Long-term treatment with imeglimin as add-on to oral antidiabetes therapy in Japanese patients with type 2 diabetes (TIMES 2) (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 assess the long-term safety and efficacy of imeglimin for 52 weeks as add-on to other individual oral antidiabetic therapies in Japanese patients with T2DM.

MATERIAL AND METHODS

This was an open-label, multicenter, Phase 3 study.

Japanese patients treated with one of the following therapies for more than 12 weeks received imeglimin 1000 mg orally twice daily as add-on therapy for 52 weeks:

- Alpha glucosidase inhibitor (AGI)
- Biguanide (BIG)
- Dipeptidyl peptidase-4 inhibitor (DDP4-I)
- Glinide (GLIN)
- Sodium glucose cotransporter 2 inhibitor (SGLT2-I)
- Sulphonylurea (SU)
- Thiazolidinedione (TZD)

Inclusion criteria:

✓ Age ≥ 20 years
✓ BMI ≥ 18.5 kg/m^2
✓ eGFR (MDRD) ≥ 60 mL/min/1.73m^2
✓ HbA1c ≥ 7.5% and < 10.5%

ENDPOINTS

Primary endpoint: safety and tolerability

Secondary endpoints at 52 weeks:

- HbA1c
- FPG

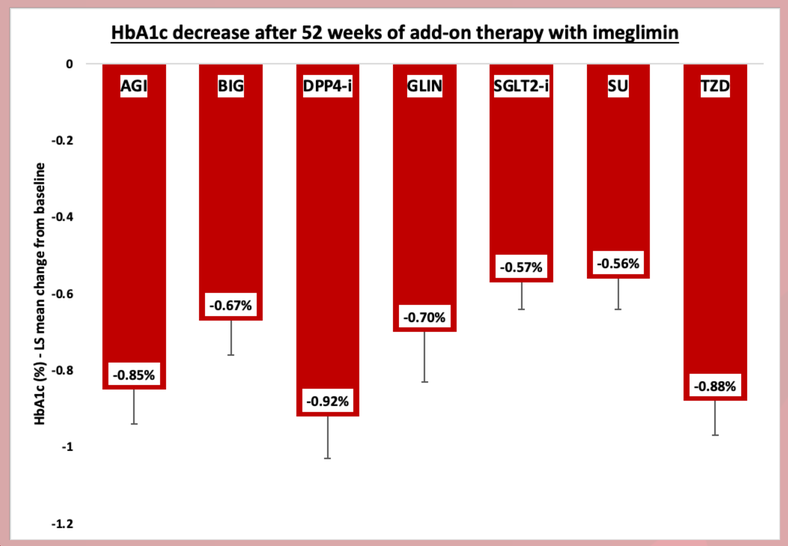
BASELINE CHARACTERISTICS

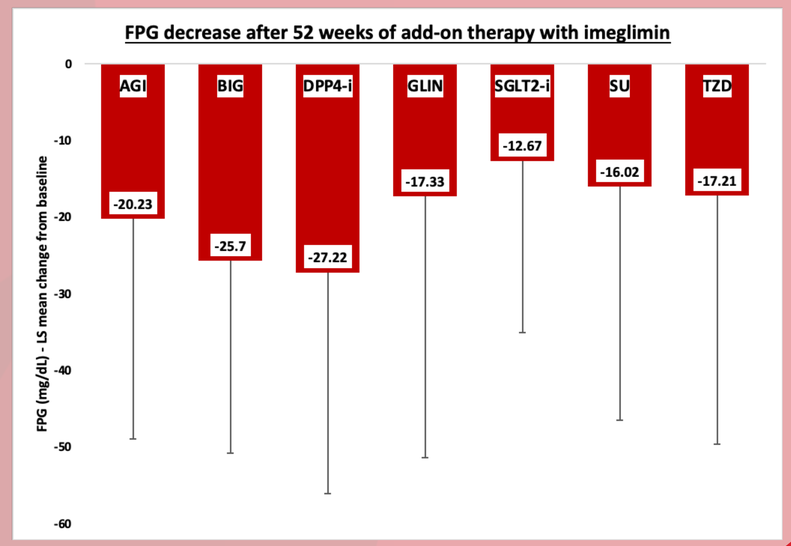
	AGI	BIG	DDP4-I	GLIN	SGLT2-I	SU	TZD
N of patients	64	64	63	64	63	127	65
Age (years) Mean (SD)	56.6 (12.01)	57.6 (10.83)	63.6 (8.95)	58.1 (10.81)	57.1 (10.04)	60.3 (10.38)	57.1 (10.72)
Males N - %	48 75.0%	46 71.9%	39 61.9%	43 67.2%	45 71.4%	101 79.5%	54 83.1%
BMI (kg/m2) Mean (SD)	26.4 (4.6)	26.3 (3.7)	24.6 (3.4)	25.3 (4.6)	26.5 (4.4)	25.6 (4.2)	27.2 (4.4)
T2DM duration Mean (SD)	7.5 (6.8)	9.0 (6.3)	8.0 (5.6)	7.9 (4.9)	9.6 (5.7)	10.6 (6.6)	9.3 (6.6)
FPG (mg/dL) Mean (SD)	174 (31)	175 (31)	180 (33)	180 (34)	166 (28)	185 (38)	171 (32)
HbA1c (%) Mean (SD)	8.37 (0.77)	8.16 (0.61)	8.23 (0.75)	8.48 (0.84)	8.50 (0.75)	8.63 (0.90)	8.72 (0.94)

SAFETY AND TOLERABILITY

	AGI	BIG	DDP4-I	GLIN	SGLT2-I	SU	TZD
N of patients	64	64	63	64	63	127	65
Any TEAEs N (%)	33 51.6%	48 75.0%	50 79.4%	54 84.4%	48 76.2%	102 80.3%	50 76.9%
Mild	32	45	50	53	47	100	48
Moderate	4	4	8	5	4	15	12
Severe	1	4	1	0	1	5	1
Drug related TEAEs, N (%)	6 9.4%	24 37.5%	14 22.2%	10 15.6%	7 11.1%	27 21.3%	6 9.2%
Serious TEAEs N (%)	4 6.3%	4 6.3%	3 4.8%	1 1.6%	4 6.3%	11 8.7%	4 6.2%
Serious drug related TEAEs	0	0	0	0	0	0	0
Severe Hypoglycemia	0	0	0	0	0	0	0
TEAE leading to discontinuation	2 3.1%	7 10.9%	5 7.9%	1 1.6%	1 1.6%	9 7.1%	4 6.2%

EFFICACY PROFILE AFTER 52 WEEKS OF TREATMENT





CONCLUSIONS

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