Comparative efficacy of Gan & Lee insulin aspart (GL-ASP) and EU-marketed insulin aspart (NN-ASP), when combined with metformin, in patients with diabetes mellitus: Post-hoc analyses from a multicenter, randomized, open-label, controlled clinical trial

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ABSTRACT #0122

Background: A 24-week, open-label, randomized, multicenter, active-controlled, non-inferiority phase 3 confirmatory trial (ChiCTR 200031290) compared the efficacy and safety of Gan & Lee insulin aspart (GL-ASP) and reference NovoRapid insulin aspart (NN-ASP), in combination with metformin, in patients with type 2 diabetes mellitus (T2DM) with inadequately controlled blood glucose[1]

Objective

Post-hoc analyses investigated the impact of patients' baseline glycated hemoglobin (HbA1c) levels on the efficacy of GL-ASP and NN-ASP.

Methods: Randomized patients (**Table 1**) with T2DM received subcutaneous mealtime GL-ASP or NN-ASP (3:1) as their sole insulin therapy, in combination with metformin (**Figure 1**). Post-hoc subgroup analysis (subgroups: patients' baseline HbA1c ≥7.5–<9%; ≥9–<11%; ≥11%) investigated mean change from baseline in HbA1c (primary efficacy endpoint) and 2-hour postprandial glucose (PPG) levels

Results: Randomized patients (N=590; GL-ASP: n=441; NN-ASP: n=149) had T2DM, with similar mean age (56 years), disease duration (8.4 years), and HbA1c levels (9.5%) across treatment groups.[1] At 24 weeks, mean HbA1c change from baseline was –2.20% with GL-ASP and –2.32% with NN-ASP; estimated treatment difference 0.04% (95% confidence interval: –0.17, 0.26).[1] Results were similar between GL-ASP and NN-ASP across baseline HbA1c subgroups (≥7.5–<9% = –1.25% vs –1.16%; ≥9–<11% = –2.52% vs –2.49%; ≥11% = –3.84% vs –4.25%, respectively, p>0.2 **Figures 2, 3**). Mean 2-hour PPG change from baseline trends observed were similar (≥7.5–<9% = –5.30 vs –5.19 mmol/L; ≥9–<11% = –6.15 vs –6.61 mmol/L; ≥11% = –8.19 vs –7.84 mmol/L, respectively, p>0.5, **Figures 3**)

Conclusion

GL-ASP demonstrated similar efficacy to NN-ASP in patients with T2DM also receiving metformin, irrespective of patients' baseline HbA1c level

Introduction

- Insulin aspart (ASP) is a rapid-acting human insulin analog approved for pre-prandial use in patients with type 1 and type 2 diabetes mellitus and may be combined with concomitant oral antidiabetic treatment[2]

Study Background

- Primary study objectives were to assess safety and demonstrate non-inferiority in efficacy (margin of 0.4, assessed by HbA1c change from baseline) of GL-ASP and NN-ASP, when administered in combination with metformin, at week 24[1]

Post-hoc analyses

- Baseline HbA1c levels and mean reductions in HbA1c over 24 weeks reported in this study were slightly higher compared to similar trials.[3,4]
- Therefore, the impact of HbA1c levels on the efficacy of GL-ASP and NN-ASP was investigated post-hoc

Additional methods

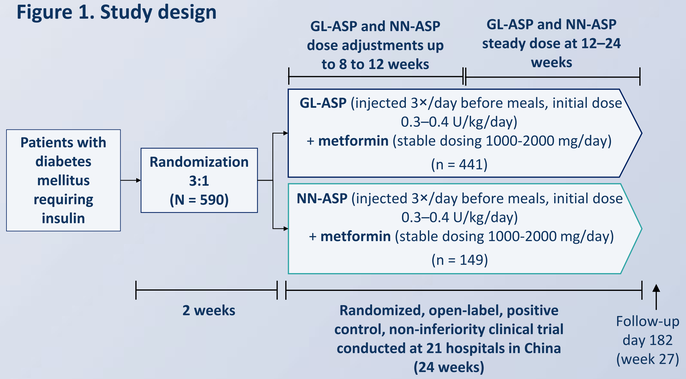
Table 1: Patient inclusion and exclusion criteria

	Patient characteristic
Inclusion criteria	Aged 18-75 years Diagnosis of type 1 or type 2 diabetes mellitus[a] Laboratory confirmed HbA1c >7.5% – ≤13% Body mass index <40 kg/m^2 Treatment for >3 months prior to screening with: • metformin (≥1000 and ≤2000 mg) or • ≤3 oral antidiabetes drugs (sulfonylureas, non-sulfonylurea insulin secretagogues, and glucosidase inhibitors)
Exclusion criteria	Insulin treatment <6 months prior to screening Thiazolidinedione, GLP-1 RA or DPP-4 inhibitor treatment <3 months prior to screening Glucocorticoid use <2 months prior to screening

[a] Although recruitment was open to patients with type 1 and type 2 diabetes, all recruited patients had a diagnosis of type 2 diabetes mellitus

GLP-1 RA, glucagon-like peptide-1 receptor agonist; DPP-4, dipeptidyl peptidase-4

Figure 1. Study design

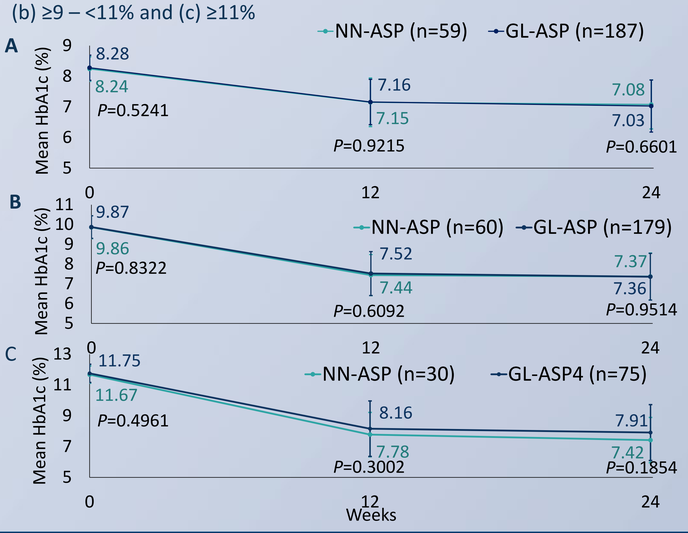


Statistical analysis

- Last observation carried forward imputation and student's t-test was used to analyse differences between treatment groups.

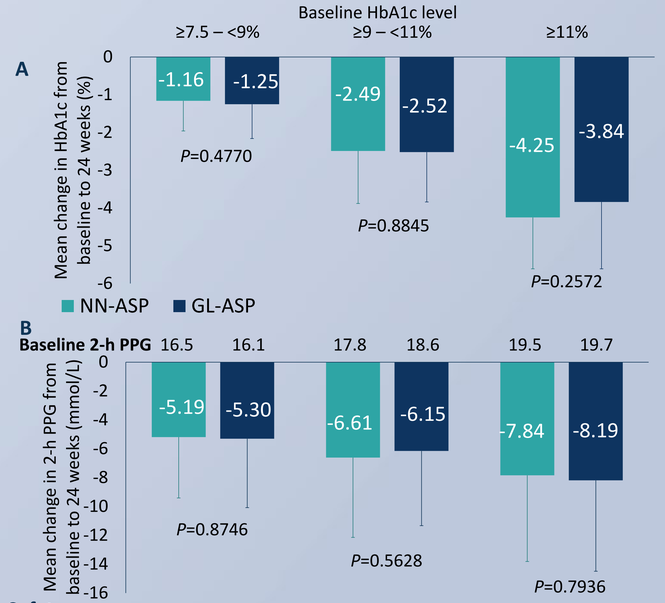
Additional results

Figure 2. Mean HbA1c in subgroups with baseline HbA1c (a) ≥7.5 – <9%, (b) ≥9 – <11% and (c) ≥11%



Efficacy

Figure 3. Change from baseline to Week 24 in (a) HbA1c and (b) 2-hour PPG for GL-ASP versus NN-ASP across HbA1c subgroups



Safety

- Similar proportions of patients reported adverse events (AEs) (43.7 vs 41.6, P=0.651) and serious AEs (3.9% vs 0.7%, P=0.054) in GL-ASP and NN-ASP groups, respectively[1]

Discussion

- Baseline HbA1c levels were comparable between treatment groups (**Table 1**), and slightly higher than in other studies of insulin aspart published to date.[3,4] This was primarily due to ~20% of patients reporting a baseline HbA1c level over 11%
- Although not pre-specified, and so to be interpreted with caution, this post-hoc subgroup analysis suggested that patients with higher baseline HbA1c levels experienced greater reductions in HbA1c and 2-h PPG over 24 weeks, as would be expected

References:1. Yao, J. 2021; Diabetologia , 64 (Suppl 1): S269; 2. Novo Nordisk A/S. Novo Rapid SmPC. Available at: https://www.ema.europa.eu/en/documents/product-information/novorapid-epar-product-information_en.pdf; 3. Hermansen K, Drugs. 2016;76:41-74; 4. Garg SK, Diabetes Technol Ther. Feb 2020;22(2):85-95.

Conflicts of interest: Damei Wang is an employee of Gan & Lee Pharmaceuticals; Jun Yao and Xiaohui Guo have no conflicts to declare

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