

## Consistency Between Network Meta-Analysis and Real-World Data Analysis: Comparison of Changes in Hemoglobin A1c Levels After Treatment by Oral Antidiabetics in Japanese Patients with Type 2 Diabetes

Nakamura M<sup>1</sup>, Mizoroki K<sup>1</sup>, Iwasaki K<sup>2</sup>, Takeshima T<sup>2</sup>, Ha C<sup>2</sup>, Chida A<sup>2</sup>

<sup>1</sup>Medical Data Vision Co., Ltd, Tokyo, Japan, <sup>2</sup>Milliman, Inc., Tokyo, Japan

### OBJECTIVES

- There are two methodologies for the indirect comparisons: Network meta-analysis (NMA) with systematic review of randomized controlled trials and Real-world data analysis (RWDA).
- They have their pros and cons. NMA may lack external validity, where RWDA may lack internal validity.
- We examined the consistency of results between them. We chose a published NMA study. Then we did a RWDA using the same methodology and compared the two results.

### METHODS

- We chose a NMA study, Nishimura 2022, which compared the outcome, change in hemoglobin (Hb) A1c after  $\geq 12$ -week treatment, between metformin 1500 mg/day and the other oral antidiabetics.
- We analyzed a clinical database provided by Medical Data Vision Co., Ltd.(Tokyo, Japan). Eligibility criteria for the analysis was the same as the NMA study: adult patients with type 2 diabetes who remained first-line treatment (combinations of drug types and dosages) for  $\geq 90$  days and had HbA1c data to assess the outcome. Treatments used for  $>100$  patients were compared to the outcome with metformin 1500 mg/day.
- The MDV database is derived from hospitals accredited as providing acute care services in Japan and participating in the Diagnostic Procedure Combination / Per-Diem bundled payment system (termed DPC hospitals). As of April 1, 2023, the MDV database included anonymized data from 475 contracted hospitals, representing 27% of the 1,761 DPC hospitals in Japan.

### RESULTS

- Of 105,096 patients who used any treatment assessed in the NMA and had  $\geq 1$  HbA1c data, 19,850 remained on the same treatment for  $\geq 90$  days and 11,096 had HbA1c data to assess the outcome (Table 1).
- Of the 36 treatment types, other than metformin 1500 mg/day, in the NMA, 13 types had  $>100$  patients. Metformin 1500 mg/day decreased HbA1c greater than all the 13 types in both NMA and RWD analyses (Table 2).
- The second largest decrease of HbA1c was shown in metformin 750 mg/day followed by vildagliptin 100 mg/day in the RWD analysis, whereas it was canagliflozin 100 mg/day followed by vildagliptin 100 mg/day and tofogliflozin 20 mg/day in the NMA (Table 2).

### CONCLUSIONS

- The largest effect was observed for metformin 1500 mg/day in both analyses
- Both studies appear to be roughly consistent. The reasons for the differences will be investigated.
- Differences in other patient characteristics could be contributing to the outcomes which we have not examined.

### REFERENCE

- Nishimura R, Taniguchi M, Takeshima T, Iwasaki K. Efficacy and Safety of Metformin Versus the Other Oral Antidiabetic Drugs in Japanese Type 2 Diabetes Patients: A Network Meta-analysis. Adv Ther. 2022 Jan;39(1):632-654. doi: 10.1007/s12325-021-01979-1. Epub 2021 Nov 30. PMID: 34846709; PMCID: PMC8799586.

	N
Having T2DM fixed diagnosis and at least one A1C (anytime)	276,957
Initial T2DM diagnosis dates were within observation periods	190,182
Having no T1DM fixed diagnosis	186,447
Having no OAD before Initial T2DM diagnosis	177,136
Having prescription of single OAD after initial T2DM diagnosis (=index)	105,096
Having no OAD before index	47,634
Age 20+ as of index	47,517
Having 90+ days of OAD script after index date	22,454
Having no OAD other than index within 90 days after index	19,850
Having A1c within 30 days before index (=baseline A1c)	13,050
Having A1C between 90 and 120 days after index (=outcome A1c)	11,096

**Table 1: Cascade chart for the patients selected for the analysis**

276,954 patients having at least one T2DM fixed diagnosis and at least one A1c value as laboratory test data at anytime in the MDV dataset. 11,096 patients were identified with criteria for this analysis

T2DM: Type 2 Diabetes Mellitus; A1c: hemoglobin A1C; OAD: Oral Antidiabetic Drug

	RWDA				NMA	
	N	$\Delta$ A1c	$\Delta$	P	$\Delta$	P
Alogliptin 25mg/day	469	-1.19	0.47	0.000	0.47	0.007
Canagliflozin 100mg/day	195	-0.82	0.84	0.000	0.28	0.066
Dapagliflozin 10mg/day	422	-0.13	1.53	0.000	0.92	0.000
Dapagliflozin 5mg/day	434	-0.59	1.07	0.000	0.96	0.000
Empagliflozin 10mg/day	781	-0.77	0.89	0.000	0.59	0.000
Linagliptin 5mg/day	2,143	-0.84	0.82	0.000	0.60	0.001
Metformin 1500mg/day	58	-1.66	n/a	n/a	n/a	n/a
Metformin 750mg/day	322	-1.51	0.15	0.000	0.40	0.000
Pioglitazone 15mg/day	128	-0.59	1.08	0.000	0.46	0.036
Saxagliptin 5mg/day	103	-0.97	0.69	0.000	0.49	0.007
Sitagliptin 50mg/day	2,265	-0.99	0.67	0.000	0.46	0.004
Teneligliptin 20mg/day	1,098	-0.92	0.74	0.000	0.50	0.002
Tofogliflozin 20mg/day	150	-1.03	0.63	0.000	0.32	0.052
Vildagliptin 100mg/day	463	-1.22	0.44	0.000	0.32	0.041

**Table 2: Comparison of the outcomes of RWDA and NMA**

Both studies appear to be roughly consistent in the colors of  $\Delta$  in the two analyses.

$\Delta$  and P of NMA are in Nishimura 2021

$\Delta$  and P of Metformin 1500mg/day were not available because it is the comparison.

RWDA: Real World Data Analysis; NMA: Network Meta-Analysis;  $\Delta$ A1c=outcome A1c – baseline A1c;  $\Delta$ =  $\Delta$ A1c of each drug –  $\Delta$ A1c of Metformin 1500mg/day; P: p-value against the null hypothesis that  $\Delta=0$ .