

Evaluation of Ranolazine in Patients with Type 2 Diabetes Mellitus and Chronic Stable Angina

Results from the TERISA Randomized Clinical Trial

Mikhail Kosiborod, Suzanne V. Arnold, John A. Spertus, Darren K. McGuire,
Yan Li, Patrick Yue, Ori Ben-Yehuda, Amos Katz, Phillip G. Jones,
Ann Olmsted, Luiz Belardinelli, Bernard R. Chaitman

On behalf of the TERISA Investigators



Saint Luke's

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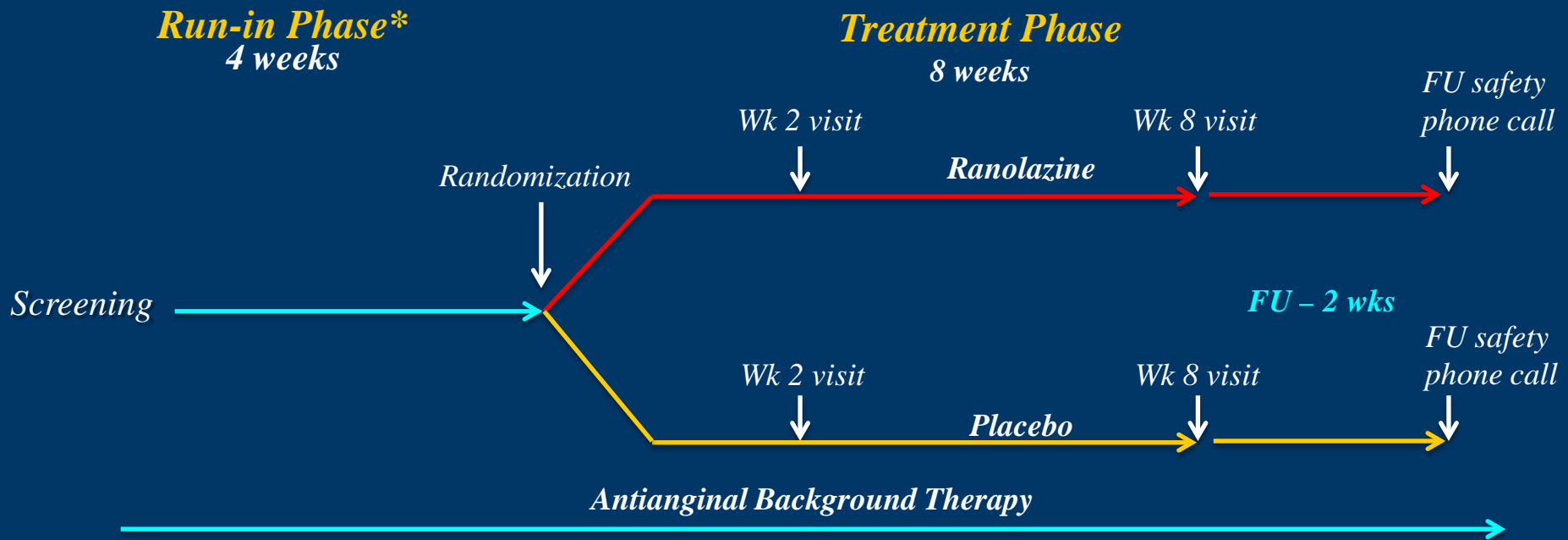


TERISA: Primary Objective

- Evaluate efficacy of ranolazine versus placebo on angina frequency in subjects with type 2 diabetes, CAD, and chronic stable angina who remain symptomatic despite treatment with 1 or 2 anti-anginal medications

TERISA: Study Design

- **Run-in Phase:** Single-blind placebo (4 weeks)
- **Treatment Phase:** Randomized double-blind parallel group phase (8 weeks): ranolazine (target dose 1000 mg bid vs. matching placebo)



Study Endpoints

- **Primary:** Average weekly number of angina episodes from weeks 2-8 of treatment
- **Key Secondary:** Average weekly number of SL NTG doses from weeks 2-8 of treatment

Data Acquisition

- Angina frequency and SL NTG use captured daily using electronic diary
- Daily data transfer



TERISA Sites



105 Sites from 14 Countries

Enrollment and Randomization

Assessed for Eligibility (n=1185)

Excluded (n=236)

- Not meeting inclusion criteria (n=43)
- Failed run-in (n=193)

Randomized (n=949)

Randomized to Ranolazine (n=473)

Randomized to Placebo (n=476)

Discontinuation of Treatment (n=11)

Discontinuation of Treatment (n=11)

Analyzed (n=462)

Analyzed (n=465)

Baseline Characteristics by Study Group

	Ranolazine n=462	Placebo n=465
Age (yr)	63.2	64.2
Men (%)	61.3	61.5
White (%)	98.7	99.4
Hypertension (%)	95.0	95.9
Dyslipidemia (%)	79.4	80.3
Current smoking (%)	15.4	16.6
Prior myocardial infarction (%)	75.4	72.7
Prior angioplasty (%)	42.7	38.8
Prior bypass graft surgery (%)	18.2	18.9

Baseline Characteristics by Study Group

	Ranolazine n=462	Placebo n=465
Duration of diabetes (yr)	7.2±6.7	7.7±7.0
HbA1c (%)	7.3±1.5	7.3±1.5
Glucose Lowering Medication (%)	93.3	92.7
Insulin (%)	17.5	20.6

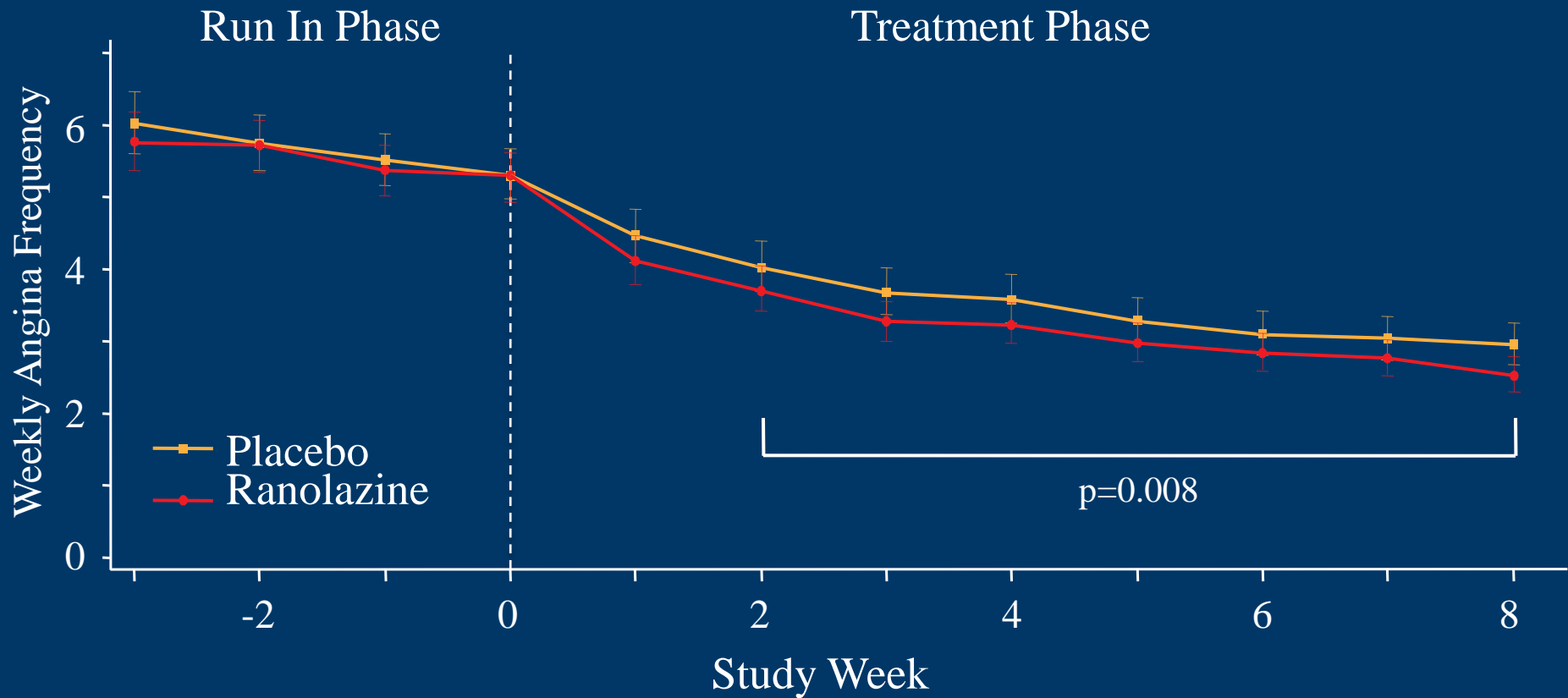
Baseline Characteristics by Study Group

	Ranolazine n=462	Placebo n=465
Antianginal medications		
on 1 (%)	56.1	55.7
on 2 (%)	43.9	44.3
Beta blockers (%)	90.5	89.9
Calcium channel blockers (%)	26.8	30.8
Long acting nitrates (%)	34.8	32.5
Statins (%)	82.5	82.4
Antiplatelet agents (%)	89.8	86.5
ACE-I/ARBs (%)	88.1	87.5
Diary compliance - median % (IQR)	98 (95-98)	98 (95-98)

Primary Endpoint

	Ranolazine n=462	Placebo n=465	p-value
<i>Least squares mean (95% CI)</i>			
Angina frequency, baseline (#/wk)	6.6 (6.3-7.0)	6.8 (6.4-7.2)	0.54
Angina frequency, on treatment (#/wk)	3.8 (3.6-4.1)	4.3 (4.0-4.5)	0.008

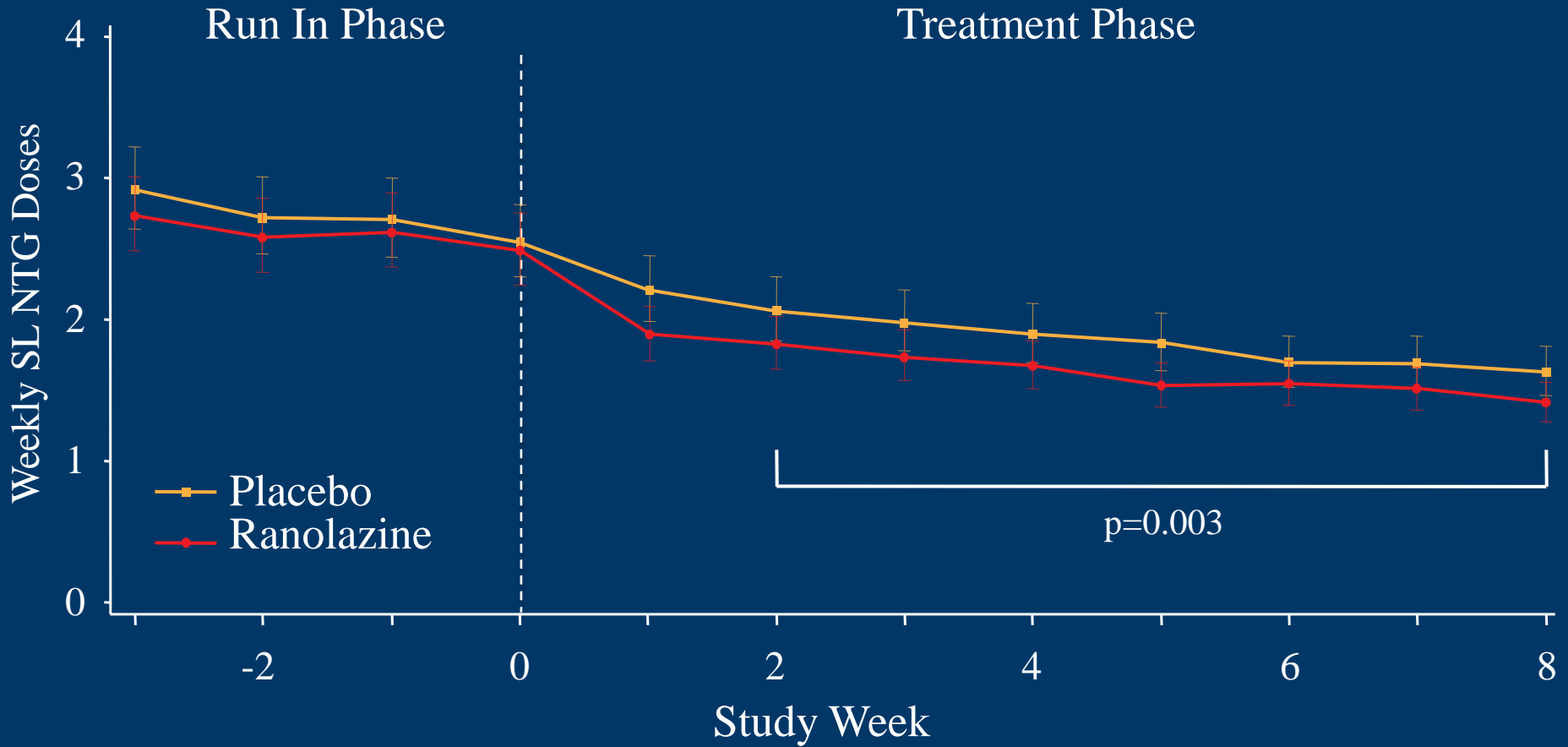
Weekly Angina Frequency by Study Group



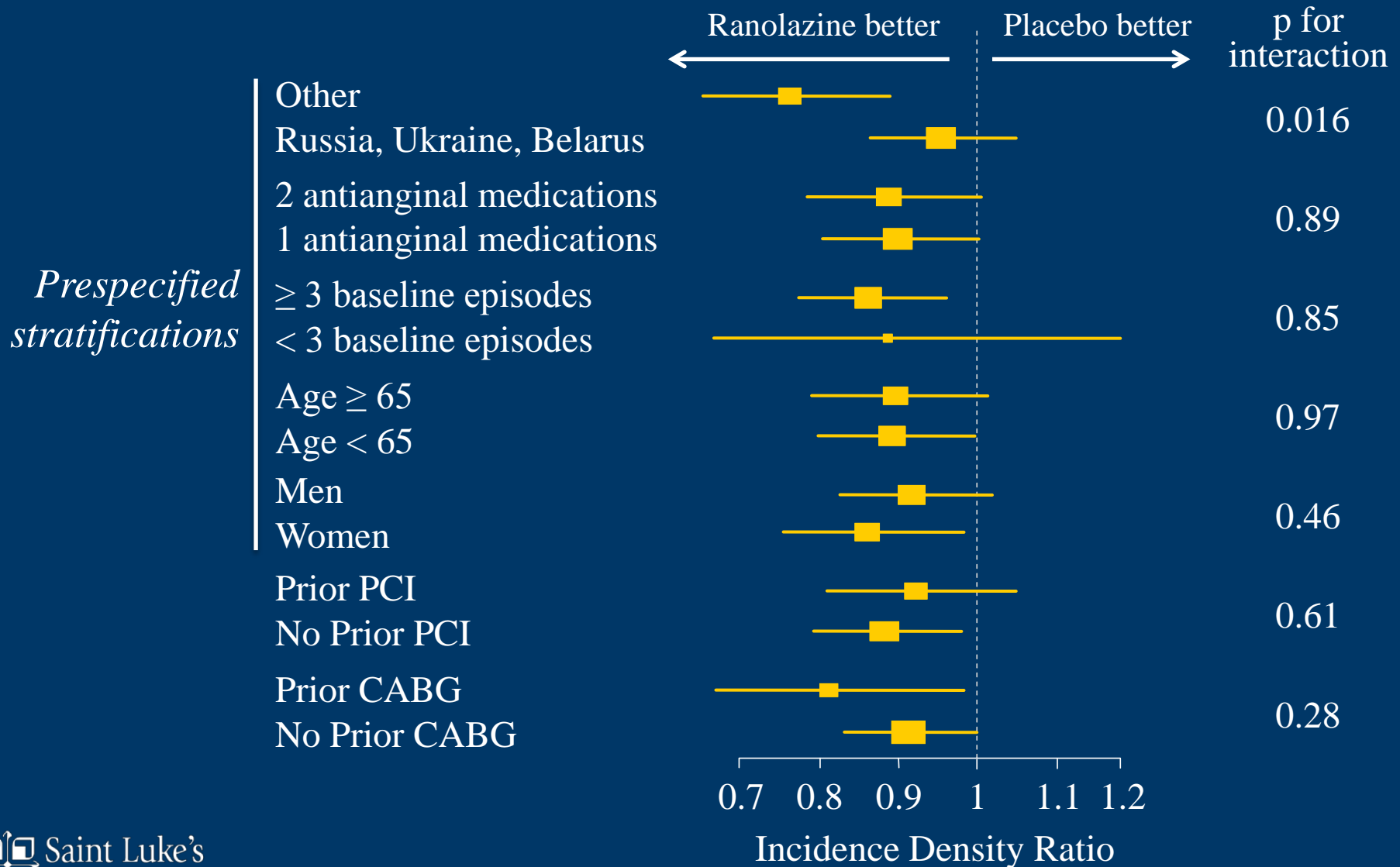
Key Secondary Endpoint

	Ranolazine n=462	Placebo n=465	p-value
<i>Least squares mean (95% CI)</i>			
SL NTG doses, baseline – (#/wk)	4.1 (3.7-4.6)	4.5 (4.1-5.0)	0.27
SL NTG doses, on treatment (#/wk)	1.7 (1.6-1.9)	2.1 (1.9-2.3)	0.003

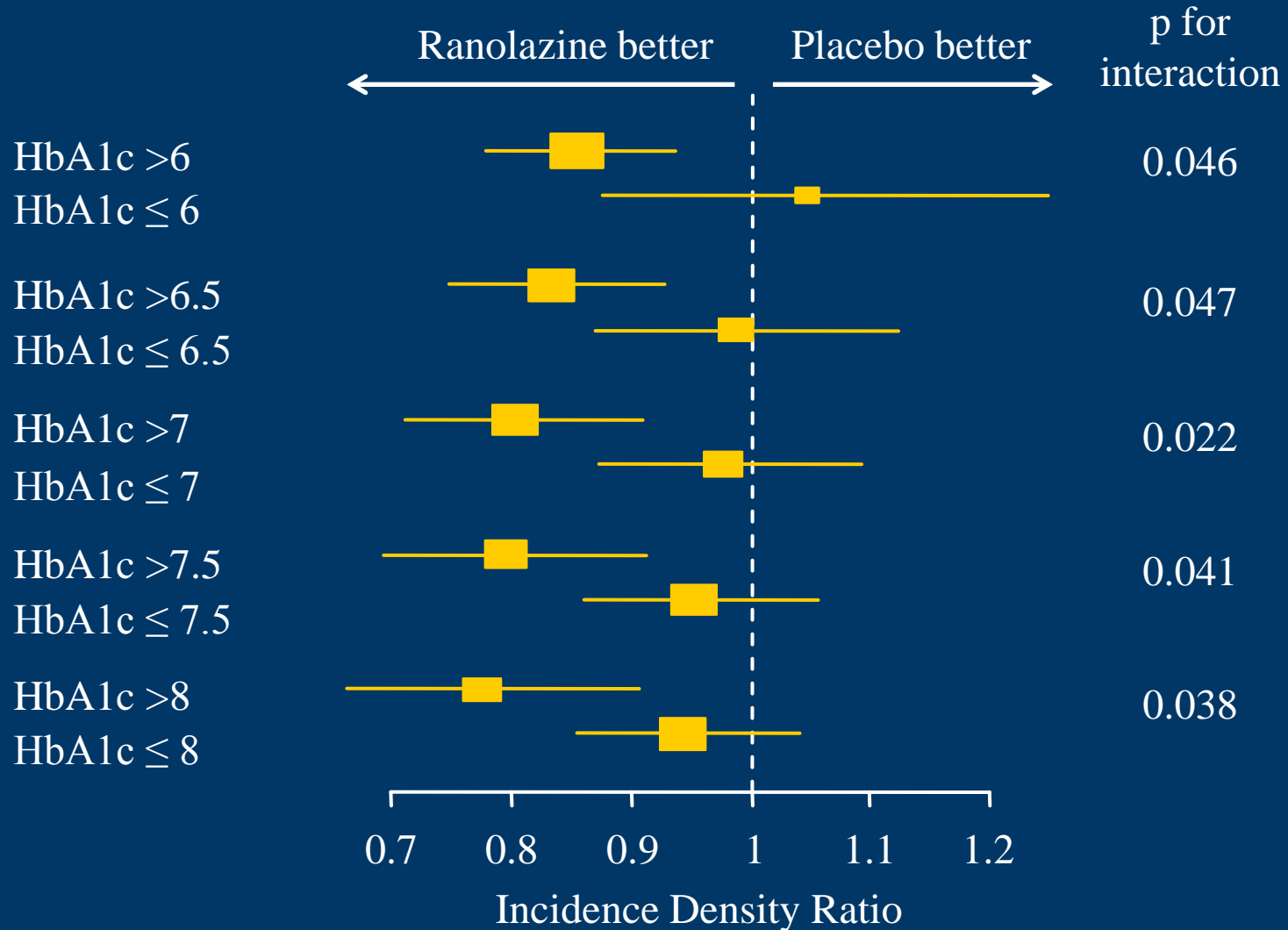
SL NTG Doses



Subgroup Analyses of the Primary End Point of Weekly Angina Frequency



Exploratory Analysis – HbA1c



Conclusions

- Ranolazine was more effective than placebo in reducing angina frequency and SL NTG use in patients with type 2 diabetes, CAD and chronic angina
- The therapeutic effectiveness of ranolazine was more pronounced
 - In patients enrolled outside of Russia, Ukraine and Belarus
 - In those with higher baseline HbA1c
- Future studies are needed to explore potential dual effects of ranolazine on angina and glucose control in patients with type 2 diabetes