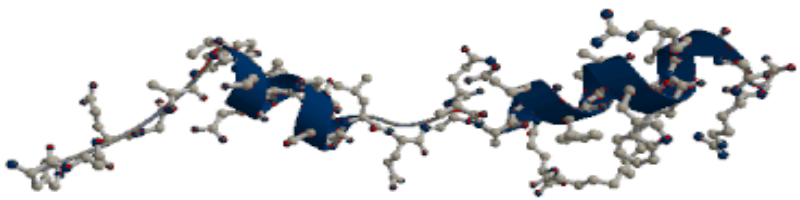

Liraglutide

Peter Kristensen, SVP
Global development

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Liraglutide demonstrates higher efficacy than active comparators across phase 3 studies

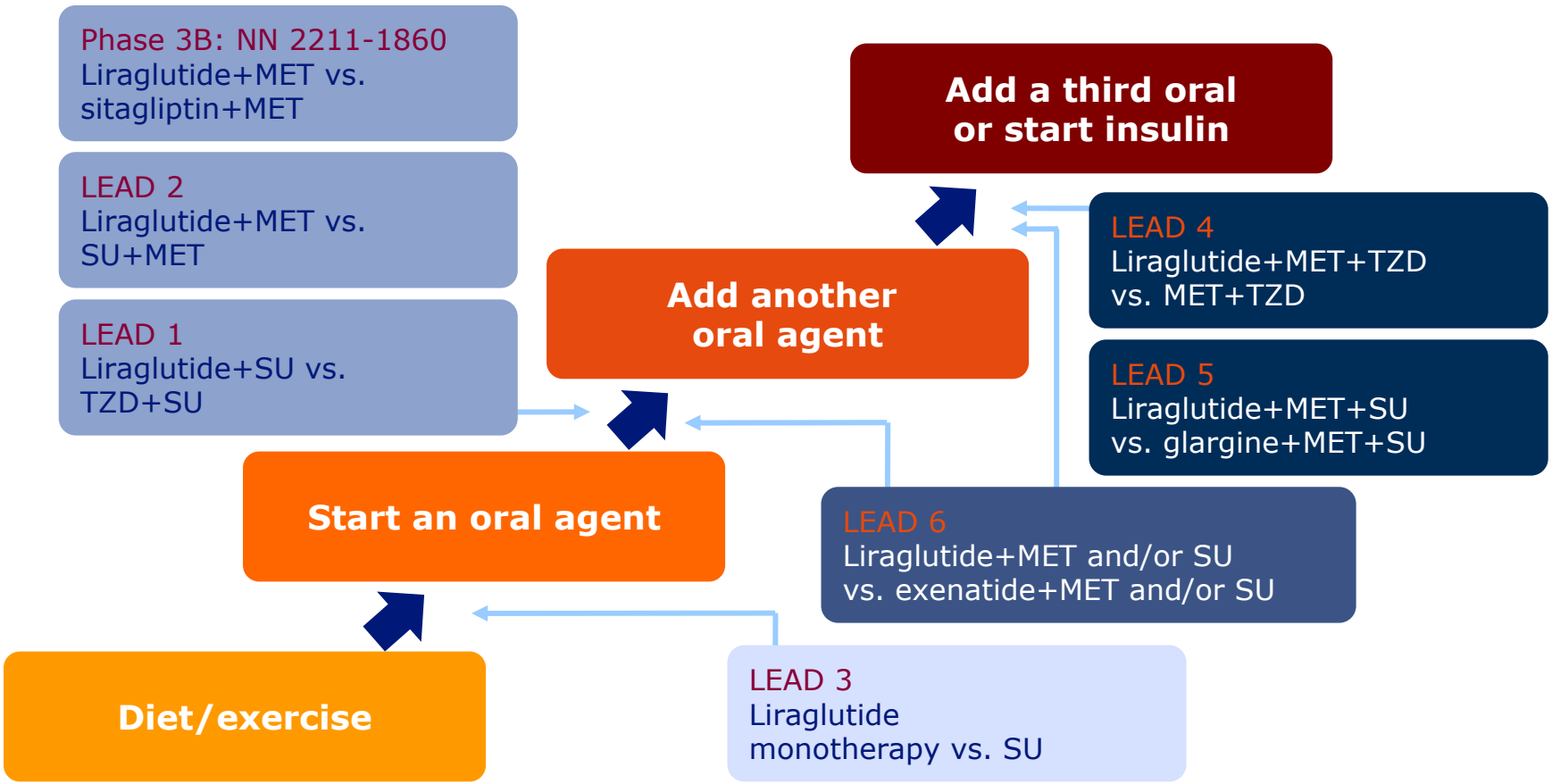
Liraglutide has shown statistically significantly better HbA_{1c} reductions compared to the following active comparators in large phase 3 studies:

- ✓ glimepiride (SU)*
- ✓ rosiglitazone (TZD)
- ✓ insulin glargine (basal insulin)
- ✓ exenatide (GLP-1)

→ Head-to-head data versus sitagliptin expected in the third quarter of 2009

*For patients previously in monotherapy

Liraglutide phase 3 programme
Exposure across type 2 diabetes disease progression



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LEAD: Liraglutide Effect and Action in Diabetes. All studies 26 weeks' duration (LEAD 3=52 weeks); all RCT; all with double dummy except LEAD 5 vs. glargine. Studies NN2211-1436, -1572, -1573 and -1697 presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

LEAD demographics and baseline characteristics

	LEAD 3 Mono-therapy	LEAD 2 Metformin	LEAD 1 SU	LEAD 4 Metformin +TZD	LEAD 5 Metformin+ SU	LEAD 6 Metformin, SU, Met+SU
Patients randomized	746	1091	1041	533	581	464
Age (years)	53.0	56.8	56.1	55.1	57.5	56.7
Duration of diabetes (years)	5.4	7.4	7.9	9.2	9.4	8.2
Previously on mono:combi (%)	(36:64)*	36:64	30:70	18:82	6:94	73:27
FPG (mM)	9.5	10.0	9.8	10.1	9.2	9.6
HbA_{1c} (%)	8.3	8.4	8.4	8.5	8.2	8.2
BMI (kg/m^2)	33.1	31.0	30.0	33.5	30.5	32.9
Weight (kg)	98.8	88.6	81.6	96.3	85.4	93.1

Source: Data originally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1): Poster 898 (LEAD 4); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

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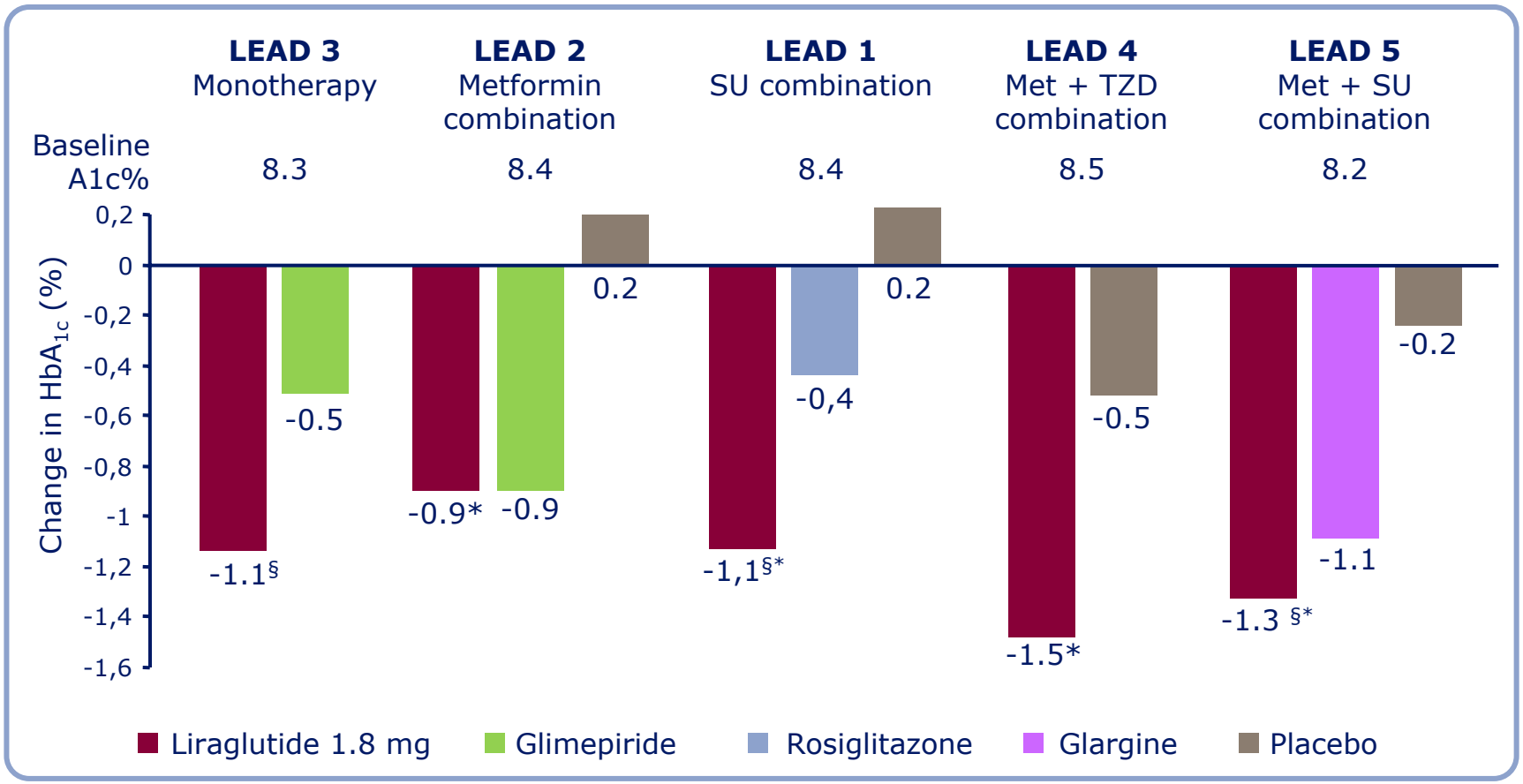
Note: * Ratio of patients previously on diet/exercise vs monotherapy

LEAD demographics and baseline characteristics

	LEAD 3 Mono-therapy	LEAD 2 Metformin	LEAD 1 SU	LEAD 4 Metformin +TZD	LEAD 5 Metformin+ SU	LEAD 6 Metformin, SU, Met+SU
Treatment period	52 w	26 w	26 w	26 w	26 w	26 w
Dosage (in mg)	• 1.2 • 1.8	• 0.6 • 1.2 • 1.8	• 0.6 • 1.2 • 1.8	• 1.2 • 1.8	• 1.8	• 1.8
Active comparator	SU	SU	TZD	Placebo	Lantus	Exenatide
Extension study	260 w	104 w	N/A	N/A	N/A	14 + 38 w

Source: Data originally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1): Poster 898 (LEAD 4); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

Changes in HbA_{1c} from baseline for liraglutide 1.8 mg vs comparator and placebo



Source: Data originally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1): Poster 898 (LEAD 4); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

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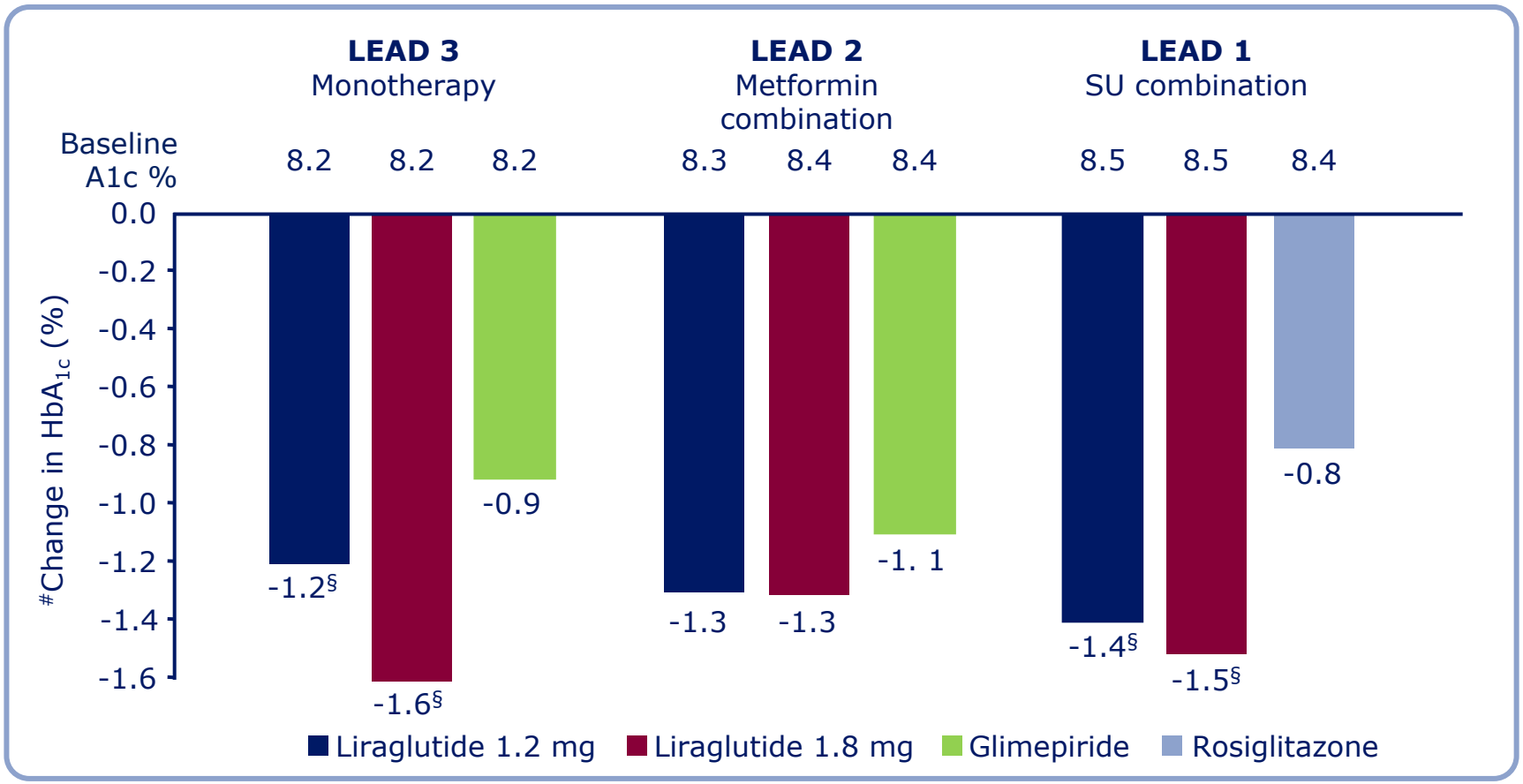
Note: *Significant vs placebo; §Significant vs active comparator

Reductions in HbA_{1c} for patients previously on monotherapy



Source: Data originally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1)

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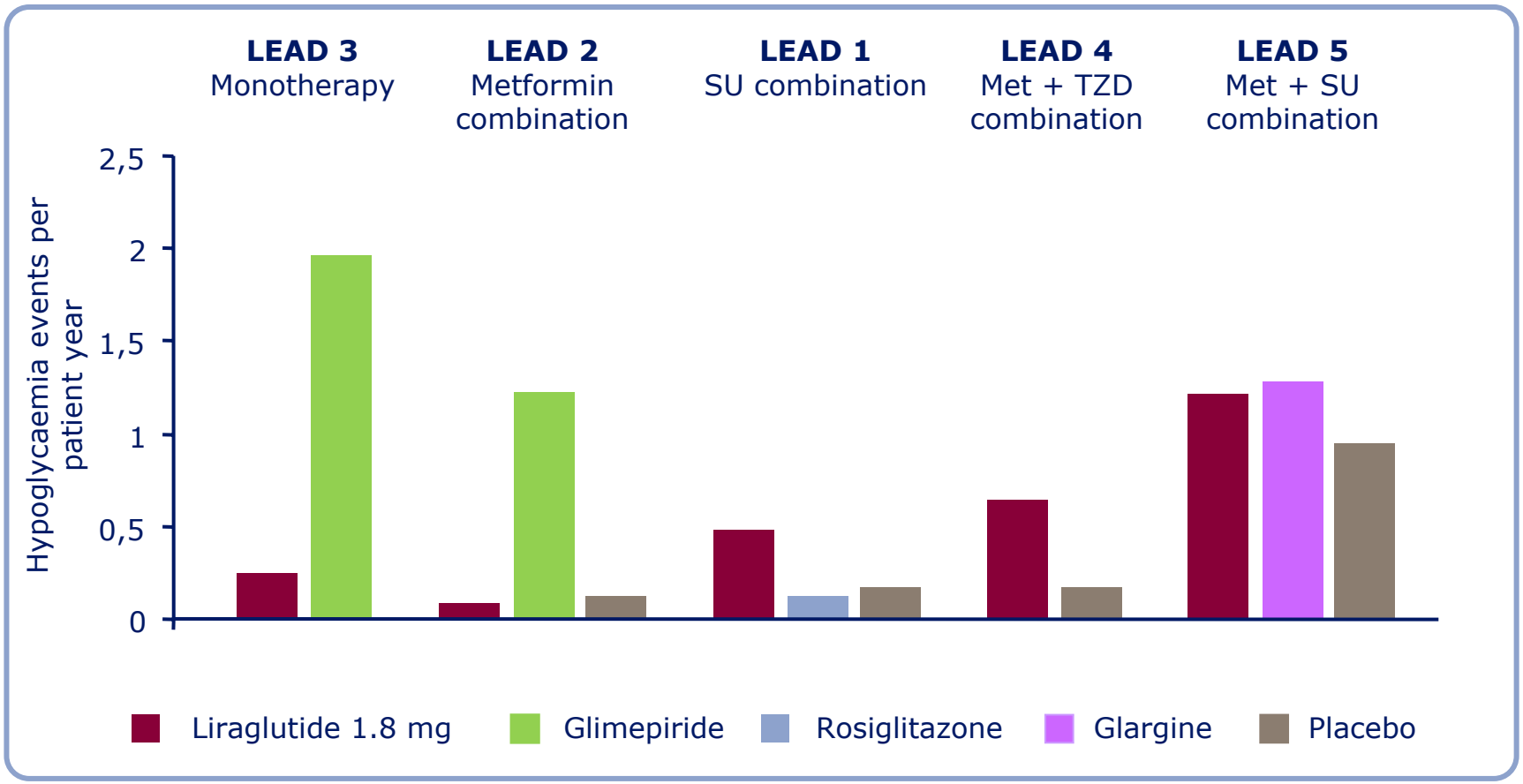
Note: *Significant vs placebo; §Significant vs active comparator. Included patients: add-on to diet and exercise failure (LEAD 3); or add-on to previous OAD monotherapy (LEAD 2,1). LEAD 4 and 5 data excluded due to low number of patients previously on monotherapy.

Hypoglycaemia: liraglutide 1.8 mg vs comparator and placebo



Source: Data originally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1): Poster 898 (LEAD 4); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

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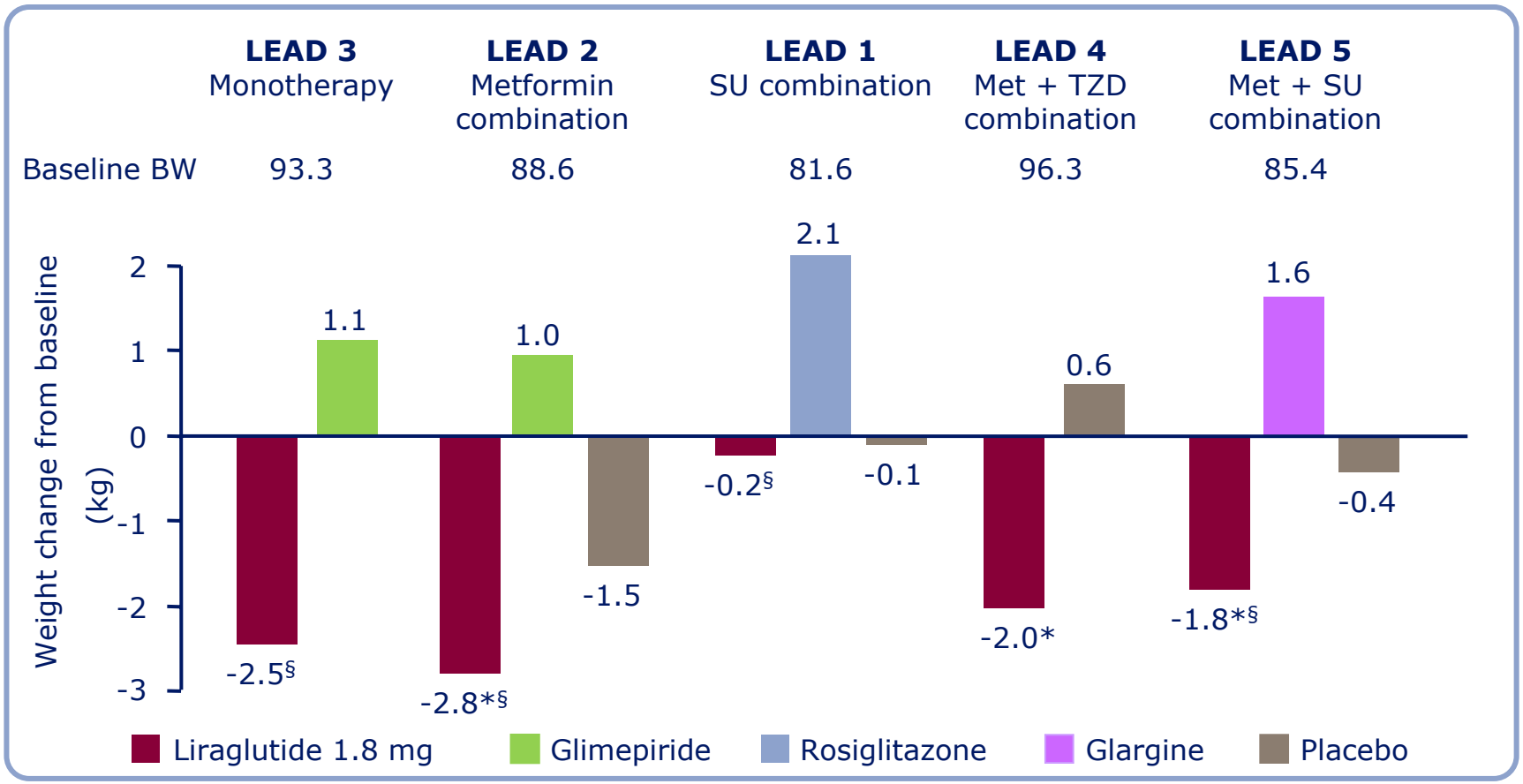
Body weight change: liraglutide 1.8 mg vs comparator and placebo



Source: Data originally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1): Poster 898 (LEAD 4); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

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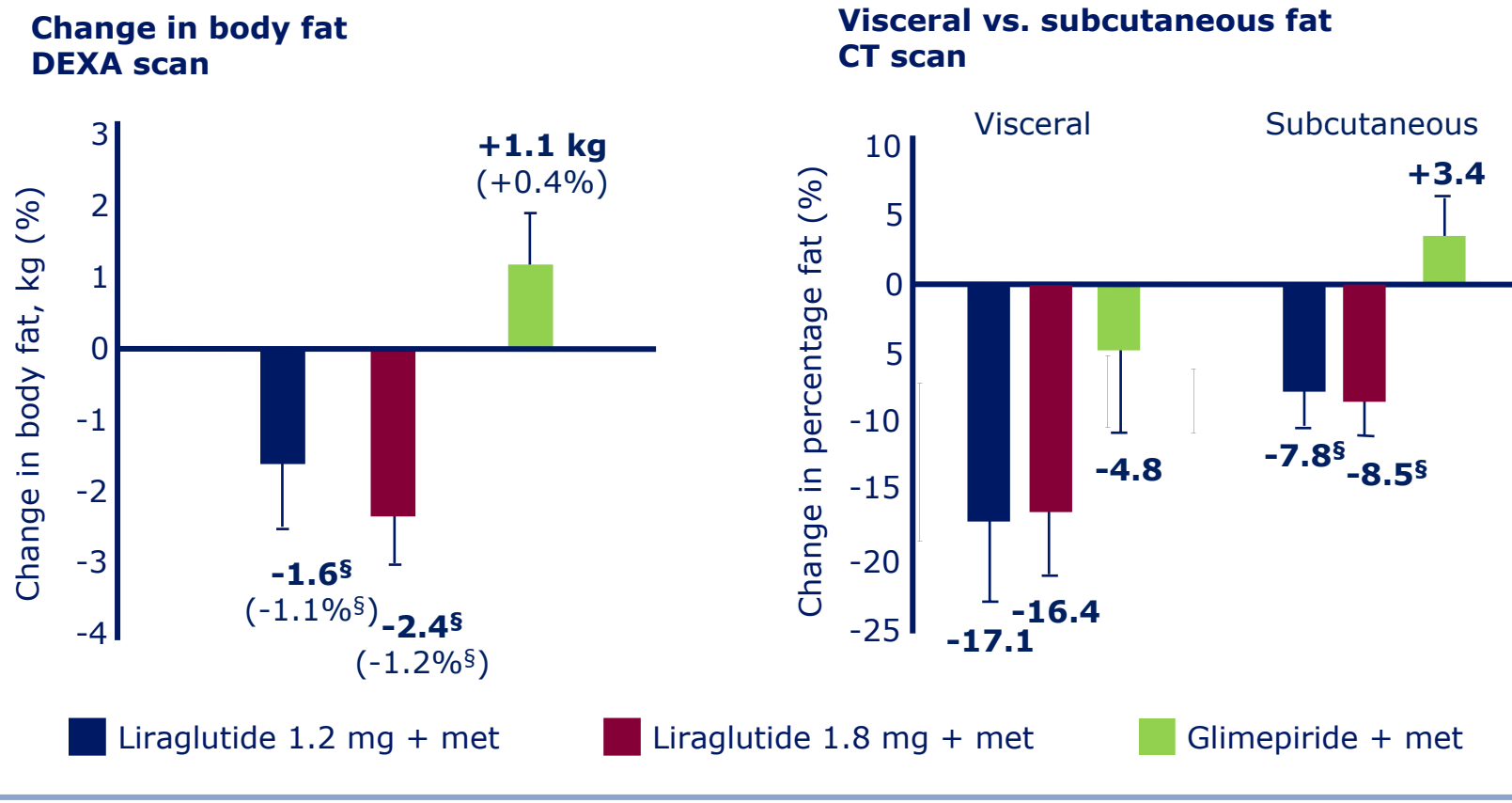
Note: *Significant vs placebo; §Significant vs active comparator

Liraglutide reduces visceral and subcutaneous fat

86% of liraglutide induced weight loss was fat mass



Source: LEAD 2 substudy, originally presented as Jendle et al. Diabetes 2008;57(Suppl. 1):A32.

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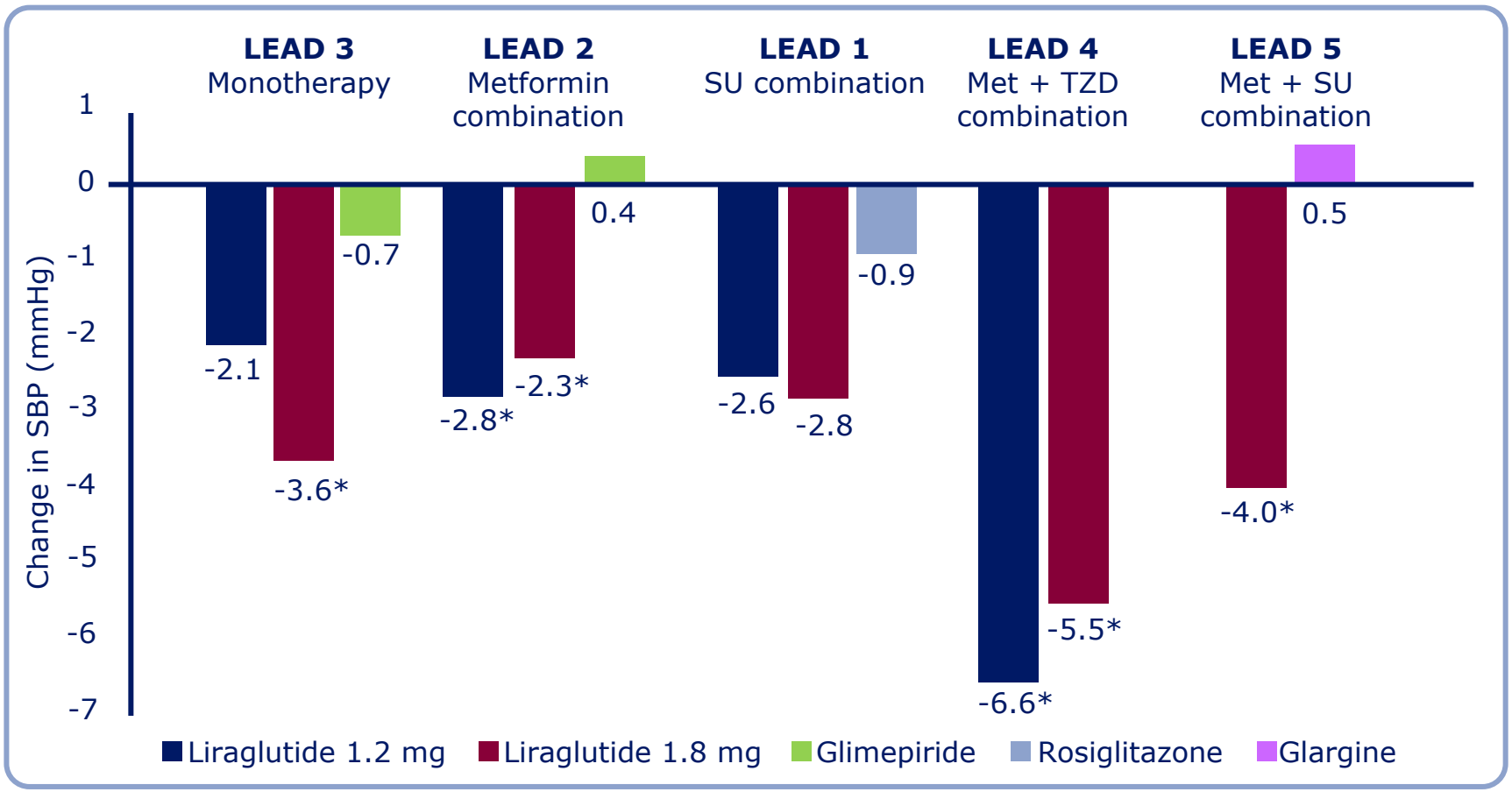
Note: Data are mean±SEM; §Significant vs active comparator

Liraglutide consistently reduces systolic blood pressure



Source: Data originally presented as Colagiuri et al. Diabetes 2008;57(Suppl. 1):A16.

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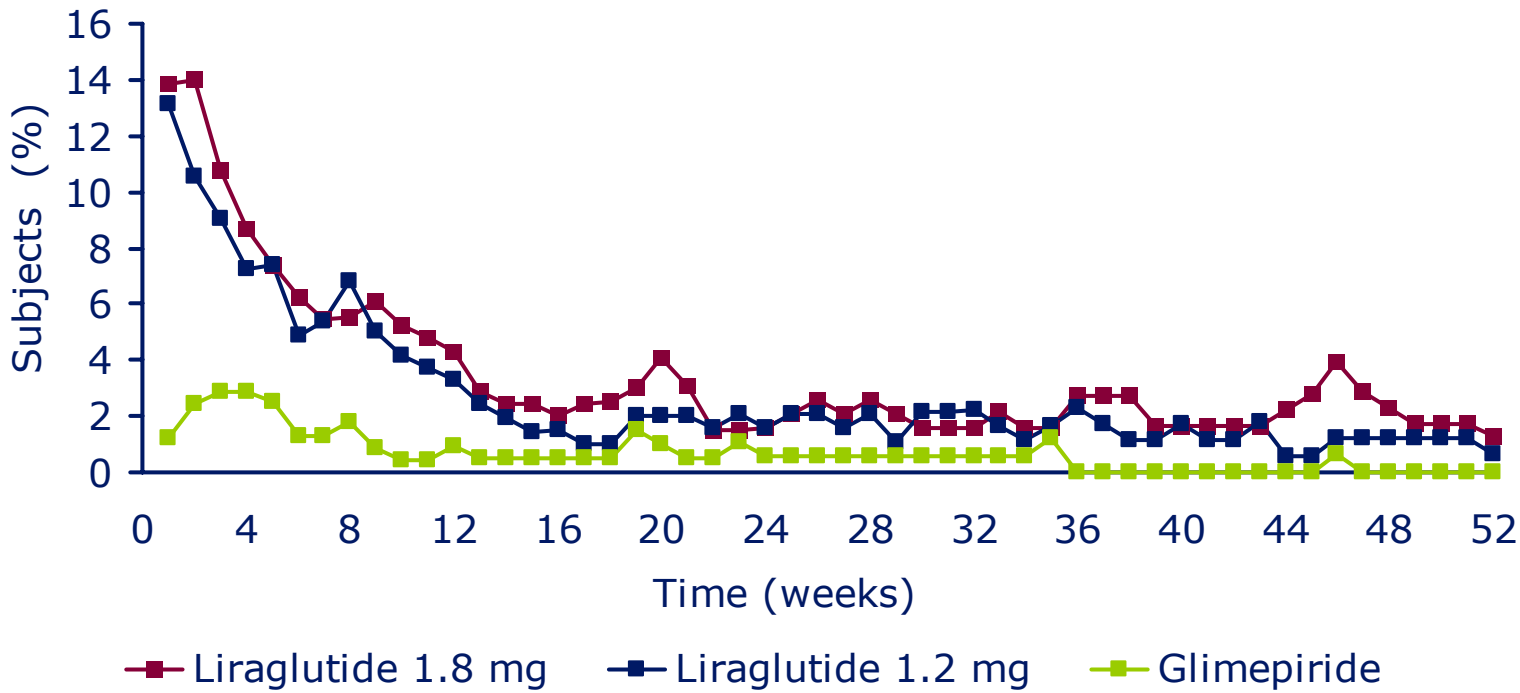
Note: *Significant vs baseline

Nausea almost at background level after 3 months

Lead 3: 5 withdrawals from liraglutide 1.8 mg arm due to nausea

Proportion of subjects with nausea by week and treatment – safety population



Source: The Lancet, accepted for publication (LEAD 3)

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Few patients withdrew due to nausea

Study	Treatment	Nausea reported at least once (%)	Withdrawals due to nausea (n/total patients)
LEAD 3 Mono	Liraglutide 1.8 mg	29	5/246
	Glimepiride	9	0/248
LEAD 2 Metformin combination	Liraglutide 1.8 mg	19	15/242
	Glimepiride	3	0/242
LEAD 1 SU combination	Liraglutide 1.8 mg	7	2/234
	Rosiglitazone	3	0/231
LEAD 4 Met +TZD combination	Liraglutide 1.8 mg	40	16/178
	Placebo	9	0/175
LEAD 5 Met + SU combination	Liraglutide 1.8 mg	14	2/230
	Glargine	1	0/232

Data orginally presented as Marre *et al. Diabetes* 2008;57(Suppl. 1):A4 (LEAD 1); Nauck *et al. Diabetes* 2008;57(Suppl. 1):A150 (LEAD 2); Garber et al, The Lancet, accepted for publication (LEAD 3); Zinman *et al. Diabetologia* 2008;51(Suppl. 1): Poster 898 (LEAD 4); Russell-Jones *et al. Diabetes* 2008;57(Suppl. 1):A159 (LEAD 5).

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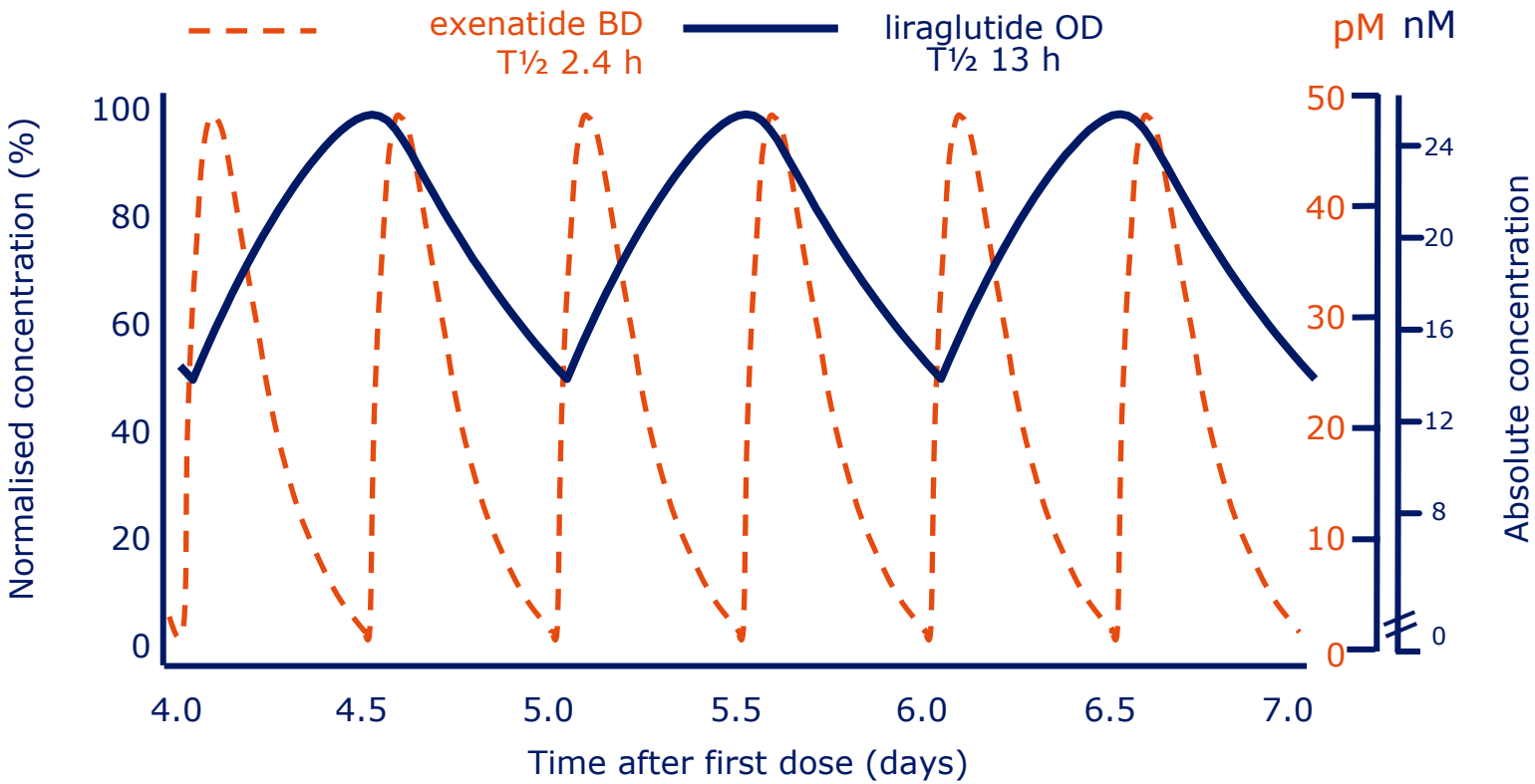
Liraglutide profile

Area	Risk / benefit profile
Antibodies	• Less than 10% of patients across the LEAD trials • No neutralising antibodies • No impact on glycemic control
Cardiovascular profile	• Significant weight loss • Significant reduction in systolic blood pressure • Significant HbA1c reduction • Positive trend on triglycerides and cholesterol (LDL/HDL ratio) • Transient heart rate increase of 2-3 beats per minute
Injection	• Convenient and safe injections
Acute Pancreatitis	• Low number of incidents observed. No cases of hemorrhagic or necrotising pancreatitis. • Incidence rate in the normal range for type 2 diabetes

Steady state levels of GLP-1 after treatment with liraglutide and exenatide



- Modelling of plasma concentration of active drug vs maximal concentration at steady state achieved following clinically relevant doses OD or BD. Based on published exenatide data and modelled liraglutide data.

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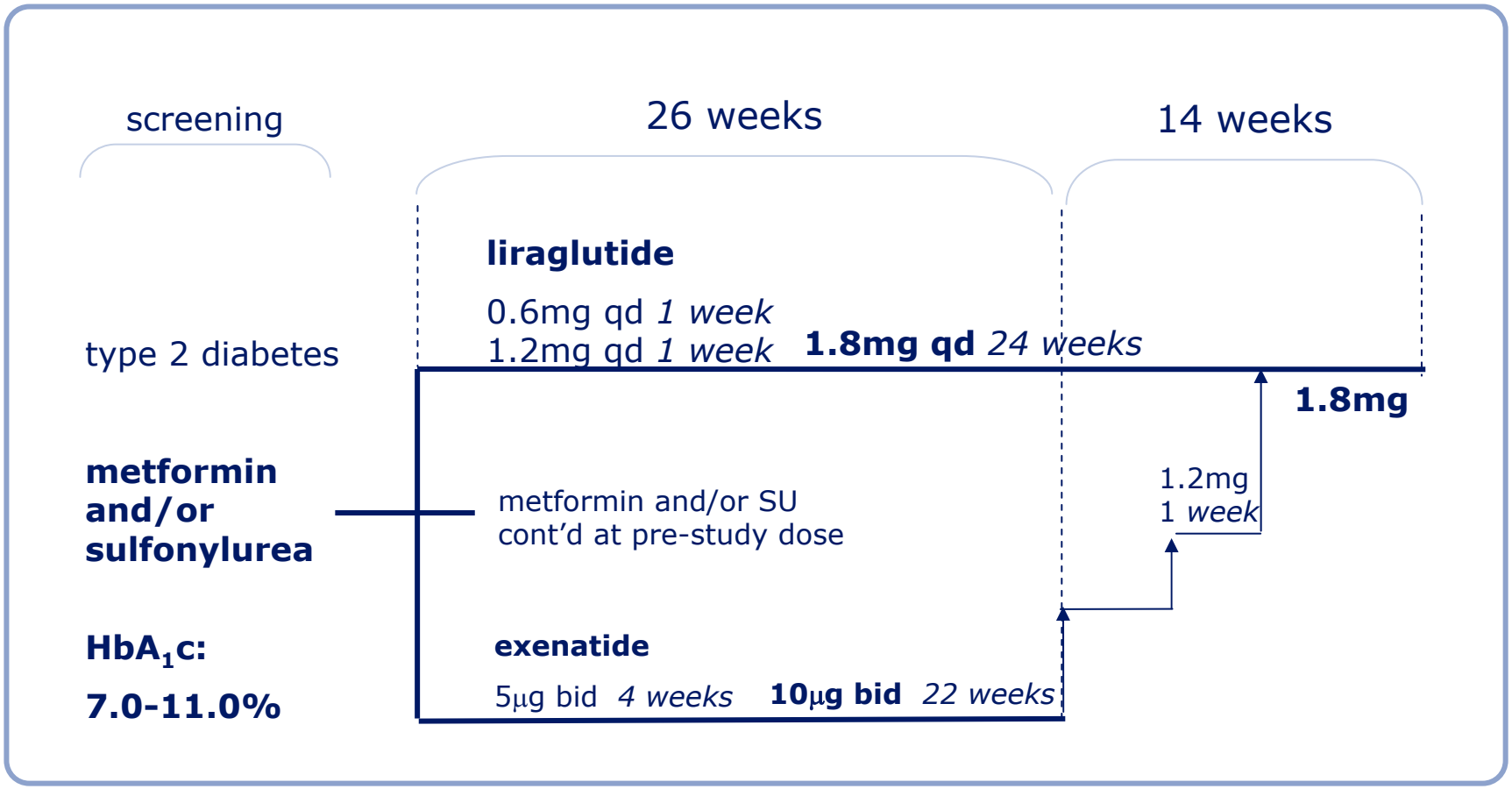
Source: Jonker *et al. Diabetes* 56 (Suppl. 1):A160 (Abstract 0605-P from ADA 2007)

Outline of LEAD 6 study design



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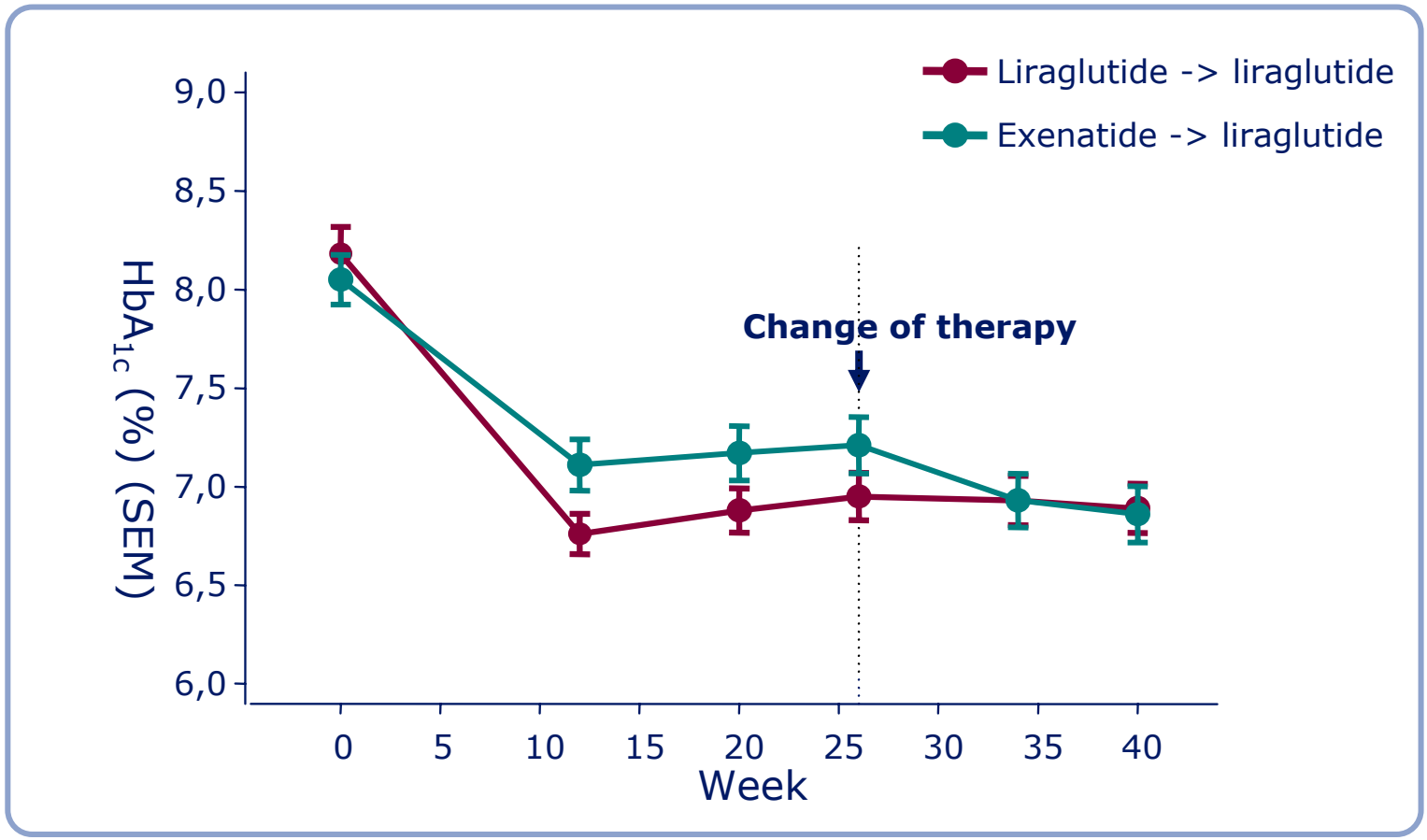
LEAD 6 - headline efficacy data for the first 26 weeks

- Average baseline HbA1c level was slightly above 8%
- Patient treated with liraglutide achieved a statistically significantly larger reduction in HbA1c
  - Liraglutide: Reduction of more than 1.1%
  - Exenatide: Reduction of less than 0.8%
- The most frequently reported adverse event was nausea
  - Liraglutide: the percentage of patients reporting nausea fell to low single-digit numbers after 8–10 weeks
  - Exenatide: the percentage of patients reporting nausea was around 10% throughout the study
- The overall rate of hypoglycaemia in the study was low
  - The rate of minor hypoglycaemia was statistically significantly lower in the liraglutide group

Detailed clinical data will be presented 16 October 2008 at the annual Canadian Diabetes Association meeting in Montreal

LEAD 6 14-week extension: shift of patients to liraglutide improves control: HbA_{1c}



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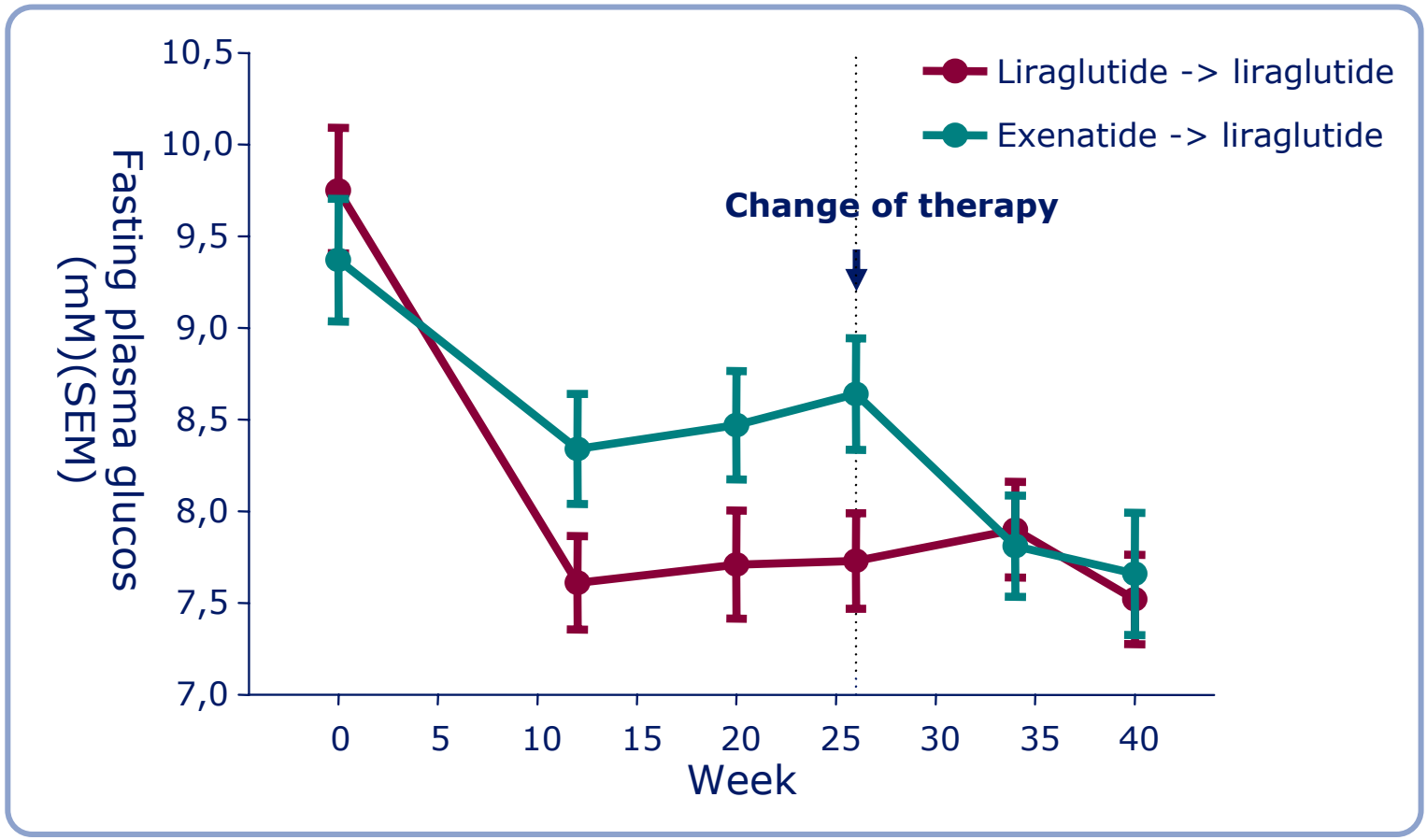
LEAD 6 14-week extension: shift of patients to liraglutide improves control: FPG



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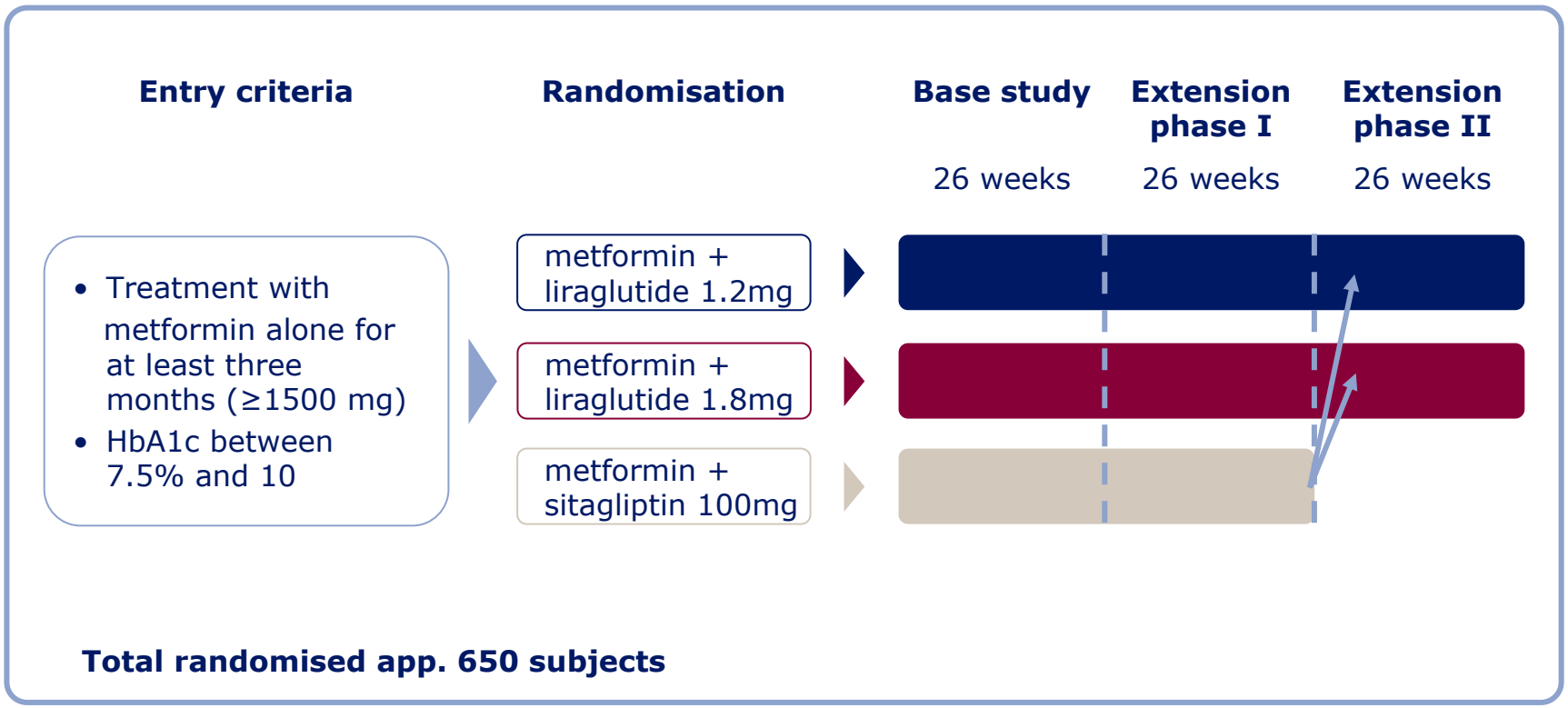
LEAD 6 14-week extension: headline data

- Patients that switched from exenatide to liraglutide:
  - HbA_{1c} statistically significantly decreased by 0.3 percentage points
  - FPG statistically significantly decreased by 0.9 mmol/L
  - Average body weight statistically significantly reduced by approximately 1 kg
  - Systolic blood pressure statistically significantly reduced by close to 4 mmHg
- Tolerability profile of liraglutide confirmed

Design of phase 3b study vs. sitagliptin



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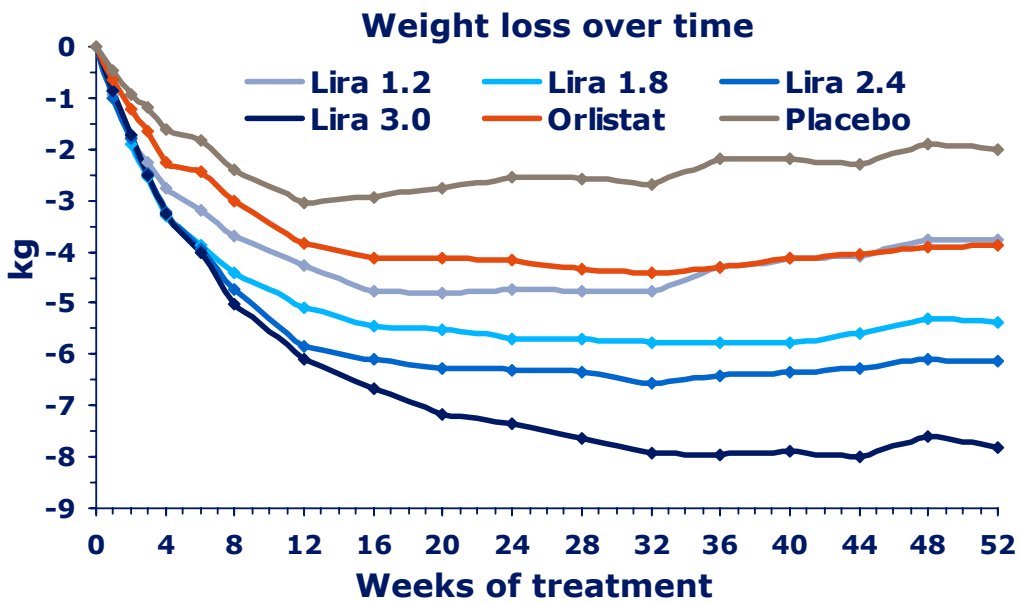
Weight loss over time with liraglutide

- App. 75% treated with 3.0 mg liraglutide achieved a weight loss larger than 5%
- More than 35% treated with 3.0 mg liraglutide achieved a weight loss larger than 10%
- Signs of prediabetes disappeared for 80% of prediabetics treated with 3.0 mg liraglutide



Note: ANCOVA analysis of ITT population, LOCF

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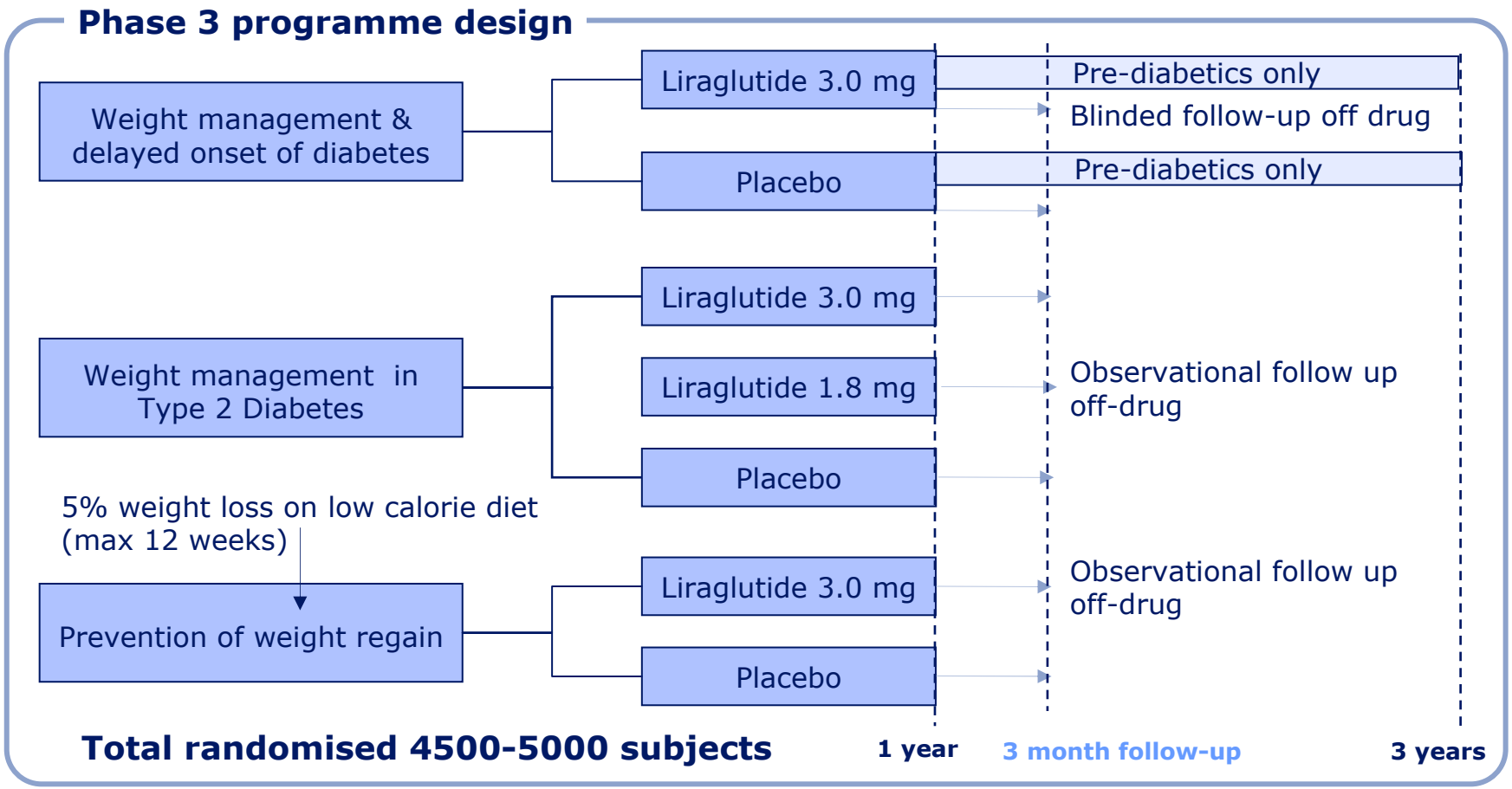
Design of the phase 3 programme



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Timeline for phase 3 study and pursued indication in obesity

Phase 3 timeline

Programme planning:

- Programme expected to start before year-end 2008
- 1 year data expected early 2011

Expected indication

Weight Management:

- Obese subjects (BMI>30)
- …or overweight subjects with co-morbidities
  (BMI > 27 + hypertension / dyslipidaemia / type 2 diabetes)

Concluding remarks

Compound	Type	Indication	Phase
Liraglutide	Once-daily GLP-1 analogue	Type 2 diabetes	Filed in the US, EU and Japan
Liraglutide	Once-daily GLP-1 analogue	Obesity	Phase 2 completed
NN9535	Once-weekly GLP-1 analogue	Type 2 diabetes	Phase 2
	Non-invasive GLP-1 analogue	Type 2 diabetes	Pre-clinical