SUPPLEMENTARY DATA

Exenatide:
The Investigator's brochure from Eli Lilly and Company (http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/021773s9s11s18s22s25lbl.pdf) indicates that the 'mean apparent clearance of exenatide in humans is 9.1L/h and the mean terminal half-life is 2.4 h. These pharmacokinetic characteristics of exenatide are independent of the dose. In most individuals, exenatide concentrations are measureable for approximately 10 h post-dose.

Sitagliptin:
The Investigator's brochure from Merck (http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/021995lbl.pdf) indicates that after 'oral administration of a 100 mg dose to healthy volunteers, the apparent terminal half-life (t1/2) was 12.4 hours. The pharmacokinetics were similar in type 2 diabetics'.

Glimepiride:
The Investigator's brochure from Sanofi-Aventis (http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020496s021lbl.pdf) indicates the half-life of glimepiride obtained from a dose-proportionality study in type 2 diabetes is 5.0 ± 2.5 hr for single dose and 9.2 ± 3.6 hrs for multiple-dose administration up to 4 mg (the maximum dose in our study). Glimepiride is completely metabolized after oral dosing.

We, therefore, used 5 days off drug to allow >10 half-lives for drug clearance to ensure no active drug would remain in the subjects.

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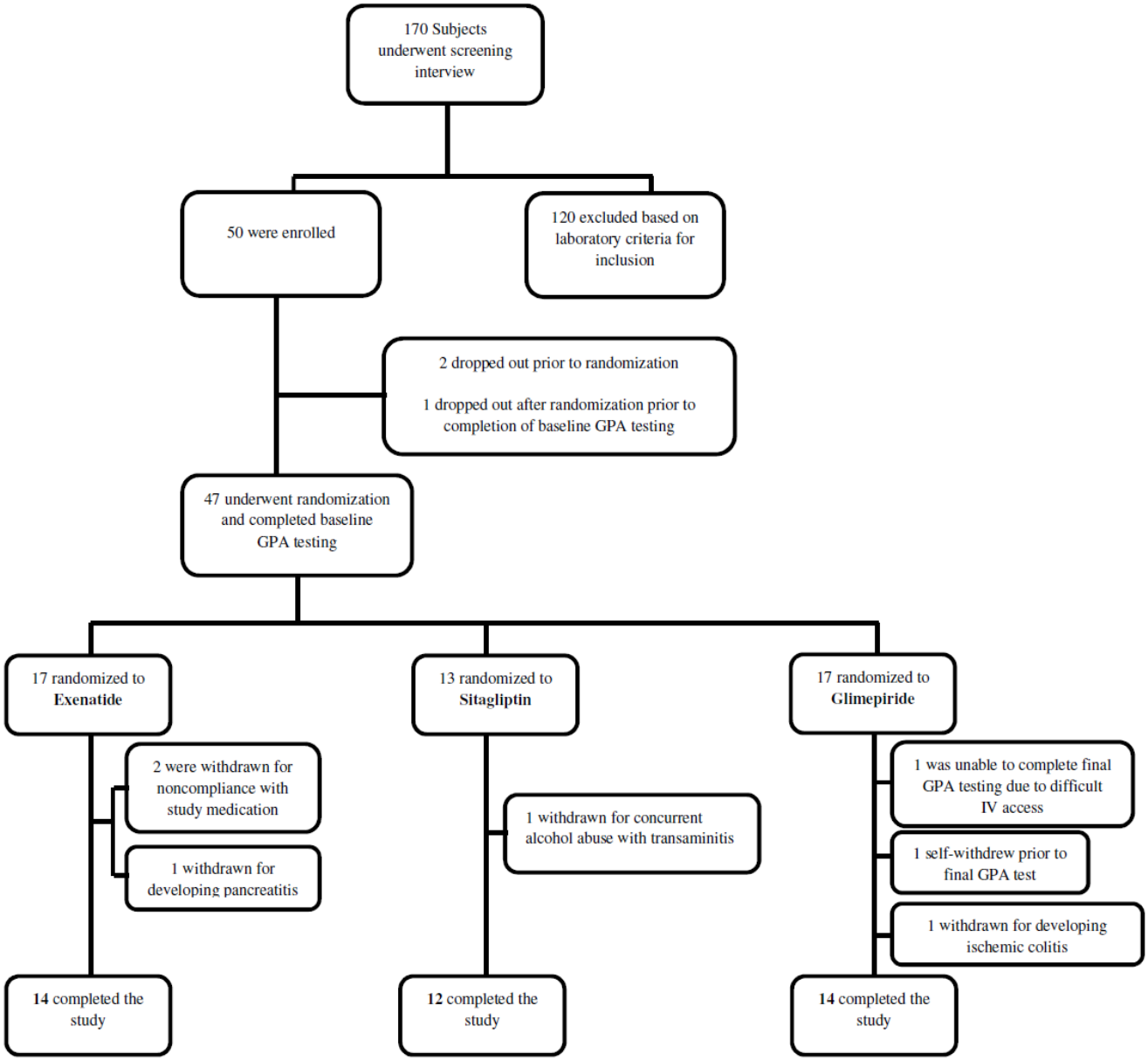
SUPPLEMENTARY DATA

Supplementary Figure 1. Flowchart describing subject recruitment, randomization and disposition of all the trial participants.



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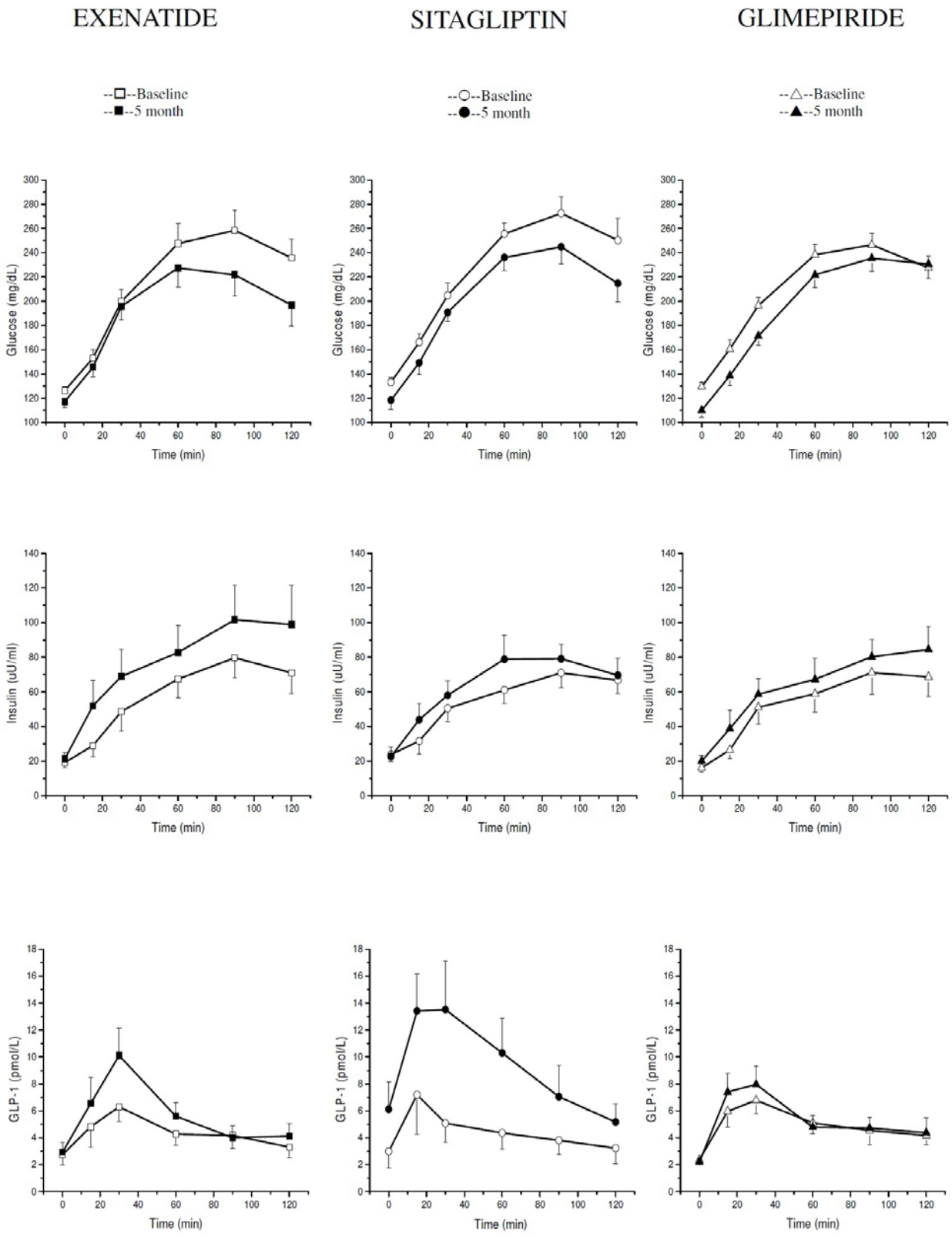
SUPPLEMENTARY DATA

Supplementary Figure 2. Plasma levels of glucose (top panel), insulin (middle panel) and GLP-1 (bottom panel) during the oral glucose tolerance test at baseline (open) and after 5 months (black) of therapy with exenatide (left, squares), sitagliptin (middle, circles) or glimepiride (right, triangles) panel.



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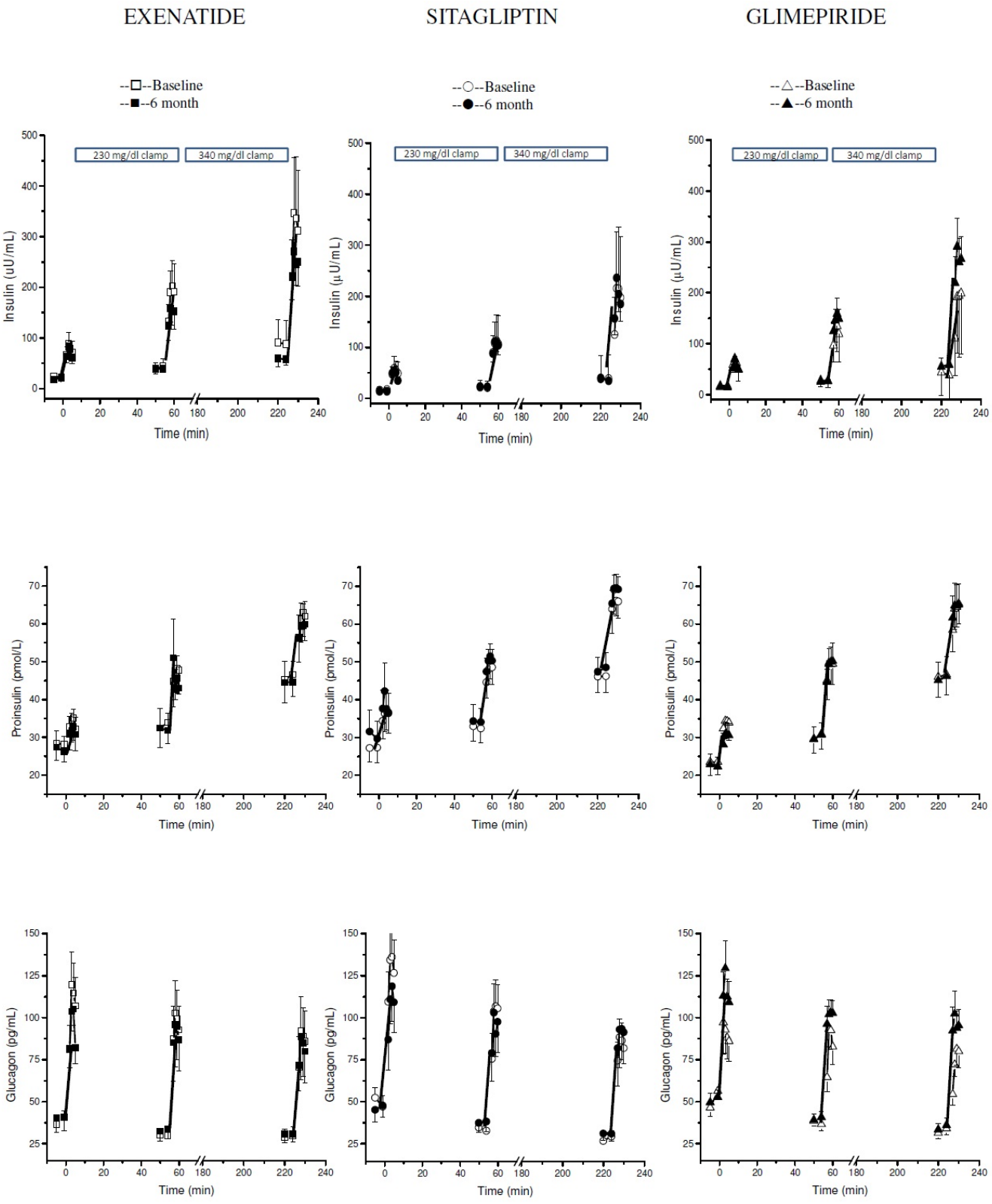
SUPPLEMENTARY DATA

Supplementary Figure 3. Plasma insulin (top panel), proinsulin (middle panel) and glucagon (bottom panel) during the glucose-potentiated arginine test at baseline (open) and after 5 days of washout following 6 months (black) of therapy with exenatide (left, squares), sitagliptin (middle, circles) or glimepiride (right, triangles) panel.



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