A Single Ascending Dose Study of a Once-monthly Liraglutide Formulation in Participants with Type 2 Diabetes

J. Hans DeVries,[1] Tim Heise,[1] Grit Andersen,[1] Erik Westrin,[2] Maria Nehlin,[3] Marie Gårdmark,[3] Kristine Bäck,[3] Owe Luhr.[3]

[1]Profil, Neuss, Germany; [2]CTC Clinical Trial Consultants AB, Uppsala, Sweden; [3]Nanexa AB, Uppsala, Sweden.

Poster
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NEX-22, a novel once-monthly formulation of liraglutide with PharmaShell® technology, showed exposure for 36 days after a single subcutaneous injection

Introduction and objectives

- → Liraglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) administered once-daily for treating type 2 diabetes[1] and obesity.[2] Other currently available GLP-1RAs are dosed once-weekly.[3] Extending the dosing interval may increase convenience and adherence.[4]
- → NEX-22 is a prolonged-release formulation of liraglutide achieved through PharmaShell® technology. This approach aims to release liraglutide over a longer duration for once-monthly administration.
- → This open, single ascending dose, phase 1 study assessed the pharmacokinetics (PK), safety and tolerability of a single subcutaneous (s.c.) injection of NEX-22 in participants with type 2 diabetes.

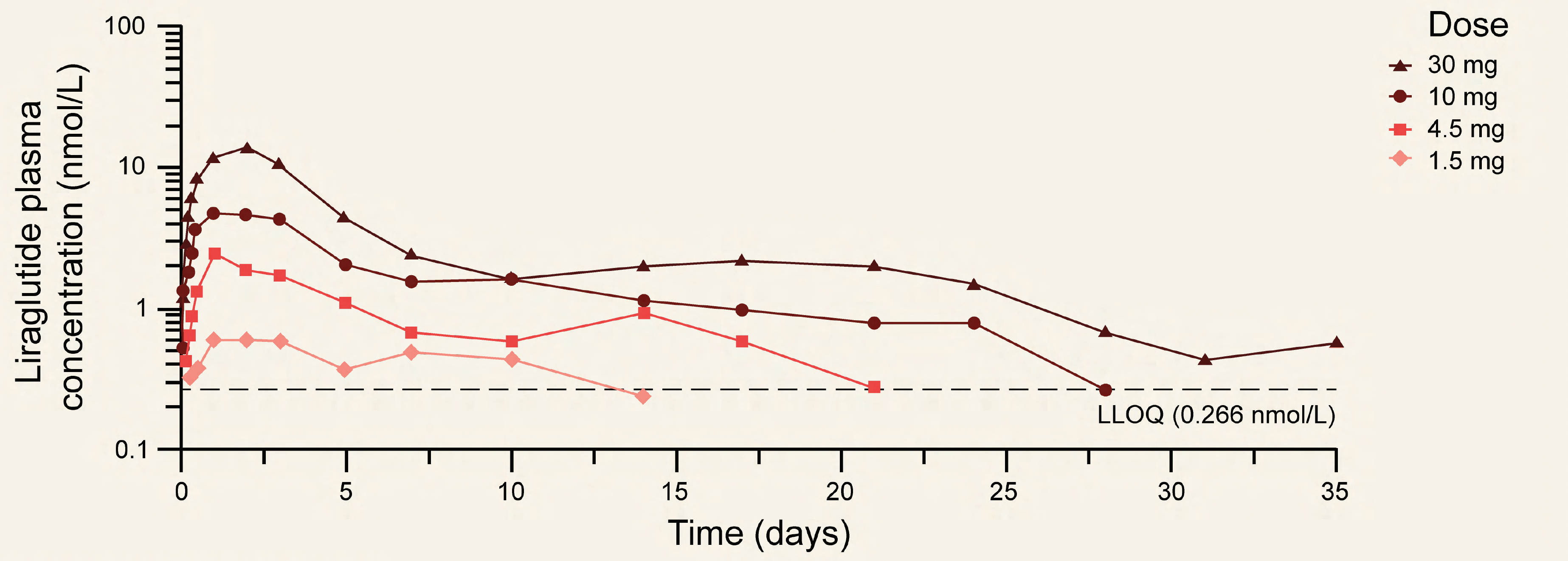
Methods

- → Twelve participants were enrolled into one of four sequential cohorts and received one single s.c. injection of NEX-22 of either 1.5 mg, 4.5 mg, 10 mg or 30 mg.
- → Eligible participants were 18–65 years old and had type 2 diabetes, a body mass index (BMI) of 18.5–35 kg/m^2, and normal kidney and liver function.
- → PK and safety profiles were followed for 36 days.

Key results

Key result

Figure 1: Liraglutide plasma concentrations over time, up to 35 days after injection of NEX-22 at doses 1.5 mg, 4.5 mg, 10 mg and 30 mg (geometric mean).



LLOQ, lower limit of quantification.

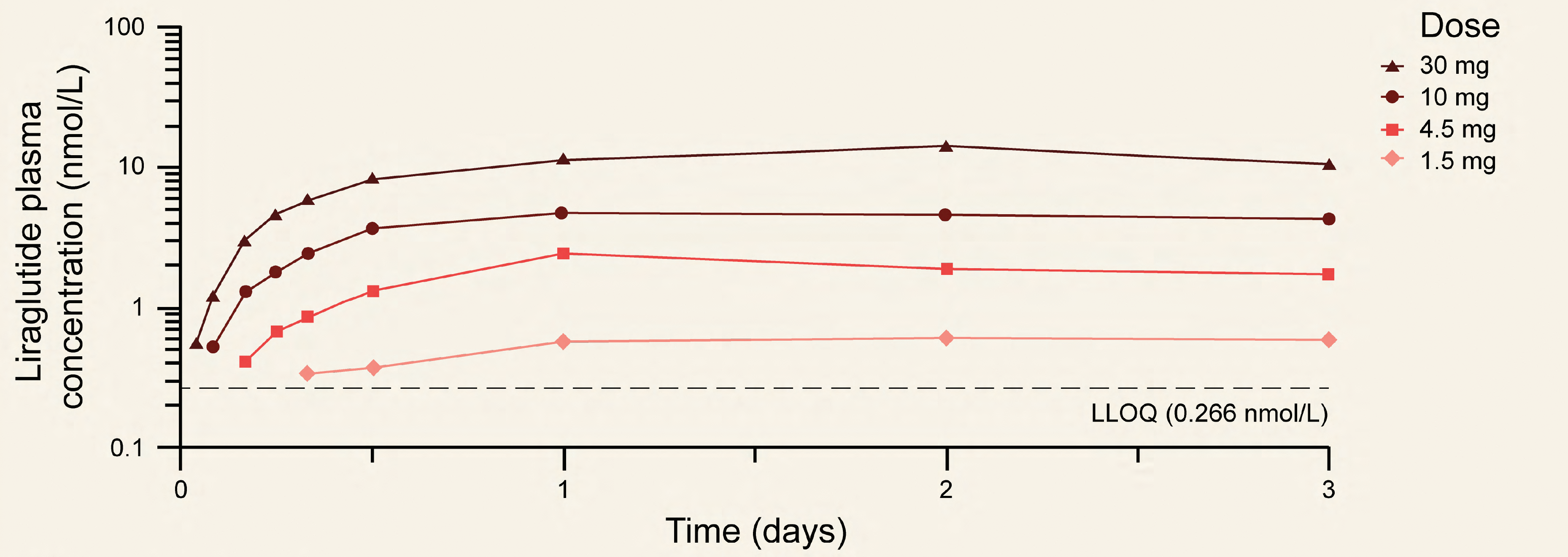
Table 1: Pharmacokinetic parameters of NEX-22 1.5 mg, 4.5 mg, 10 mg and 30 mg, based on concentrations above the lower limit of quantification (LLOQ).

	NEX-22, 1.5 mg (n=3)	NEX-22, 4.5 mg (n=3)	NEX-22, 10 mg (n=3)	NEX-22, 30 mg (n=3)
T_{max}, h	48 (48–168)	24 (24–24)	48 (24–48)	48 (48–48)
C_{max} (nmol/L)	0.697 (32.1%)	2.43 (0.00%)	4.94 (82.3%)	14.2 (55.3%)
$AUC_{0–24h}$ (h*nmol/L)	6.13 (18.6%)	29.9 (41.8%)	73.8 (83.2%)	172 (66.8%)
$AUC_{0–Last}$ (h*nmol/L)	86.0 (127%)	394 (83.0%)	1050 (104%)	2350 (48.1%)
Absorption-dependent half-life, h	279 (NA)	158 (256%)	180 (72.0%)	148 (89.7%)

Data are presented as geometric mean (geometric CV%) or median (min–max).
AUC, area under curve; C_{max}, maximum concentration; CV, coefficient of variation; T_{max}, time to maximum concentration.

- → At baseline, participants (3 female and 9 male) had a mean±SD age of 59.4±3.5 years, BMI of 28.1±3.8 kg/m^2 and HbA_{1c} of 7.3±0.4%.
- → The exposure in terms of C_{max} and AUC was, in general, dose-proportional for NEX-22 for the range of 1.5 mg to 30 mg **(Figure 1)**.
- → Within 24 hours of administration of NEX-22 4.5 mg, 10 mg, and 30 mg, the initial release was 5.7–6.0%.
- → Following administration of NEX-22 30 mg, the maximum liraglutide plasma concentration (C_{max}) was 14.2 nmol/L and concentrations were detected for up to 36 days (**Figure 1**). The absorption-dependent terminal half-life for NEX-22 30 mg was 148 hours (**Table 1**).
- → Across all cohorts, NEX-22 demonstrated a T_{max} of 24–48 hours (**Table 1**), **(Figure 2).**
- → Ten participants showed injection site reactions, most commonly erythema which usually resolved within 1 week. For some patients with erythema, the investigator noted a palpable mild swelling decreasing over time (**Table 2**).

Figure 2: Liraglutide plasma concentrations over time, up to 72 hours after injection of NEX-22 (geometric mean).



LLOQ, lower limit of quantification.

Table 2: Safety and tolerability of NEX-22.

	Total (N=12)
Any AE	9
SAE	0
TEAE	6
Gastrointestinal AE	2
Participants with any ISR*	10
Mild erythema	7
Moderate erythema	1
Mild tenderness	3
Mild induration / swelling	6
Mild pain	3

* None of the ISRs were severe or considered clinically significant by the investigator and were therefore not reported as an AE per study protocol.
AE, adverse event; ISR, injection-site reaction; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Conclusion

- → The PK profiles of s.c. NEX-22 demonstrated a **prolonged release of liraglutide**, with a **duration of up to 36 days** for the highest dose (30 mg).
- → The increase in plasma exposure was proportional with an increase of dose and **supports the potential of NEX-22 for once-monthly s.c. administration**.
- → Subcutaneous NEX-22 was well tolerated.
- → These data support continued development of s.c. prolonged-release formulations of GLP-1RAs with PharmaShell® technology.

References
1. Novo Nordisk. VICTOZA® (liraglutide) [package insert]; November 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/022341Orig1s042lbl.pdf. 2. Novo Nordisk. SAXENDA® (liraglutide) [package insert]; November 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/206321s019lbl.pdf. 3. Jain A, et al. Int J Clin Pract. 2020;75:e13731. 4. Giorgino F, et al. Patient Prefer Adherence. 2018;12:707–19.

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