# Cost-Effectiveness Model of Ranolazine for Treating Chronic Stable Angina Patients from the Kingdom of Saudi Arabia Perspective

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## Introduction

- Chronic stable angina (CSA) is a common cardiovascular condition characterized by chest pain or discomfort that occurs during physical activity or emotional stress.
- Ranolazine is approved for the treatment of CSA as an add-on therapy in patients who remain symptomatic despite optimal medical therapy with beta blockers and nitrates.
- Despite advancements in medical treatment, CSA poses a significant burden on the Saudi Arabian healthcare system. The cost-effectiveness of ranolazine in this system is presented here for the first time.

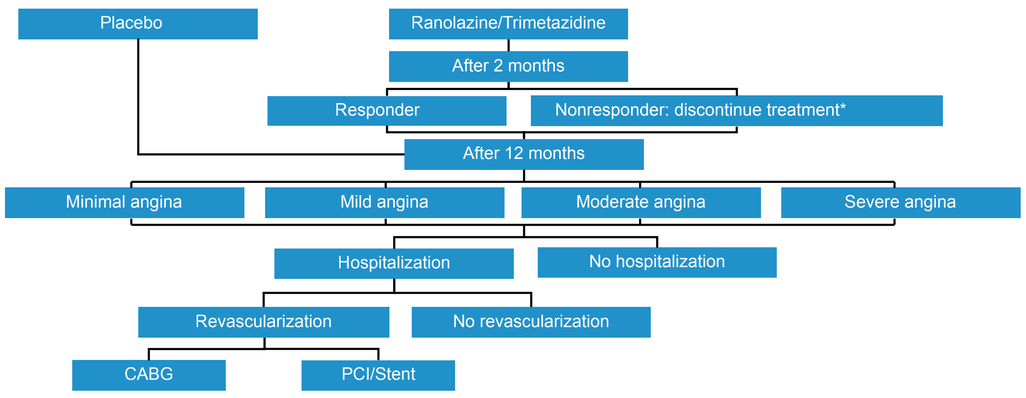
## Objective

**To investigate the cost-effectiveness of ranolazine compared with placebo or trimetazidine among adult patients with CSA who remain symptomatic despite treatment with anti-anginal agents from a Kingdom of Saudi Arabia (KSA) public/institution payer perspective.**

## Methods

- A 1-year decision tree model (**Figure 1**) was designed to compare the three treatment arms, stratifying outcomes by angina severity (using the Seattle Angina Questionnaire [SAQ]) and including the economic impact of revascularization (coronary artery bypass grafting [CABG] or percutaneous coronary intervention [PCI]/stent).
- Discounting was not applied due to the short 1-year time horizon.
- The analysis focused on direct healthcare costs and effects (quality adjusted life years [QALYs]), derived from the frequency of minimal, mild, moderate, or severe angina from the SAQ, hospitalization rate, and proportion of patients requiring revascularization.

### Figure 1: One-year decision tree.




*At 2 months, for the ranolazine and trimetazidine groups, responders were assessed by adherence and improvement; nonresponders were switched to placebo, and then all groups were assessed at 12 months.
CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

## Model Inputs

### Table 1: Model inputs – probability of angina frequency outcomes at 2 and 12 months (%).

| | Ranolazine & placebo: ERICA trial[1] | | | | Ranolazine & Trimetazidine: Tolunay H 2021[2] | | | |
|---|---|---|---|---|---|---|---|---|
| | Ranolazine | | Placebo | | Ranolazine | | Trimetazidine | |
| **Probability (%)** | **Responders** | **Nonresponders** | **Responders** | **Nonresponders** | **Responders** | **Nonresponders** | **Responders** | **Nonresponders** |
| **At the end of 2 months** | 99 | 1 | NA | NA | 99[1] | 1[1] | 95[3,4] | 5[3,4] |
| **At the end of 12 months (SAQ)[2]** | **Responders** | **Nonresponders** | **Responders** | **Nonresponders** | **Responders** | **Nonresponders*** | **Responders** | **Nonresponders*** |
| Minimal angina | 4.1 | 0 | 0 | 0 | 27.1 | 0.1 | 2.2 | 0.1 |
| Mild Angina | 60.5 | 7.1 | 7.1 | 7.1 | 71.7 | 90.3 | 97.8 | 90.3 |
| Moderate Angina | 21.8 | 68.8 | 68.8 | 68.8 | 1.3 | 9.6 | 0.03 | 9.6 |
| Severe Angina | 13.6 | 24.1 | 24.1 | 24.1 | 0 | 0 | 0 | 0 |

NA, not applicable; SAQ, Seattle Angina Questionnaire.*Non-responder values were based on trimetazidine pre-treatment arm; the severity of angina frequency was estimated indirectly by applying normal distribution to the established SAQ cut-off scores5, with the distribution's parameters informed by post-treatment data

- The model used hospitalization probabilities from the MERLIN-TIMI 36 trial (acute coronary syndrome [ACS] specific),[6] also reported by previous ranolazine economic models for CSA (**Table 2**). An annual probability of 50% of hospitalized patients undergoing revascularization has been reported,[7] of which 28% is CABG and 72% is PCI/stent.
- National cost data were used for drug costs, hospitalization rates, and CABG/PCI costs.
- The utilities used in the model, where no hospitalization occurred, are outlined in **Table 3**. A -0.01 disutility was applied for hospitalization and -0.05 disutility for hospitalization with revascularization.[8-10]

### Table 2: Annual probability of hospitalization associated with angina severity (not treatment specific).*,[6]

| Angina severity | Annual probability (%) of hospitalization for patients |
|---|---|
| Minimal | 14 |
| Mild | 18 |
| Moderate | 20 |
| Severe | 29 |

*8-month rates from MERLIN-TIMI 36 were converted into annual probability using the standard formula

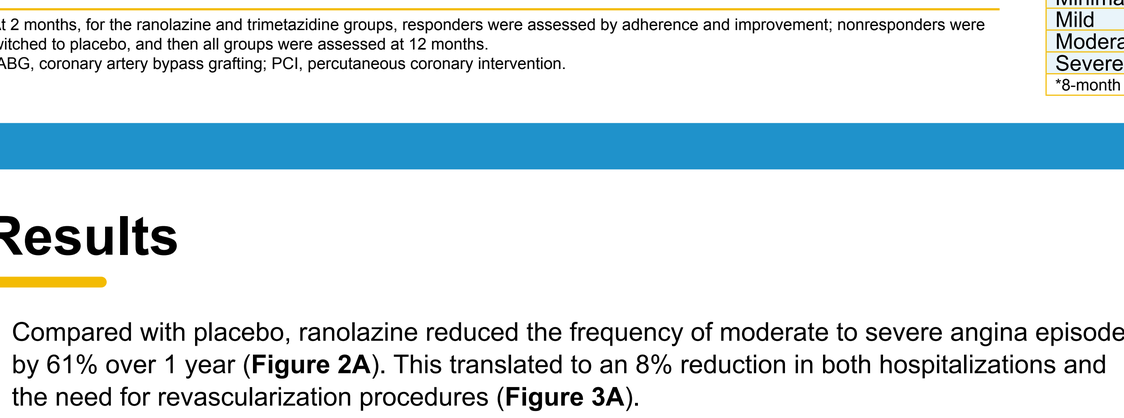
### Table 3: Utilities of angina severity.[8,9]

| Angina severity | No hospitalization[8,9] |
|---|---|
| Minimal angina | 0.81 |
| Mild angina | 0.75 |
| Moderate angina | 0.6 |
| Severe angina | 0.39 |

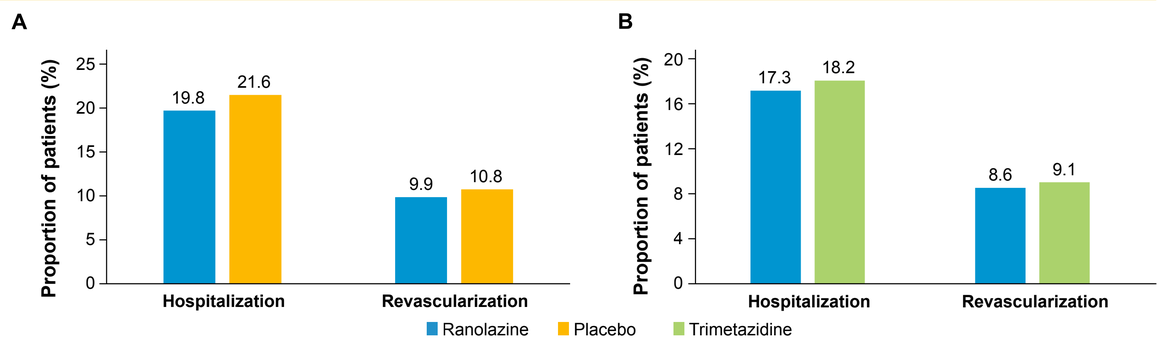
## Results

- Compared with placebo, ranolazine reduced the frequency of moderate to severe angina episodes by 61% over 1 year (**Figure 2A**). This translated to an 8% reduction in both hospitalizations and the need for revascularization procedures (**Figure 3A**).
- Ranolazine improved overall QALYs at 1 year vs placebo (**Table 4**).
- Even with a higher ranolazine drug cost, the overall difference in cost was minimal (<10%) due to the added expense of Saudi Arabian Riyal (SAR)/Saudi Riyal (SAR) 449/patient toward hospitalization with/without revascularization with placebo.
- Ranolazine was cost effective against placebo at a willingness to pay (WTP) of SAR 50,000/QALY (**Table 4**).

### Figure 2: Distribution of patients based on angina severity by treatment, A. Ranolazine vs placebo, B. Ranolazine vs trimetazidine.




### Figure 3: Proportion of patients needing hospitalization and revascularization, A. Ranolazine vs placebo, B. Ranolazine vs trimetazidine.




- Compared with trimetazidine, ranolazine reduced the frequency of mild to severe angina episodes by 25% over 1 year (**Figure 2B**). This translated to a 5% reduction in both hospitalizations and the need for revascularization procedures (**Figure 3B**).
- Ranolazine improved overall QALYs at 1 year vs trimetazidine (**Table 4**).
- Even with a higher ranolazine drug cost, the overall difference in cost was minimal (<7%) due to the added expense of SAR 230/patient toward hospitalization ± revascularization with trimetazidine.
- Ranolazine was cost effective vs trimetazidine at a WTP of SAR 50,000/QALY (**Table 4**).

### Table 4: Summary of costs and QALY results.

| | Ranolazine vs placebo | | Ranolazine vs trimetazidine | |
|---|---|---|---|---|
| | Ranolazine | Placebo | Ranolazine | Trimetazidine |
| Total costs | SAR 7,127 | SAR 6,481 | SAR 6,494 | SAR 6,109 |
| Total QALYs | 0.6623 | 0.5525 | 0.7579 | 0.7441 |
| Incremental costs | - | SAR 646 | - | SAR 385 |
| Incremental QALYs | - | 0.1098 | - | 0.0137 |
| ICER (SAR/QALY) | - | SAR 5,883 | - | SAR 28,017 |

ICER, incremental cost-effectiveness ratio; QALY: quality adjusted life year; SAR: Saudi Riyal

## Conclusions

- This is the **first model from a KSA public/institution payer perspective** that compared the cost-effectiveness of ranolazine vs placebo or trimetazidine for CSA.
- Ranolazine is a **cost-effective treatment** compared with placebo and trimetazidine from a KSA public/institution payer perspective, consistent with previously published evaluations.
- The cost-effectiveness of ranolazine is due to **reduced angina severity and subsequent lower healthcare resource utilization**.

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