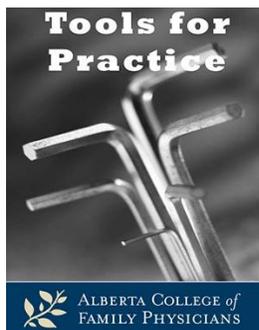


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Evidence Updated: None.
Bottom Line: Unchanged
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Rosiglitazone – Reasonable Option or Regrettable Choice?

Clinical Question: Is rosiglitazone a reasonable second or third line agent in the management of Type 2 Diabetes (DM2)?

Bottom Line: Strong evidence supports increased cardiovascular risk, specifically MI, in Type 2 Diabetes patients receiving rosiglitazone. In the absence of any demonstrated patient-oriented benefits, there is no indication for its use.

Evidence:

- A 2007 meta-analysis (42 randomized controlled trials, 27,847 patients) first assessed the impact of rosiglitazone on cardiovascular (CV) outcomes in DM2 patients.
 - Rosiglitazone caused a statistically significant increase in myocardial infarction (MI) over placebo or other drugs, Relative Risk Increase 43% (Confidence Interval (CI) 3%-97%).¹
 - No difference in cardiovascular deaths.
 - Some questioned the meta-analysis validity due to inclusion of low-quality studies and concern that analysis may have overestimated CV events.²
- Two larger 2010 meta-analyses^{3,4} support the increased risk of MI with rosiglitazone
 - 56 trials, 35,531 patients Odds Ratio 1.28 (CI 1.02-1.63), Number Needed to Harm (NNH) 52 over five years.³
 - 52 trials, 16,995 patients Odds Ratio 1.80 (CI 1.03-3.25).⁴
 - FDA analysis⁴ found the researchers' management of some data potentially masked rosiglitazone harms.
- An FDA mandated re-analysis of the open-label, manufacturer-sponsored RECORD data did not find increased risk of MI (Hazard Ratio 1.13 (CI 0.80-1.59) or related outcomes with rosiglitazone.⁵
- Rosiglitazone is known to increase heart failure, Odds Ratio 1.93 (CI 1.30-2.93).⁴

Context:

- Rosiglitazone was approved based on its ability to improve glycemic control, without any evidence of improvement in patient-oriented outcomes.
- A systematic review reported a strong link between author's views on rosiglitazone and financial conflicts of interest with manufacturer.⁶
- The American Diabetes Association and the European Association for the Study of Diabetes released a consensus statement in 2009 recommending against the use of rosiglitazone in DM2.⁷
- In 2013, the FDA relaxed restrictions on rosiglitazone based on re-analysis of the RECORD trial, despite remaining concerns on its safety.^{8,9}

Original Authors:

Christina Korownyk MD CCFP, G. Michael Allan MD CCFP

Updated:

Ricky D. Turgeon BSc(Pharm) ACPR PharmD

Reviewed:

G. Michael Allan MD CCFP

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