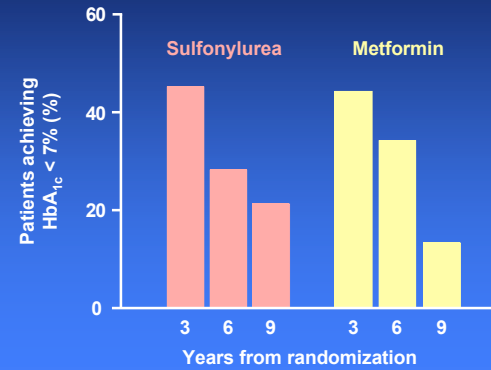


Comparison of Anti-Hyperglycemic Agents

	Approx. drop in A _{1c} *	Effect on body weight	Hypo-glycemia	Contra-indications	Cost per month [†]
Metformin	1.0-1.5	Neutral or reduction	None	Renal, hepatic, cardiac failure	\$19
Insulin sensitizers	1.0-1.5	↑ 2-5 kg	None	Cardiac failure	\$100
Secretagogues	1.0-1.5	↑ 2-5 kg	10-30%		\$8-50
Insulin	1.0-3.0	↑ 2-5 kg	100%		\$30-60
Acarbose	0.5-0.8	Neutral	None		\$30

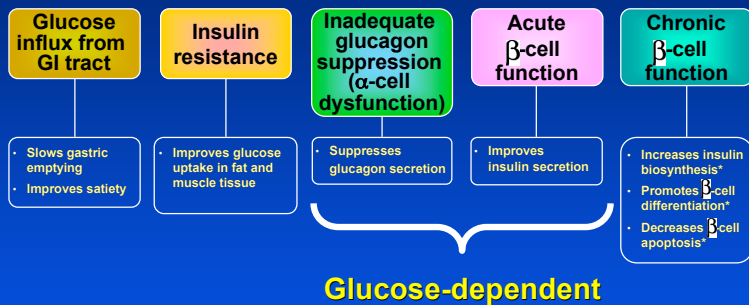
* when used as new therapy or added to existing therapy
[†] estimated cost at maximum dose, Quebec formulary 2006

UKPDS: time-dependent reduction in percentage of patients achieving HbA_{1c} < 7%



UKPDS 49. JAMA 1999; 281:2005-2012.

GLP-1 Actions Address the Multiple Metabolic Defects in T2DM



GLP-1 = glucagon-like peptide-1

*Preclinical data

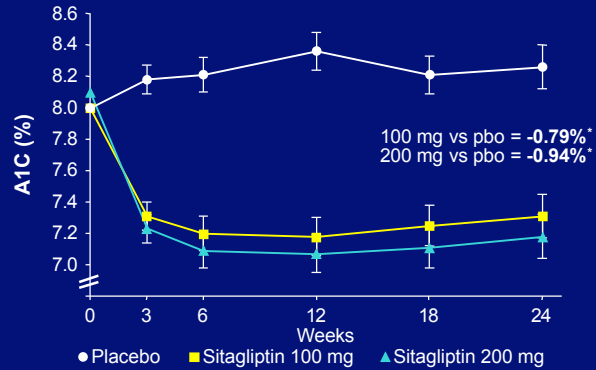
Adapted from Drucker DJ. *Diabetes Care* 2003;26:2929-2940.

Potential Strategies for Incretin-Based Therapies

- GLP-1 continuous infusion: impractical
- Agents that mimic GLP-1 action:
GLP-1 analogues
(e.g. exenatide, liraglutide)
- Agents that prevent incretin degradation:
DPP-IV inhibitors
(e.g. sitagliptin, vildagliptin, saxagliptin)

Drucker DJ et al. *Diabetes Care* 2003;26:2929-2940.
 Sinclair EM, Drucker DJ. *Physiology* 2005;20:352-365.
 Baggio LL, Drucker DJ. *Annu Rev Med* 2006;57:269-281.
 Baggio LL et al. *Diabetes* 2004;53:2492-2500.

Improvement in A1C over 24 weeks with Sitagliptin Monotherapy



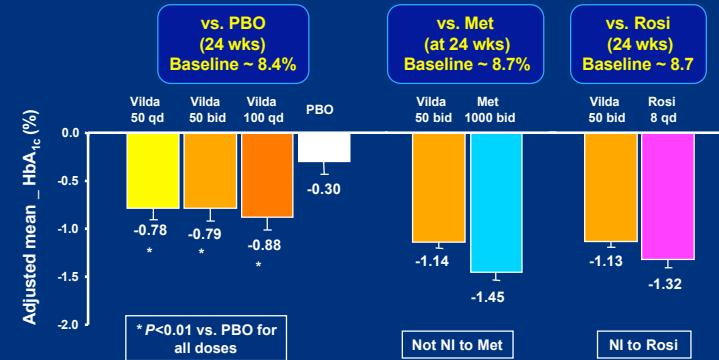
100 mg vs pbo = $-0.79\%^*$
200 mg vs pbo = $-0.94\%^*$

*Difference in LS mean change from baseline vs. placebo at Week 24; $p < 0.001$

Protocol 021.

Aschner P et al Diabetes Care 2006; 29(12):2632-2637

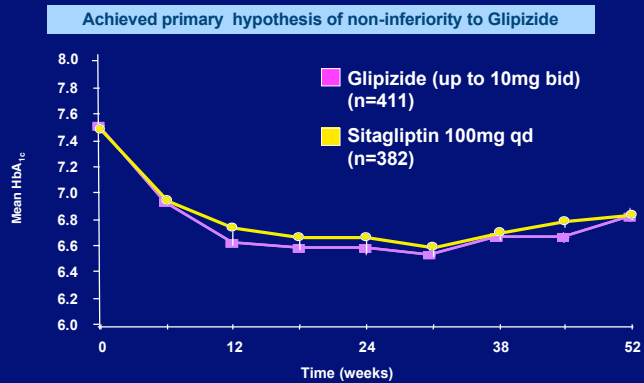
Vildagliptin Shows Consistent Lowering of HbA_{1c} in Monotherapy



Primary efficacy ITT population
Diabetes 2006;55(S1):A557
Diabetes 2006;55(S1):A120
Data on file, Novartis

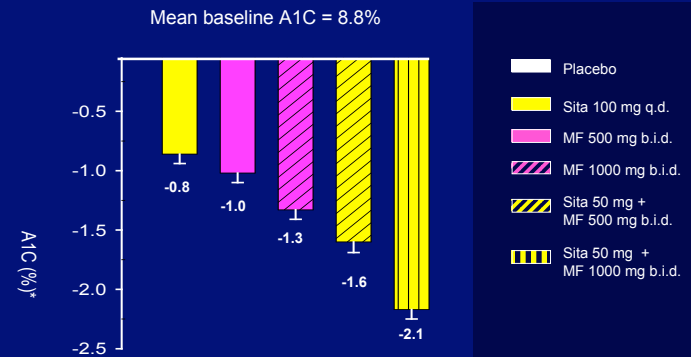
6

Sitagliptin shows Comparable Glycemic Efficacy to Glipizide when added to Metformin (52 weeks)



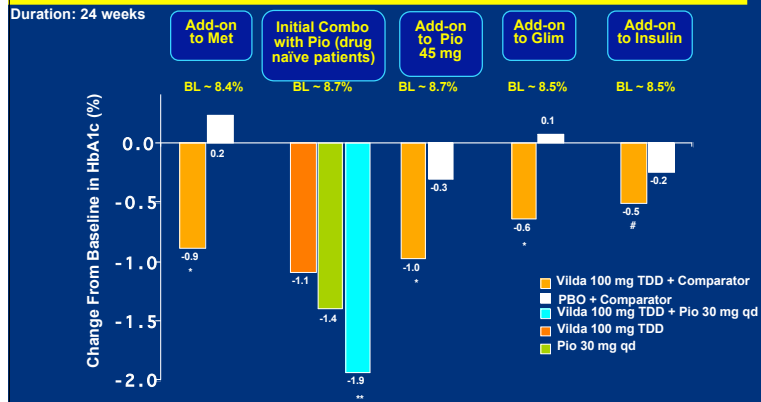
Presented at ADA 2006

Improvements in A1C with Initial Co-administration of Sitagliptin and Metformin



*Placebo-subtracted LS mean change from baseline at Week 24

Vildagliptin: Clinically Relevant Efficacy



Vilda=vildagliptin, Met=metformin, SU=sulfonylurea, Pio=Pioglitazone PBO=placebo, Primary efficacy ITT population
 * P<0.001, # P=0.022 (vs PBO), ** P<0.001 vs Pio 30 mg qd
 Dose regimen in 2355 is 100 mg qd, and 50 mg bid in 2303, 2304, 2305, 2311
 Diabetes 2006;55(S1):A121-A467. Nathwani A. Late-Breaking Trials 66th Scientific Sessions ADA 2006

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Summary of clinical trials with gliptins

Gliptin monotherapy:

- Substantially improved glycemic control A_{1c} , FPG, and PPG
 - Greater proportion achieved A_{1c} targets
 - Greater A_{1c} reductions with higher baseline A_{1c}
 - Improved β -cell function
- Demonstrated overall safety and tolerability similar to placebo
 - Slightly higher incidence of mild GI AEs
 - Low incidence of hypoglycemia, similar to placebo
 - No change in body weight relative to baseline