

第28回MGR

トピックス：境界型糖尿病、GI

発表者：古屋佑子（専修医）

コメンテーター：井上正晴（糖尿病内分泌内科）

文献

Voglibose for prevention of type 2 diabetes mellitus : a randomised, double-blind trial in Japanese individuals with impaired glucose tolerance

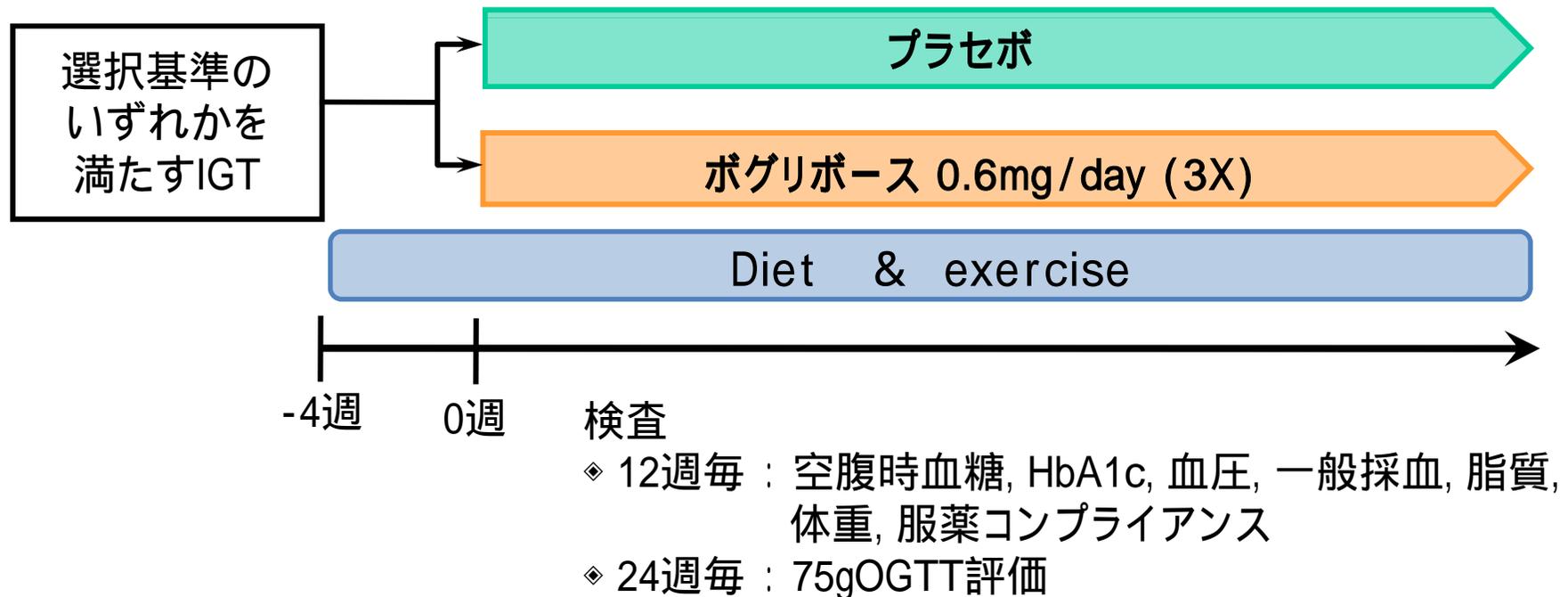
Ryuzo Kawamori, Naoko Tajima, Yasuhiko Iwamoto, Atsunori Kashiwagi, Kazuaki Shimamoto, Kohei Kaku, on behalf of the Voglibose Ph-3 study group

Lancet 2009; 373, 1607-1614

2011年9月26日

ボグリボースによる糖尿病発症予防

- 経口血糖降下薬である α -GI (voglibose) がハイリスク患者で2型糖尿病への進展を防止できるか評価
- Primary endpoint : 2型糖尿病に進展
- Secondary endpoint : 正常血糖になった時



方法

- Randomized double-blind study
- 103施設を対象として、2003年4月から登録
- 対象:

空腹時血糖 126mg/dL未満

75gOGTT 2時間値 140 ~ 199mg/dL

HbA1c 6.5%未満

少なくとも1つ2型糖尿病のリスクファクター

Risk factor

血圧 : sBP 130mmHg, dBP 85mmHg または治療中

脂質 : T-cho 220mg/mL, TG 150mg/mL, HDL < 40mg/mL

肥満 : BMI 25

1-2親等以内での糖尿病家族歴

Trial profile

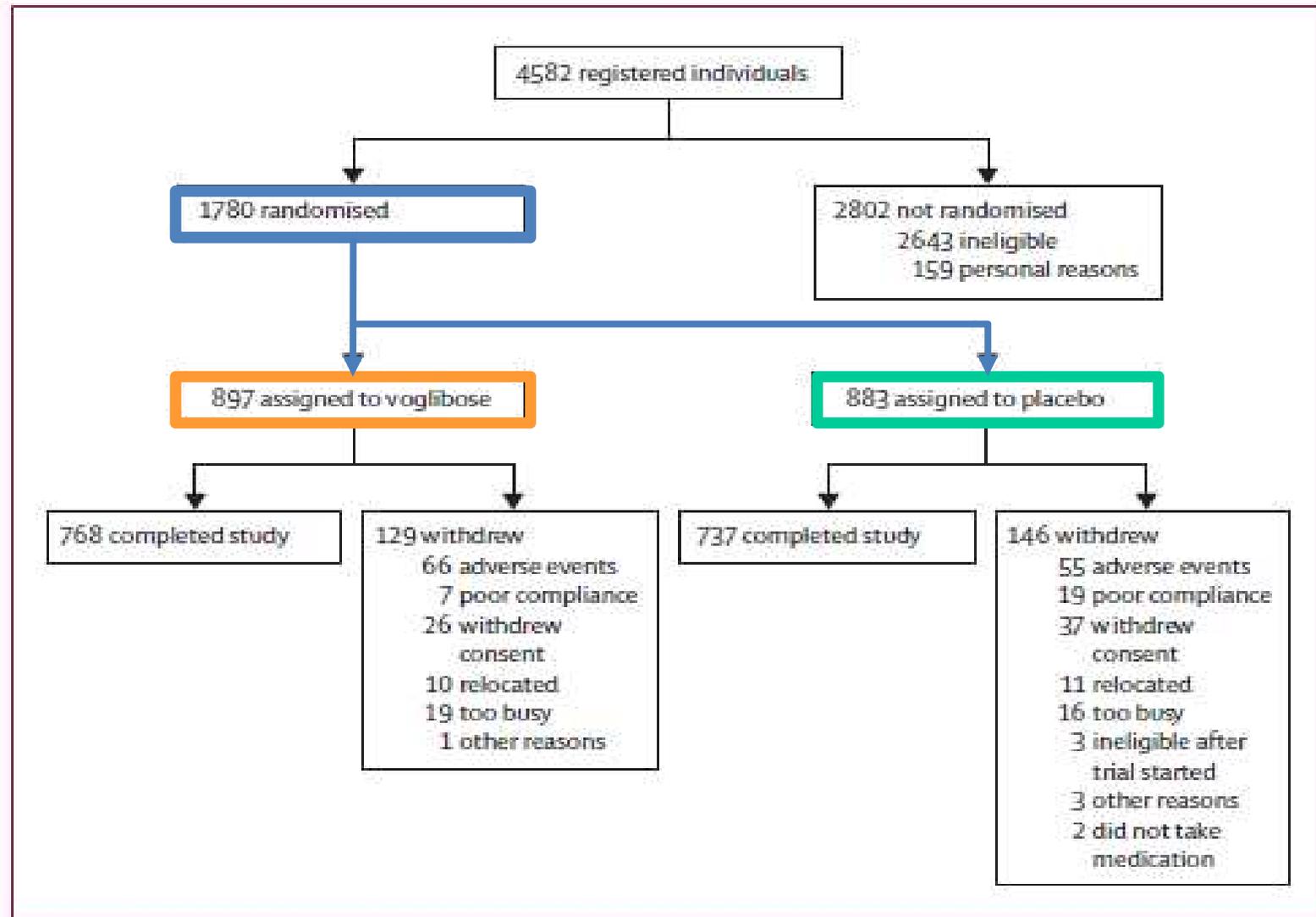


Figure 1: Trial profile

Kawamori R. et al., Lancet, 373, 1607, 2009.

患者背景

	ボグリボース (n=897)	プラセボ (n=881)
男性	541 (60%)	530 (60%)
女性	356 (40%)	351 (40%)
年齢(歳)	55.7 ± 9.08	55.7 ± 9.16
BMI(kg/m ²)	25.76 ± 3.70	25.89 ± 3.82
空腹時血糖値(mg/dL)	104.4 (9.9)	105.3 (10.1)
食後2時間血糖値(mg/dL)	164.1 (16.6)	165.5 (17.0)
肥満(BMI ≥ 25)	502 (56%)	500 (57%)
高脂血症	695 (77%)	667 (76%)
高血圧症	528 (59%)	510 (58%)
糖尿病家族歴あり	337 (38%)	336 (38%)
食後2時間血糖値(170 ~ 199mg/dL)	323 (36%)	345 (39%)
リスク因子の保有数		
2個以下	340 (38%)	330 (37%)
3個以上	557 (62%)	551 (63%)

2型糖尿病新規発症率

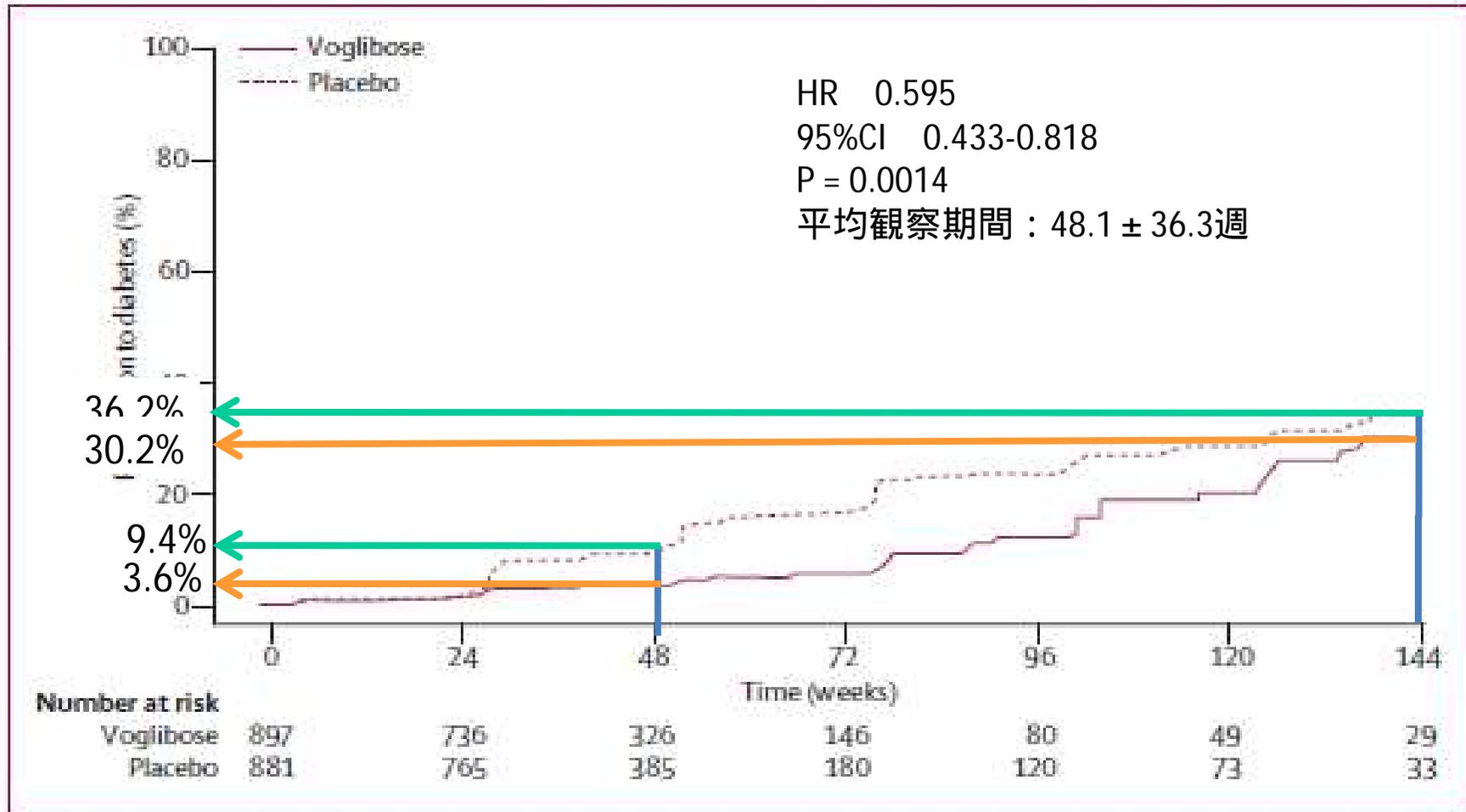


Figure 2: Effect of voglibose and placebo on the cumulative probability of individuals developing type 2 diabetes (Kaplan-Meier method)

リスク数別2型糖尿病新規発症率

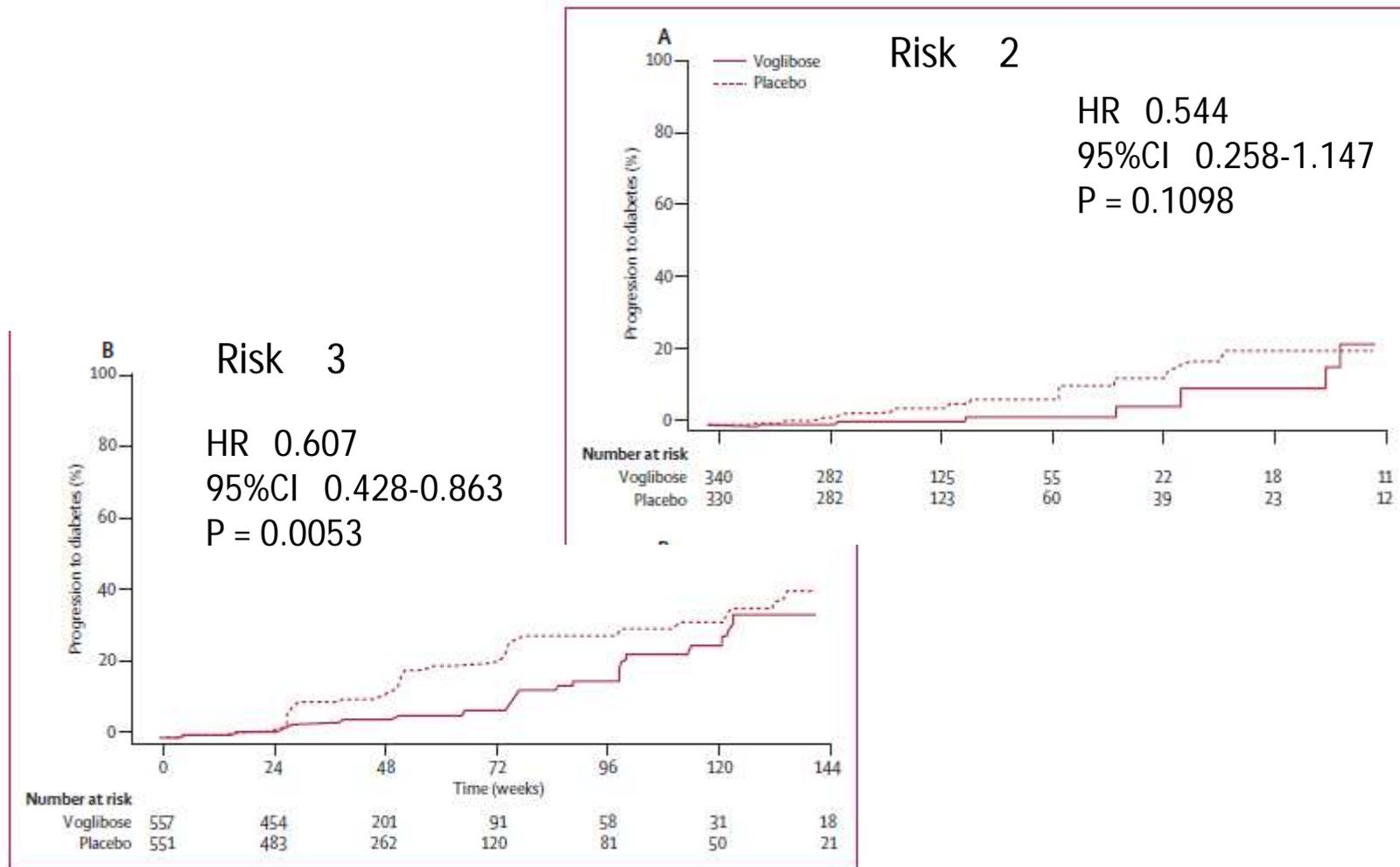


Figure 3: Effect of voglibose and placebo on the cumulative probability of individuals developing type 2 diabetes based on the number of risk factors (Kaplan-Meier method)
(A) At most two risk factors. (B) At least three risk factors.

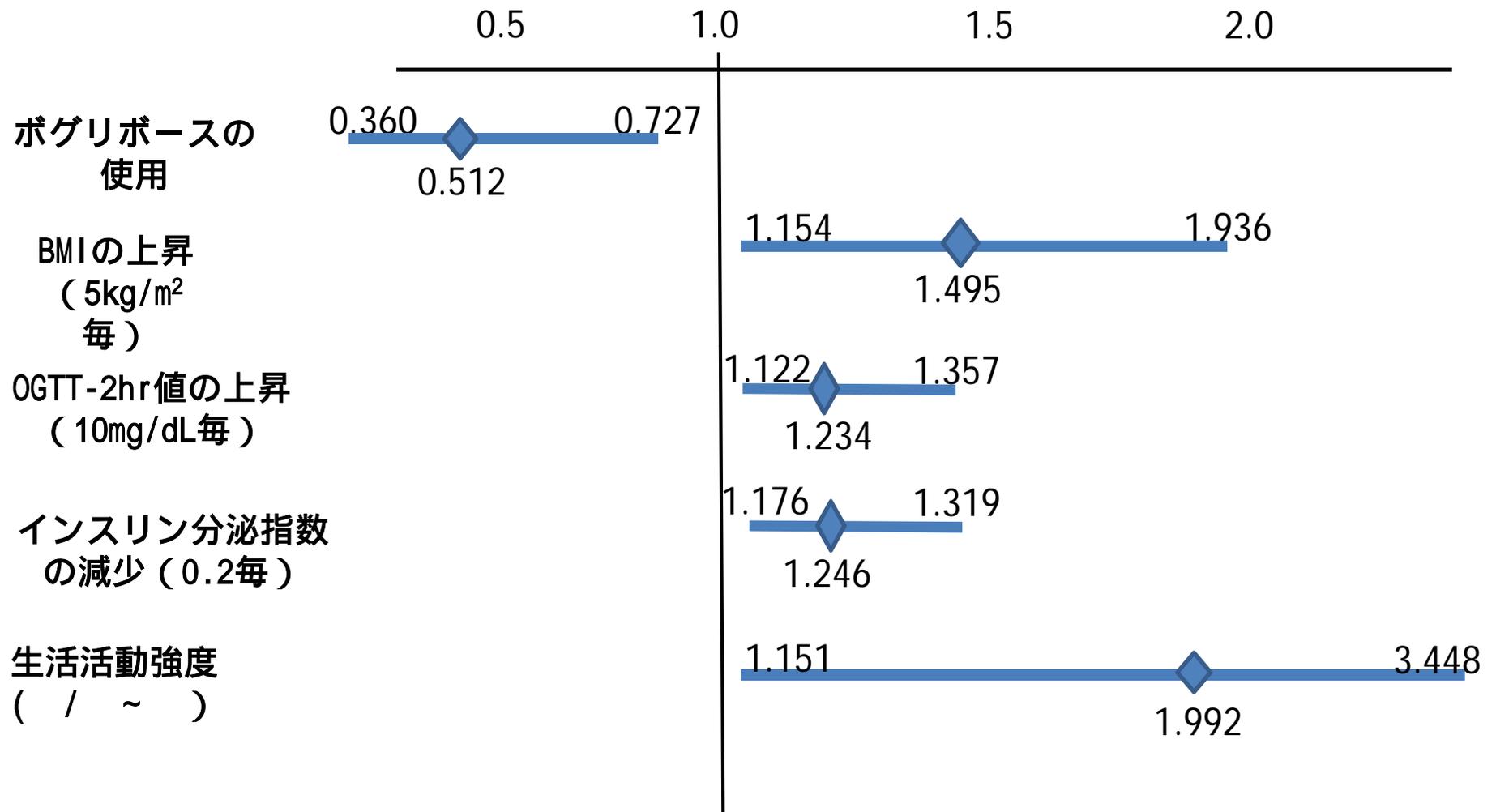
患者背景での多変量解析

	Direction estimation	Univariable analysis		Multivariable analysis	
		Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Treatment group	Voglibose/placebo	0.564 (0.403-0.790)	0.0009	0.512 (0.360-0.727)	0.0002
Age	10-year increase	0.839 (0.708-0.995)	0.0433	0.909 (0.731-1.130)	0.3893
Sex	Men/women	1.365 (0.973-1.915)	0.0715	1.278 (0.883-1.849)	0.1936
BMI	5 kg/m ² increase	1.445 (1.180-1.770)	0.0004	1.495 (1.154-1.936)	0.0023
Dyslipidaemia	Yes/no	1.305 (0.888-1.918)	0.1750	1.284 (0.868-1.899)	0.2107
Hypertension	Yes/no	0.829 (0.603-1.138)	0.2456	0.916 (0.614-1.367)	0.6665
Family history of diabetes	Yes/no	1.365 (0.994-1.875)	0.0546	1.253 (0.903-1.739)	0.1771
2hPG	0.55 mmol/L increase	1.278 (1.164-1.404)	<0.0001	1.234 (1.122-1.357)	<0.0001
Insulinogenic index	0.2 decrease	1.165 (1.103-1.230)	<0.0001	1.246 (1.176-1.319)	<0.0001
HOMA-R	1 increase	1.066 (0.999-1.148)	0.0927	1.094 (0.984-1.216)	0.0983
Smoker	Yes/no	1.648 (1.184-2.294)	0.0030	1.327 (0.931-1.893)	0.1182
Intensity of daily activity	I/III to IV	2.109 (1.231-3.614)	0.0066	1.992 (1.151-3.448)	0.0138
Intensity of daily activity	II/III to IV	1.513 (0.894-2.562)	0.1229	1.340 (0.784-2.288)	0.2842
Concomitant use of ACE inhibitor or ARB	Yes/no	0.859 (0.618-1.194)	0.3648	0.996 (0.663-1.496)	0.9834

2hPG=2 h plasma glucose concentration during oral glucose tolerance test. ACE=angiotensin-converting enzyme. ARB=angiotensin receptor blocker. BMI=body-mass index. HOMA-R=homeostasis model assessment for insulin resistance.

Table 3: Simultaneous adjustment analysis by multivariables (Cox regression analysis)

患者背景での多変量解析



血糖正常化率

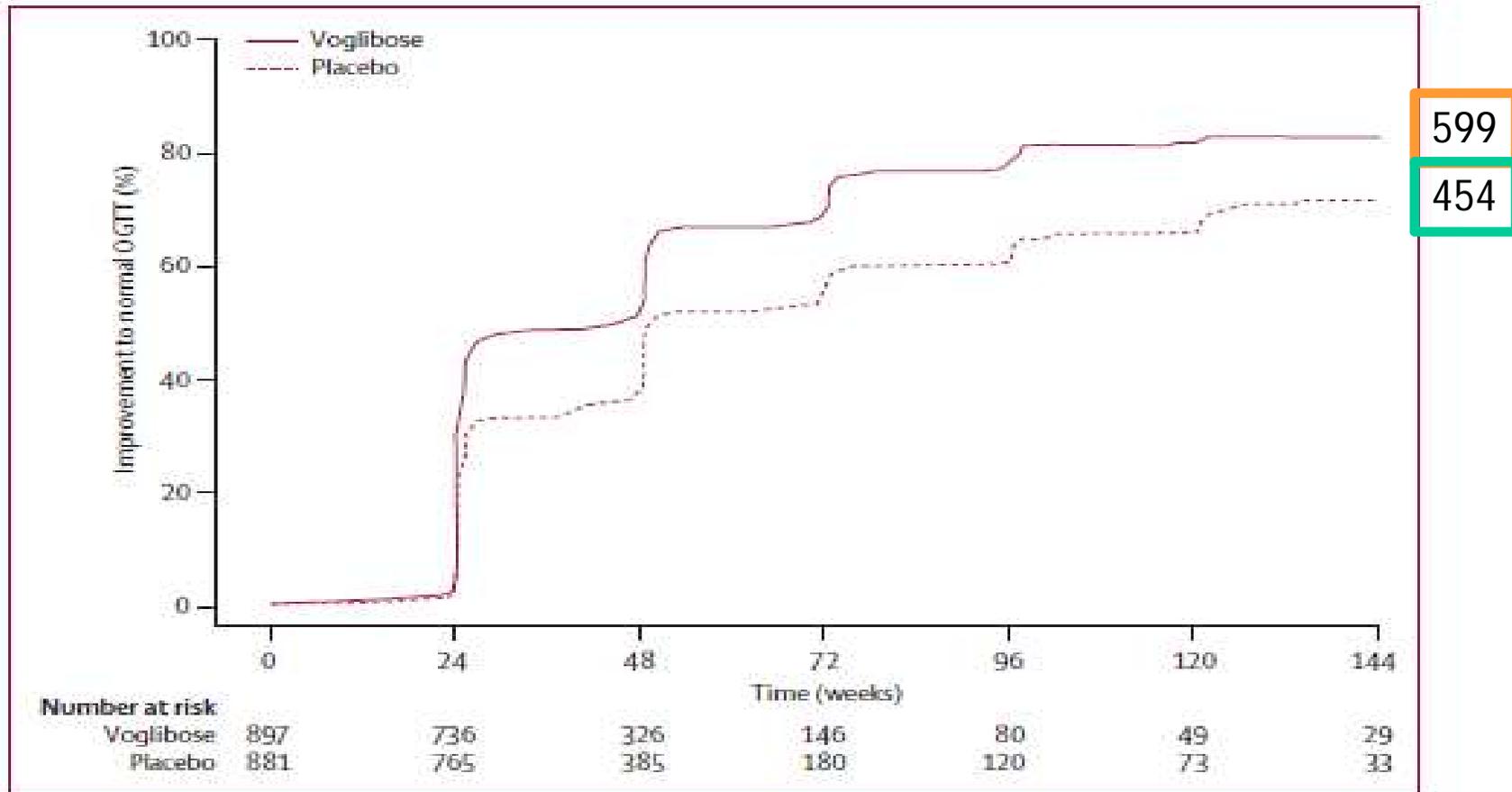


Figure 4: Effect of voglibose and placebo on the cumulative probability of individuals achieving normoglycaemia (Kaplan-Meier method)

OGTT=oral glucose tolerance test.

有害事象

	ボグリボース (n=897)	プラセボ (n=881)	P値		ボグリボース (n=897)	プラセボ (n=881)	P値
因果関係が否定できない有害事象	428 (47.7%)	257 (29.2%)	< 0.0001	因果関係が否定できない有害事象で服薬中止	46 (5.1%)	24 (2.7%)	0.0092
胃腸障害				生化学検査			
鼓腸	156 (17.4%)	63 (7.2%)	< 0.0001	CPK上昇	12 (1.3%)	9 (1.0%)	0.5372
腹部膨満	120 (13.4%)	49 (5.6%)	< 0.0001	ALT上昇	30 (3.3%)	17 (1.9%)	0.0630
下痢	110 (12.3%)	45 (5.1%)	< 0.0001	AST上昇	21 (2.3%)	11 (1.2%)	0.0832
便秘	39 (4.3%)	22 (2.5%)	0.0321	-GTP上昇	14 (1.6%)	18 (2.0%)	0.4443
腸雑音異常	39 (4.3%)	11 (1.2%)	< 0.0001				
胃不快感	10 (1.1%)	6 (0.7%)	0.3328				
上腹部痛	4 (0.4%)	4 (0.5%)	0.9796				
一般症状							
頭痛	2 (0.2%)	3 (0.3%)	0.6398				
浮動性めまい	11 (1.2%)	3 (0.3%)	0.0346				
湿疹	2 (0.2%)	2 (0.2%)	0.9856				

結論

- α -GI (voglibose) は耐糖能異常の改善・進展防止に明らかに効果があった。
- lifestyleの変更に加え、境界型糖尿病のHigh-risk患者での α -GI (voglibose) 内服は、2型糖尿病進展予防となりえる。