In the Type 2 Diabetes Evaluation of Ranolazine in Subjects with Chronic Stable Angina (TERISA) trial, ranolazine reduced the frequency of angina episodes and use of sublingual nitroglycerin in patients with type 2 diabetes mellitus (T2DM) and stable angina, as assessed by a daily diary. Using data from the same trial, we evaluated the effect of ranolazine on a broader range of patients’ health status and quality of life.

Table. Mean Change From Baseline in Disease-Specific Health Status and QOL Scores by Treatment Group

<table>
<thead>
<tr>
<th>Health Status/QOL</th>
<th>Baseline Score, Mean (SD)</th>
<th>LS Mean Change (95% CI)</th>
<th>Treatment Effect, Δ (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAQ angina frequency</td>
<td>46.3 (19.0)</td>
<td>16.1 (14.0 to 18.1)</td>
<td>13.3 (11.2 to 15.4)</td>
<td>2.8 (0.6 to 5.0)</td>
</tr>
<tr>
<td>SAQ physical limitation</td>
<td>57.3 (19.2)</td>
<td>4.3 (2.8 to 5.9)</td>
<td>4.0 (2.4 to 5.5)</td>
<td>0.3 (−1.4 to 2.1)</td>
</tr>
<tr>
<td>SAQ QOL</td>
<td>50.2 (19.6)</td>
<td>9.6 (7.7 to 11.5)</td>
<td>7.8 (5.9 to 9.7)</td>
<td>1.8 (−0.2 to 3.9)</td>
</tr>
<tr>
<td>SAQ treatment satisfaction</td>
<td>75.5 (15.4)</td>
<td>6.2 (4.7 to 7.6)</td>
<td>4.5 (3.0 to 6.0)</td>
<td>1.7 (0.1 to 3.3)</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>38.2 (6.8)</td>
<td>2.9 (2.3 to 3.5)</td>
<td>1.9 (1.3 to 2.5)</td>
<td>1.0 (0.3 to 1.6)</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>44.9 (10.1)</td>
<td>1.0 (0.2 to 1.8)</td>
<td>1.1 (0.3 to 1.9)</td>
<td>−0.1 (−1.0 to 0.8)</td>
</tr>
<tr>
<td>Rose Dyspnea Scale score</td>
<td>2.0 (1.2)</td>
<td>−0.28 (−0.39 to −0.17)</td>
<td>−0.18 (−0.29 to −0.07)</td>
<td>−0.11 (−0.23 to 0.01)</td>
</tr>
</tbody>
</table>

Abbreviations: LS, least squares; MCS, mental component summary; PCS, physical component summary; QOL, quality of life; SAQ, Seattle Angina Questionnaire; SF-36, Medical Outcomes Short Form-36.

Scores range from 0 to 100, with higher scores indicating improved health status/QOL for all measures except for dyspnea, where scores range from 0 to 4, with lower scores indicating less severe symptoms.
antianginals (17 vs 8 for 1 vs 2 medications) and among patients with more angina at baseline (7 vs 49 for SAQ angina frequency <50 vs ≥50).

Discussion | In a multinational trial of patients with T2DM and stable angina, ranolazine modestly improved key measures of disease-specific and generic health status, with benefits generally consistent across each prespecified subgroup. Furthermore, a greater proportion of patients experienced clinically meaningful improvements in angina with ranolazine vs placebo, particularly among those with more baseline angina and taking more antianginal medications. These data complement our prior reports of reduced angina frequency using an electronic diary by revealing that, from patients’ perspectives, multiple health status domains improved more with ranolazine than with placebo.

TERISA was limited by a racially narrow patient population. Furthermore, our interaction analyses may have been underpowered, leading to potential type II error. Specifically, the interaction of geography by treatment was significant in the underpowered, leading to potential type II error. Specifically, the interaction of geography by treatment was significant in the main TERISA study using an angina diary, but not from patients’ perspectives using the SAQ.

In conclusion, ranolazine reduced angina, particularly among those with more severe angina, improved treatment satisfaction and physical functioning in patients with T2DM and chronic stable angina.

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Author Contributions: Dr Arnold had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition, analysis, or interpretation of data: Arnold, Kosiborod, Li, Yue, Ben-Yehuda, Spertus.

Drafting of the manuscript: Arnold, Ben-Yehuda.

Critical revision of the manuscript for important intellectual content: Arnold, Kosiborod, Li, Yue, Ben-Yehuda, Spertus.

Statistical analysis: Arnold, Li.

Obtained funding: Kosiborod, Yue, Ben-Yehuda.

Administrative, technical, or material support: Yue.

Study supervision: Kosiborod, Ben-Yehuda, Spertus.

Conflict of Interest Disclosures: Dr Arnold received research support from Gilead Sciences, Genentech, and sanofi-aventis. Dr Kosiborod received research support from Gilead Sciences, American Heart Association, Medtronic Minimed, Genentech, sanofi-aventis, Glumetrics, and Maquet; is a consultant for Gilead Sciences, Genentech, F Hoffmann-La Roche, Medtronic Minimed, AstraZeneca, Abbvie, and Regeneron; and served on the advisory board for Gilead Sciences. Dr McGuire is a consultant for Janssen Pharmaceuticals, Daiichi Sankyo, Pfizer, Boehringer-Ingelheim, Regeneron, Genentech, F Hoffmann-La Roche, Merck, Bristol-Myers Squibb, Tethys Biosciences, AstraZeneca, Orexigen, Eli Lilly, and Takeda. Dr Yue is an employee of and owns stock and stock options in Gilead Sciences. Dr Ben-Yehuda is a former employee of Gilead Sciences. Dr Spertus has received research support from Gilead Sciences, National Heart, Lung, and Blood Institute, American College of Cardiology, American Heart Association, Patient-Centered Outcomes Research Institute, Amrocyte, Genentech, and Eli Lilly; is a consultant for Gilead Sciences, Genentech, Amgen, and United Healthcare (Scientific Advisory Group); is a board member for Health Outcomes Sciences; and holds the copyrights for the Seattle Angina Questionnaire, Kansas City Cardiomyopathy Questionnaire, and Peripheral Artery Questionnaire. No other disclosures are reported.

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Role of the Sponsor: As the present study was a planned secondary analysis of the TERISA trial, Gilead Sciences had a role in the design and conduct of the study. The data were collected by Gilead Sciences, who had a role in
interpretation of the data and in the preparation and review of the manuscript. An independent statistical analysis of the data was conducted by the study authors. The sponsor had no role in approval of the manuscript and decision to submit the manuscript for publication.

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Trial Registration: clinicaltrials.gov Identifier: NCT01425359


Blood conservation strategies effectively decrease red blood cell (RBC) use in specific patient groups.1-3 However, the impact of RBC transfusion reduction on mortality in a diverse inpatient population remains poorly described. We detail the impact of declining RBC use on 30-day mortality within Kaiser Permanente Northern California (KPNC), an integrated health care delivery system serving 3.5 million members at 21 hospitals.

Methods | The KPNC and University of California, San Francisco (UCSF) institutional review boards approved this study and waived the requirement for informed consent based on the nature of the study. Beginning in 2010, KPNC initiated a regional blood conservation program whose key features included (1) clinician education in evidence-based transfusion guidelines; (2) focused multidisciplinary conservation efforts in specific high-use departments (eg, orthopedics, cardiovascular surgery); and (3) guideline-based clinical decision support embedded within the electronic medical record.

To study the impact of these initiatives, we quantified RBC transfusion in an inpatient cohort composed of all nonobstetric patients 18 years or older admitted to KPNC hospitals between July 1, 2009, and August 31, 2013. We evaluated the impact of decreased RBC use on unadjusted and risk-adjusted 30-day mortality prior to (2010) and following (2012-2013) reductions in blood use. We examined these rates in patients with hemoglobin levels below 10 g/dL (to convert to grams per liter, multiply by 10) during hospitalization (n = 218,056), accounting for nearly all (81,897 of 83,461 [98.1%]) transfused patients. We quantified patients’ predicted 30-day mortality rates based on prior methods adjusting for age, sex, comorbid disease burden, emergency or elective presentation, medical or surgical admission, admission diagnosis, severity of illness, first inpatient ward, and hospital facility.4 We also adjusted for patients’ preadmission hemoglobin level and lowest hospital hemoglobin level.5 We then compared standardized mortality ratios for transfused vs nontransfused patients using Poisson regression. Trends in RBC use and unadjusted 30-day mortality were assessed using linear regression. Statistical analyses were performed in Stata 11 software (StataCorp).

Results | The number of RBC units transfused decreased 8.6% annually from 41.8 units per 100 patients in 2010 (95% CI, 41.1-42.6 units) to 31.0 units per 100 patients in 2013 (95% CI, 30.3-31.8 units) (P < .001) (Figure 1). From 2009 to 2013, the number of RBC units transfused per 100 patients and median pretransfusion hemoglobin level decreased following initiation of blood conservation strategies in 2010 (P < .001). To convert hemoglobin to grams per liter, multiply by 10. KPNC indicates Kaiser Permanente Northern California; and RBC, red blood cells.

Figure 1. Trends in Inpatient RBC Use and Pretransfusion Hemoglobin Levels Across 21 KPNC Facilities

The number of RBC units transfused per 100 patients and median pretransfusion hemoglobin level decreased following initiation of blood conservation strategies in 2010 (P < .001). To convert hemoglobin to grams per liter, multiply by 10. KPNC indicates Kaiser Permanente Northern California; and RBC, red blood cells.