Efficacy and safety of imeglimin in combination with insulin in Japanese patients with type 2 diabetes: results of TIMES 3 trial (Phase 3)

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BACKGROUND

Imeglimin is the first in a new tetrahydrotriazine-containing class of oral antidiabetic agents referred to as “glimins”.

Imeglimin ameliorates the two key defects in type 2 diabetes mellitus (T2DM) improving both:

- insulin secretion in response to glucose
- insulin sensitivity, through a unique mechanism of action targeting mitochondria.

AIMS

To confirm the efficacy and safety of imeglimin 1000 mg orally twice daily versus placebo in combination with insulin in Japanese T2DM patients inadequately controlled by insulin monotherapy.

MATERIAL AND METHODS

Phase 3 randomised, multicenter, double-blind, placebo-controlled trial.

Randomisation in 2 groups and stratification on:

- ✓ Baseline HbA1c
- ✓ Previous antidiabetic treatment status (insulin monotherapy / insulin in combination with one oral hypoglycemic agent)

Insulin therapy fixed during the 16-week double-blind treatment period.

Inclusion criteria:

✓ Japanese T2DM patients with inadequate glycemic control on insulin monotherapy or on insulin in combination with one oral hypoglycemic agent

✓ Age ≥ 20 years

✓ BMI ≥ 18.5 kg/m^2

✓ eGFR (MDRD) ≥ 60 mL/min/1.73m^2

✓ Insulin daily dose ≥ 8 to ≤ 40 UI/day, stable during the 12 weeks prior to randomization

ENDPOINTS

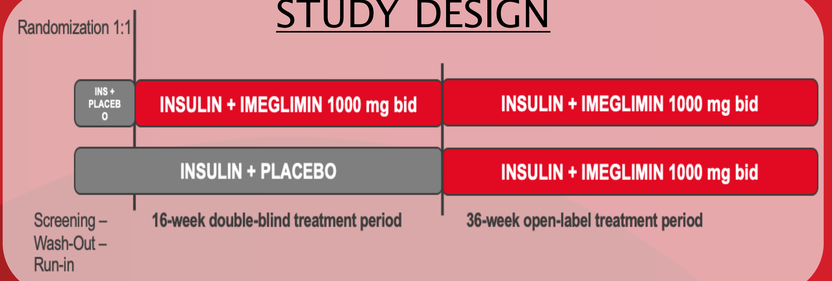
Primary efficacy endpoint: Placebo-adjusted dose-dependent reduction in HbA1c from baseline after 16 weeks of treatment

Secondary endpoints:

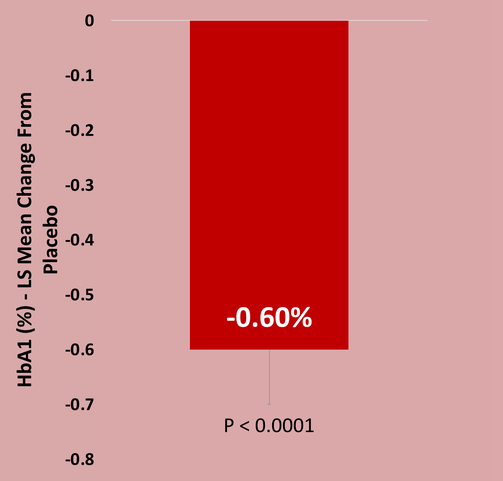
✓ HbA1c change from baseline after 52 weeks of treatment

✓ Safety and tolerability

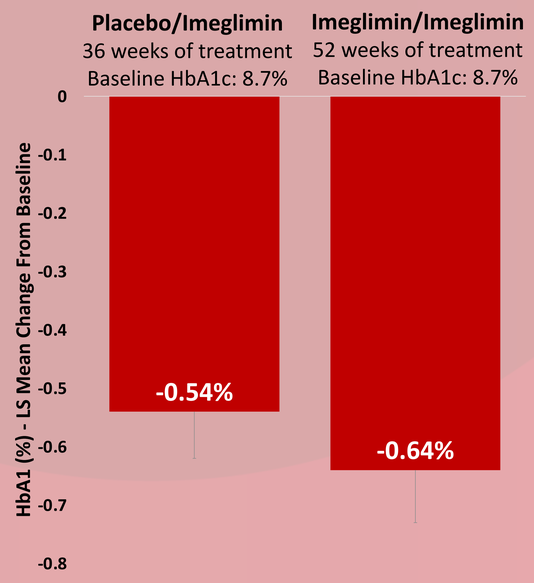
STUDY DESIGN



PRIMARY ENDPOINT MET



HbA1c AFTER 52 WEEKS



BASELINE CHARACTERISTICS

	Imeglimin 1000 mg bid + insulin	Placebo bid + insulin
N of patients	108	107
Age (years)	59.3 (10.5)	57.6 (10.1)
Males, n (%)	66 (61.1%)	69 (64.5%)
T2D duration; years	13.26 (8.15)	13.37 (7.40)
HbA1c (%)	8.7 (0.7)	8.8 (0.8)
FPG (mg/dL)	153.0 (37.7)	146.8 (37.9)
Insulin monotherapy, n (%)	87 (80.6%)	86 (80.4%)
Basal insulin therapy, n (%)	73 (67.6%)	78 (72.9%)
Insulin daily dose (IU/day)	20.5 (10.0)	22.2 (9.8)
BMI (kg/m2)	25.2 (3.6)	24.9 (3.5)

Data are expressed in mean (SD) unless otherwise specified

SAFETY - Double-Blind Period

	Imeglimin 1000 mg bid + insulin	Placebo bid + insulin
N of patients	108	107
Any TEAE	57 (52.8%)	51 (47.7%)
Drug related TEAEs	16 (14.8%)	13 (12.1%)
Serious TEAEs	1 (0.9%)	4 (3.7%)
Serious drug related TEAEs	0	1 (0.9%)
Any hypoglycemia	23 (21.3%)	17 (15.9%)
Severe Hypoglycemia	0	0
TEAE leading to discontinuation	1 (0.9%)	3 (2.8%)

Data are expressed as N(%)

CONCLUSIONS

Imeglimin, in combination with insulin therapy in Japanese patients with type 2 diabetes was well tolerated and led to clinically meaningful and sustained improvements in glycemic control.

Imeglimin did not significantly increase the number of patients with hypoglycemia and no events of severe hypoglycemia were reported.