



Who could benefit from Ranexa®?

>> Choose a case study to find out



>> Intolerant to first-line treatment



>> Uncontrolled on first-line treatment



>> CAD & diabetes



>> Stable angina in female patients



Lately, Lim hasn't
been tolerating his
angina treatment

***Is it time to
add-on Ranexa®?***

On his current treatment plan, Lim has angina symptoms and fatigue that bother him when he's walking

**Reduce angina,
keep them active¹⁻⁸**

*Lim, 62 yrs old
Outdoor enthusiast*

- ❖ Clinical picture
- ❖ Current treatment
- ❖ Presenting symptoms

On his current treatment plan, Lim has angina symptoms and fatigue that bother him when he's walking

**Reduce angina,
keep them active¹⁻⁸**

*Lim, 62 yrs old
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⚡ Clinical picture

- Chronic stable angina
- Revascularisation with percutaneous coronary intervention (PCI) 9 months ago

⚡ Current treatment

⚡ Presenting symptoms

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⚡ Clinical picture

- Chronic stable angina
- Revascularisation with percutaneous coronary intervention (PCI) 9 months ago

⚡ Current treatment

		+		+		+	
Atenolol (50 mg)	Amlodopine (10 mg)		Glyceryl trinitrate (400 mcg prn)		Aspirin (75 mg)		Rosuvastatin (20 mg)

⚡ Presenting symptoms

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Atenolol (50 mg)	Amlodopine (10 mg)	Glyceryl trinitrate (400 mcg prn)	Aspirin (75 mg)	Rosuvastatin (20 mg)

⚡ Presenting symptoms

- Fatigue, cold hands and feet, and angina with mild exercise
- Heart rate: 54 bpm
- Blood pressure: 118/58 mmHg

Lim's not alone: most patients have relative intolerances to maximum doses of antianginal agents⁹⁻¹¹

Reduce angina,
keep them active¹⁻⁸



Lim still experiences angina despite maximum doses of his CCB⁹ and beta blocker,¹⁰ and he may be experiencing some adverse effects¹¹

Lim's not alone: most patients have relative intolerances to maximum doses of antianginal agents⁹⁻¹¹

Reduce angina,
keep them active¹⁻⁸








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What can
Ranexa[®] do?

Ranexa[®] could help reduce the frequency of Lim's angina with no substantial haemodynamic effects¹²

Reduce angina,
keep them active¹⁻⁸

In a meta-analysis, Ranexa[®] was shown to be substantially haemodynamically neutral in patients with chronic stable angina¹²






 Supine		Supine SBP NEUTRAL	(MD: -0.647; 95% CI: -1.431 to 0.0136; comparison p = 0.105; heterogeneity p = 0.734; i2 = 0.0%)
		Supine DBP NEUTRAL	(MD: 0.016; 95% CI: -0.425 to 0.280; comparison p = 0.944; heterogeneity p = 0.932; i2 = 0.0%)
		Supine HR NEUTRAL	(MD: -0.051; 95% CI: -0.549 to 0.447; comparison p = 0.841; heterogeneity p = 0.374; i2 = 3.7%)
 Standing			

Data from Savarese G *et al.* 2013¹² See 'i' button for study design information. CI, confidence interval; DBP, diastolic blood pressure; HR, heart rate; MD, mean difference; SBP, systolic blood pressure. Ranexa[®] is indicated as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as betablockers and/or calcium antagonists).¹³ Ranexa[®]'s recommended initial dose is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily, and according to the patient's response, further titrated to a recommended maximum dose of 750 mg twice daily.¹³

Ranexa[®] could help reduce the frequency of Lim's angina with no substantial haemodynamic effects¹²

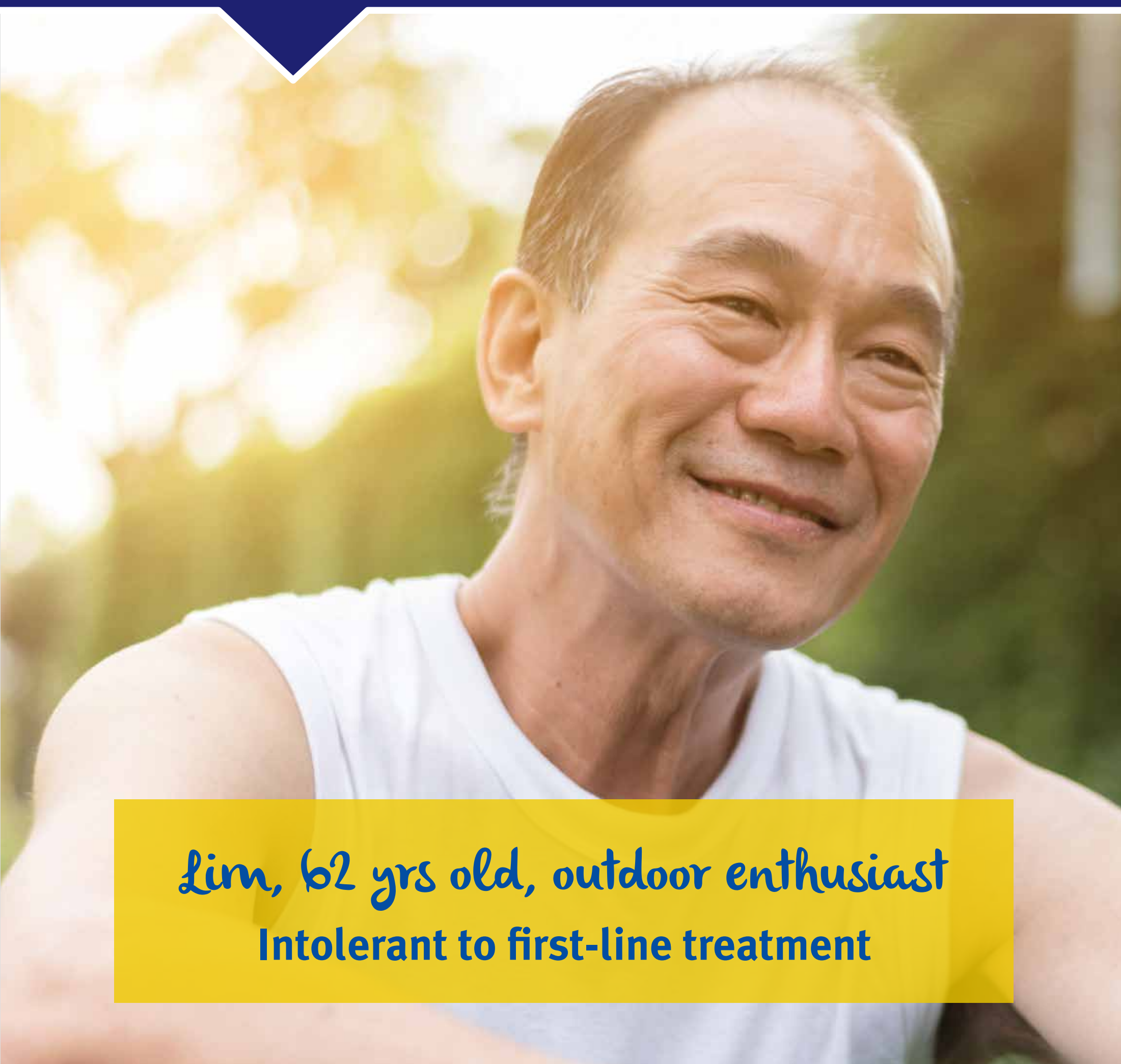
Reduce angina,
keep them active¹⁻⁸

In a meta-analysis, Ranexa[®] was shown to be substantially haemodynamically neutral in patients with chronic stable angina¹²

 Supine		Standing SBP MODESTLY REDUCED (-1.55 mmHg)	(MD: -1.553; 95% CI: -2.363 to -0.743; comparison p=0.000; heterogeneity p=0.672; i2 = 0.0%)
		Standing DBP NEUTRAL	(MD: -0.404; 95% CI: -0.862 to -0.055; comparison p = 0.084; heterogeneity p = 0.287; i2 = 20.4%)
		Standing HR NEUTRAL	(MD:-0.162; 95% CI:-0.697 to 0.374; comparison p = 0.555; heterogeneity p = 0.143; i2 = 44.7%)
 Standing			

Data from Savarese G *et al.* 2013¹² See 'i' button for study design information. CI, confidence interval; DBP, diastolic blood pressure; HR, heart rate; MD, mean difference; SBP, systolic blood pressure. Ranexa[®] is indicated as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as betablockers and/or calcium antagonists).¹³ Ranexa[®]'s recommended initial dose is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily, and according to the patient's response, further titrated to a recommended maximum dose of 750 mg twice daily.¹³

Ranexa[®]: Help patients like Lim reconnect with the life they love¹⁻⁷



Lim, 62 yrs old, outdoor enthusiast
Intolerant to first-line treatment

In a meta-analysis, in patients with chronic stable angina, Ranexa[®] was shown to:



Reduce the frequency of angina symptoms while remaining haemodynamically neutral¹²

Reduce angina, keep them active¹⁻⁸

Ranolazine is indicated in adults as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists). The patient presented is not real but used only for illustrative purposes. For the treatment of any underlying disease, please do refer to the appropriate guidelines.

Ranexa®: Help patients like Lim reconnect with the life they love¹⁻⁷



Study design: Saravese G *et al.* 2013.¹²

Meta-analysis of six clinical trials assessing the effects of Ranexa® on angina, nitroglycerin consumption, functional capacity, electrocardio-graphic signs of ischaemia and haemodynamic parameters in patients with chronic stable CAD (coronary artery disease). Three clinical trials involving 8,216 patients were included in the blood pressure and heart rate analysis.

References:

1. Muhlestein JB *et al.* *Drugs R D* 2013;13:207–213.
2. Chaitman BR *et al.* *J Am Coll Cardiol* 2004;43:1375–82.
3. Chaitman BR *et al.* *JAMA* 2004;291:309–16.
4. Alexopoulos D *et al.* *Int J Cardiol* 2016;205:111-116.
5. Stone PH *et al.* *J Am Coll Cardiol* 2006;48(3):566–75.
6. Wilson SR *et al.* *J Am Coll Cardiol* 2009;53:1510–6.
7. Diedrichs H *et al.* *J Clin Exp Cardiol* 2015;6(12):16.
8. Hasenfuss G, Maier LS. *Clin Res Cardiol* 2008;97:222–26.
9. Amlodipine 10 mg Tablet. Summary of Product Characteristics, October 2013.
10. APO-Atenolol tablets. Product Information, May 2018.
11. Al Mobeirek AF *et al.* *Int J Clin Med* 2014;5:249–59.
12. Savarese G *et al.* *Int J Cardiol* 2013; 169:262–270.
13. Ranexa® Summary of Product Characteristics, July 2014.

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Lee's been taking his angina medicines like his doctor told him, but he's just suffered his 4th angina attack this week

Is it time to add-on Ranexa®?

Lee's inadequate angina control is interfering with his work

**Reduce angina,
keep them active¹⁻⁸**

*Lee, 50 yrs old
Business manager*

❖ Clinical picture

❖ Current treatment

❖ Presenting symptoms

Lee's inadequate angina control is interfering with his work

**Reduce angina,
keep them active¹⁻⁸**

*Lee, 50 yrs old
Business manager*

⚡ Clinical picture

- Stable angina
- Revascularised with percutaneous coronary intervention (PCI) 1 year ago with optimal result as seen on angiography*

*Normal coronary artery flow and <50% stenosis in the luminal diameter after balloon angioplasty and <20% after coronary stent implantation.

⚡ Current treatment

⚡ Presenting symptoms

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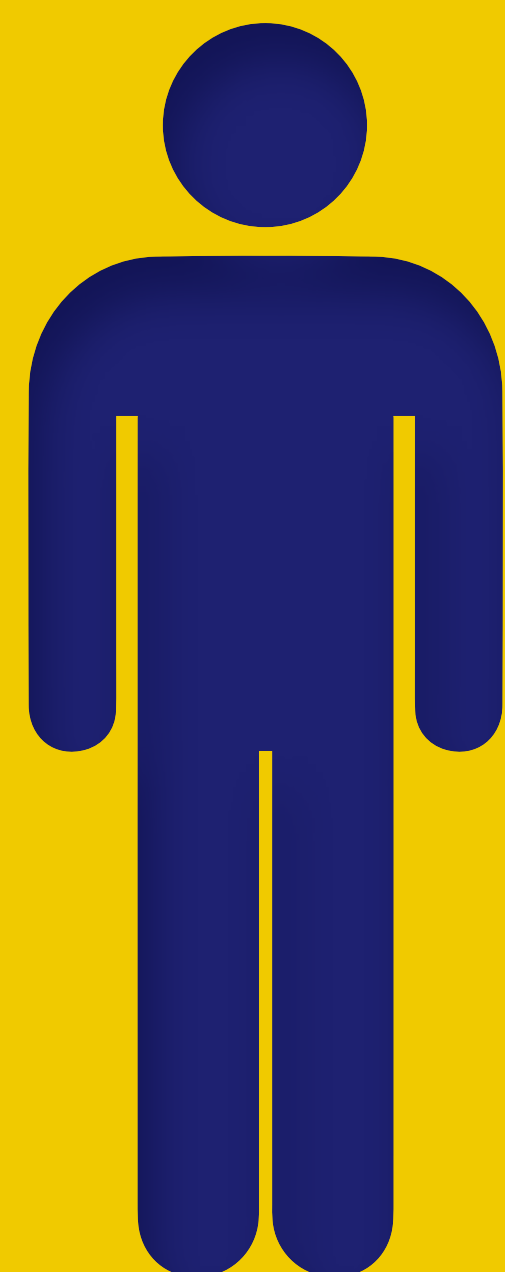
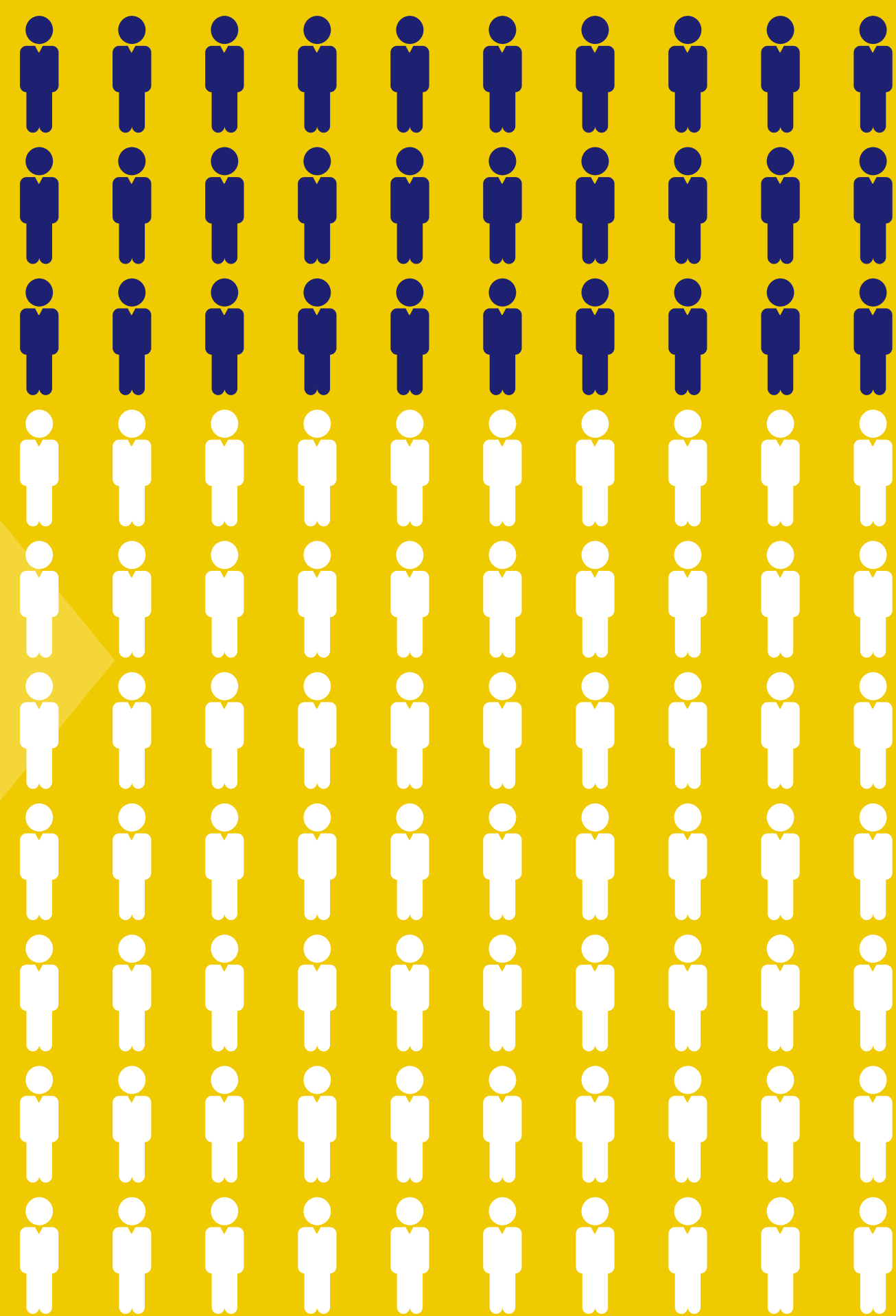
				
Atenolol (100 mg)	Amlodopine (10 mg)	Glyceryl trinitrate (400 mcg prn)	Aspirin (100 mg)	Rosuvastatin (10 mg)

⚡ Presenting symptoms

- Angina attack (4th episode this week)
- ECG: normal

Lee's not alone: many patients have recurring symptoms

Reduce angina,
keep them active¹⁻⁸



Up to
~30%
of angina patients
experience recurrent
angina pectoris and
require multi-drug
regimens⁹

What can
Ranexa[®] do?



MENARINI
ASIA - PACIFIC

Intolerant

Uncontrolled

CAD & diabetes

Female patients



Ranexa[®] could help provide further symptom relief
and improve daily activities for Lee^{4,5,7}

Reduce angina,
keep them active¹⁻⁸

Observational studies of 'real-world' symptomatic patients taking Ranexa[®]

Reduction in mean number of weekly angina attacks⁷

4.4 Baseline

1.1 3 months ($p < 0.0001$)

>3 fewer
angina attacks
per week vs.
baseline⁷

Adapted from Diedrichs H *et al.* 2015⁷ See 'i' button for study design information.



ARETHA



OSCAR-GR

Ranexa[®] could help provide further symptom relief
and improve daily activities for Lee^{4,5,7}

Reduce angina,
keep them active¹⁻⁸

Observational studies of 'real-world' symptomatic patients taking Ranexa[®]

Reduction in % patients experiencing 1–3 angina
attacks in the indicated time intervals⁴

88.4% Baseline

26.5% 6 months ($p < 0.001$)

A clear declining
trend in angina symptoms
after both 3 and 6 months
of therapy ($p < 0.0001$)⁴

IMPROVED DAILY
ACTIVITY SCORES

Adapted from Alexopoulos D *et al.* 2016⁴ See 'i' button for study design information.



ARETHA



OSCAR-GR



MENARINI
ASIA - P A C I F I C

Intolerant

Uncontrolled

CAD & diabetes

Female patients



Ranexa® could help provide further symptom relief and improve daily activities for Lee^{4,5,7}

Reduce angina,
keep them active^{1,2}

In OSCAR-GR there was a significant improvement in patients' daily activity scores ($p < 0.001$), with the greatest improvement seen in employment activities:⁴



37% improvement in mean scores over 6 months

(change in employment activity score, 3.81 to 2.39 measured on a visual analogue scale where 0=no limitation and 10=severe limitation).

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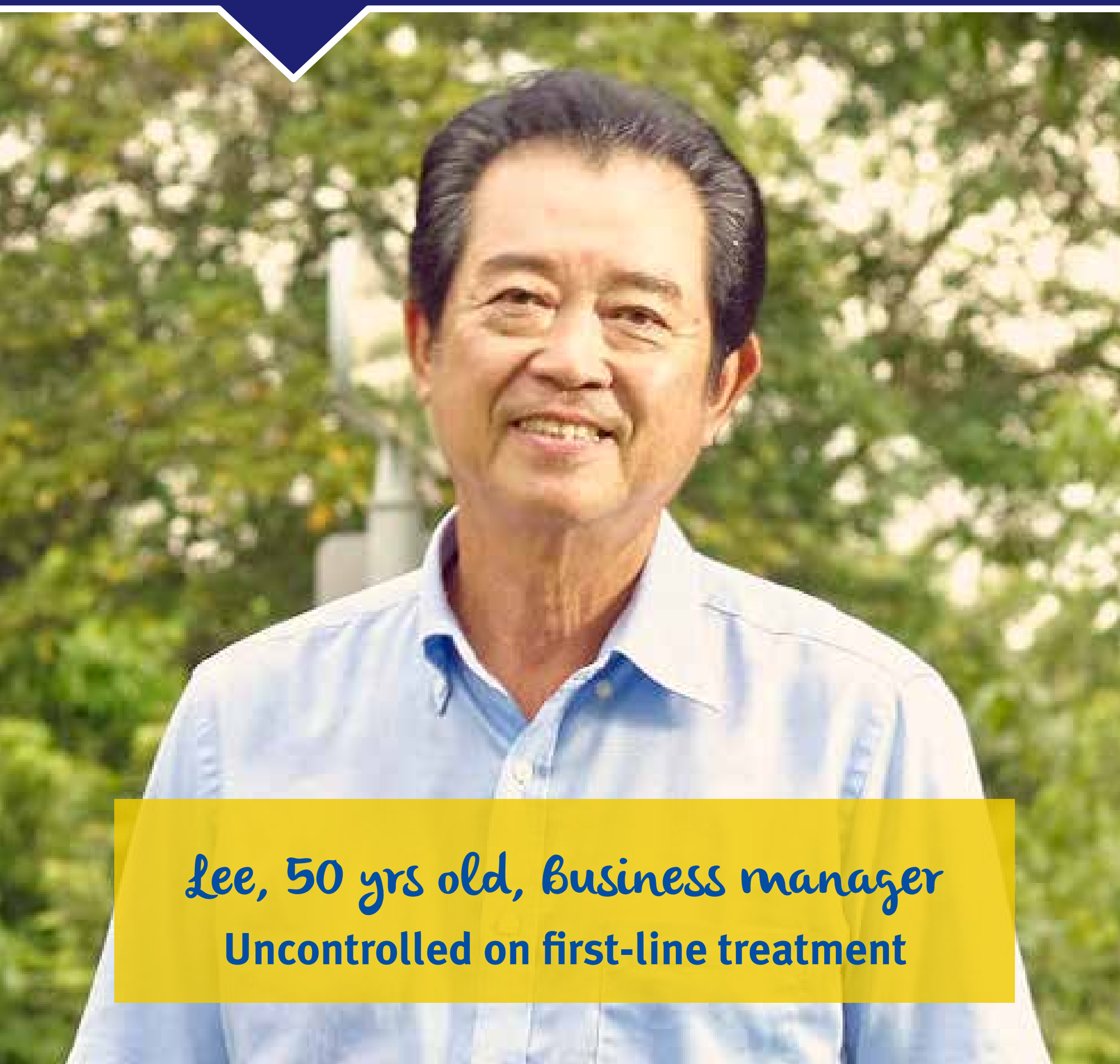


ARETHA



OSCAR-GR

Ranexa[®]: Help patients like Lee reconnect with the life they love¹⁻⁷



Lee, 50 yrs old, business manager
Uncontrolled on first-line treatment



Decrease frequency
of angina attacks^{3,5,7}



Reduce angina
symptoms⁴



Improve daily
activity⁴

Reduce angina, keep them active¹⁻⁸

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Ranexa®: Help patients like Lee reconnect with the life they love¹⁻⁷



Study design: Diedrichs H *et al.* 2015⁷

ARETHA: Application of ranolazine in stable angina pectoris therapy. Patients (n=1,537, full analysis set) with stable angina pectoris receiving ranolazine were enrolled and monitored at baseline and after 3 months. Only patients receiving ranolazine for the first time were monitored (provided that therapy did not start earlier than 2 to a maximum of 4 weeks previously and the dosage still equalled the recommended starting dose).

Study design: Alexopoulos D *et al.* 2016⁴

OSCAR-GR: Prospective, multicentre, observational, study in 189 patients with chronic stable angina. Ranolazine was prescribed, and 6 months' follow-up was performed, with study visits at baseline, 3 and 6 months.

References:

1. Muhlestein JB *et al.* *Drugs R D* 2013;13:207–213. **2.** Chaitman BR *et al.* *J Am Coll Cardiol* 2004;43:1375–82. **3.** Chaitman BR *et al.* *JAMA* 2004;291:309–16. **4.** Alexopoulos D *et al.* *Int J Cardiol* 2016;205:111. **5.** Stone PH *et al.* *J Am Coll Cardiol* 2006;48(3):566–75. **6.** Wilson SR *et al.* *J Am Coll Cardiol* 2009;53:1510–6. **7.** Diedrichs H *et al.* *J Clin Exp Cardiol* 2015;6(12):16. **8.** Hasenfuss G, Maier LS. *Clin Res Cardiol* 2008;97:222–26. **9.** Manolis AJ *et al.* *Int J Cardiol* 2016;445–43. **10.** Ranexa® Summary of Product Characteristics. July 2014.

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Sam is diabetic and he is being treated for stable coronary artery disease, but he still experiences angina symptoms

Is it time to add-on Ranexa®?



Despite his angina treatments, Sam still has frequent symptoms that worry him

**Reduce angina,
keep them active¹⁻⁸**

Sam, 64 yrs old
Music teacher



- ❯ Clinical picture
- ❯ Current treatment
- ❯ Presenting symptoms

Despite his angina treatments, Sam still has frequent symptoms that worry him

**Reduce angina,
keep them active¹⁻⁸**

*Sam, 64 yrs old
Music teacher*



⚡ Clinical picture

- Chronic stable angina
- 1-year history of stable coronary artery disease (CAD) with daily symptoms
- Type 2 diabetes

⚡ Current treatment

⚡ Presenting symptoms

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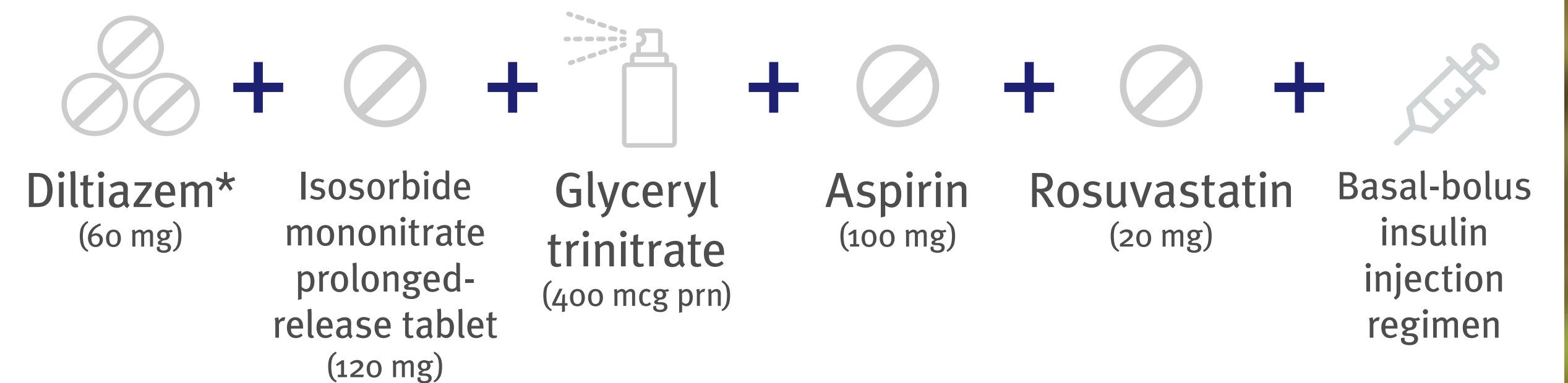
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⚡ Clinical picture

- Chronic stable angina
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⚡ Current treatment



*For the interactions between Diltiazem and Ranolazine please refer to the full SmPC for Ranolazine.

⚡ Presenting symptoms

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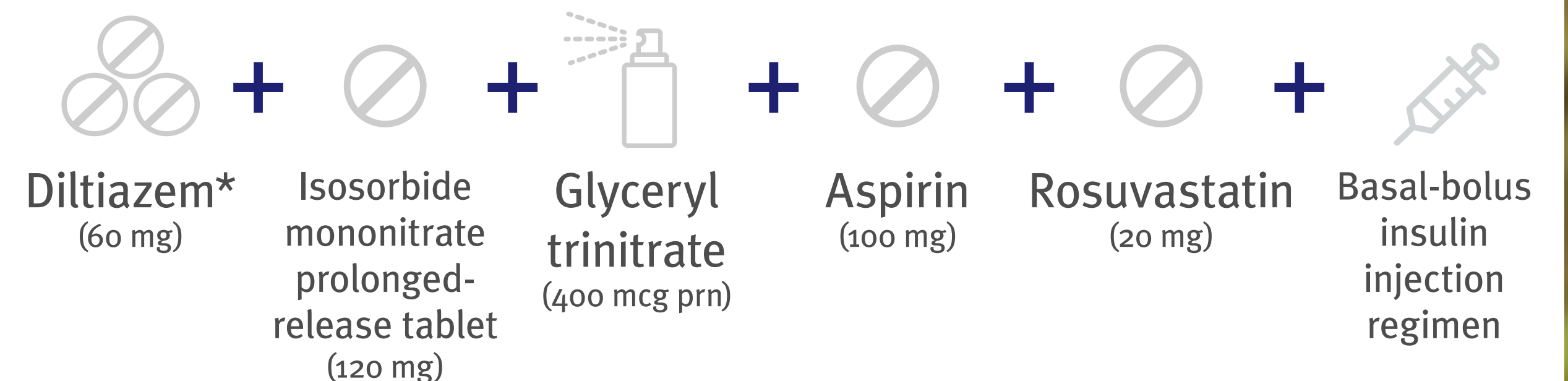
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- Type 2 diabetes

⚡ Current treatment



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⚡ Presenting symptoms

- Fatigue
- Frequent angina

Sam's on the maximum dose of his sustained-release nitrate⁹ and a high dose of non-dihydropyridine CCB¹⁰

**Reduce angina,
keep them active¹⁻⁸**

Older traditional beta-blockers have the potential to:

- Facilitate or accelerate new-onset diabetes in predisposed patients, or
- Aggravate the glycaemic profile in patients with pre-existing diabetes¹¹

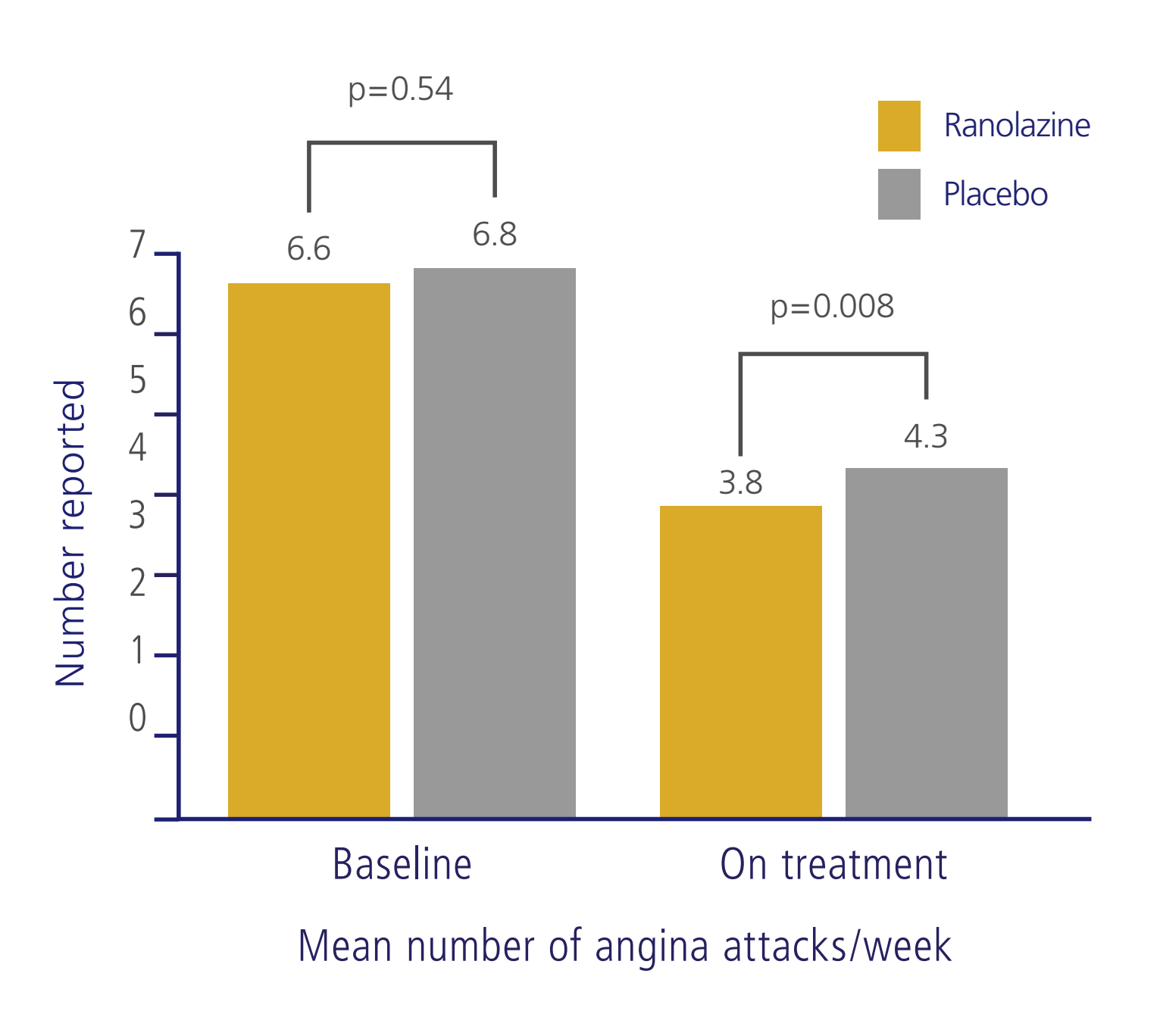


**What can
Ranexa[®] do?**

Ranexa[®] could help reduce Sam's angina symptoms and medication use¹²

Reduce angina,
keep them active¹⁻⁸

Efficacy endpoints in CAD/CSA patients with diabetes treated with Ranexa[®] for 8 weeks¹²



In patients with type 2 diabetes CAD and chronic stable angina who were being treated with 1 to 2 anti-anginal agents:¹²



Ranexa[®] significantly reduced the frequency of angina symptoms (p=0.008)

Adapted from Kosiborod M *et al.*¹² See 'i' button for study design information.

EXPERT OPINION

ANGINA
ATTACKS

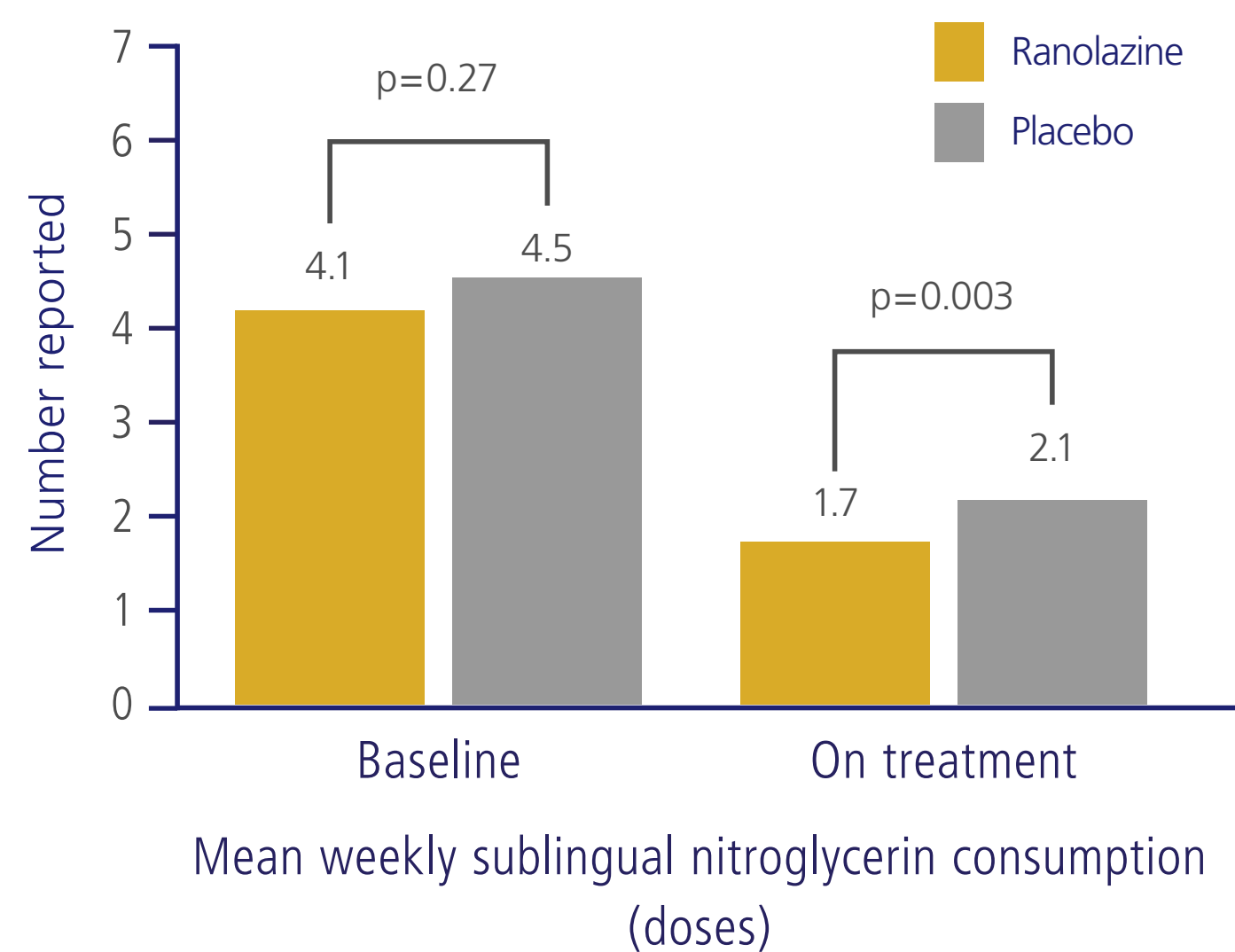
NITROGLYCERIN
CONSUMPTION

CAD, coronary artery disease; CCB, calcium channel blocker; CSA, chronic stable angina.
Ranexa[®]'s recommended initial dose is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily, and according to the patient's response, further titrated to a recommended maximum dose of 750 mg twice daily.¹⁴

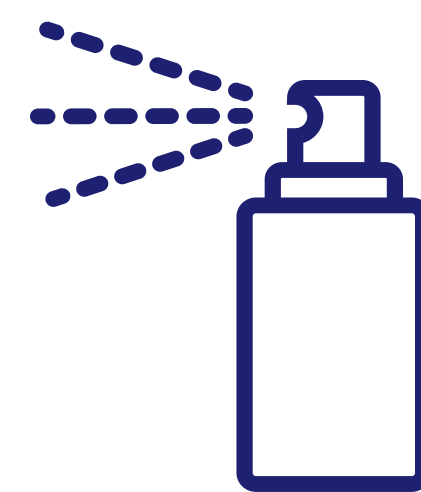
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Reduce angina,
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In patients with type 2 diabetes CAD and chronic stable angina who were being treated with 1 to 2 anti-anginal agents:¹²



Ranexa[®] significantly reduced sublingual nitroglycerin use (p=0.003)

Adapted from Kosiborod M *et al.*¹² See 'i' button for study design information.

EXPERT OPINION

ANGINA
ATTACKS

NITROGLYCERIN
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Ranexa® could help reduce Sam's angina symptoms
and medication use¹²

Reduce angina,
keep them active¹²



The combined anti-ischaemic and HbA1c
lowering effects of Ranexa® indicate that
this agent may become the preferred
anti-anginal agent for the management of
stable coronary artery disease in patients
who also have diabetes¹¹⁻¹³

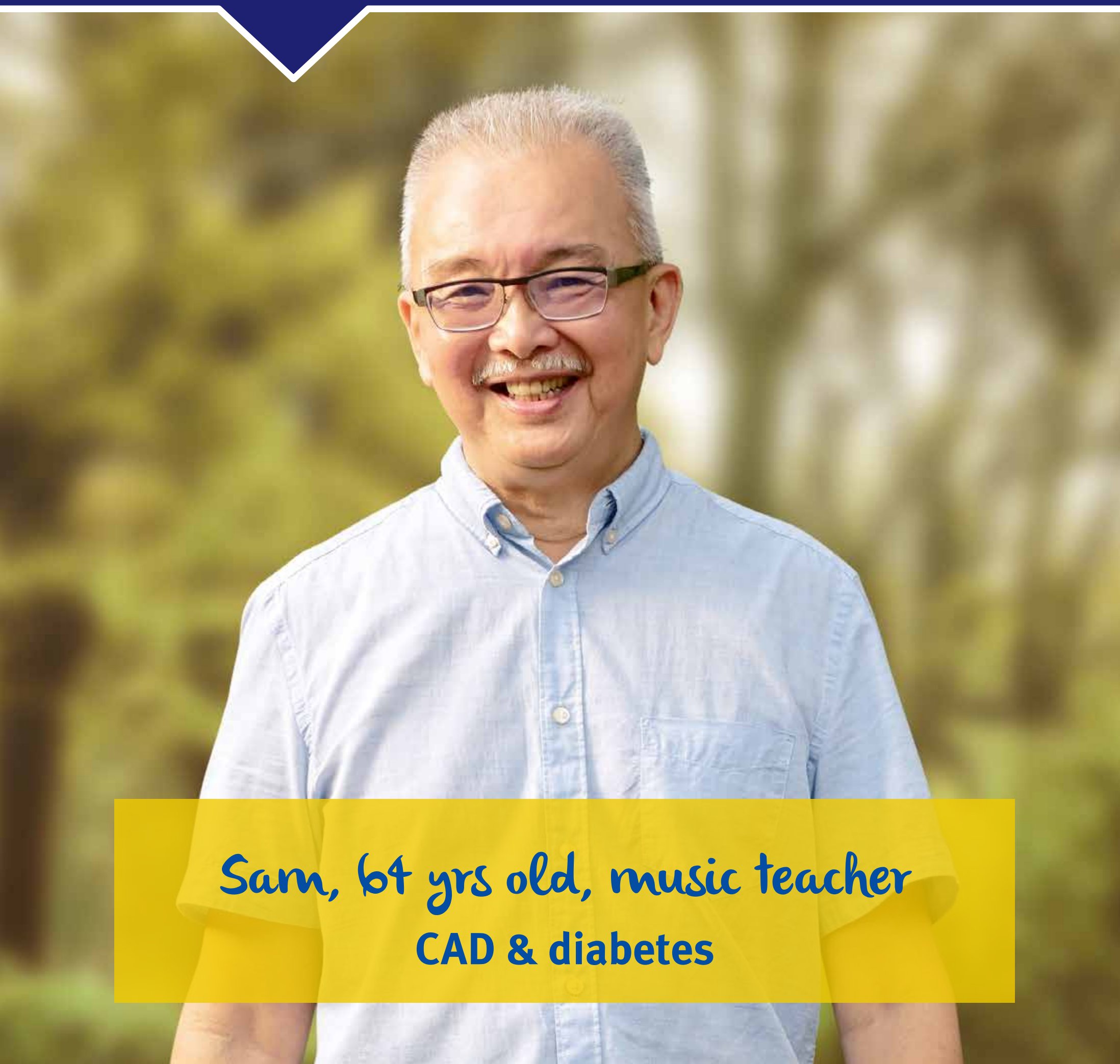
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Ranexa[®]: Help patients like Sam reconnect with the life they love¹⁻⁷



In patients with type 2 diabetes, CAD, and chronic stable angina, who were being treated with 1 to 2 anti-anginal agents Ranexa[®] helped:



Decrease frequency of angina attacks¹²



Reduce angina symptoms¹²

Reduce angina, keep them active¹⁻⁸

Ranolazine is indicated in adults as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists). The patient presented is not real but used only for illustrative purposes. For the treatment of any underlying disease, please do refer to the appropriate guidelines.

Ranexa®: Help patients like Sam reconnect with the life they love¹⁻⁷



Study Design: Kosiborod M *et al.*¹²

TERISA (Type 2 Diabetes Evaluation of Ranolazine in Subjects with Chronic Stable Angina): a randomised, double-blind, international multicentre trial of ranolazine versus placebo in 949 patients with diabetes, coronary artery disease and stable angina treated with 1–2 antianginals. After a 4-week placebo run-in, patients were randomised to 8 weeks of double-blind ranolazine (target dose 1000 mg bd) or placebo. Anginal episodes and nitroglycerin use were recorded daily. Primary outcome was the average weekly number of anginal episodes over the last 6 weeks of the study.

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8. Hasenfuss G, Maier LS. *Clin Res Cardiol* 2008;97:222–26.
9. Monomax XL (Isosorbide mononitrate) 60 mg Prolonged Release Tablets. Summary of Product Characteristics, January 2017.
10. Diltiazem Hydrochloride Tablets 60 mg. Summary of Product Characteristics, April 2016.
11. Manolis AJ *et al. Int J Cardiol* 2016;220:445–53.
12. Kosiborod M *et al. J Am Coll Cardiol* 2013 May 21;61(20):2038-45.
13. Ambrosio G *et al. Diab Vasc Dis Res* 2016;13(2):98-112.
14. Ranexa® Summary of Product Characteristics, July 2014.

Ranolazine
beta-block

as
ines.





Sharon started the day with chest pain. Again.

Is it time to add-on Ranexa®?



MENARINI
ASIA - PACIFIC

Intolerant

Uncontrolled

CAD & diabetes

Female patients



Despite her current treatment, Sharon has continuing angina in the early morning that she finds distressing

**Reduce angina,
keep them active¹⁻⁸**

Sharon, 60 yrs old
Restaurateur

- ❖ Clinical picture
- ❖ Current treatment
- ❖ Presenting symptoms

Despite her current treatment, Sharon has continuing angina in the early morning that she finds distressing

**Reduce angina,
keep them active¹⁻⁸**

Sharon, 60 yrs old
Restaurateur

⚡ Clinical picture

- Stable angina
- ECG changes
- Exercise-induced angina and ischaemia (ST-depression on exercise ECG)
- Non-obstructed coronary arteries at coronarography

⚡ Current treatment

⚡ Presenting symptoms

Despite her current treatment, Sharon has continuing angina in the early morning that she finds distressing

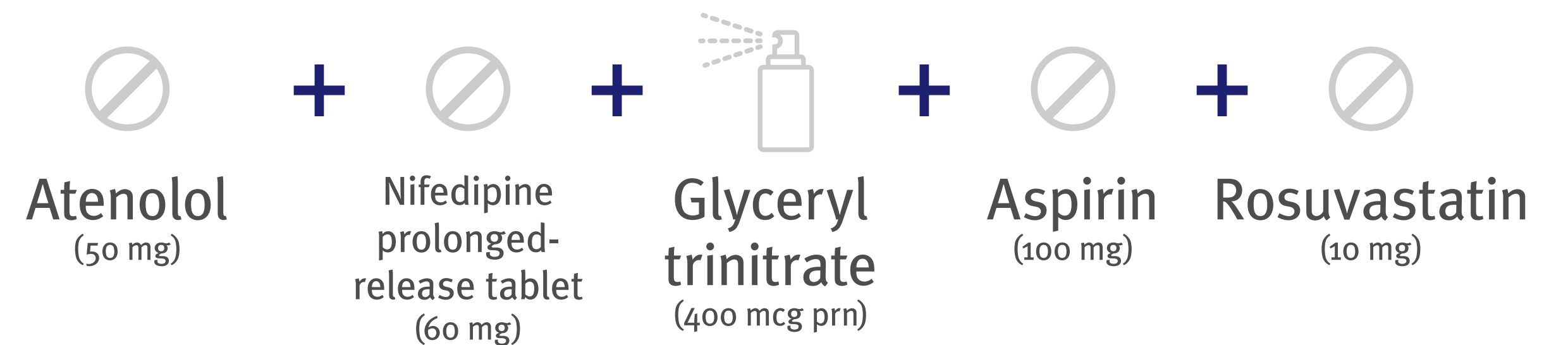
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- Stable angina
- ECG changes
- Exercise-induced angina and ischaemia (ST-depression on exercise ECG)
- Non-obstructed coronary arteries at coronarography

⚡ Current treatment



⚡ Presenting symptoms

- Chest pains

Sharon is not alone: women are more likely than men to present with chest pain uncomplicated by myocardial infarction and unstable angina⁹

**Reduce angina,
keep them active¹⁻⁸**

Uncomplicated chest pain incidence
(Framingham heart study):



86%
of women vs
66% of men⁹

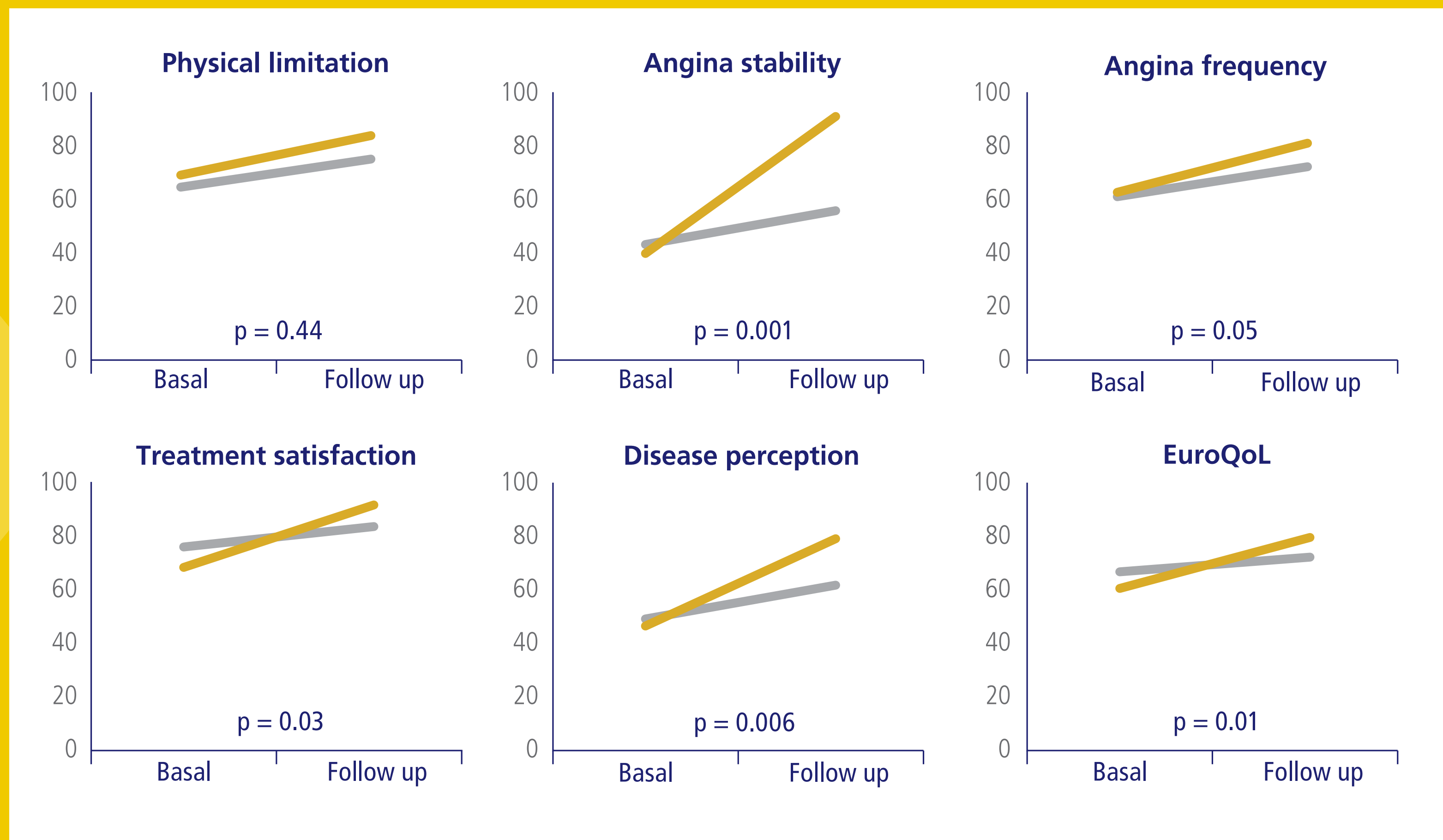
**What can
Ranexa[®] do?**

Ranexa[®] is an effective add-on antianginal therapy for women¹⁰⁻¹²

**Reduce angina,
keep them active¹⁻⁸**

Ranolazine and ivabradine both significantly improved angina symptoms and QoL vs baseline in patients (80% women) with effort-induced angina without obstructive coronary artery disease¹⁰

**IMPROVED SAQ
SCORES**



Adapted from Villano *et al.* 2013.¹⁰ See 'i' button for study design information.

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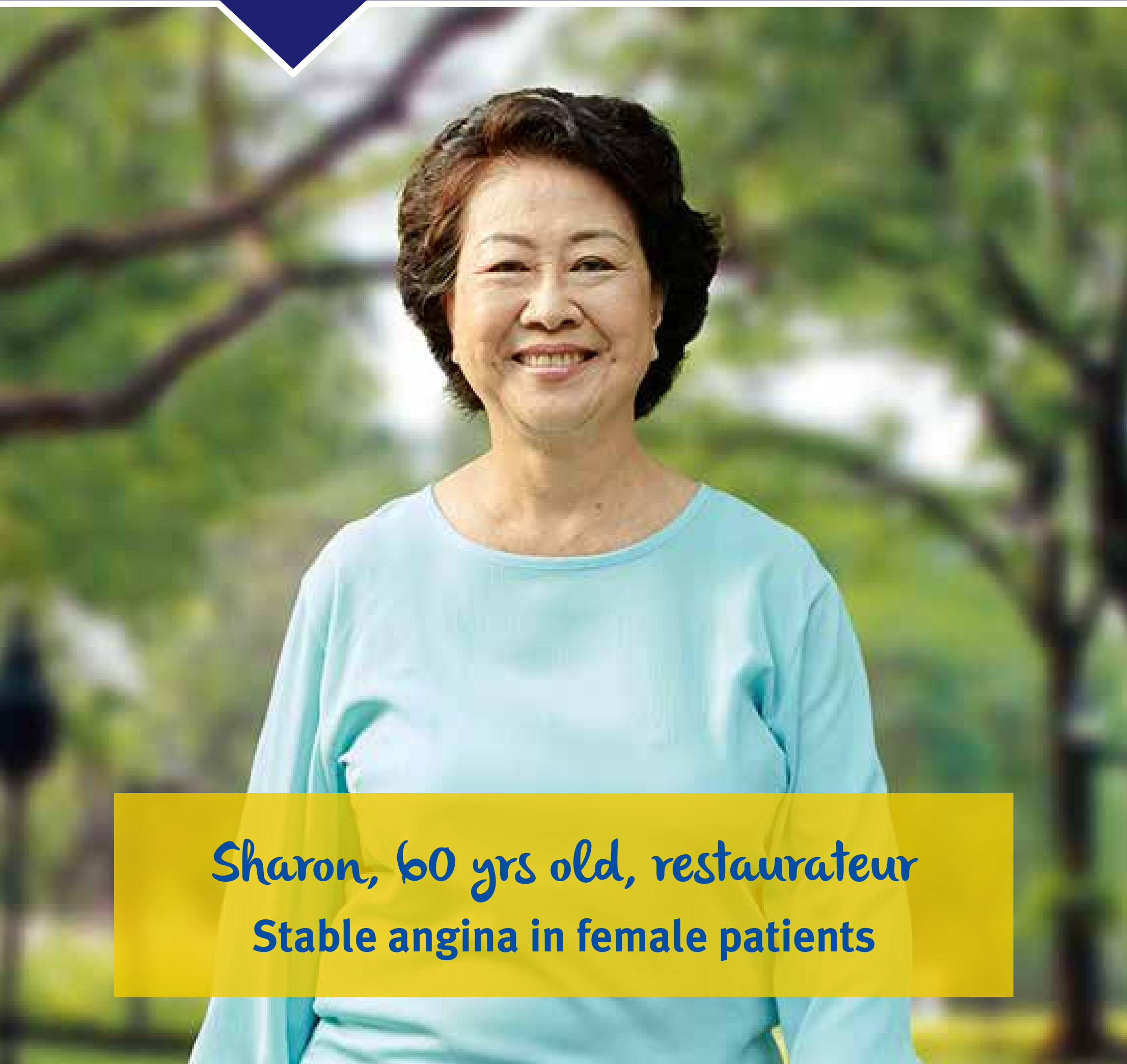
There was a significant benefit for Ranexa®
vs placebo in objective SAQ scores for:¹¹⁻¹³

- Anginal stability
- Physical functioning
- Quality of life
(Women with angina, evidence of ischaemia and no obstructive coronary artery disease)

Ranexa®'s recommended initial dose is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily, and according to the patient's response, further titrated to a recommended maximum dose of 750 mg twice daily.¹³

Adapted from Villano *et al.* 2013.¹⁰ See 'i' button for study design information.

Ranexa[®]: Help patients like Sharon reconnect with the life they love¹⁻⁷



Sharon, 60 yrs old, restaurateur
Stable angina in female patients

In patients (80% women) with effort-induced angina without obstructive coronary artery disease, Ranexa[®] was shown to (vs baseline):



Improve angina symptoms¹⁰



Improve quality of life¹⁰



Significantly increase treatment satisfaction¹⁰

Reduce angina, keep them active¹⁻⁸

Ranolazine is indicated in adults as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists). The patient presented is not real but used only for illustrative purposes. For the treatment of any underlying disease, please do refer to the appropriate guidelines.

Ranexa[®]: Help patients like Sharon reconnect with the life they love¹⁻⁷



Study Design: Villano *et al.* 2013.¹⁰

n=46 patients with stable microvascular angina (effort angina, positive exercise stress test, normal coronary angiography, coronary flow reserve <2.5), who had symptoms inadequately controlled by standard anti-ischaemic therapy, were randomised to ivabradine (5 mg bd), ranolazine (375 mg bd), or placebo for 4 weeks. Primary endpoints were anginal status assessed by the Seattle Angina Questionnaire, items (physical limitation, angina frequency, angina stability, treatment satisfaction, disease perception) scored on a 0 to 100 scale (higher scores indicate better functional status); and quality of life (QoL) assessed by the validated EuroQoL visual analogue scale, from 0 (worst condition) to 100 (best condition).

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Ranexa[®]: Help patients like Sharon reconnect with the life they love¹⁻⁷

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RG/RAN/XX/2019/XXX



Intolerant

Uncontrolled

CAD & diabetes

Female patients

