Semaglutide Depot, a Long-Acting Injection of Semaglutide Administered Once Every Four Weeks Demonstrate Similar Efficacy and PK Profile to Daily weekly Semaglutide Administration

Shai Rubnov PhD, Galina Zats, Nadav Bleich Kimelman PhD DMD, Laura Popper MD, Uri Danon, Ehud Marom

Mapi Pharma Ltd (Ness Ziona, Israel)

Introduction and Objective

Semaglutide Depot consists of extended-release microspheres administered once every 28 days, aiming to provide an improved dosing regimen over the currently available once weekly dosed Semaglutide. Depot efficacy and PK profile were evaluated in mice and minipigs. The study aimed to assess the efficacy and the PK profile of Semaglutide Depot injected once compared to Semaglutide solution administered daily in mice or every 72 hours in minipigs.

Design/Methods

In the PK study, db/db mice received a SC injection of 2mg/kg Semaglutide Depot on day 0 or daily injections of 0.02mg/kg Semaglutide API for 42 days. In a parallel in the PD study, db/db mice were IM injected with 2mg/Kg Semaglutide Depot on day 0 or daily injections of 0.06-0.4mg/kg Semaglutide solution, for 28 days. The PK profile, fasting blood glucose, HbA1c levels and feed intake were measured. In the minipigs PK study, animals were injected with 0.5mg/kg Semglutide Depot IM on day 0 or with 0.008mg/Kg Semaglutide solution SC once every 72 hours for 28 days.

Results

PK studies in both species demonstrate sustained release profile maintaining plasma concentrations within the therapeutic range for at least 30 days (figure 1). The PK profile is correlated with PD in mice. Significant reductions in fasting glucose levels at days 14 and 28, as well as HbA1c levels at day 28 in Semaglutide Depot-treated mice were noted, compared with vehicle treated controls (Figure 2). Additionally, feed intake was significantly lower in Semaglutide Depot-treated mice. Notably, a single dose of Semaglutide Depot given on day 0 was comparable to 28 daily doses of Semaglutide solution (Figure 2).

Figure 1: PK profile of Semaglutide Depot in Minipigs and in db/db/mice

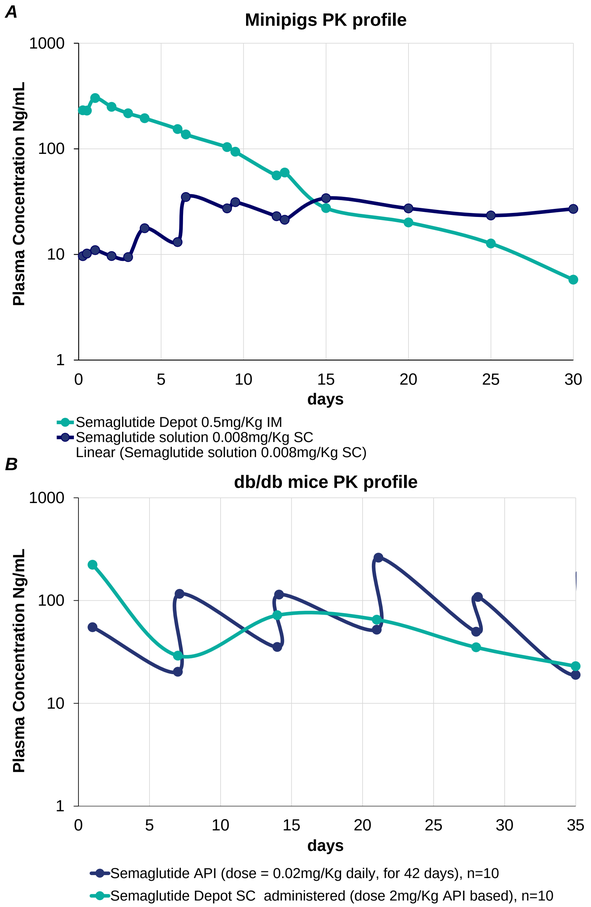
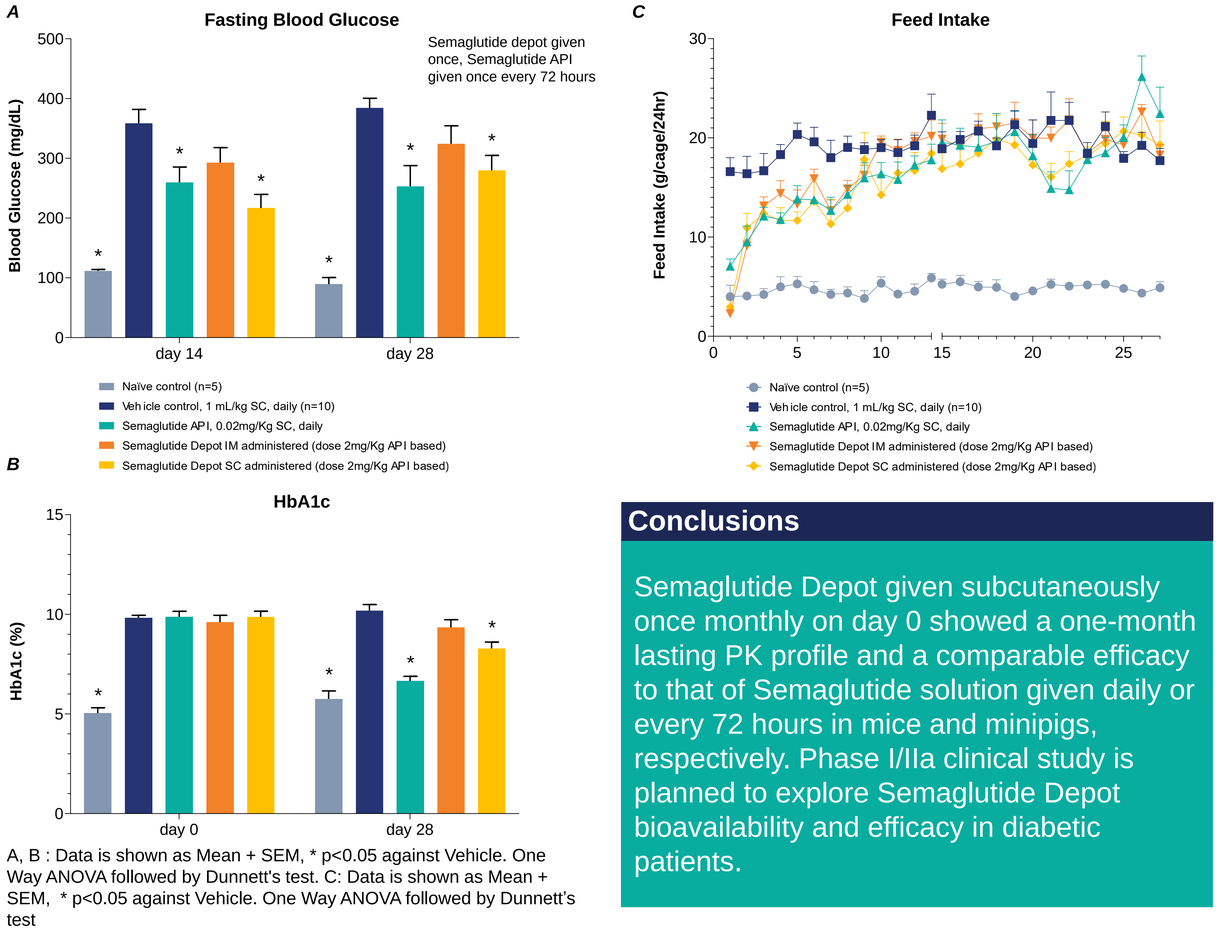


Figure 2: PD of Semaglutide in db/db/mice



A, B : Data is shown as Mean + SEM, * p<0.05 against Vehicle. One Way ANOVA followed by Dunnett's test. C: Data is shown as Mean + SEM, * p<0.05 against Vehicle. One Way ANOVA followed by Dunnett's test

Conclusions

Semaglutide Depot given subcutaneously once monthly on day 0 showed a one-month lasting PK profile and a comparable efficacy to that of Semaglutide solution given daily or every 72 hours in mice and minipigs, respectively. Phase I/IIa clinical study is planned to explore Semaglutide Depot bioavailability and efficacy in diabetic patients.

Disclosure: Galina Zats, Laura Popper, Nadav Bleich Kimelman, Shai Rubnov (co-inventor of SG Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom is a co-inventor of SG Depot, founder and CEO of Mapi Pharma.

Study Supported by: Mapi Pharma Ltd.