

### Evidence Tables

#### INS 4: Are multiple analogue insulin injection regimens effective (meal time and basal insulin) compared to basal insulin or biphasic insulin regimes?

Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect size	Source of funding
Joshi SR et al. Designer Insulins Regimens in Clinical Practice-Pilot Multicentre Indian Study. JAPI Vol. 53, September 2005. Id 28	Cohort study conducted at four diabetes care clinics in India. It collected data on the use of either of the two regimes.  Evidence grading 2+	N= 145	Compiled data of 145 consecutive patients recruited with T2D who were prescribed either of the two regimes between March and August 2004.  Baseline demography was comparable in the two groups as there was no statistically difference in the various parameters including age (premix analogue: 52.4± 10 basal-bolus analogue: 51.1±14); duration of diabetes (premix analogue: 9.5± 5 basal-bolus analogue: 11.9± 9); weight (premix analogue: 70.4± 12 basal-bolus analogue: 69.6± 10); and glycaemic parameters (HbA1c premix analogue: 8.7± 1.1 HbA1c basal-bolus analogue:8.5± 1.2)	Premix insulin analogue given twice-a-day (biphasic insulin aspart 30/70) N=114	Basal-bolus analogue regimen (insulin aspart as the bolus insulin given with every meal and insulin glargine as the basal insulin given once-a-day) N=31	12 weeks	HbA1c FPG PPPG Body weight Insulin dose Adverse events	*HbA1c Both regimes lowered HbA1c significantly as compared to baseline  - Premix analogue: baseline 8.79± 1.13 12-weeks 7.20 ±0.83 - Basal-bolus analogue: baseline 8.53± 1.22 12-weeks 7.37± 0.83  However, premix insulin analogue fared better than the basal-bolus analogue therapy in lowering HbA1c (1.58% vs. 1.16% respectively, p<0.05).  Also 41% more patients in the premix group could achieve target HbA1c of <7% at the end of 12 weeks (45.61% vs. 32.26%)  *FPG Both regimes lowered FPG levels significantly as compared to baseline  - Premix analogue: baseline 186.5± 47.3 12-weeks 114.8± 18.7 - Basal-bolus analogue:	Novo Nordisk

			<p>The two groups were comparable on usage of oral antidiabetic drugs which continued throughout the study for the majority of patients along with both the insulin regimes.</p>					<p>baseline 190.2± 55.3  12-weeks 110.6± 16.8  <i>No statistical comparison between groups</i></p> <p>*PPPG  Both regimes lowered PPPG levels significantly as compared to baseline</p> <p>- Premix analogue:  baseline 287.3± 58.4  12-weeks 171.5± 28.7  - Basal-bolus analogue:  baseline 281.4± 68.8  12-weeks 177.5± 24.7</p> <p><i>No statistical comparison between groups</i></p> <p>*Body weight  The body weight did not change significantly in either group at the end of the study</p> <p>*Insulin dose, units/day</p> <p>- Premix analogue:  baseline 38.2± 11.8  12-weeks 40.2± 16.9</p> <p>- Basal-bolus total daily dose  baseline 57.4± 24.5  12-weeks 52.8± 29.9  - Basal analogue  baseline 23.3± 10.7  12-weeks 24.5± 12.1  -Bolus analogue  baseline 34.1± 17.5</p>	
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								<p>12-weeks 28.3± 23.2 No statistical comparison between groups</p> <p>Adverse events</p> <p>Hypoglycaemia Throughout the study period of 12 weeks, there were no major hypoglycaemic episodes reported in both the treatment groups.</p> <p>The % of patients experiencing a minor hypoglycaemia was significantly lower in the premix group than in the basal-bolus group at 12 weeks (16.7% vs. 58.06%, p&lt;0.05)</p> <p>No other adverse drug reactions were reported in both groups throughout the study period.</p>	
Davies M, Storms F, Shutler S. Initiation of Insulin Glargine in Type 2 patients with suboptimal glycaemic control on twice-daily premix insulin: results from the AT.LANTUS trial ( <b>abstract</b> ). Diabetologia 2004;	Open label – multinational RCT comparing two treatment algorithms* This abstracts	N= 888 <sup>†</sup>	Participants with type 2 diabetes suboptimally controlled on their previous antidiabetic treatment were Included. Inclusion criteria included: age ≥18 years; on antidiabetic treatment	PRIOR BD PREMIX INSULIN  Insulin glargine alone (n=169)	PRIOR BD PREMIX INSULIN + OADs  Insulin glargine + OAD (n=311)	24 weeks	HbA1c Hypoglycaemia	<p><b>PRIOR BD PREMIX INSULIN</b></p> <p><b>Insulin glargine alone</b></p> <p>-Algorithm 1 Baseline: 8.9 ± 1.3 Endpoint: 8.2 ± 1.5</p> <p>-Algorithm 2 Baseline: 8.8 ± 1.3 Endpoint: 8.3 ± 1.3</p>	Sanofi-Aventis

\* Alg 1 was a visit-base titration using 2-8 IU increments (10 IU initiation dose for insulin-naïve). Alg 2 involved patient self-titration of 2 IU every 3 days (first dose was based on FBG for insulin-naïve). The titration was based on target FBG ≤5.5 mmol/l

<sup>†</sup> Sub-population relevant to the INS4 question

<sup>‡</sup> Prandial includes regular and short acting, unless otherwise stated

<p>47(suppl 1):319. Ref ID: 3207</p>	<p>reports change in glycaemic control for the sub-population of patients who changed from twice-daily premix insulin to once-daily insulin glargine alone or with prandial insulin and/or OADs.</p> <p>Evidence grading: N/A</p>		<p>(any oral and/or insulin therapy) for &gt;6 months requiring, in the opinion of the investigating physician, basal long-acting insulin therapy for the control of hyperglycaemia; HbA1c levels &gt;7.0 and &lt;12.0%; BMI values &lt;40 kg/m<sup>2</sup>; and confirmed written informed consent.</p> <p>Subject demographics and baseline characteristics were similar between the two treatment groups (Table 2). Patients had long-standing diabetes, with a mean duration of disease of 12 years and a 5-year mean duration of insulin pre-treatment. It is noteworthy that 72% of patients were insulin pre-treated at inclusion (of these, 40.5% with NPH and 23.2% with premixed insulin).</p>	<p>Insulin glargine + BD prandial (n=89)</p> <p>Insulin glargine+ &gt;BD prandial<sup>†</sup> (n=83)</p> <p>Insulin glargine + OD prandial‡ (n=15)</p>	<p>Insulin glargine + BD prandial<sup>†</sup> + OAD (n=74)</p> <p>Insulin glargine + &gt;BD prandial‡ + OAD (n=78)</p> <p>Insulin glargine + &gt;BD short-acting insulin + OAD (n=43)</p> <p>Insulin glargine + OD prandial‡ + OAD (n=26)</p>			<p>Overall baseline-endpoint difference -0.7 ± 1.6 (p&lt;0.001)</p> <p>Hypoglycaemia 1.2%</p> <p><b>Insulin glargine + BD prandial</b> -Algorithm 1 Baseline: 9.2 ± 1.3 Endpoint: 7.6 ± 1.3</p> <p>-Algorithm 2 Baseline: 9.3 ± 1.1 Endpoint: 8.0 ± 1.1</p> <p>Overall baseline-endpoint difference -1.4 ± 1.4 (p&lt;0.001)</p> <p>Hypoglycaemia 2.2%</p> <p><b>Insulin glargine+ &gt;BD prandial‡</b> -Algorithm 1 Baseline 9.0± 1.1 Endpoint: 7.8 ± 1.1</p> <p>-Algorithm 2 Baseline: 9.3 ± 1.2 Endpoint: 7.7 ± 1.2</p> <p>Overall baseline-endpoint difference -1.4 ± 1.3 (p&lt;0.001)</p> <p>Hypoglycaemia 0%</p> <p><b>Insulin glargine + OD prandial‡</b></p>	
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								<p>-Algorithm 1 Baseline 8.1 ± 1.0 Endpoint: 7.9 ± 1.2</p> <p>-Algorithm 2 Baseline: 9.4 ± 1.6 Endpoint: 7.9 ± 1.0</p> <p>Overall baseline-endpoint difference -0.8 ± 2.0</p> <p>Hypoglycaemia 0%</p> <p><b>PRIOR BD PREMIX INSULIN + OADs</b></p> <p><b>Insulin glargine + OAD</b></p> <p>-Algorithm 1 Baseline 8.9 ± 1.3 Endpoint: 8.3 ± 1.4</p> <p>-Algorithm 2 Baseline: 8.7 ± 1.1 Endpoint: 8.0 ± 1.2</p> <p>Overall baseline-endpoint difference -0.7 ± 1.4 (p&lt;0.001)</p> <p>Hypoglycaemia &lt;1%</p> <p><b>Insulin glargine + BD prandial<sup>†</sup> + OAD</b></p> <p>-Algorithm 1 Baseline 9.0 ± 1.3 Endpoint: 7.7 ± 1.0</p> <p>-Algorithm 2</p>	
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								<p>Baseline: <math>8.9 \pm 1.3</math>  Endpoint: <math>7.7 \pm 1.4</math></p> <p>Overall baseline-endpoint difference  <math>-1.3 \pm 1.3</math> (<math>p &lt; 0.001</math>)</p> <p>Hypoglycaemia  0%</p> <p><b>Insulin glargine + &gt;BD prandial† + OAD</b></p> <p>-Algorithm 1  Baseline <math>9.3 \pm 1.1</math>  Endpoint: <math>7.8 \pm 1.1</math></p> <p>-Algorithm 2  Baseline: <math>9.0 \pm 1.2</math>  Endpoint: <math>7.4 \pm 0.9</math></p> <p>Overall baseline-endpoint difference  <math>-1.5 \pm 1.2</math> (<math>p &lt; 0.001</math>)</p> <p>Hypoglycaemia  0%</p> <p><b>Insulin glargine + &gt;BD short-acting insulin + OAD</b></p> <p>-Algorithm 1  Baseline <math>9.2 \pm 1.0</math>  Endpoint: <math>7.8 \pm 0.8</math></p> <p>-Algorithm 2  Baseline: <math>8.8 \pm 1.0</math>  Endpoint: <math>7.5 \pm 0.8</math></p> <p>Overall baseline-endpoint difference  <math>-1.3 \pm 1.1</math> (<math>p &lt; 0.001</math>)</p>	
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								<p>Hypoglycaemia 0%</p> <p><b>Insulin glargine + OD prandial† + OAD</b></p> <p>-Algorithm 1 Baseline 8.8± 1.1 Endpoint: 7.7 ± 0.9</p> <p>-Algorithm 2 Baseline: 9.2 ± 1.4 Endpoint: 7.3 ± 0.6</p> <p>Overall baseline-endpoint difference -1.4 ± 1.4 (p&lt;0.001)</p> <p>Hypoglycaemia 0%</p>	
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