Overview and place in therapy of insulin glargine 300 units/mL (Gla-300)

Kim Tran, PharmD
12 Sept 2015

Disclosure

I have no financial relationships to disclose.

I will not discuss off label use and/or investigational use in my presentation.

Learning Objectives

Participants will be able to describe the appropriate clinical use of insulin glargine 300 units/mL for treating diabetes.
Diabetes Management: Type 1

- Insulin
  - Multiple dose
  - Continuous subcutaneous infusion
- Insulin analogs (for those with increased risk of hypoglycemia)
  - Pramlintide

Diabetes Management: Type 2

Basal Insulin Therapy

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Onset of Action (h)</th>
<th>Peak Action (h)</th>
<th>Duration of Action (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate-acting</td>
<td>NPH 1-2  5-7  13-18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting analogues</td>
<td>Glargine 1-3  N/A  20-24</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Detemir 1-3  6-9  12-24</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Insulin glargine 300 U/mL (Gla-300)³

- Approved by the US FDA on 2/25/2015
  - For use in adults with diabetes mellitus
- Gla-300 has a reduced redissolution rate as compared with Gla-100
  - Onset of action: 6 hours
  - Peak action: N/A
  - Duration of action: up to 36 hours
- Only 1/3 the volume per unit compared with Gla-100

EDITION 1 Trial⁴

- 6-month, multicenter, randomized controlled, parallel-group, noninferiority
- Comparing the safety & efficacy of Gla-300 to Gla-100 in 807 participants with type 2 diabetes mellitus (T2DM)
  - Mean hemoglobin A1c (HbA1c): 8.15%
- Inclusion: prior use of Gla-100 or NPH ± mealtime insulin ± metformin, HbA1c 7%–10%
- Gla-300 dosing:
  - direct 1:1 conversion from once daily Gla-100 or NPH. If used NPH twice daily, study dose was 80% of total daily dose.

EDITION 1 Trial⁴

- Results:
  - HbA1c reduction equivalent between regimens - least squares mean difference was -0.00% (95% CI -0.11 to 0.11)
  - Both groups had 0.9kg weight gain
  - Hypoglycemia rates initially lower in Gla-300 group, but eventually no difference throughout treatment
  - No difference in adverse events
  - Gla-300 group required a higher basal insulin dose compared to Gla-100 (1.03 U/kg/day vs 0.90 U/kg/day)
EDITION 3 Trial

- 6-month, multicenter, open-label, parallel-group
- Comparing the safety and efficacy of Gla-300 to Gla-100 in 878 insulin-naïve subjects with uncontrolled T2DM
  - Mean HbA1c: 8.54%
- Inclusion: T2DM diagnosis for at least 1 year along with use of an oral antidiabetic drug (OAD) for at least 6 months, insulin naïve
- Gla-300 dosing:
  - Start at 0.2 units/kg/day
  - Adjustments made once weekly to target fasting plasma glucose (FPG) 80-100 mg/dL

EDITION 3 Trial

- Results:
  - HbA1c decreased by equivalent amounts between both treatment groups – least square mean difference was 0.04% (95% CI 0.09 to 0.17)
  - Mean increase in weight was lower with Gla-300 [0.49 kg (95% CI 0.14 to 0.83)] than with Gla-100 [0.71 kg (95% CI 0.36 to 1.06)]
  - Hypoglycemia risk non-significantly lower with Gla-300 over 6 months
  - Gla-300 group required higher basal insulin doses as compared to Gla-100 (0.62 U/kg/day vs 0.53 U/kg/day)

EDITION 4 Trial

- 6-month, multicenter, open-label, parallel-group
- Comparing the safety and efficacy of Gla-300 to Gla-100 in 549 adults with type 1 diabetes mellitus (T1DM)
  - Mean HbA1c: 8.12%
- Inclusion: T1DM using basal + mealtime insulin for at least 1 year, with stable insulin dosing for at least 30 days previous
- Gla-300 dosing:
  - Either AM or PM administration
  - Continued mealtime insulin
  - No details provided on starting doses or dose adjustments of Gla-300
**EDITION 4 Trial**

- **Results:**
  - Change in HbA1c was equivalent in both treatment groups – mean difference was 0.04% (95% CI -0.10 to 0.19)
  - No difference in hypoglycemic events or weight gain
  - No difference in glucose profiles, hypoglycemic events, or adverse events between AM and PM injections
  - Higher doses of Gla-300 as compared to Gla-100 were required (0.19 U/kg/day vs 0.10 U/kg/day)

---

**Trial Summary**

- Gla-300 shown to be noninferior to Gla-100 both in efficacy and safety
- Higher doses of Gla-300 were required to achieve same glycemic controls as Gla-100 in clinical trial (about 11% to 17.5% more with Gla-300)
- Limitations:
  - Open label design
  - Short duration (6 months)
  - Study participants predominantly Caucasian and Japanese
  - study only in participants with moderately elevated HbA1c (at 10% or 11% max)
  - Lacking data on use with other OADs and conversion from basal insulins other than Gla-100 or NPH

---

**Gla-300 in practice**

- Availability – Toujeo® Solostar
  - 300 units/mL of insulin glargine
  - 1.5 mL disposable prefilled pen (450 units/1.5 mL)
- Storage/Disposal
  - In-use pen store at room temperature for maximum of 28 days
- Once daily dosing (pen goes up to 80 units per injection)
- Insulin conversion to once daily Gla-300:
  - If on previous once daily long-acting basal insulin: use 1:1 ratio
  - If on previous twice daily NPH: use 80% of the total daily dose
**Gla-300 in practice**

- **Cost:**
  - Lantus® Solostar (15mL) = $416.43
  - Toujeo® Solostar (4.5mL) = $401.16
- **Consider as an alternative to currently available long-acting basal insulins for patients with either T1DM or T2DM**
  - May be beneficial for patients who require twice-daily dosing to maintain full basal insulin coverage
- **Lower incidence of hypoglycemia during first several weeks in EDITION 1, 2, and 4 trials suggest safer titration with Gla-300**

**Question #1**

60 year old woman with T2DM x 10 years. She is currently using Gla-100 - 50 units in the morning and 50 units before bedtime. FPG have been relatively controlled on current dosing. However, she would like to switch to Gla-300 insulin to be dosed just at bedtime for easier convenience. What would be her Gla-300 dose?

A. Two injections (given at bedtime): 50 units plus 50 units
B. One injection (given at bedtime): 100 units
C. One injection (given at bedtime): 80 units
D. Given her good level of control, no change is needed.
Conclusion

Efficacy and safety of Gla-300 have been studied in more than 4500 subjects with T1DM and T2DM – data demonstrates potential of Gla-300 to improve glycemic control with similar efficacy and safety as Gla-100

Future studies:
- Conversion from basal insulins other than Gla-100 or NPH
- More flexible dosing given the extended duration of action?
- More data for use in other populations (ie. peds, elderly, pregnant, renal/hepatic disease)

References

4. Riddle MC, et al. New insulin glargine 300 units/mL versus glargine 100 units/mL in people with type 2 diabetes using basal and mealtime insulin: Glucose control and hypoglycemia in a 6-month randomized controlled trial (EDITION 1). Diabetes Care 2014; 37: 2755-2762.
5. Bolli GB, et al. New insulin glargine 300 U/mL compared with glargine 100 U/mL in insulin-naive people with type 2 diabetes on oral glucose-lowering drugs: a randomized controlled trial (EDITION 3). Diabetes Obes Metab 2015; 17(4): 386-394.
6. Home PD, et al. New insulin glargine 300 units/mL versus glargine 100 units/mL in people with type 1 diabetes: a randomized, phase 3a, open-label clinical trial (EDITION 4). Diabetes Care 2015.