

# ALTERNATIVE VIEWPOINTS

## Sitagliptin-Lovastatin and Possible Rhabdomyolysis: Correlation and Mechanism Unknown

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We read with interest the case report describing concomitant sitagliptin and lovastatin resulting in potential rhabdomyolysis.<sup>1</sup> We believe other issues require further discussion.

Statin-induced myotoxicity (SIM) is commonly the result of a culmination of factors. This patient's specific risks included female gender, advanced age, diabetes mellitus, concomitant diltiazem, hypothyroidism, and recent back surgery.<sup>2,3</sup> These factors are all established as contributors to SIM; thereby indicating the presence of substantial risk prior to sitagliptin initiation.

The authors eliminated hypothyroidism as a cause due to her long-standing treatment and normal thyroid panel 3 months earlier. Although reassuring this does not indicate euthyroidism at the time of the adverse event. Secondly, SIM typically results from pharmacokinetic or pharmacodynamic interactions involving concomitant agents increasing statin serum concentrations (e.g., itraconazole) or also possessing myotoxic effects (e.g., colchicine).<sup>2,4</sup> A PubMed search yielded no reports of other forms of myotoxicity with sitagliptin. Additionally, simvastatin, closely

related to lovastatin with comparable metabolic pathways, showed 'no significant or meaningful' pharmacokinetic changes when administered with sitagliptin in healthy subjects.<sup>5</sup>

A recent report implicated sitagliptin and simvastatin with rhabdomyolysis in another complex patient with multiple risk factors for myotoxicity.<sup>6</sup> Unlike the present report this patient had existing renal impairment, which the authors hypothesized was worsened by high-dose sitagliptin, resulting in elevated simvastatin serum levels and ultimately rhabdomyolysis. The report was however disputed because of concomitant amiodarone<sup>7</sup>; well established for increasing simvastatin concentrations and potentiating rhabdomyolysis.<sup>8</sup>

We agree with the authors that it is imperative to be watchful of newer agents and report suspected adverse events. It is possible that the addition of sitagliptin further increased this patient's risk of myotoxicity; however presently it is difficult to determine any association. If causation between sitagliptin and rhabdomyolysis is indeed someday determined, the mechanism will likely be unique compared to traditional interacting agents or the occurrence more frequent among patients with renal impairment.

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### Authors' Reply

The authors declined the opportunity to reply.