Real-world outcomes for the Safety of SGLT2 Inhibitor Luseogliflozin in Elderly Patients with Type 2 Diabetes Mellitus

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Background and Aims

- Sodium glucose co-transporter-2 (SGLT2) inhibitors have been developed recently as a new class of anti-diabetic drug, and have been widely used in the management of type 2 diabetes (T2D) worldwide. As glucose-lowering mechanisms of SGLT2 inhibitors are considerably different from those of other previously available anti-diabetic drugs, safe use of this drug class needs to be evaluated based on data available in real-world studies.
- In particular, safety of SGLT2 inhibitors among elderly patients with T2D need to be investigated as they are more vulnerable to potential adverse drug reactions (ADRs), and physiological functional capacity declines with age.
- The aim of this study was to evaluate of safety of luseogliflozin in a real-world clinical setting for elderly patients with T2D by conducting a post-marketing surveillance (PMS).

Methods

Patients and treatment

- T2D patients aged ≥65 years who started luseogliflozin treatment within 3 months after its launch (between 23 May 2014 and 31 Aug 2014) were included in this surveillance. The observation period was 1-year from the first luseogliflozin treatment.

Survey design

- Survey items included demographics, treatment, ADRs, vital signs, and laboratory variables.
- Each cohorts for safety and efficacy analysis included 1262 and 1249 patients.

Results

Table 1. Demographics and baseline characteristics

	n=1262	Number of concomitant anti-diabetic drug		Type of concomitant anti-diabetic drug	
Male, n(%)	621 (49.2)	0	281 (22.3)	DPP-4 inhibitor	695 (55.1)
Age, years	73.0 ± 6.5	1 drug	437 (34.6)	Sulfonylurea	327 (25.9)
Duration, years	10.2 ± 7.4	2 drugs	315 (25.0)	Biguanide	280 (22.2)
HbA1c, %	7.63 ± 1.32	over 3 drugs	229 (18.1)	α-Glucosidase inhibitor	130 (10.3)
Body weight, kg	65.7 ± 12.6	n (%)		Thiazolidine	107 (8.5)
BMI, kg/m ²	26.2 ± 4.4			Insulin	98 (7.8)
eGFR, mL/min/1.73m ²	67.6 ± 19.6			Fast-acting insulin secretagogue	37 (2.9)
	Mean ± S.D.			GLP-1 receptor agonist	18 (1.4)
				n (%)	

Table 2. Summary of ADRs: comparison between at-preapproval and PMS

	At-approval		PMS
	All ages (n = 1262)	≥65 years (n = 454)	≥65 years (n = 1262)
Any ADRs	236 (18.7)	99 (21.8)	169 (13.39)
Events related to body fluid volume reduction	20 (1.6)	4 (0.9)	28 (2.22)
Genital infection	24 (1.9)	11 (2.4)	9 (0.71)
Urinary tract infection	41 (3.2)	20 (4.4)	22 (1.74)
Hypoglycemia	31 (2.5)	16 (3.5)	4 (0.32)
Polyuria / Urinary frequency	39 (3.1)	3 (0.7)	21 (1.66)
Skin disease	10 (0.8)	4 (0.9)	31 (2.46)
Ketone body-related events	38 (3.0)	7 (1.5)	3 (0.24)
	n (%)		

- There was no ADRs about lower limb amputation and bone fracture in PMS.
- Luseogliflozin has a favorable safety profile in both preapproval clinical trials and PMS in elderly patients.

Figure 1. Time-Course of HbA1c

Figure 2. Time-Course of FPG

Figure 3. Time-Course of Body Weight

Figure 5. Time-Course of eGFR in PMS

Figure 4. Timing of occurrence for ADRs after luseogliflozin administration

Table 3. Factors associated with the incidence of ADRs of special interest in PMS

	No. of evaluable patients	Events related to body fluid volume reduction*	Genital infection	Urinary tract infection	Hypoglycemia	Polyuria/Urinary frequency	Skin disease	Ketone body-related events
Sex								
Male	621	11 (1.77)	2 (0.32)	3 (0.48)	0 (0.00)	13 (2.09)	17 (2.74)	2 (0.32)
Female	641	17 (2.65)	7 (1.09)	19 (2.96)	4 (0.62)	8 (1.25)	14 (2.18)	1 (0.16)
Age, years								
≥65 to <75	808	15 (1.86)	4 (0.50)	17 (2.10)	3 (0.37)	11 (1.36)	17 (2.10)	2 (0.25)
≥75	454	13 (2.86)	5 (1.10)	5 (1.10)	1 (0.22)	10 (2.20)	14 (3.08)	1 (0.22)
BMI, kg/m ²								
<18.5	18	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (5.56)	0 (0.00)
≥18.5 to <22.0	132	4 (3.03)	0 (0.00)	0 (0.00)	2 (1.52)	3 (2.27)	7 (5.30)	1 (0.76)
≥22.0 to <25.0	238	4 (1.68)	2 (0.84)	7 (2.94)	1 (0.42)	5 (2.10)	8 (3.36)	0 (0.00)
≥25.0	563	13 (2.31)	4 (0.71)	8 (1.42)	1 (0.18)	12 (2.13)	11 (1.95)	2 (0.36)
eGFR, mL/min/1.73m ²								
<30	10	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
≥30 to <45	57	0 (0.00)	0 (0.00)	1 (1.75)	0 (0.00)	1 (1.75)	4 (7.02)	0 (0.00)
≥45 to <60	208	8 (3.85)	1 (0.48)	5 (2.40)	1 (0.48)	5 (2.40)	5 (2.40)	0 (0.00)
≥60 to <90	439	5 (1.14)	5 (1.14)	7 (1.59)	3 (0.68)	4 (0.91)	9 (2.05)	3 (0.68)
≥90	87	4 (4.60)	1 (1.15)	0 (0.00)	0 (0.00)	4 (4.60)	2 (2.30)	0 (0.00)

* Acute myocardial infarction, Thirst, Hematocrit increased, Hemoglobin increased, Red blood cell count increased, Dehydration, Cerebral infarction, Hypotension, Blood urea increased, Myocardial infarction, Acute prerenal failure, Blood pressure decreased, Blood uric acid increased

- Even though the patients with low BMI (i.e. BMI <22.0kg/m²) or renal dysfunction (i.e. eGFR <45 mL/min/1.73m²), the frequency of ADRs of special interest were not increased.

Conclusions

- HbA1c, FPG and body weight were decreased significantly after luseogliflozin treatment in real-world outcomes as well as in preapproval clinical trials.
- No safety concerns requiring a new precaution were obtained from PMS in Japanese elderly T2D patients.
- The SGLT2 inhibitor luseogliflozin has a favorable safety profile in real-world outcomes as well as in preapproval clinical trials.
- No significant change was observed in eGFR after introduction of luseogliflozin treatment in any subgroup of patients stratified according to eGFR at the time of the first luseogliflozin treatment.