The Depth Understanding of TECOS Trial of Sitagliptin

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TECOS : Primary Objective

To assess the long-term **CV safety** of adding sitagliptin to usual care, as compared with usual care alone, in patients with type 2 diabetes and established CV disease

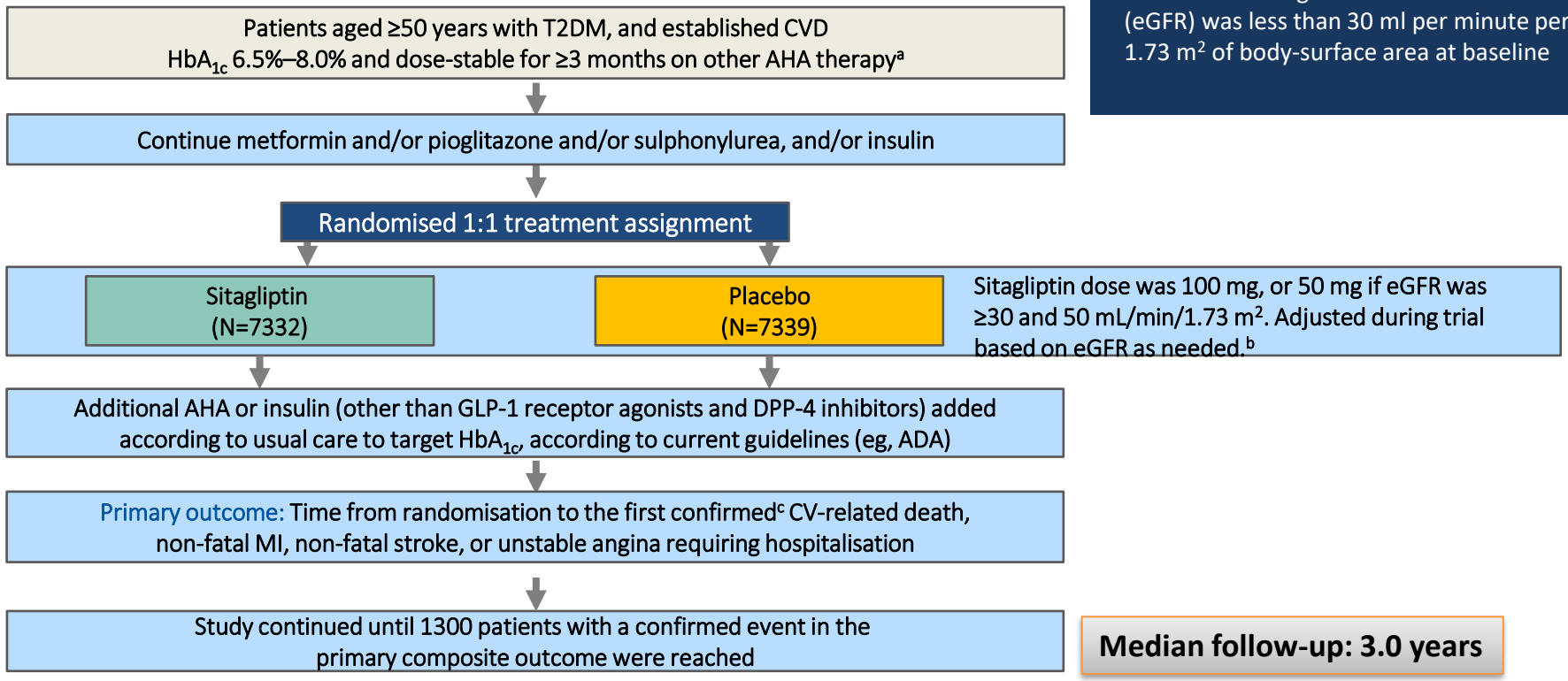
Usual care defined as care provided by patient's physicians based on local and institutional practice and regional guidelines, and included continuation of existing therapy at baseline and adjustment of open-label therapy as required during study

1. Green JB et al. *N Engl J Med*. 2015;373:232–242.

CV = cardiovascular

Design

Excluded if they had taken a:
- DPP-4 inhibitor
- Glucagon-like peptide-1 receptor agonist
- Thiazolidinedione (other than pioglitazone) during the preceding 3 months
- Two or more episodes of severe hypoglycemia (during the preceding 12 months)
- If the estimated glomerular filtration rate (eGFR) was less than 30 ml per minute per 1.73 m^2 of body-surface area at baseline



[a]Monotherapy or dual therapy with metformin, sulfonylurea, or pioglitazone, or insulin alone or in combination with metformin.

[b]If eGFR is ≥50 mL/min/1.73 m^2, dose of sitagliptin or placebo will be 100 mg/day; if eGFR is 30 to <50 mL/min/1.73 m^2 at screening, dose of sitagliptin or placebo will be 50 mg/day; if eGFR is <30 mL/min/1.73 m^2 during the study, dose will be reduced to 25 mg/day. [c]CV events were adjudicated by an independent committee, blinded to study therapy.

ADA = American Diabetes Association; AHA = antihyperglycaemic agent; CV = cardiovascular; CVD = cardiovascular disease; DPP-4 = dipeptidyl peptidase-4; eGFR = estimated glomerular filtration rate; GLP-1 = glucagon-like peptide-1; T2DM = type 2 diabetes mellitus; TECOS = Trial Evaluating Cardiovascular Outcomes With Sitagliptin

1.Adapted from Green JB et al. *N Engl J Med*. 2015;373:232–242.

Primary composite[1]

First confirmed event of

- Cardiovascular death
- Nonfatal myocardial infarction
- Nonfatal stroke
- Hospitalisation for unstable angina
- *Cardiovascular death*
- *Nonfatal myocardial infarction*
- *Nonfatal stroke*

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Table 1. Rates of Composite Cardiovascular Outcomes and Key Secondary Outcomes.

Outcome	Sitagliptin		Placebo		Hazard Ratio (95% CI)	P Value
	no. (%)	*no. per 100 person-yr*	*no. (%)*	*no. per 100 person-yr*		
Per-protocol analysis						
No. of patients in analysis	7257		7266			
Cardiovascular outcome						
Cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina: primary composite outcome	695 (9.6)	3.73	695 (9.6)	3.82	0.98 (0.88–1.09)	<0.001*
Cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke: secondary composite outcome	609 (8.4)	3.24	602 (8.3)	3.28	0.99 (0.89–1.11)	<0.001*
Noncardiovascular outcome						
Acute pancreatitis	20 (0.3)	0.10	11 (0.2)	0.06	1.80 (0.86–3.76)	0.12
Charter-defined cancer	248 (3.4)	1.30	260 (3.6)	1.40	0.93 (0.78–1.10)	0.38
Pancreatic cancer	9 (0.1)	0.05	10 (0.1)	0.05	0.91 (0.37–2.25)	0.85
Severe hypoglycemia	144 (2.0)	0.77	125 (1.7)	0.68	1.13 (0.89–1.44)	0.31

PER PROTOCOL ANALYSIS

Sitagliptin was noninferior to placebo for cardiovascular outcomes

✓ Primary: 0.98 (0.88-1.09); *P*<0.001

1. Adapted from Green JB et al. *N Engl J Med*. 2015;373:232–242.

TECOS Key Summary[1]

The TECOS CV Safety Trial showed that treatment with sitagliptin did not increase the risk of major CV events in patients with type 2 diabetes and established CV disease

- ✓ No increase in risk of all-cause mortality, CV death, or non-CV death
- ✓ No increase in risk of hospitalisation for heart failure

HR: Hazard Ratio

1. Green JB et al. *N Engl J Med*. 2015;373:232–242.