

R&D Strategy for diabetes

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Focusing on diabetes

		Therapeutic Classification	Marketed Products	Development Compounds	Research Stage
Metabolic Syndrome	Diabetes	Insulin Secretagogue	Glimicron	Repaglinide	◎
		Insulin Sensitizer	Melbin	Metformin	◎
		Glucose Absorption Inhibitor	Seibule		◎*
		Complication Treatment		Ranirestat	◎
	Cardio-vascular	Hypertension etc.	Amlodin Cetapril Almarl	Irbesartan	◎

* SGLT1 (Selective Glucose Transporter 1) Inhibitor ²

Antidiabetic Agents at Clinical Stage (P2 or higher)

	P2	P3	Marketed
Insulin Secretagogue (SU) ¹⁾			Glimicron
Rapid Insulin Secretagogue (RIS)	SMP-508 (repaglinide)		
Insulin Sensitizer (BG) ²⁾	SMP-862 (metformin)		Melbin
Glucose Absorption Inhibitor (α GI)			Seibule*
Diabetic Complications Treatment (ARI) ³⁾	AS-3201 (ranirestat) (Japan)	AS-3201 (ranirestat) (overseas)	

¹⁾Sulfonylurea ²⁾ Biguanide, ³⁾ Aldose Reductase Inhibitor * Co-promotion with Sanwa Chemical

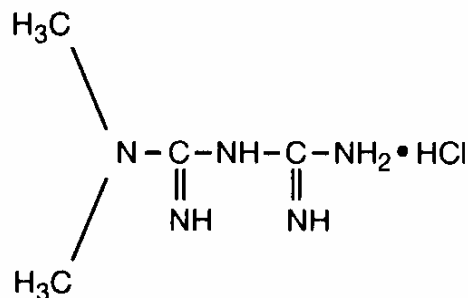
SMP-862

【P II b in Japan】

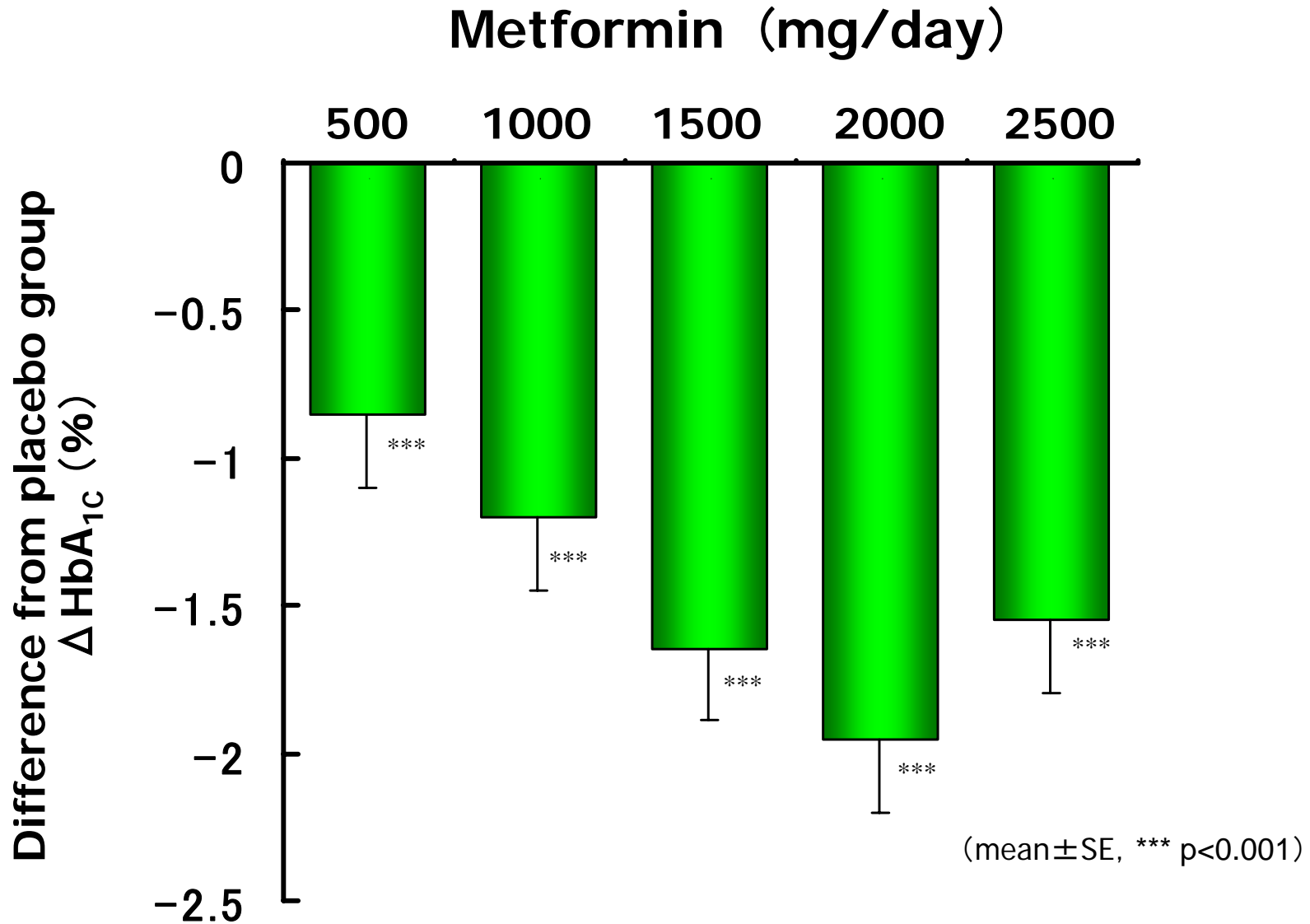
- **Generic Name: Metformin (INN)**
- **Brand Name: To be decided**
- **Regulatory Category for Japanese NDA:**
1-(4) New Indication, 1-(6) New Strength

★ **First-line treatment** for Type II Diabetes
 ★ **New dosage higher than currently approved 750 mg/day** with evidence based on results from on-going clinical studies

- **Target Disease: Type 2 Diabetes**
- **Pharmacological Classification: Biguanide**
 (Suppression of hepatic gluconeogenesis and improvement of insulin sensitivity by increasing peripheral glucose uptake and utilization)



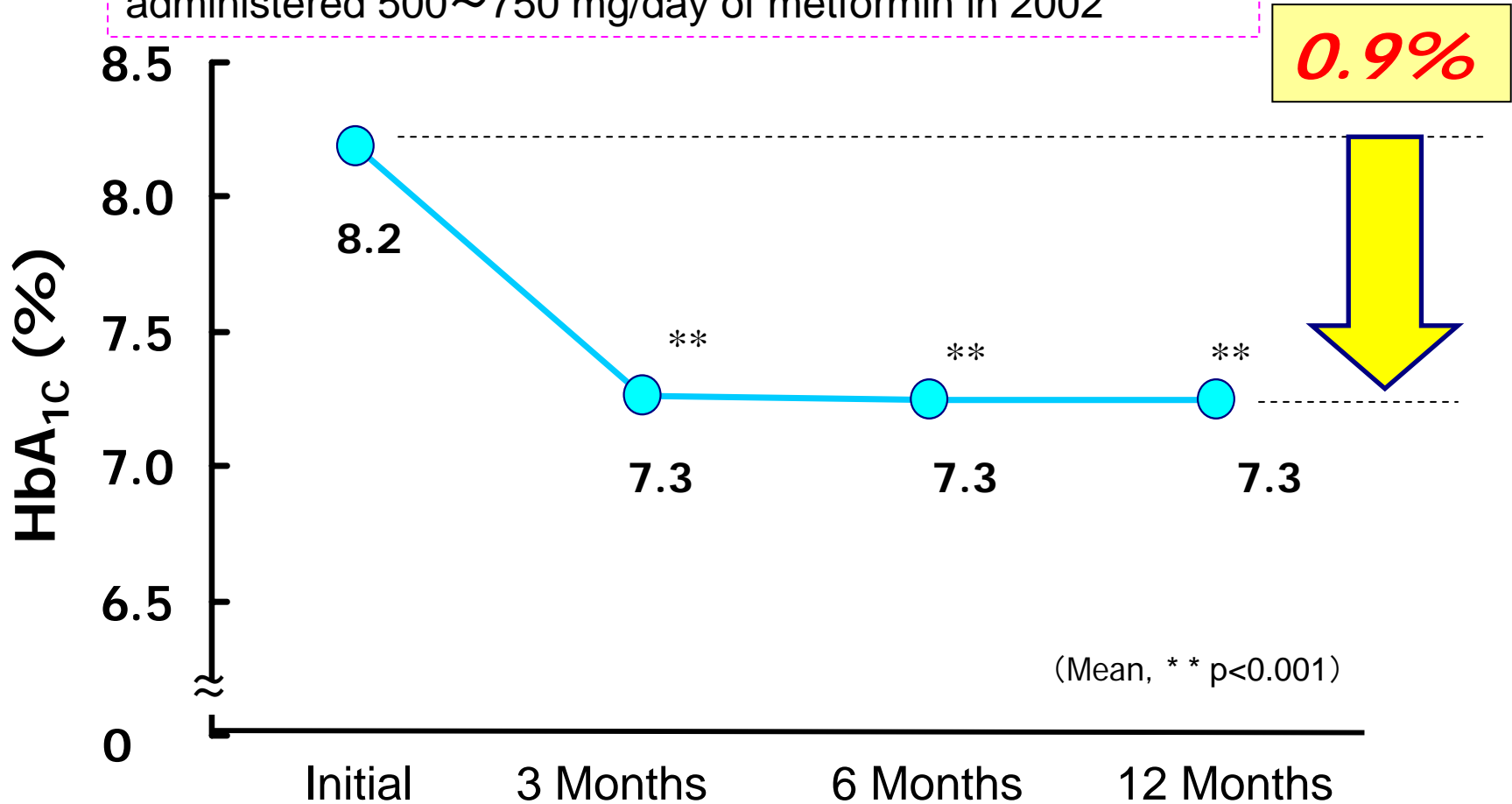
Metformin: Blood Glucose Lowering Effect (US)



Melbin (Metformin) Observational Research (MORE) Study: Effect of metformin on Type 2 diabetes

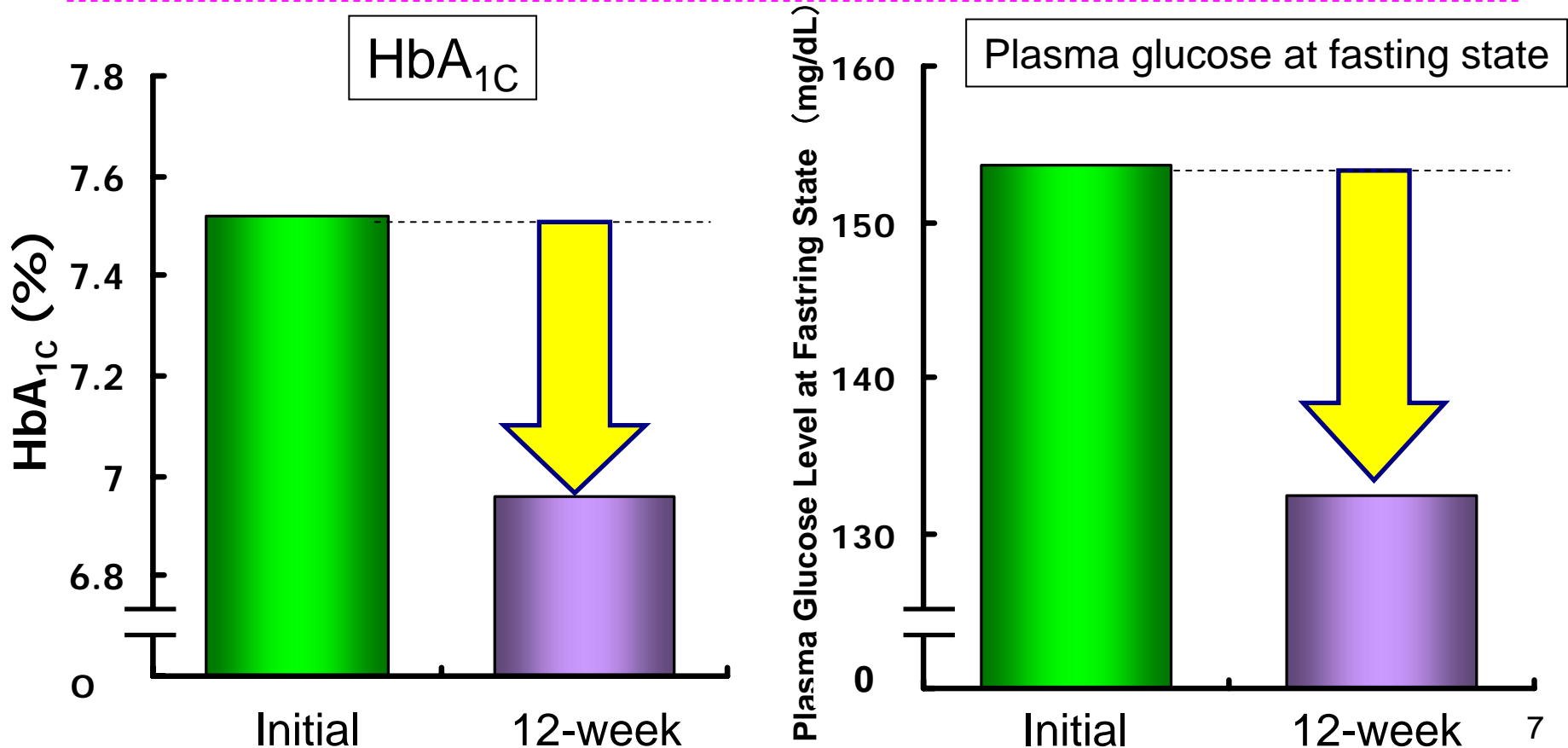


Results from 1197 type II diabetic patients in 74 sites newly administered 500~750 mg/day of metformin in 2002

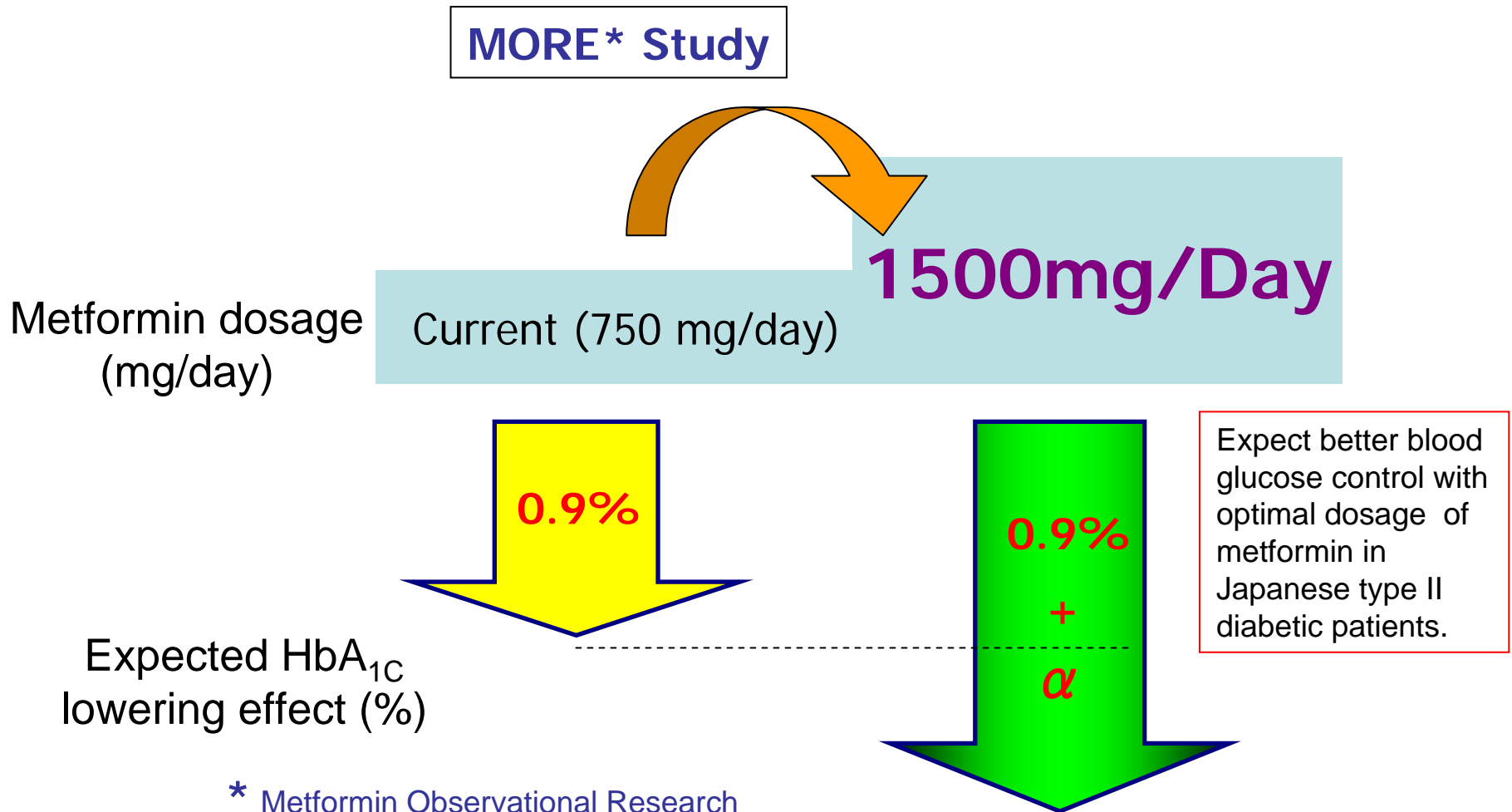


Effect of increased dosage of metformin on HbA_{1c} and plasma glucose level at fasting state

12-week treatment with 1500 mg/day of SMP-862 (metformin) in Type II diabetic patients whose blood glucose is insufficiently controlled with currently approved metformin dosage of 750 mg/day



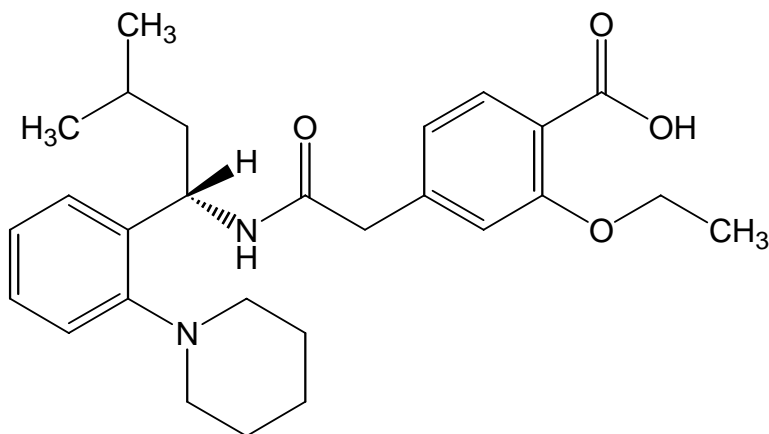
Expected blood glucose lowering effect of metformin in Japanese type II diabetic patients



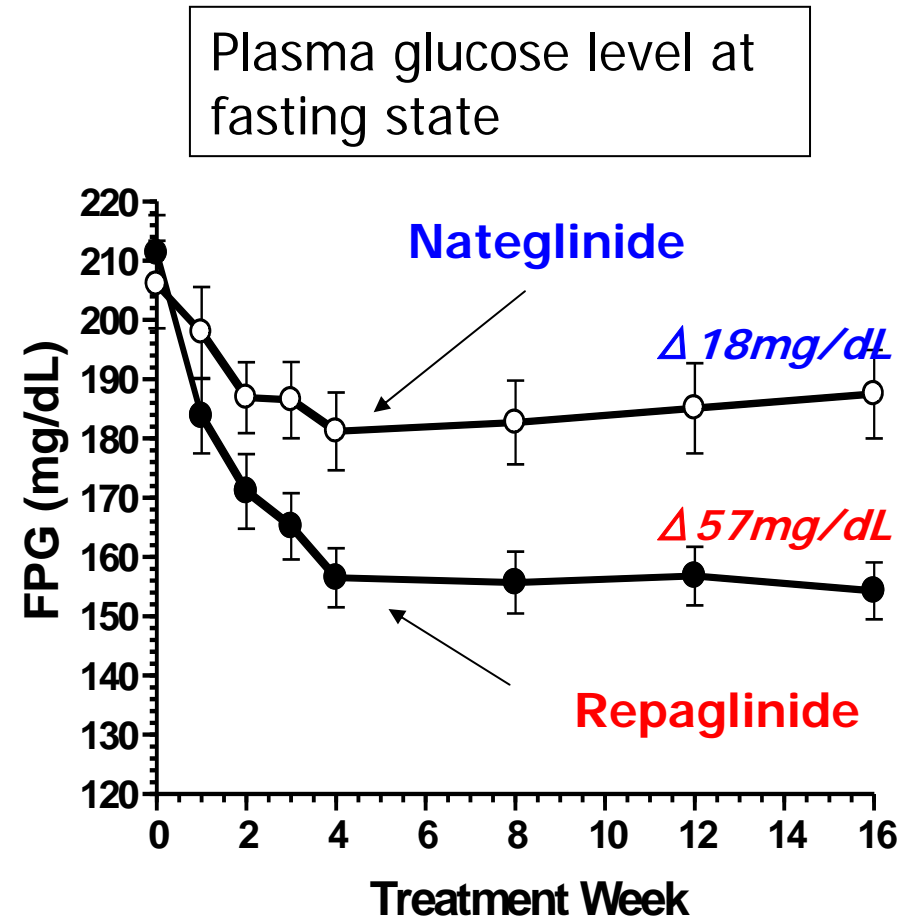
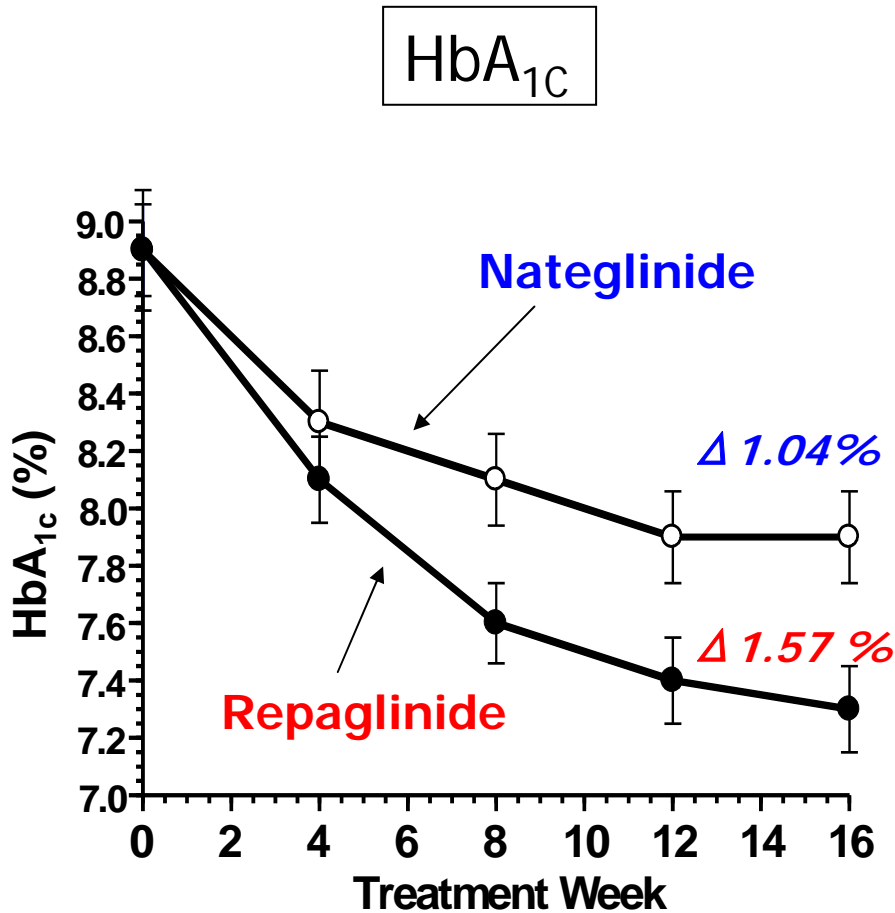
SMP-508

【P II b in Japan】

- **Generic Name:** Repaglinide (INN)
- **Brand Name:** To be decided
- **Regulatory category for Japanese NDA:**
1-(1) New chemical entity
- **Target disease:** Type II diabetes
- **Pharmacological classification:** Rapid insulin secretagogue



— Plasma glucose control with RIS* — Comparison between Repaglinide and Nateglinide



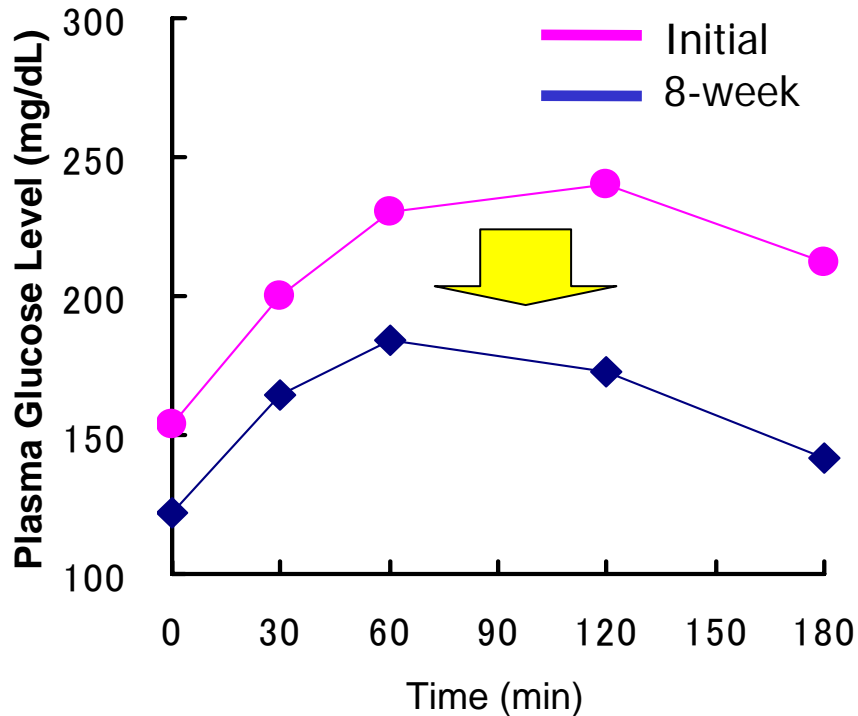
* Rapid Insulin Secretagogue

Rosenstock, J et al. Diabetes Care 27; 1265,2004.

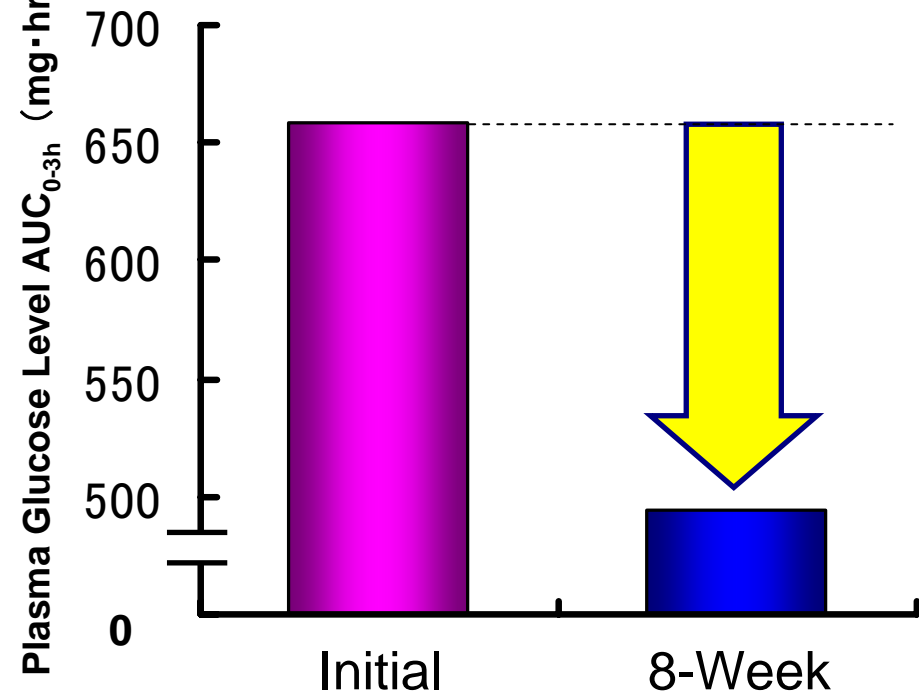
Concomitant Treatment with SMP-508 added to α -GI (P2a Study): Postprandial plasma glucose level

Effect of 8-week treatment with SMP-508 added to α -GI used at its approved dosage in patients with insufficient control of plasma glucose

Postprandial plasma glucose level

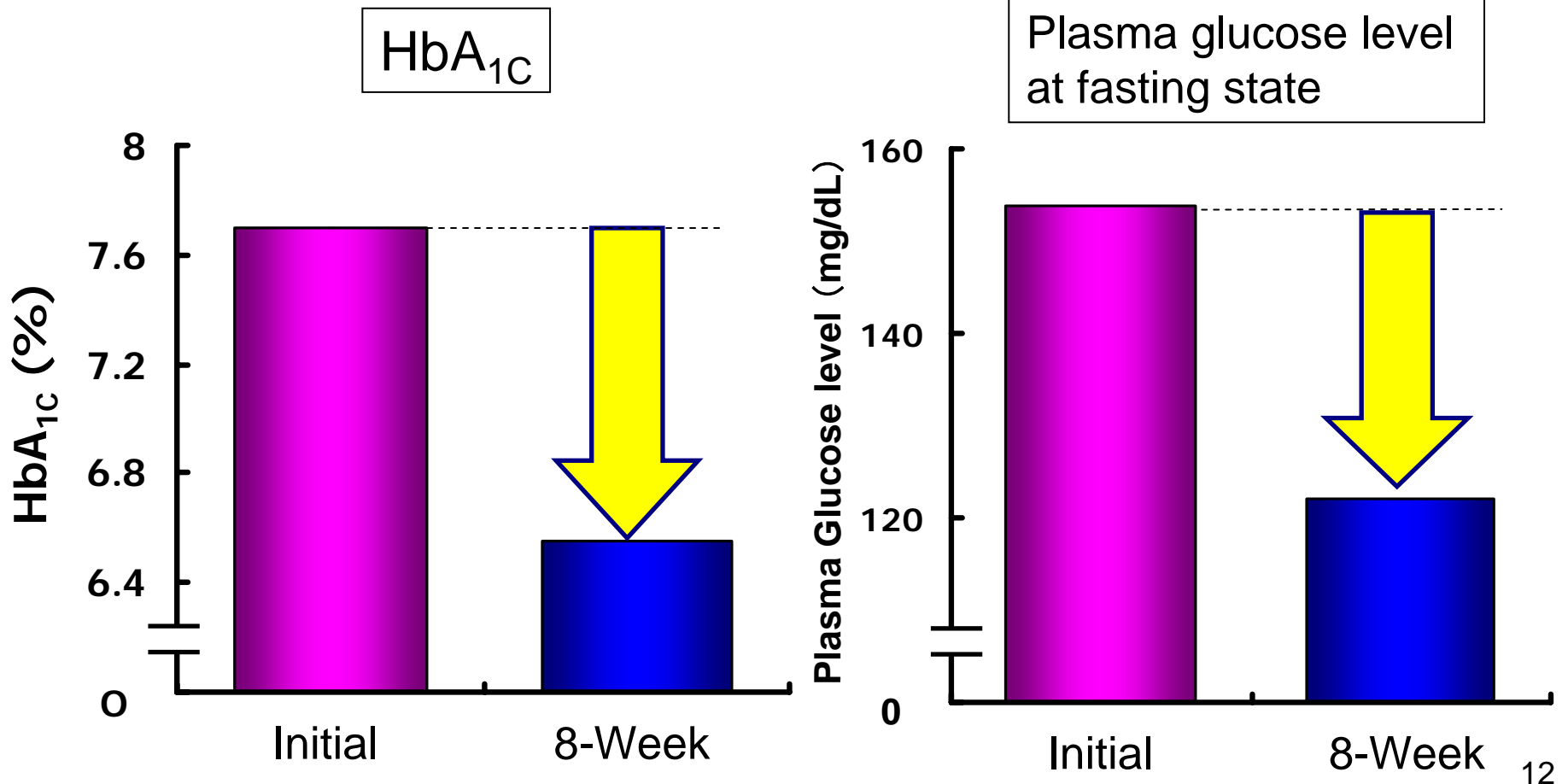


Postprandial plasma glucose level AUC_{0-3h}



Concomitant Treatment with SMP-508 added to α -GI (P2a Study): HbA_{1c} and Plasma Glucose Level at Fasting State

Effect of 8-week treatment with SMP-508 added to α -GI used at its approved dosage in patients with insufficient control of plasma glucose



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