**Insulin-Only STAR: Liège Clinical Trial Interim Results on Safety and Efficacy**

Vincent Uyttendaele$^{1,2}$, J Knopp$^2$, M Pirotte$^3$, J Guiot$^3$, P Morimont$^3$, B Lambermont$^3$, GM Shaw$^4$, T Desaive$^1$ and JG Chase$^2$

$^1$GIGA – In silico Medicine, University of Liège, Belgium; $^2$Department of Mechanical Engineering, University of Canterbury, New Zealand; $^3$Department of Intensive Care, University Hospital of Liège, Belgium; $^4$Department of Intensive Care, Christchurch Hospital, New Zealand

**Background**

- Stress-hyperglycaemia is a common complication in the ICU.
- Glycaemic control (GC) has shown improved outcomes but was proven difficult to achieve safely, increasing risks of hypoglycaemia.
- STAR is a model-based GC protocol with proven safety and performance. It uses a unique risk-based dosing approach accounting for both intra- and inter-patient variability.
- STAR determines the best insulin and nutrition treatment option by assessing the likelihood of future metabolic variability based on current identified insulin sensitivity, as depicted in Figure 1.

**Objectives**

- Most GC design uses insulin-only intervention while STAR uses both insulin and nutrition.
- This study uses an insulin only version of STAR with nutrition set clinically in the University Hospital of Liège, Belgium, to assess safety and efficacy in this use.

**Methods**

Ethics approval was granted by the University Hospital of Liège Ethics Committee for the STAR-Liège clinical trial. STAR-Liège offers 1-3 hourly blood glucose (BG) measurements options. Insulin is administered through IV catheter continuously and nutrition clinically set.

- **Target band:** 4.4-8.0 mmol/L (80-145 mg/dL)
- **Starting criteria:** 2 BG measurements > 8.0 mmol/L (145 mg/dL)
- **Stopping criteria:** BG stable for 6h at low insulin rates (≤ 2U/h) or 72h after inclusion.
- **Insulin:** Max. 9U/h with maximum increment of 2U/h.

STAR is fully computerised and implemented on a tablet running Android. Nurses are free to choose any possible treatment option (1-3 hourly).

Results from the first 11 patients are analysed.

**Results**

BG traces from clinical data are shown in **Figure 2** and results are shown in **Table 1**.

**Table 1** – Clinical data from 11 STAR-Liège patients. Results are given as median[IQR].

<table>
<thead>
<tr>
<th># patients</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hours of control</td>
<td>645</td>
</tr>
<tr>
<td>Workload (#measurements/day)</td>
<td>16</td>
</tr>
<tr>
<td>Median BG (mmol/L)</td>
<td>6.7 [5.9 7.7]</td>
</tr>
<tr>
<td>Insulin rate (U/h)</td>
<td>3.5 [1.5 6.0]</td>
</tr>
<tr>
<td>Nutrition (dextrose) rate (g/h)</td>
<td>6.1 [4.9 9.2]</td>
</tr>
<tr>
<td>%BG within 4.4-8.0 mmol/L (80-145 mg/dL)</td>
<td>78</td>
</tr>
<tr>
<td>%BG &gt; 10.0 mmol/L (180 mg/dL)</td>
<td>10</td>
</tr>
<tr>
<td>%BG &lt;4.4 mmol/L (80 mg/dL)</td>
<td>1</td>
</tr>
<tr>
<td>%BG &lt;2.2 mmol/L (40 mg/dL)</td>
<td>0</td>
</tr>
<tr>
<td>Unchanged intervention (%)</td>
<td>86</td>
</tr>
</tbody>
</table>

- **High performance:** median [IQR] BG of 6.7 [5.9 7.7] mmol/L (122 [106 147] mg/dL) and 78% BG in band.
- **High safety:** only 1% BG < 4.4 mmol/L (80 mg/dL), no incidence of severe hypoglycaemia (BG < 40 mg/dL or 2.2 mmol/L), and 10% of BG > 180 mg/dL (10.0 mmol/L).
- **High compliance:** only 14% of intervention changed by clinical staff.

> **High safety and efficacy for nearly all patients!**

**Conclusions**

- Insulin-only GC with the STAR-Liège protocol succeeds in providing equally high safety and quality for nearly all patients.
- Failed to reduce BG in 1 consistently highly resistant patient. Reducing nutritional input as per the original STAR design could reduce BG to safer range for this patient.
- These results are encouraging, comparable to previous studies, and support STAR’s risk-based dosing approach as a robust solution across different ICU settings and usages.