Elevating the role of basal insulin therapy in T2D management: From CGM use to fixed-ratio combinations and once-weekly regimens

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions*
- *The presenting faculty have been advised by USF Health and touchIME to ensure that they disclose any such references made to unlabelled or unapproved use*
- *No endorsement by USF Health and touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in USF Health and touchIME activities*
- *USF Health and touchIME accept no responsibility for errors or omissions*

A conversation between:

Dr Alice YY Cheng
Endocrinologist
Trillium Health Partners & Unity Health
Toronto, ON, Canada

Dr Viswanathan Mohan
Endocrinologist
Dr Mohan's Diabetes Specialities Centre
Chennai, India

touch™ ENDOCRINOLOGY

Agenda

Why is timely initiation of basal insulin treatment important, and how can the barriers to insulin intensification in T2D be overcome?

What is the role of continuous glucose monitoring and time-in-range in optimizing outcomes in patients with T2D on basal insulin?

What is the clinical evidence for once-weekly insulins in T2D, and what are the practicalities of their use?

T2D, type 2 diabetes.

Why is timely initiation of basal insulin treatment important, and how can the barriers to insulin intensification in T2D be overcome?

Dr Alice YY Cheng

Trillium Health Partners & Unity Health
Toronto, ON, Canada

touch™ ENDOCRINOLOGY

Timely initiation of basal insulin in T2D is important to improve long-term clinical outcomes[1]

Treatment intensification with insulin is recommended in people living with T2D who do not meet glycaemic targets with non-insulin glucose-lowering agents[1,2]

Delayed initiation of basal insulin

Chronic hyperglycaemia[3]

- Microvascular complications, e.g. retinopathy, nephropathy, neuropathy and lower extremity amputation[4,5]
- Macrovascular complications, e.g. coronary heart disease, stroke and peripheral vascular disease[4,5]
- Reduced QoL and psychological wellbeing[4,6]

Increased risk of early mortality[1,6]

Once macrovascular complications occur, they cannot be reversed by tighter glucose control[7]

QoL, quality of life; T2D, type 2 diabetes.

1. Khunti K, et al. *Diabetes Obes Metab*. 2020;22:722–33; 2. Davies MJ, et al. *Diabetes Care*. 2022;45:2753–86; 3. Zografou I, et al. *Hippokratia.* 2014;18:306–9; 4. Martinez M, et al. *BMJ Open Diab Res Care*. 2021;9:e002032; 5. Harding JL, et al. *Diabetologica*. 2019;62:3–16; 6. Kim SG, et al. *J Diabetes Investig*. 2017;8:346–53; 7. Lovre D, Fonseca V. *J Diabetes Complications*. 2015;29:295–301.

touch™ ENDOCRINOLOGY

Initiation of insulin therapy is often delayed[1]

Clinical inertia[2]

The failure to initiate or intensify therapy according to the guidelines

A systematic literature review found that **clinical inertia was reported in >50%** of people living with T2D in most studies (range 18.1–85.8%)

Barriers to daily basal insulin initiation

- Injection burden[3]
- Social stigma[4]
- Complex dosing schedules[3]
- Fear of weight gain[3,4]
- Difficult administration[4]
- Fear of hypoglycaemia[3–5]
- Local injection site reactions[5]
- Anticipation of pain[5]
- Lack of healthcare provider time or resources[3]

T2D, type 2 diabetes.

1. Harris S, Seidu S. *Prim Care Diabetes*. 2023;17:535–47; 2. Almigbal TH, et al. *Medicina (Kaunas)*. 2023;59:182; 3. Khunti K, et al. *Diabetes Obes Metab*. 2020;22:722–33; 4. Alhagawy AJ, et al. *Int J Environ Res Public Health*. 2022;19:16794; 5. Mohan V, et al. *Endocr Metab Sci*. 2021;4:100103.

touch™ ENDOCRINOLOGY

What is the role of continuous glucose monitoring and time-in-range in optimizing outcomes in patients with T2D on basal insulin?

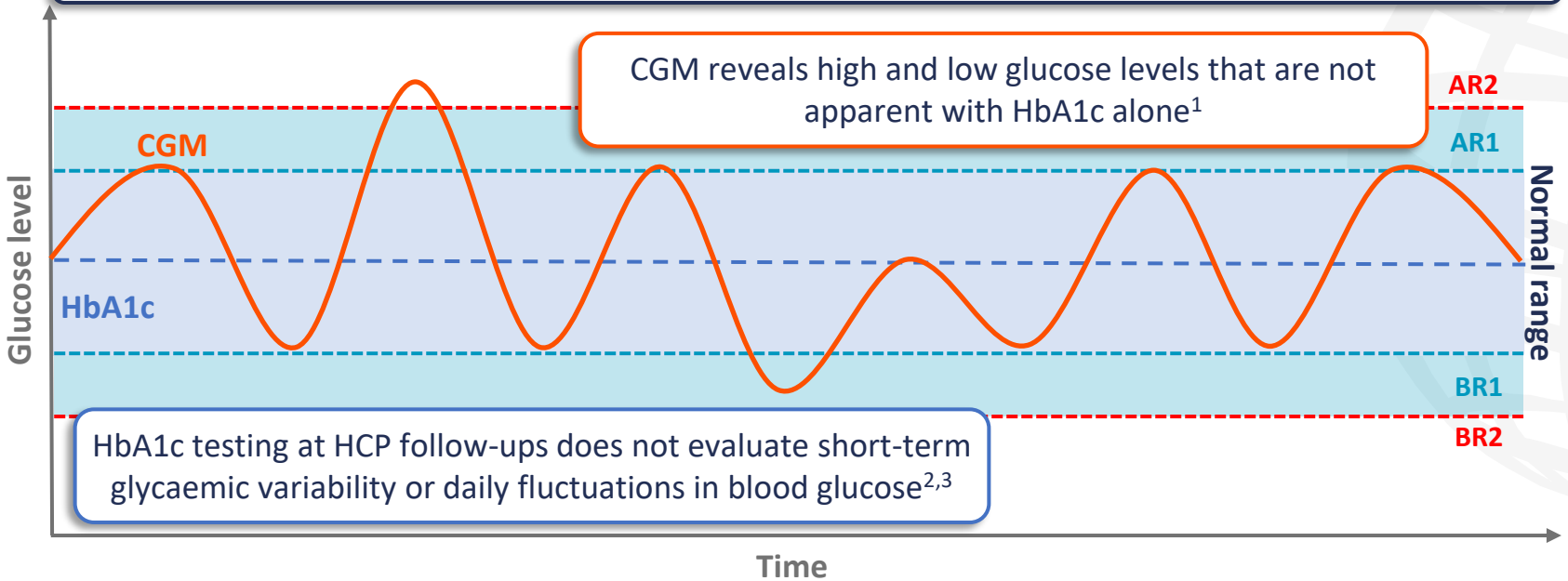
Alice YY Cheng

Trillium Health Partners & Unity Health
Toronto, ON, Canada

touch™ ENDOCRINOLOGY

CGM provides a comprehensive assessment of an individual's glucose profile[1]

CGM uses a subcutaneous sensor to measure interstitial glucose concentrations every few minutes[1]



AR, above range; BR, below range; CGM, continuous glucose monitoring; HbA1c, glycated haemoglobin; HCP, healthcare professional.

1. Kushner PR, Kruger DF. *Clin Diabetes*. 2020;38:348–56; 2. Martinez M, et al. *BMJ Open Diab Res Care.* 2021;9:e002032;
3. Eyth E, Naik R. 2023. Available at: www.ncbi.nlm.nih.gov/books/NBK549816/ (accessed 23 February 2024).

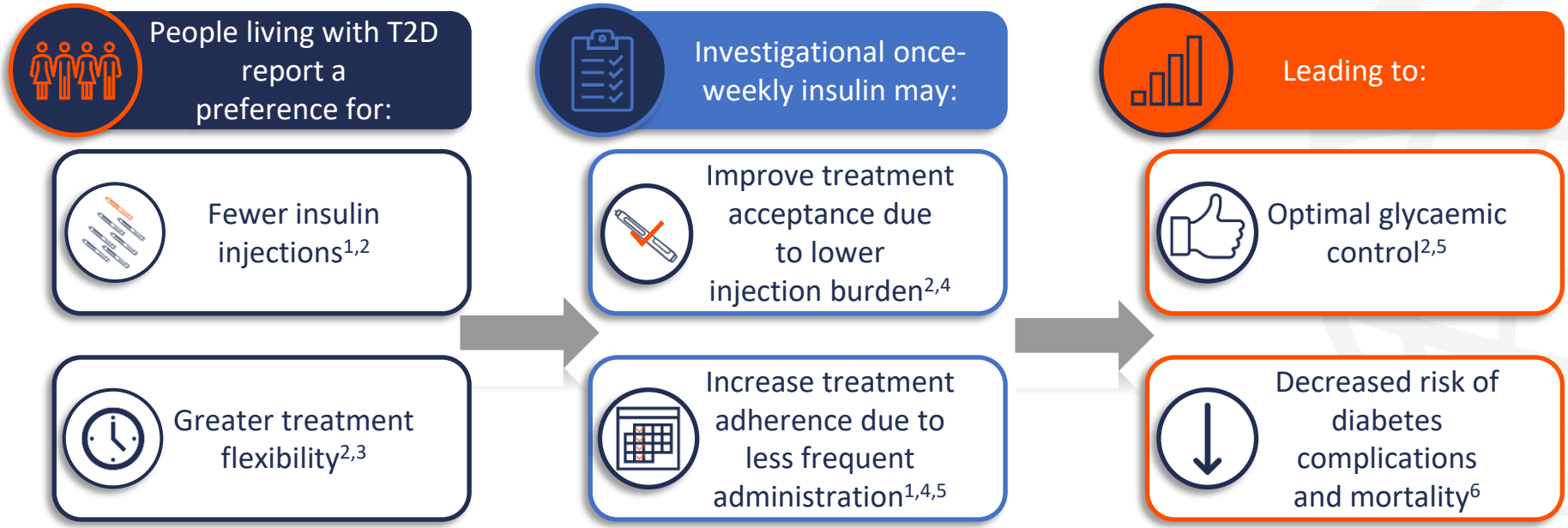
What is the clinical evidence for once-weekly insulins in T2D, and what are the practicalities of their use?

Alice YY Cheng

Trillium Health Partners & Unity Health
Toronto, ON, Canada

touch™ ENDOCRINOLOGY

Investigational once-weekly insulins may help meet an unmet treatment need in T2D



T2D, type 2 diabetes.

1. Polonsky WH, et al. *Diabetes Obes Metab*. 2011;13:144–9; 2. Rosenstock J, et al. *N Engl J Med*. 2020;383:2107–16; 3. Peyrot M, et al. *Diabet Med*. 2012;29:682–9; 4. Wang PW, et al. *Diabetol Metab Syndr*. 2024;16:3; 5. Polonsky WH, et al. *Diabetes Ther*. 2022;13:175–87; 6. Khunti N, et al. *Br J Diabetes*. 2019;19:99–104.

touch™ ENDOCRINOLOGY

Clinical trial data for once-weekly insulin icodec in T2D

	ONWARDS 1 (N=984)[1]		ONWARDS 3 (N=588)[2]		ONWARDS 2 (N=526)[3]		ONWARDS 4 (N=582)[4]	
	78-week, phase IIIa • Insulin naive		26-week, phase IIIa • Insulin naive		26-week, phase IIIa • On basal insulin (pre-trial)		26-week, phase IIIa • On basal-bolus insulin (pre-trial)	
	Icodec	Glargine	Icodec	Degludec	Icodec	Degludec	Icodec†	Glargine†
Estimated mean change in HbA1c	-1.6%	-1.4%	-1.6%	-1.4%	-0.9%	-0.7%	-1.2%	-1.2%
Rate of level 2 or 3 hypoglycaemia (per PYE)‡	0.3	0.2	0.3	0.2	0.7	0.3	0.8	1.0
Adverse event rate	81%	79%	60%	57%	61%	51%	59%	57%

HbA1c: Non-inferiority and superiority for icodec vs comparator*[1–3]

HbA1c: Non-inferiority for icodec vs glargine[4]

Direct comparisons between trials should not be made due to differences in trial design.

*Non-inferiority and superiority for HbA1c demonstrated for ONWARDS 1, 2 and 3. ONWARDS 1: non-inferiority (p<0.001), superiority (p=0.02);[1] ONWARDS 3: non-inferiority (p<0.001), superiority (p=0.002);[2] ONWARDS 2: non-inferiority (p<0.0001), superiority (p=0.0028);[3] ONWARDS 4: non-inferiority for HbA1c (p<0.0001).[4] †Combined with 2–4 daily bolus aspart injections.[4] ‡Level 2=clinically significant; glucose level <54 mg/dL (3 mmol/L), confirmed by blood glucose meter. Level 3=severe; hypoglycaemia associated with severe cognitive impairment requiring external assistance for recovery. All rates shown were not statistically significant between groups.[1-4] HbA1c, glycated haemoglobin; PYE, patient year of exposure; T2D, type 2 diabetes.

1. Rosenstock J, et al. *N Engl J Med*. 2023;389:297–308; 2. Lingvay I, et al. *JAMA*. 2023;330:228–37; 3. Philis-Tsimikas A, et al. *Lancet Diabetes Endocrinol*. 2023;11:414–25; 4. Mathieu C, et al. *Lancet*. 2023;401:1929–40.

touch™ ENDOCRINOLOGY

Clinical trial data for once-weekly insulin efsitora alfa in T2D

	NCT04450394 (N=278)[1]		NCT03736785 (N=399)[2]	
	26-week, phase II • Insulin naive		32-week, phase II • Insulin ± ≤3 OADs (pre-trial)	
	BIF	Degludec	BIF*	Degludec
Estimated mean change in HbA1c	-1.2%	-1.3%	-0.6%†	-0.7%
Rate of level 2 hypoglycaemia (PPPY)††	0.22	0.15	BIF-A1: 2.2 BIF-A2: 2.4	3.0
TEAE rate	49%‡	44%	62%†	56%

HbA1c: Non-inferiority for BIF vs degludec§[1,2]

Direct comparisons between trials should not be made due to differences in trial design.

*Two fasting glucose targets were used for patients receiving BIF. Fasting glucose targets for BIF-A1 and BIF-A2 were ≤7.8 mmol/L titrated every 2 weeks and ≤6.7 mmol/L titrated every 4 weeks, respectively.[2] †Pooled data.[2] ‡Contained patients from the discontinued digital algorithm (n=135).[1] ††Level 2=clinically significant; glucose level <54 mg/dL (3 mmol/L), confirmed by blood glucose meter. All rates shown were not statistically significant between groups.[1,2] §Non-inferiority margin of 0.4%. Insulin-naive patients vs degludec 0.06%,[1] insulin ± ≤3 OADs BIF pooled data vs degludec 0.1%.[2] BIF, insulin efsitora alfa; HbA1c, glycated haemoglobin; OADs, oral antidiabetes agents; PPPY, per patient per year; T2D, type 2 diabetes; TEAE, treatment-emergent adverse event.

1. Bue-Valleskey JM, et al. *Diabetes Care*. 2023;46:1060–7; 2. Frias J, et al. *Lancet Diabetes Endocrinol*. 2023;11:158–68.

touch™ ENDOCRINOLOGY