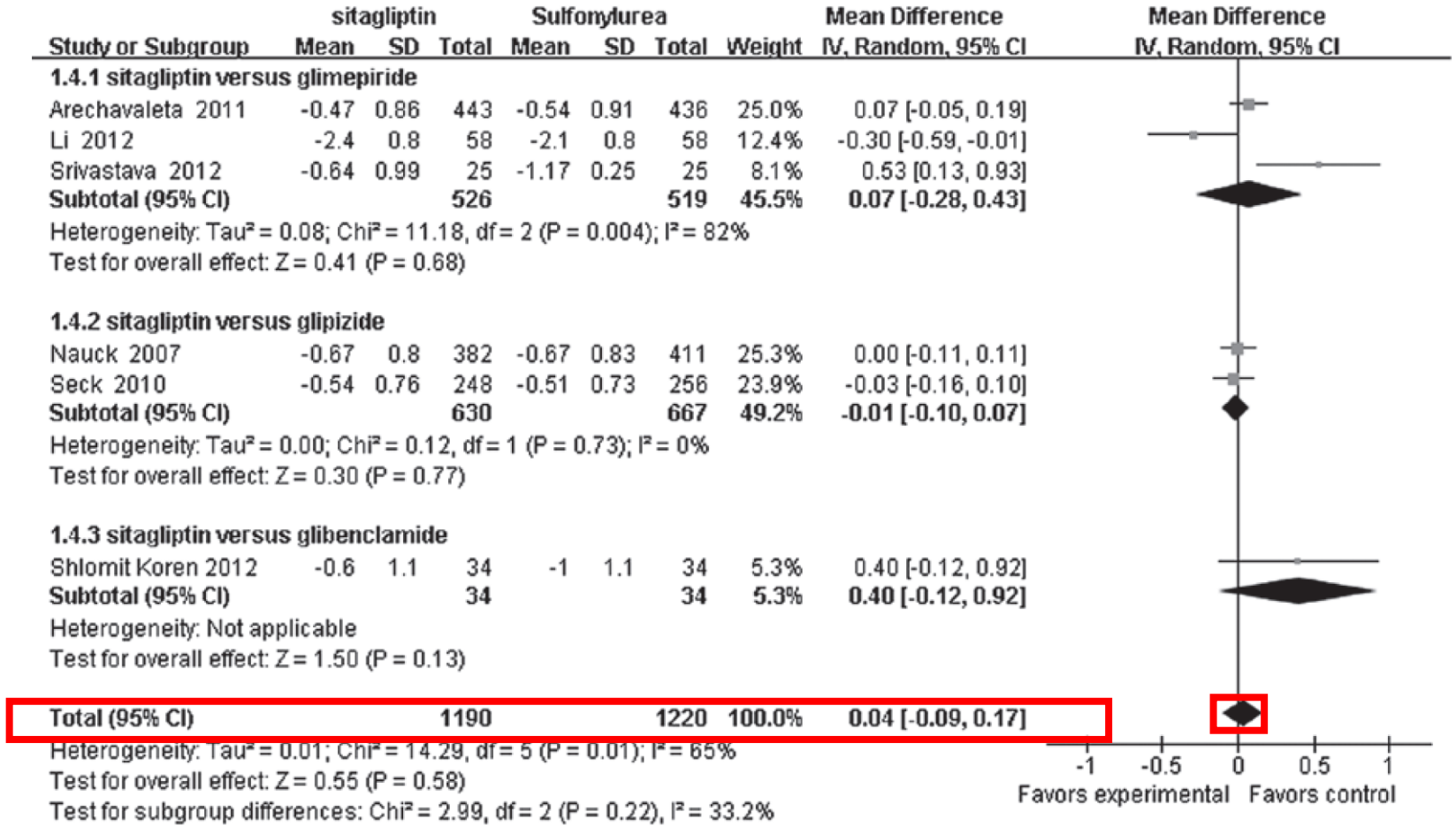
Received June 18, 2014; Accepted January 26, 2015

1-Exp Ther Med. 2015. 9(4): 1528–1536.c

HbA1c Changes Were not Significant Between Sitagliptin and Sulfonylurea Groups[1]



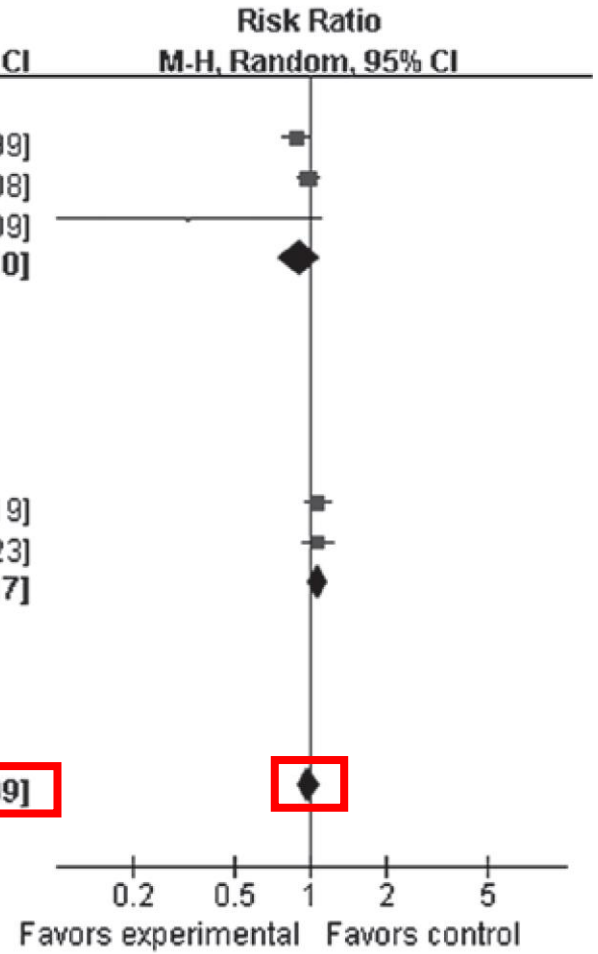
Study or Subgroup	sitagliptin Mean	SD	Total	Sulfonylurea Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.4.1 sitagliptin versus glimepiride								
Arechavaleta 2011	-0.47	0.86	443	-0.54	0.91	436	25.0%	0.07 [-0.05, 0.19]
Li 2012	-2.4	0.8	58	-2.1	0.8	58	12.4%	-0.30 [-0.59, -0.01]
Srivastava 2012	-0.64	0.99	25	-1.17	0.25	25	8.1%	0.53 [0.13, 0.93]
Subtotal (95% CI)			**526**			**519**	**45.5%**	**0.07 [-0.28, 0.43]**
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 11.18$, df = 2 (P = 0.004); $I^2 = 82\%$								
Test for overall effect: Z = 0.41 (P = 0.68)								
1.4.2 sitagliptin versus glipizide								
Nauck 2007	-0.67	0.8	382	-0.67	0.83	411	25.3%	0.00 [-0.11, 0.11]
Seck 2010	-0.54	0.76	248	-0.51	0.73	256	23.9%	-0.03 [-0.16, 0.10]
Subtotal (95% CI)			**630**			**667**	**49.2%**	**-0.01 [-0.10, 0.07]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.12$, df = 1 (P = 0.73); $I^2 = 0\%$								
Test for overall effect: Z = 0.30 (P = 0.77)								
1.4.3 sitagliptin versus glibenclamide								
Shlomit Koren 2012	-0.6	1.1	34	-1	1.1	34	5.3%	0.40 [-0.12, 0.92]
Subtotal (95% CI)			**34**			**34**	**5.3%**	**0.40 [-0.12, 0.92]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.50 (P = 0.13)								
Total (95% CI)			**1190**			**1220**	**100.0%**	**0.04 [-0.09, 0.17]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 14.29$, df = 5 (P = 0.01); $I^2 = 65\%$								
Test for overall effect: Z = 0.55 (P = 0.58)								
Test for subgroup differences: $Chi^2 = 2.99$, df = 2 (P = 0.22), $I^2 = 33.2\%$								

SD, standard deviation; CI, confidence interval; df, degrees of freedom.

1-Exp Ther Med. 2015; 9(4): 1528–1536.

Target HbA1c <7% Achievement Were not Significant Between Sitagliptin and Sulfonylurea Groups

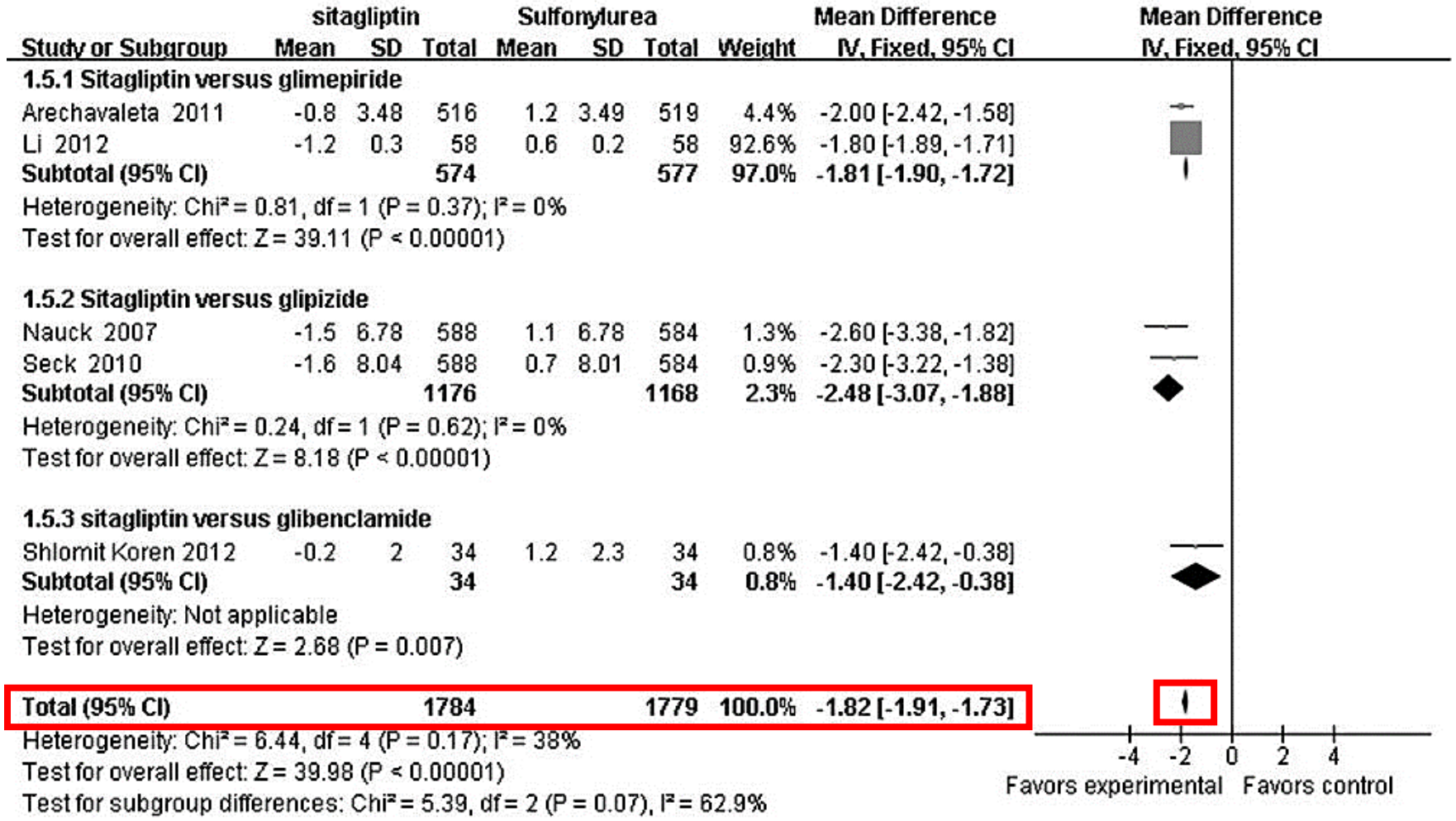
Study or Subgroup	sitagliptin Events	Total	Sulfonylurea Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 sitagliptin versus glimepiride						
Arechavaleta 2011	232	443	260	436	24.4%	0.88 [0.78, 0.99]
Li 2012	54	58	55	58	28.1%	0.98 [0.90, 1.08]
Srivastava 2012	3	25	9	25	0.7%	0.33 [0.10, 1.09]
Subtotal (95% CI)		**526**		**519**	**53.2%**	**0.91 [0.75, 1.10]**
Total events	289		324			
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 7.93$, df = 2 (P = 0.02); $I^2 = 75\%$						
Test for overall effect: Z = 1.00 (P = 0.32)						
1.2.2 sitagliptin versus glipizide						
Nauck 2007	240	382	242	411	25.3%	1.07 [0.95, 1.19]
Seck 2010	157	248	151	256	21.5%	1.07 [0.93, 1.23]
Subtotal (95% CI)		**630**		**667**	**46.8%**	**1.07 [0.98, 1.17]**
Total events	397		393			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1 (P = 0.95); $I^2 = 0\%$						
Test for overall effect: Z = 1.51 (P = 0.13)						
Total (95% CI)		**1156**		**1186**	**100.0%**	**0.99 [0.89, 1.09]**
Total events	686		717			
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 10.34$, df = 4 (P = 0.04); $I^2 = 61\%$						
Test for overall effect: Z = 0.25 (P = 0.80)						
Test for subgroup differences: Not applicable						



M-H, Mantel-Haenszel; CI, confidence interval

1-Exp Ther Med. 2015; 9(4): 1528–1536.

Sitagliptin Groups Did not Experience Weight Gain Compared to Sulfonylurea Groups[1]

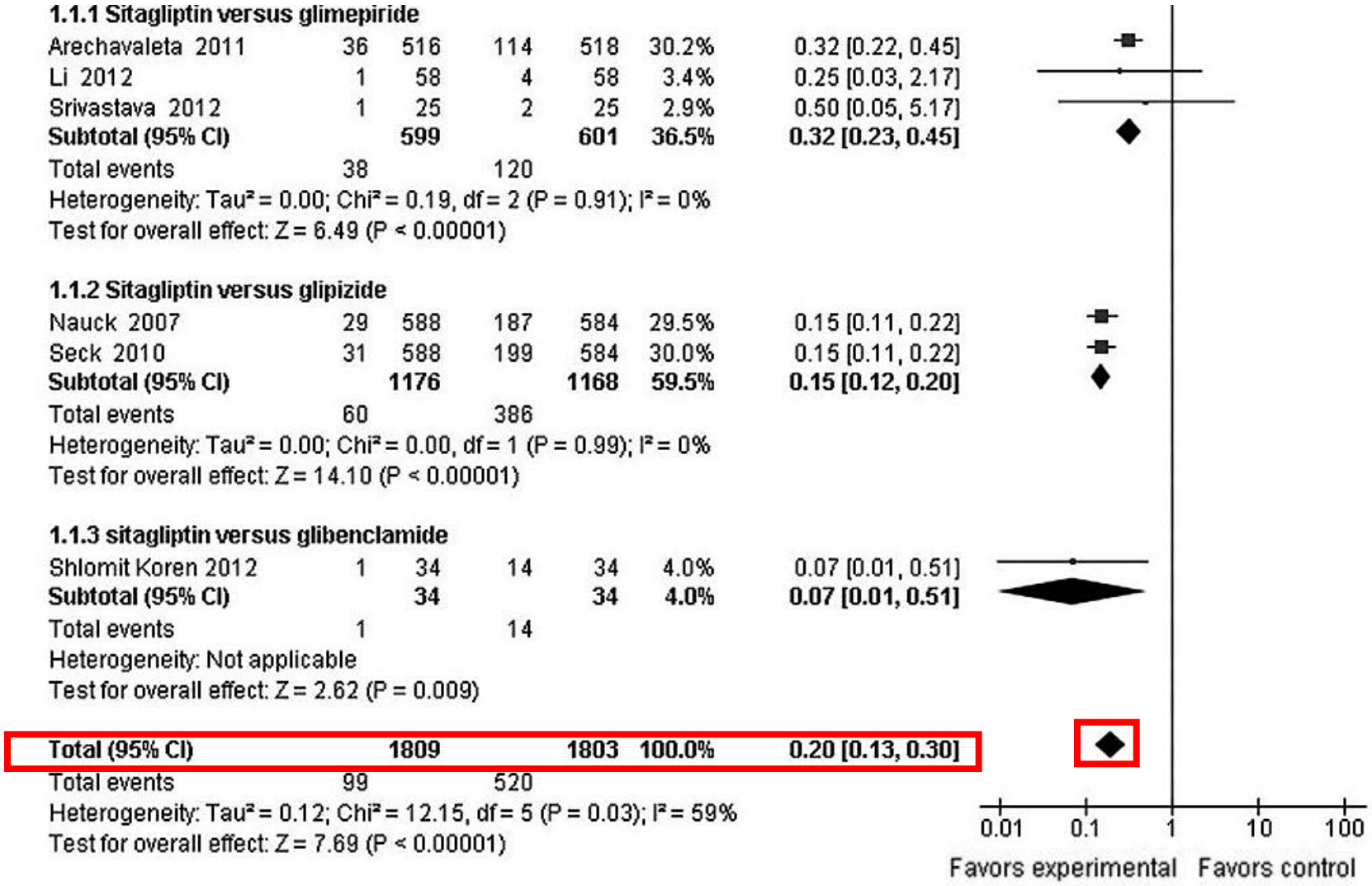


Study or Subgroup	sitagliptin Mean	SD	Total	Sulfonylurea Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.5.1 Sitagliptin versus glimepiride								
Arechavaleta 2011	-0.8	3.48	516	1.2	3.49	519	4.4%	-2.00 [-2.42, -1.58]
Li 2012	-1.2	0.3	58	0.6	0.2	58	92.6%	-1.80 [-1.89, -1.71]
Subtotal (95% CI)			**574**			**577**	**97.0%**	**-1.81 [-1.90, -1.72]**
Heterogeneity: Chi² = 0.81, df = 1 (P = 0.37); I² = 0%								
Test for overall effect: Z = 39.11 (P < 0.00001)								
1.5.2 Sitagliptin versus glipizide								
Nauck 2007	-1.5	6.78	588	1.1	6.78	584	1.3%	-2.60 [-3.38, -1.82]
Seck 2010	-1.6	8.04	588	0.7	8.01	584	0.9%	-2.30 [-3.22, -1.38]
Subtotal (95% CI)			**1176**			**1168**	**2.3%**	**-2.48 [-3.07, -1.88]**
Heterogeneity: Chi² = 0.24, df = 1 (P = 0.62); I² = 0%								
Test for overall effect: Z = 8.18 (P < 0.00001)								
1.5.3 sitagliptin versus glibenclamide								
Shlomit Koren 2012	-0.2	2	34	1.2	2.3	34	0.8%	-1.40 [-2.42, -0.38]
Subtotal (95% CI)			**34**			**34**	**0.8%**	**-1.40 [-2.42, -0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.68 (P = 0.007)								
Total (95% CI)			**1784**			**1779**	**100.0%**	**-1.82 [-1.91, -1.73]**
Heterogeneity: Chi² = 6.44, df = 4 (P = 0.17); I² = 38%								
Test for overall effect: Z = 39.98 (P < 0.00001)								
Test for subgroup differences: Chi² = 5.39, df = 2 (P = 0.07), I² = 62.9%								

SD, standard deviation; CI, confidence interval

1-Exp Ther Med. 2015; 9(4): 1528–1536.

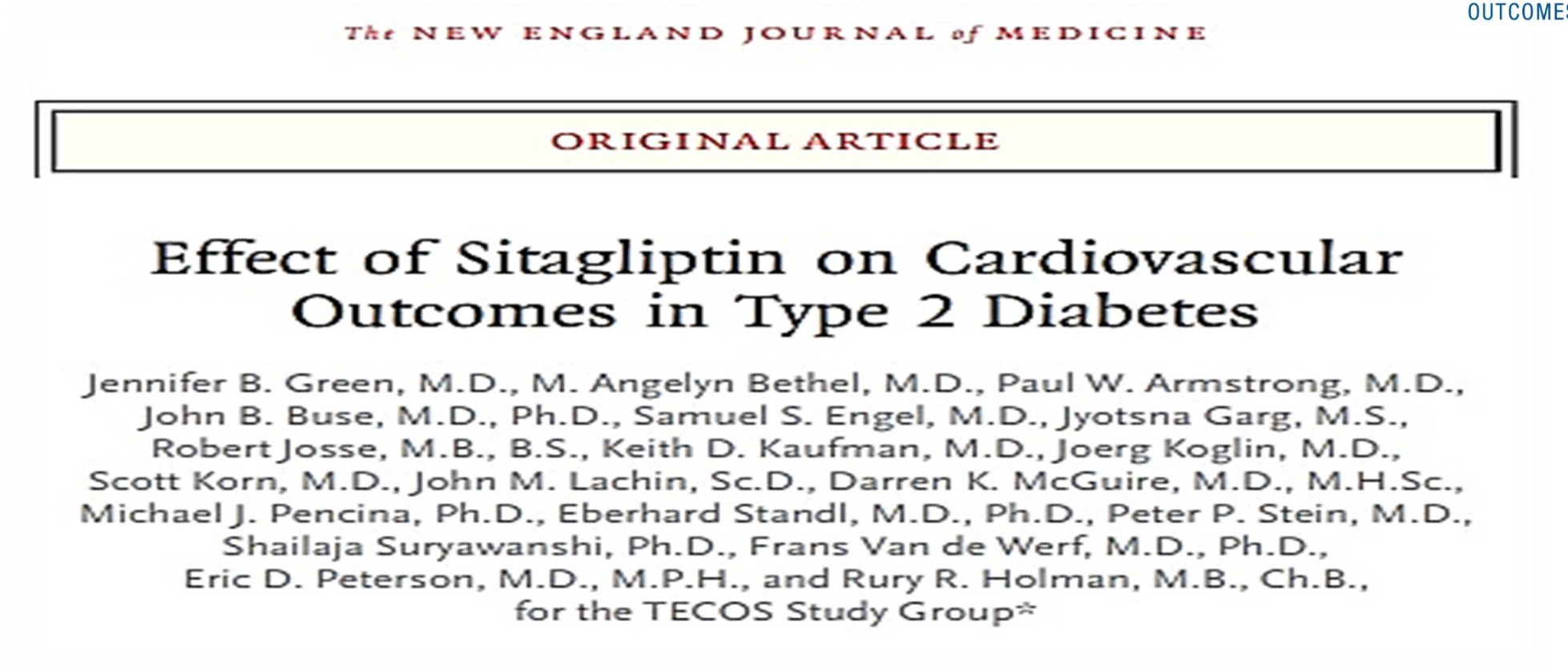
Lower Occurrence of Hypoglycemic Events in Sitagliptin Groups Compared to Sulfonylurea Groups[1]



M-H, Mantel-Haenszel; CI, confidence interval

1-Exp Ther Med. 2015; 9(4): 1528–1536.

TECOS
TRIAL EVALUATING CARDIOVASCULAR OUTCOMES WITH SITAGLIPTIN



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes

Jennifer B. Green, M.D., M. Angelyn Bethel, M.D., Paul W. Armstrong, M.D., John B. Buse, M.D., Ph.D., Samuel S. Engel, M.D., Jyotsna Garg, M.S., Robert Josse, M.B., B.S., Keith D. Kaufman, M.D., Joerg Koglin, M.D., Scott Korn, M.D., John M. Lachin, Sc.D., Darren K. McGuire, M.D., M.H.Sc., Michael J. Pencina, Ph.D., Eberhard Standl, M.D., Ph.D., Peter P. Stein, M.D., Shailaja Suryawanshi, Ph.D., Frans Van de Werf, M.D., Ph.D., Eric D. Peterson, M.D., M.P.H., and Rury R. Holman, M.B., Ch.B., for the TECOS Study Group*

Aim[1]: the long-term effect on cardiovascular events of adding sitagliptin, a dipeptidyl peptidase 4 inhibitor, to usual care in patients with type 2 diabetes and cardiovascular disease.

1-N Engl J Med. 2015.16;373(3):232-42

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Sitagliptin Cardiovascular Outcomes Study (TECOS) Study Design[1]

TECOS
TRIAL EVALUATING CARDIOVASCULAR OUTCOMES WITH SITAGLIPTIN

Main inclusion criteria

1. Patients aged ≥ 50 years with T2D
2. HbA_{1c} 6.5–8.0% receiving stable oral glucose-lowering therapy and/or insulin*
3. Pre-existing vascular disease

+ Usual care for T2D

Sitagliptin 100 mg daily* vs Placebo

N = 14,671; median follow-up 3.0 years

Primary endpoint: time to first occurrence of:

- CV-related death
- Unstable angina requiring hospitalisation
- Non-fatal stroke
- Non-fatal MI

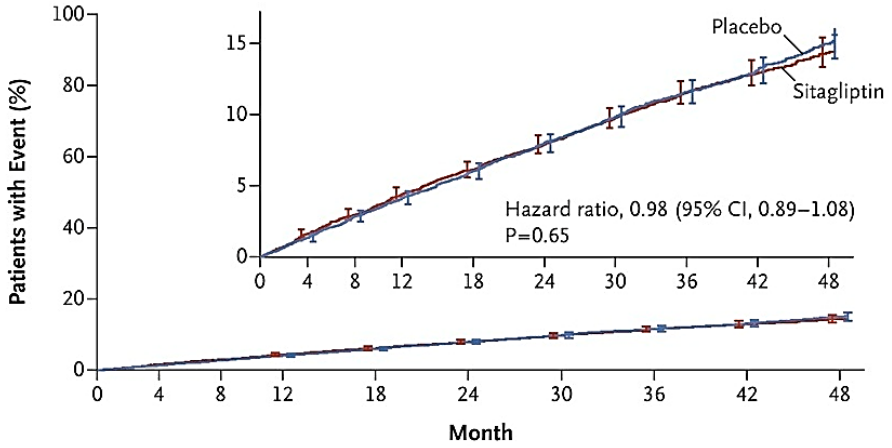
*50 mg daily if the baseline eGFR was ≥ 30 and < 50 mL per minute per 1.73 m^2.

1-N Engl J Med. 2015.16;373(3):232-42

Results[1]

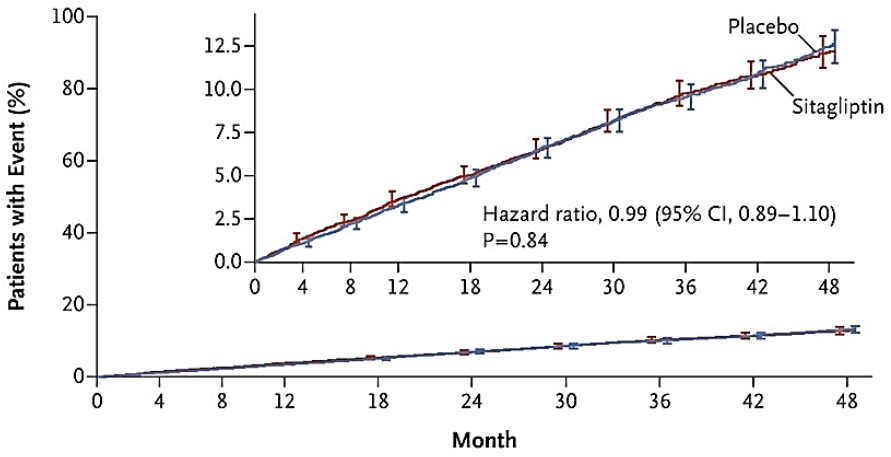
TECOS
TRIAL EVALUATING CARDIOVASCULAR OUTCOMES WITH SITAGLIPTIN

Primary Composite Cardiovascular Outcome#



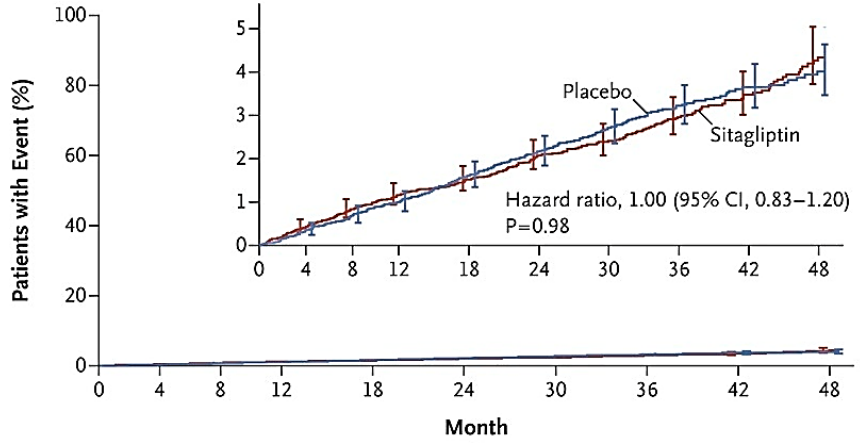
No. at Risk										
Sitagliptin	7332	7131	6937	6777	6579	6386	4525	3346	2058	1248
Placebo	7339	7146	6902	6751	6512	6292	4411	3272	2034	1234

Secondary Composite Cardiovascular Outcome*



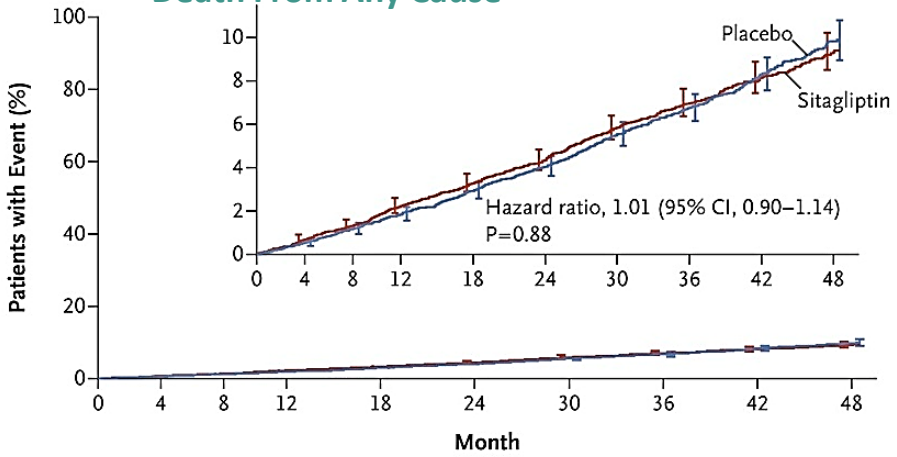
No. at Risk										
Sitagliptin	7332	7145	6969	6817	6638	6457	4584	3396	2097	1270
Placebo	7339	7161	6939	6796	6573	6359	4472	3332	2070	1260

Hospitalization for Heart Failure



No. at Risk										
Sitagliptin	7332	7189	7036	6917	6780	6619	4728	3515	2175	1324
Placebo	7339	7204	7025	6903	6712	6549	4599	3443	2131	1315

Death From Any Cause



No. at Risk										
Sitagliptin	7332	7262	7180	7103	7010	6904	4964	3739	2321	1435
Placebo	7339	7271	7176	7098	6982	6864	4891	3673	2293	1412

#The primary composite cardiovascular outcome was defined as the first confirmed event of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina. *The secondary composite cardiovascular outcome was the first confirmed event of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

1-N Engl J Med. 2015; 16;373(3):232-42

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Conclusion:

- Among patients with type 2 diabetes and established cardiovascular disease, adding **sitagliptin** to usual care **did not appear to increase the risk of major adverse cardiovascular events**, hospitalization for heart failure, or other adverse events.

1-N Engl J Med. 2015. 16;373(3):232-42

Dosage and Administration

Sitagliptin: Once-Daily Dosing Administration[1]

Usual Dosing for Sitagliptin*

The recommended dose of Sitagliptin is 100 mg once daily as monotherapy or as combination therapy with metformin or a PPARγ agonist.

Patients With Renal Insufficiency*,†

A dosage adjustment is recommended in patients with moderate or severe renal insufficiency and in patients with end-stage renal disease requiring hemodialysis or peritoneal dialysis.

50 mg once daily	25 mg once daily
Moderate **eGFR greater than or equal to 30 mL/min/1.73 m^2 to less than 45 mL/min/1.73 m^2**	**Severe and ESRD‡** **eGFR less than 30 mL/min/1.73 m^2 (including patients with end stage renal disease [ESRD] on dialysis)**

Assessment of renal function is recommended prior to Sitagliptin initiation and periodically thereafter.

*Sitagliptin can be taken with or without food. †Patients with mild renal insufficiency—100 mg once daily.
‡ESRD=end-stage renal disease requiring hemodialysis or peritoneal dialysis.
1. Sitagliptin FDA Label, 2018, Reference ID: 4219849.
PPAR agonist= Thiazolidinedione class.

Sitagliptin + Metformin: Twice-Daily Dosing Administration[1]

- Individualize the starting dose of Sitagliptin +Metformin based on the patient's current regimen.

- Adjust the dosing based on effectiveness and tolerability;

➢ not exceeding the maximum recommended daily dose:

(100 mg sitagliptin and 2000 mg metformin).

- Twice daily with meals, with gradual dose escalation:

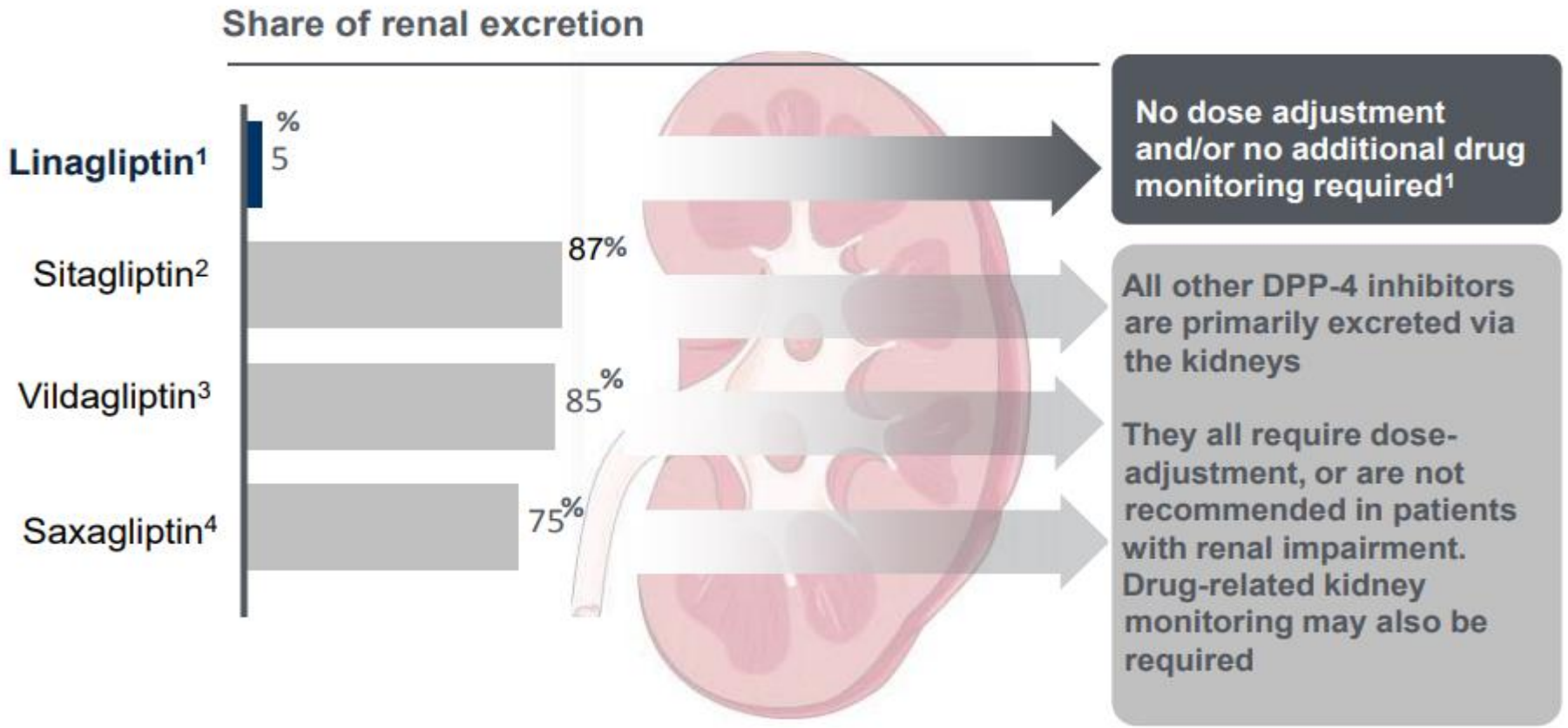
➢ to reduce the gastrointestinal effects due to metformin.

- Not use in eGFR <30 mL/min/1.73 m^2.
- Not recommended in eGFR between 30 to <45 mL/min/1.73 m^2.

1-Sitagliptin+ Metformin FDA Label,2017,Reference ID: 4043185

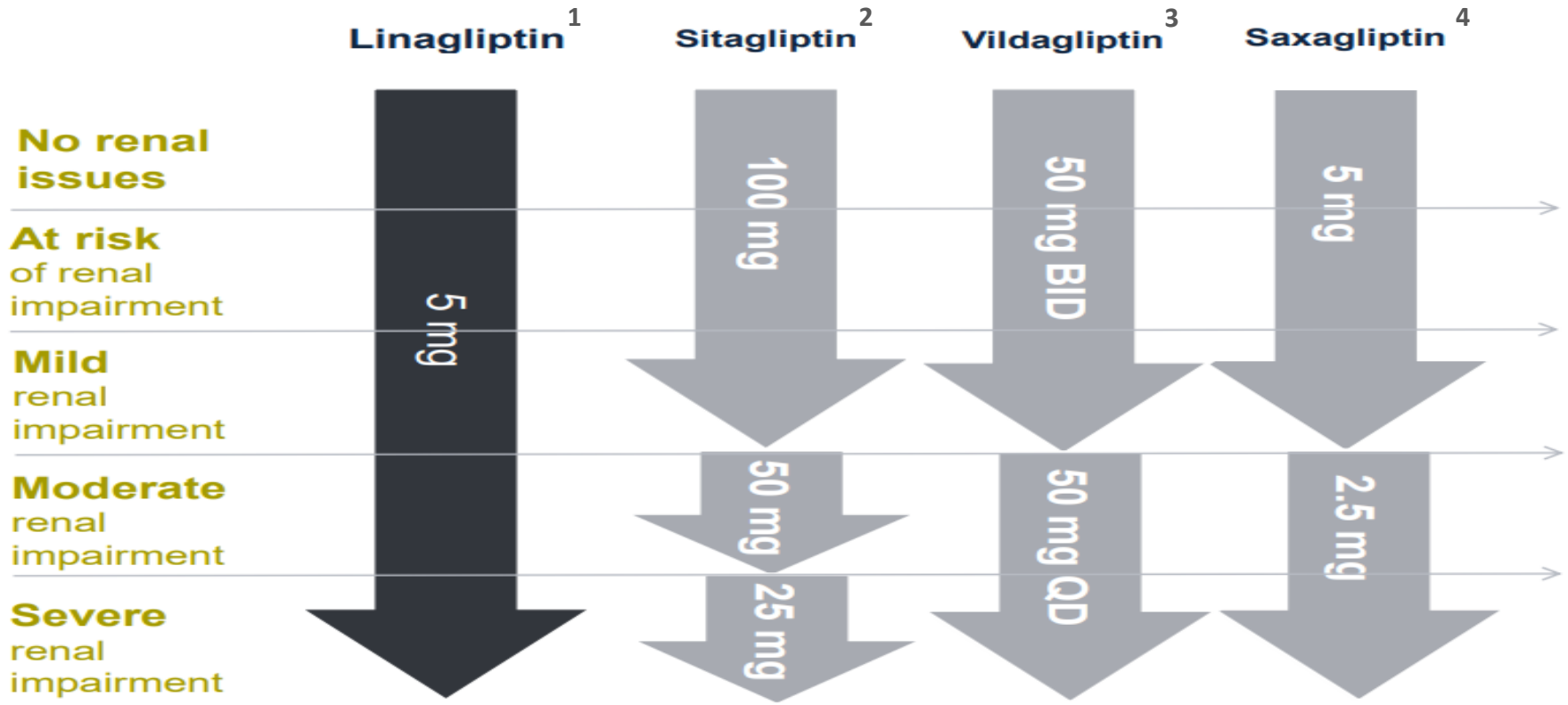
- **Linagliptin Efficacy**

Linagliptin is the only DPP-4 inhibitor which is primarily excreted by gut



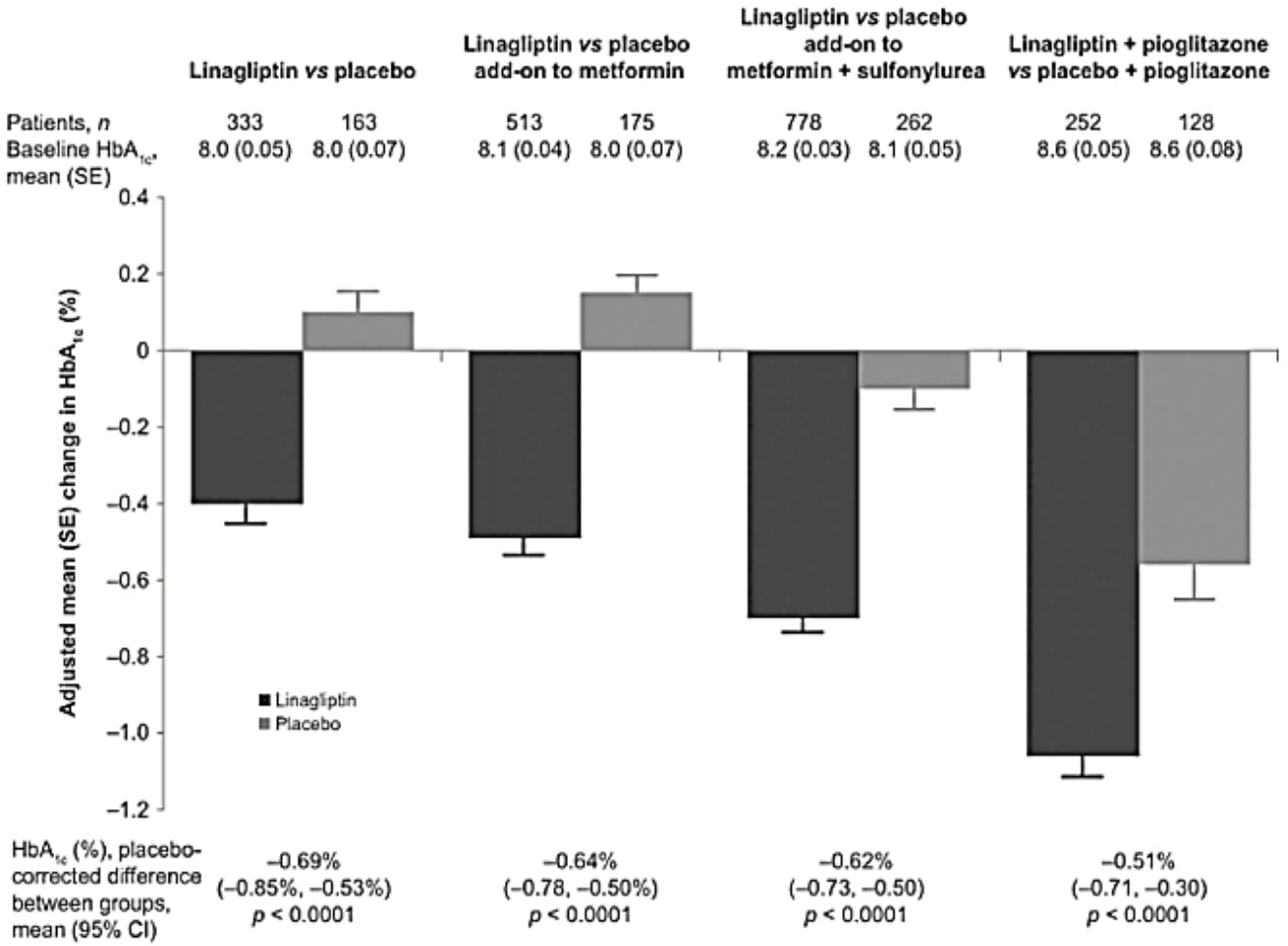
1. Linagliptin US prescribing information , 2. Vincent SH et al. Drug Metab Dispos. 2007;35(4): 533–538 , 3. He H, et al. Drug Metab. Dispos.2009 37(3):536–544 ,
4. Saxagliptin US prescribing information

Linagliptin is the first only DPP-4 inhibitor that does not require dose adjustment: Easy use



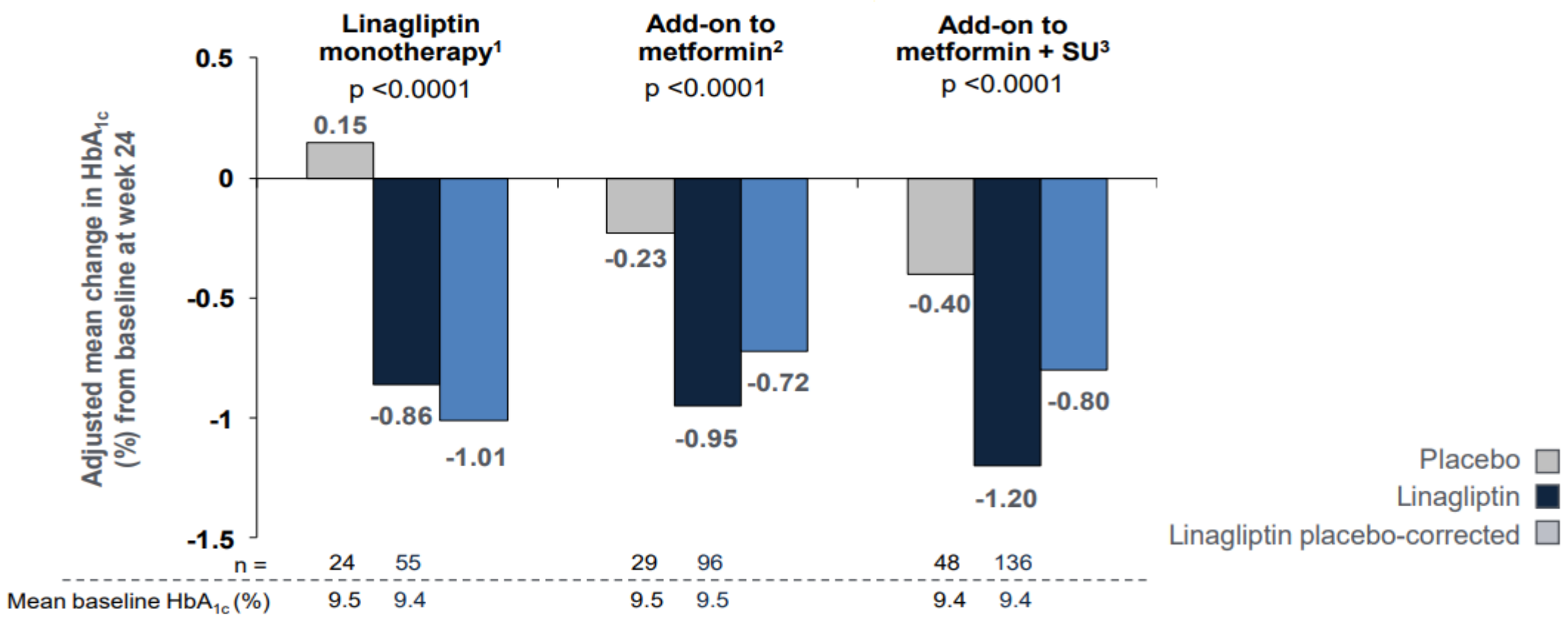
1.TRAJENTA® EMA Summary of Product Characteristics, 2.Januvia® Summary of Product Characteristics. October 2016. 3.Galvus® Summary of Product Characteristics. April 2017, 4.Onglyza® Summary of Product Characteristics. June 2017.

Δ HbA_{1c} across different background therapy Linagliptin *vs*. placebo



1. Therapeutic Advances in Endocrinology and Metabolism 2012, 3(4), 113–124.

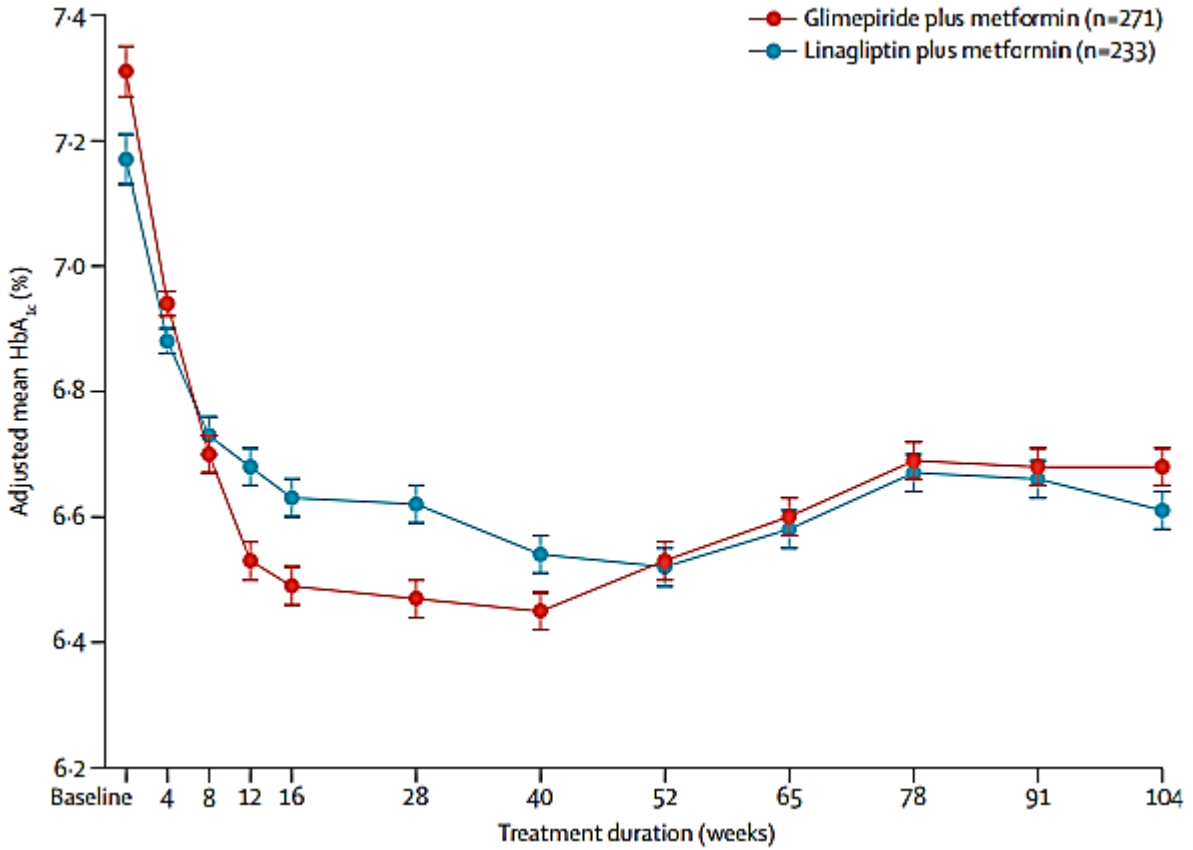
Linagliptin achieves HbA1c decrease of up to 1.2% in poorly controlled patients



Significant HbA1c reductions in type 2 diabetes patients with baseline HbA1c ≥ 9%

1. Diabetes Obesity and Metabolism 2011;13(3):258–267, 2. Diabetes Obesity and Metabolism 2011;13(1):65–74, 3. Diabetic Medicine 2011;28,1352-1361

Linagliptin sustained HbA1c reduction over 104 weeks similar efficacy as a SU over 104 weeks



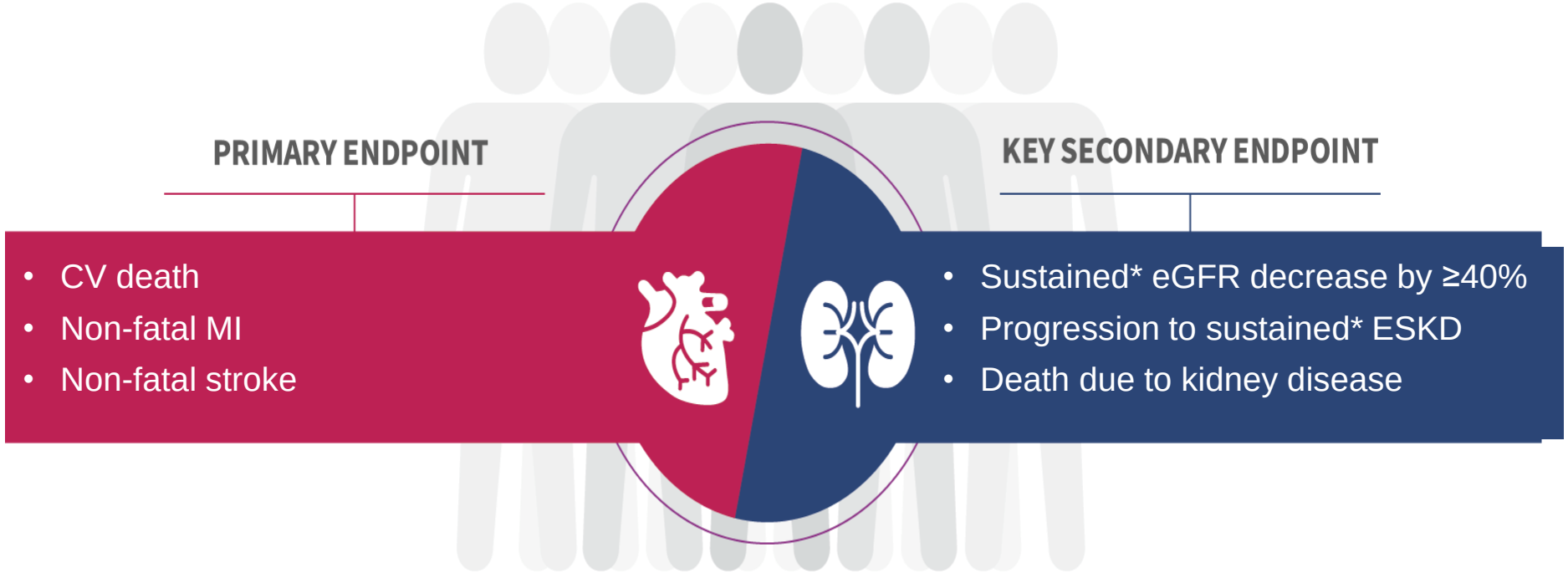
Linagliptin, has similar efficacy as a SU over 104 weeks

1. Lancet, 2012; 380(9840), 475–483

Aim: CARMELINA is a large, long-term cardiovascular (CV) outcomes trial testing the impact of linagliptin vs. placebo on top of standard care on CV and renal outcomes.

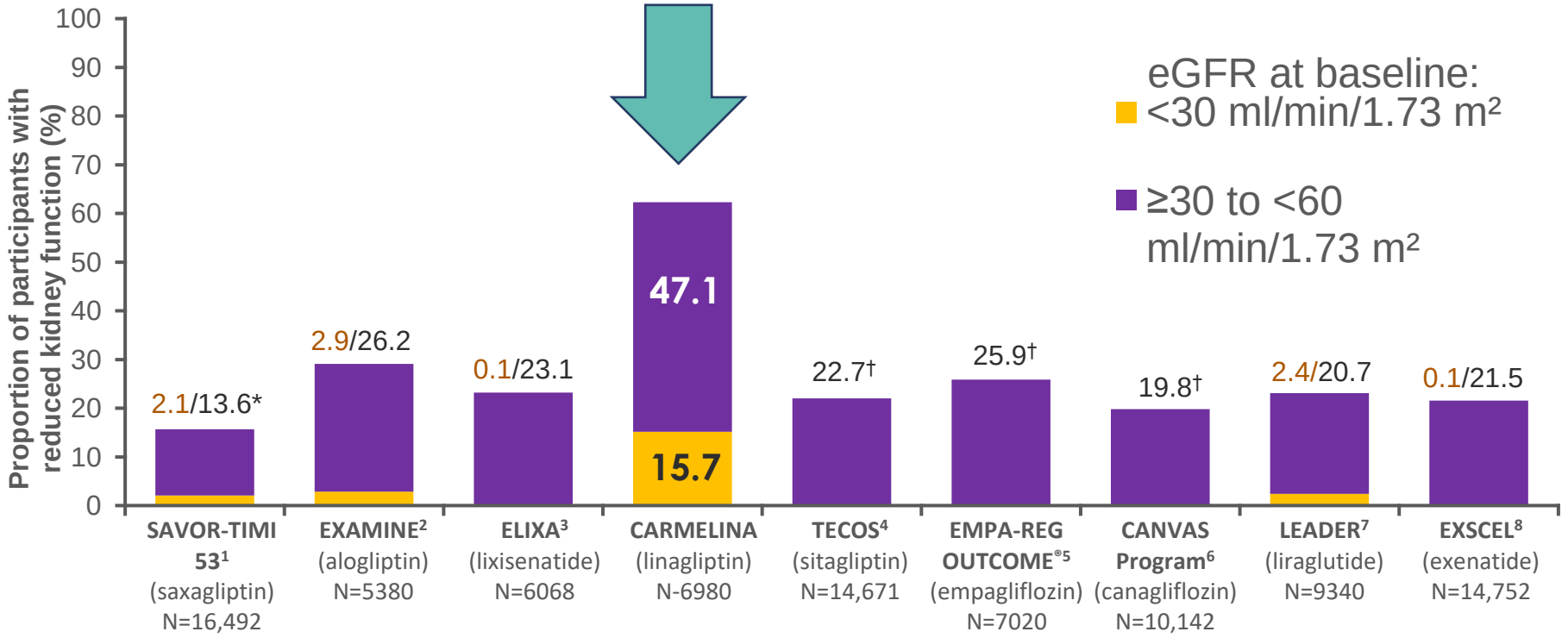
1. Cardiovasc Diabetol 2018;17:39

CARMELINA® was designed to evaluate the CV and kidney safety of linagliptin in patients with T2D[1]



1. Cardiovasc Diabetol 2018;17:39

Higher prevalence of renal impairment CARMELINA than recent CVOTs

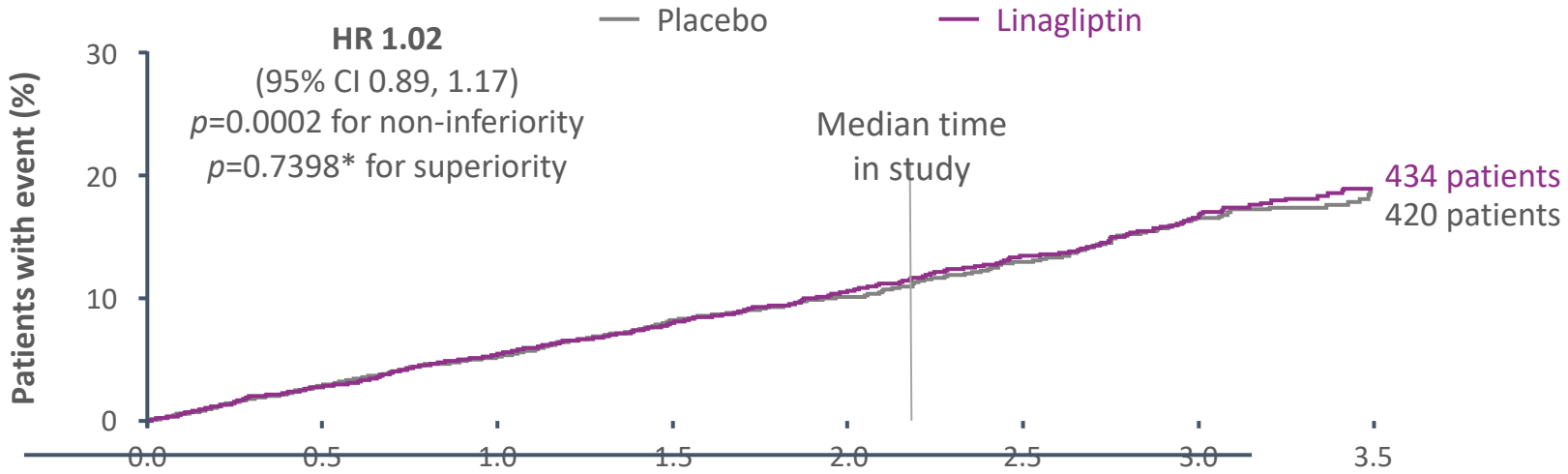


*eGFR ≥30 to <50 ml/min/1.73 m2; †Trial excluded patients with eGFR <30 ml/min/1.73 m^2 CVOT, cardiovascular outcomes trial; eGFR, estimated glomerular filtration rate

1. Scirica BM *et al. N Engl J Med* 2013;369:1317; 2. White WB *et al. N Engl J Med* 2013;369:1327 (supplementary appendix); 3. Pfeffer MA *et al. N Engl J Med* 2015;373:2247 (supplementary appendix); 4. Green JB *et al. N Engl J Med* 2015;373:232 (supplementary appendix); 5. Zinman B *et al. N Engl J Med* 2015;373:2117 6. Neal B *et al. Diabetes Obes Metabol* 2017;19:926; 7. Marso SP *et al. N Engl J Med* 2016;375:311; 8. Holman RR *et al. N Engl J Med* 2017;377:1228

The long-term CV safety profile of linagliptin was confirmed

Time to first occurrence of 3P-MACE

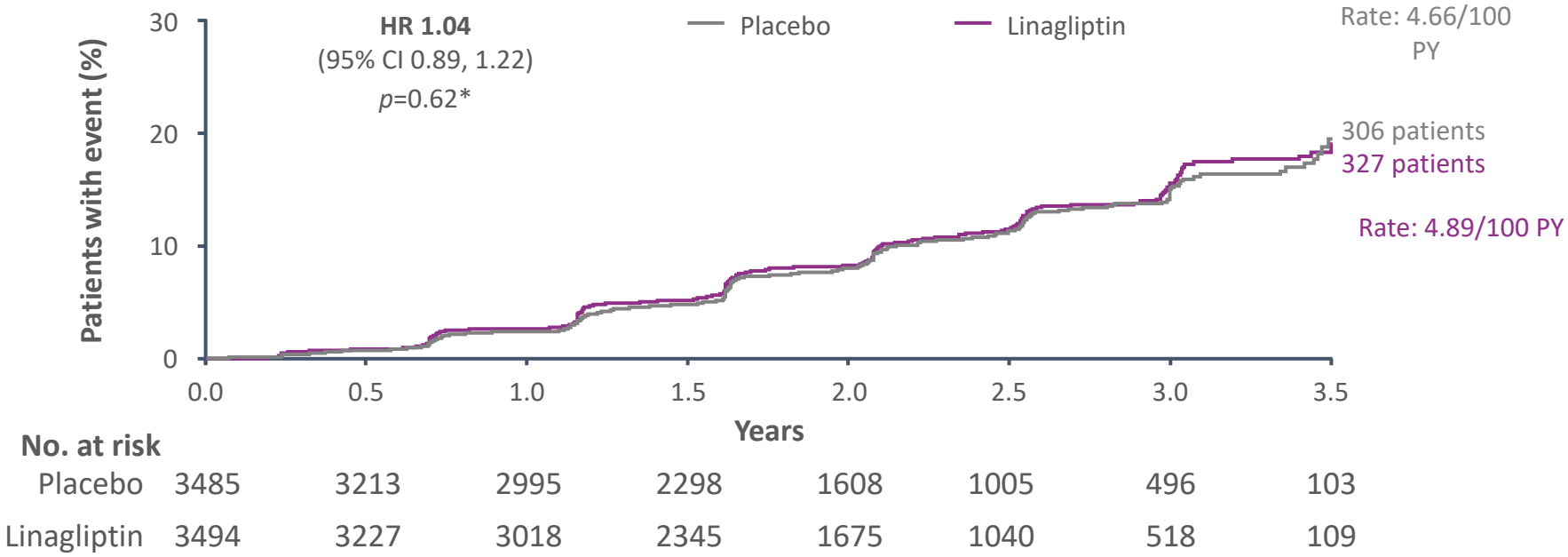


No. of patients								
Placebo (n)	3,485	3,353	3,243	2,625	1,931	1,285	758	251
Linagliptin (n)	3,494	3,373	3,254	2,634	1,972	1,306	778	269

Linagliptin event rate 5.77/100 PY Placebo event rate 5.63/100 PY
Treated set, Kaplan-Meier estimate. Hazard ratio and 95% CI based on Cox regression model with terms for treatment group (p=0.7398) and region (p=0.7878); *Two-sided
3P-MACE, 3-point major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke)
Rosenstock J, et al. JAMA. 2018 Nov 9. doi: 10.1001/jama.2018.18269

Time to first occurrence of key secondary outcome: sustained ESKD, sustained decrease of ≥40% in eGFR from baseline, or death due to kidney disease

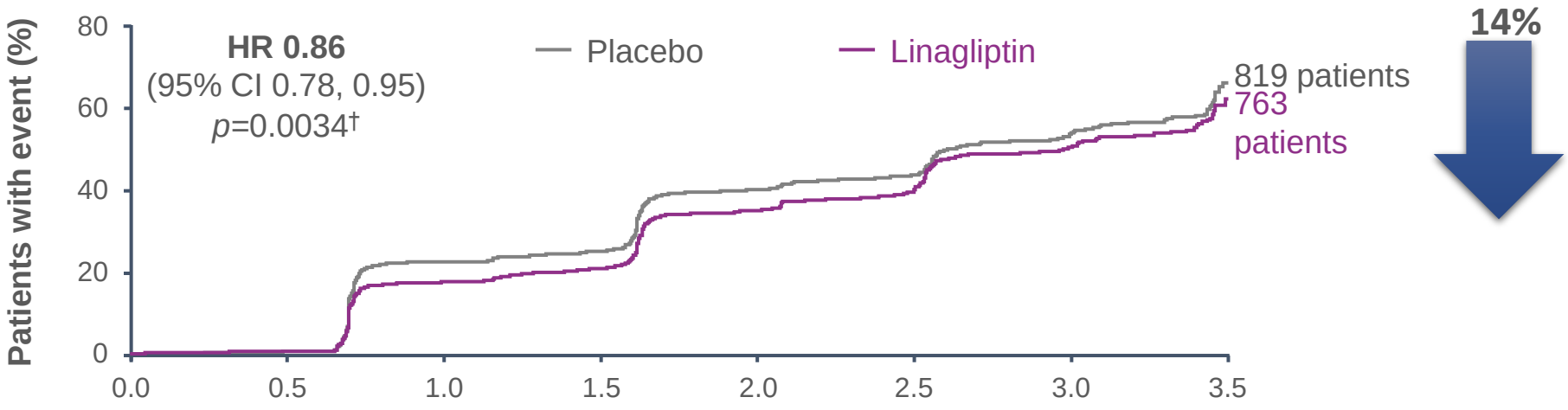
The kidney safety profile of linagliptin was confirmed



1. Cardiovasc Diabetol 2018;17:39

Linagliptin was associated with a significant reduction in albuminuria progression

Time to first occurrence of albuminuria progression*

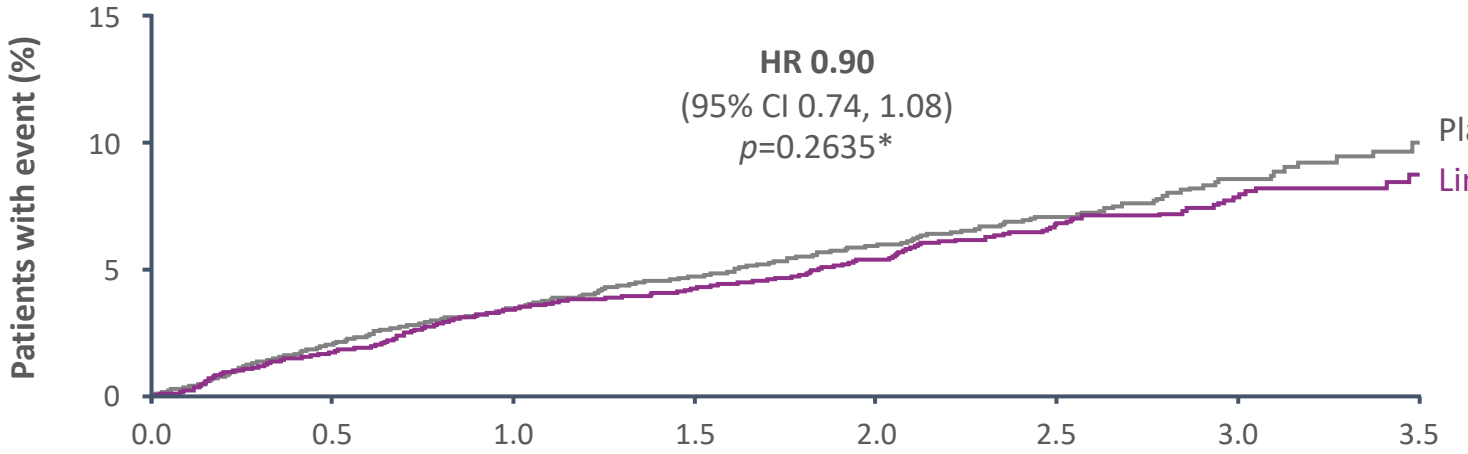


No. of patients								
Placebo (n)	2,129	1,972	1,434	1,139	667	430	200	35
Linagliptin (n)	2,162	2,004	1,554	1,263	756	487	213	39

1. Cardiovasc Diabetol 2018;17:39

There was no increased risk of hospitalization for HF with Linagliptin

Time to first occurrence of adjudication-confirmed hospitalization for HF

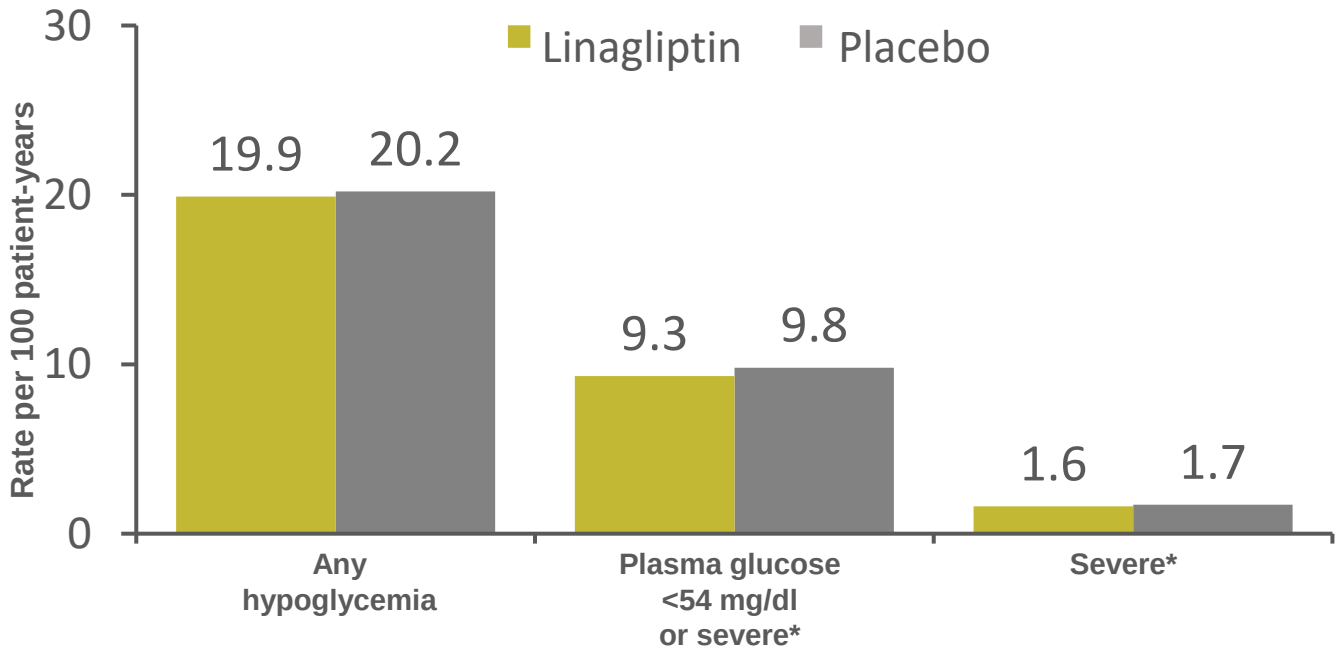


No. of patients								
Placebo (n)	3,485	3,336	3,222	2,621	1,923	1,285	767	258
Linagliptin (n)	3,494	3,361	3,243	2,647	1,979	1,317	787	280

1. Cardiovasc Diabetol 2018;17:39

Overall linagliptin did not increase the risk of hypoglycemia

Hypoglycemia: rates per 100 patient-years overall



1. Cardiovasc Diabetol 2018;17:39

Dosage And Administration [1]

Recommend dosing:

The recommended dose of Linagliptin is 5 mg once daily.

Linagliptin tablets can be taken with or without food.

1. Tradjenta (linagliptin) tablets Label – FDA 2019

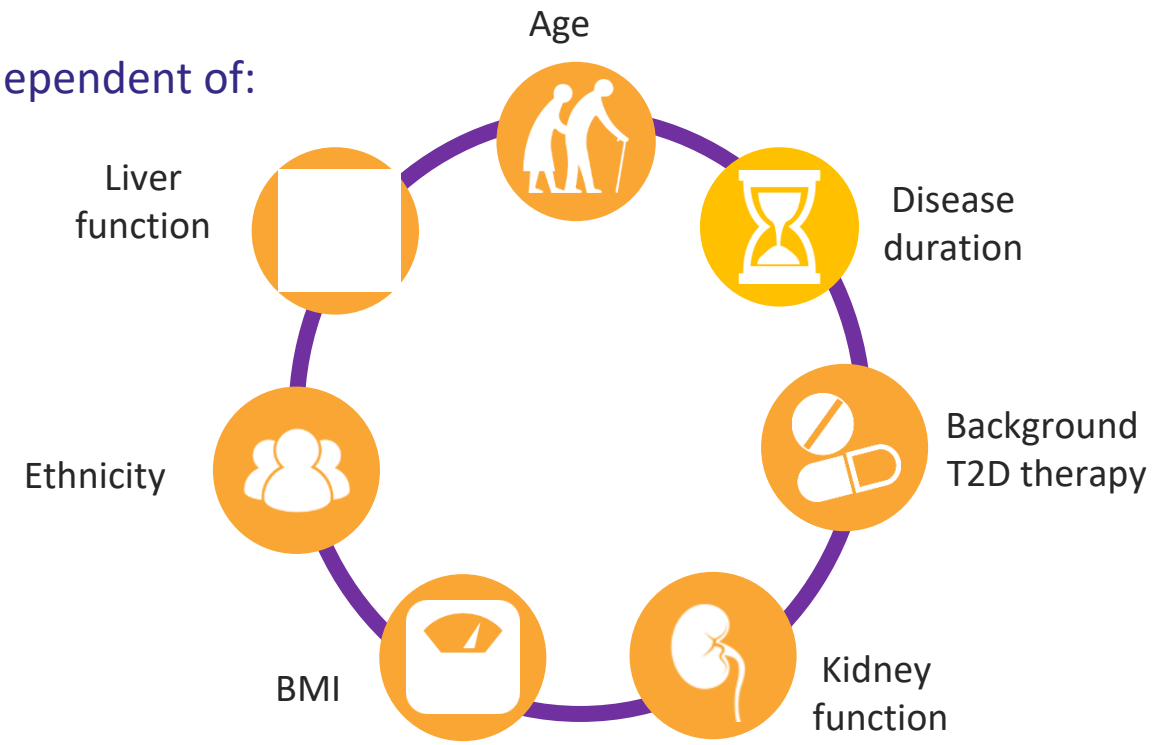
- **Conclusion**

1-Diabetes Obes Metab. 2011;13:841–849. 2- Diabetes Obes Metab. 2007;9:194–205. 3- Int J Clin Pract. 2010;64:562–576. 4-Diabetes Res Clin Pract. 2011;93(1):e15-75-Diabetes Care. 2019;42(Suppl 1):S90-S102. 6-N Engl J Med. 2015.16;373(3):232-42

Linagliptin Has Broad Therapeutic Indication

Linagliptin
5 *mg*
once daily

Independent of:



BMI, body-mass index
Boehringer Ingelheim and Eli Lilly. Trajenta®(linagliptin) Prescribing Information. 2017

Liroprim®
Linagliptin/Metformin

Dosage Forms and Strengths[1]:

- 2.5 mg linagliptin/500 mg metformin HCl
- 2.5 mg linagliptin/1000 mg metformin HCl

1- Linagliptin and Metformin FDA Label.;2019, Reference ID: 4457960.

Dosage and Administration[1]:

Individualize the starting dose of **LIROPRIM** based on the patient's current regimen.

Give **twice** daily **with meals**, with gradual dose escalation to reduce the gastrointestinal effects due to metformin.

The maximum recommended dose is **2.5 mg linagliptin/1000 mg metformin HCl** twice daily.

1- Linagliptin and Metformin FDA Label.;2019, Reference ID: 4457960.


abidi
Diabetes
Thank you