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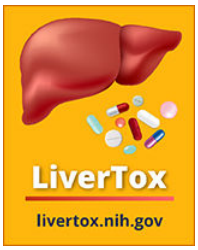

Rosuvastatin

Updated: December 1, 2021.

OVERVIEW

Introduction

Rosuvastatin is a commonly used cholesterol lowering agent (statin) that is associated with mild, asymptomatic and self-limited serum aminotransferase elevations during therapy, and rarely with clinically apparent acute liver injury.

Background

Rosuvastatin (roe soo" va stat' in) is a potent, orally available inhibitor of hepatic 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase the major rate-limiting enzyme in cholesterol synthesis. Like other members of its class (the "statins"), rosuvastatin lowers total serum cholesterol and low density lipoprotein (LDL) concentrations, thereby reducing the risk of atherosclerosis and its complications – myocardial infarction and stroke. Rosuvastatin was approved for use in the United States in 2003 and currently several million prescriptions are filled yearly. Rosuvastatin is indicated for treatment of hypercholesterolemia in persons at high risk for coronary, cerebrovascular and peripheral artery disease and for children and adults with homozygous familial hypercholesterolemia. Rosuvastatin has been shown to slow progression of atherosclerosis and to prevent cardiovascular disease, and is approved for those indications. Rosuvastatin is available in tablets of 5, 10, 20 and 40 mg generically and under the trade name Crestor. Rosuvastatin is one of the more potent statins available and is typically used in a comparably lower dose. The recommended dose in adults is 5 to 40 mg once daily, based upon tolerability and lipid levels. Persons of Asian descent should receive a lower dose (5 to 10 mg daily) because of alternations in its metabolism. Common side effects include muscle cramps, headache, joint aches, abdominal pain, nausea, and weakness, symptoms that occur with all of the currently available statins. Rare but potentially severe adverse events include liver injury, myopathy, rhabdomyolysis, and immune-mediated necrotizing myopathy.

Hepatotoxicity

Rosuvastatin therapy is associated with mild, asymptomatic and usually transient serum aminotransferase elevations in 1% to 3% of patients. ALT levels above 3 times the upper limit of normal (ULN) occur slightly more frequently among rosuvastatin treated [1.1%] than placebo [0.5%] recipients. Serum enzyme elevations are more common with higher doses of rosuvastatin, being 2.2% with 40 mg daily. Most of these elevations are self-limited and do not require dose modification. Rosuvastatin is also associated with frank, clinically apparent hepatic injury but this is rare, occurring in less than 1:10,000 patients. The onset is typically after 2 to 4 months ,and the pattern of serum enzyme elevations is usually hepatocellular, although cholestatic cases have also been reported. Rash, fever and eosinophilia are uncommon. Several statins including rosuvastatin have been linked to hepatitis

with autoimmune features marked by ANA positivity, elevations in serum immunoglobulin levels, and a clinical response to corticosteroids. Such features are not, however, invariable (Case 1). The injury is usually self-limited and resolves rapidly once rosuvastatin is stopped, but it can be severe and fatal instances have been reported.

Likelihood score: A (likely cause of clinically apparent liver injury).

Mechanism of Injury

The cause of hepatic injury from rosuvastatin is unknown. Rosuvastatin is minimally (~10%) metabolized in the liver (via CYP 2C9). The mild, self-limited ALT elevations may be due to a toxic intermediate of drug metabolism and the reversal of these elevations due to adaptation. The idiosyncratic, clinically apparent liver injury associated with rosuvastatin is often accompanied by autoimmune features and may, therefore, be caused by immune mechanisms.

Outcome and Management

The product label for rosuvastatin recommends screening for liver test abnormalities before starting therapy and repeating tests as clinically indicated. The mild ALT elevations associated with rosuvastatin therapy are usually self-limited and do not require dose modification. Rosuvastatin should be stopped if ALT levels rise above 10-fold the ULN, or persist in being above 5-fold elevated or are associated with symptoms. In the clinically apparent liver injury attributed to rosuvastatin, recovery is usually complete within 1 to 2 months. Recurrence of injury with rechallenge has been reported and should be avoided. Cases of chronic hepatitis, but no instances of vanishing bile duct syndrome attributable to rosuvastatin have been reported. In cases of autoimmune hepatitis-like injury, corticosteroids have been used when recovery does not occur promptly. If corticosteroids are used, the dose and duration of treatment should be kept to a minimum, and careful follow up after stopping is essential. Switching therapy to another statin after rosuvastatin induced injury is apparently safe, but few instances have been reported, and it should be done with careful monitoring for recurrence.

Drug Class: Antilipemic Agents

Other Drugs in the Subclass, Statins: Atorvastatin, Ezetimibe [used in combination], Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Simvastatin

CASE REPORT

Case 1. Acute self-limited hepatitis during rosuvastatin therapy.(1)

A 64 year old man developed jaundice approximately 15 weeks after starting rosuvastatin (10 mg daily) for hypercholesterolemia. He had a history of acute myocardial infarction four months previously, which was treated with angioplasty and stenting. Discharge medications included clopidogrel, aspirin, metoprolol, ramipril and atorvastatin. One week later he developed skin rash and minor ALT elevations (55 U/L), and rosuvastatin was substituted for atorvastatin. Subsequently, he felt well until 3 months later when he developed malaise, anorexia and upper abdominal discomfort followed by jaundice. On examination, he had no fever, rash or signs of chronic liver disease. Laboratory results showed elevations in serum bilirubin and aminotransferase levels, but normal alkaline phosphatase and GGT values (Table). Tests for hepatitis A, B, C, and E were negative as were routine autoantibodies. Ultrasonography of the liver and biliary tree was normal. Rosuvastatin was stopped while blood pressure and antiplatelet medications were continued. Liver test abnormalities improved promptly and were normal two weeks later.

Key Points

Medication:	Rosuvastatin (10 mg daily)

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Pattern:	Hepatocellular (aminotransferase elevations only)
Severity:	3+ (jaundice, hospitalization)
Latency:	15 weeks
Recovery:	2 weeks
Other medications:	Clopidogrel, aspirin, metoprolol, ramipril, atorvastatin

Laboratory Values

Time After Starting	Time After Stopping	ALT* (U/L)	Alk P* (U/L)	Bilirubin (mg/dL)	Other
Pre		20	Normal	Normal	Discharge after heart attack
Pre		55			Atorvastatin stopped
Atorvastatin stopped and rosuvastatin started					
2 days		40			
3 days		35			
15 weeks	0	775	Normal	2.6	Admission: rosuvastatin stopped
15 weeks	3 days	198		1.8	INR Normal
16 weeks	1 week	40		Normal	
17 weeks	2 weeks	30	Normal	Normal	
Normal Values		**<36**	**<117**	**<1.2**	

* Some values estimated from Figure 1.

Comment

The onset of hepatocellular injury approximately 3 months after starting rosuvastatin and the rapid recovery with stopping therapy makes the diagnosis of rosuvastatin induced acute hepatitis highly likely. Other diagnoses were appropriately ruled out, and there was documentation of normal liver tests before starting statin therapy. Acute, clinically apparent liver injury is rare with rosuvastatin therapy (~1:10,000 patients treated) and is rapidly reversible with prompt discontinuation of therapy. Rechallenge with rosuvastatin is inadvisable, but other statins might be initiated with careful monitoring of serum enzymes.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Rosuvastatin – Generic, Crestor®

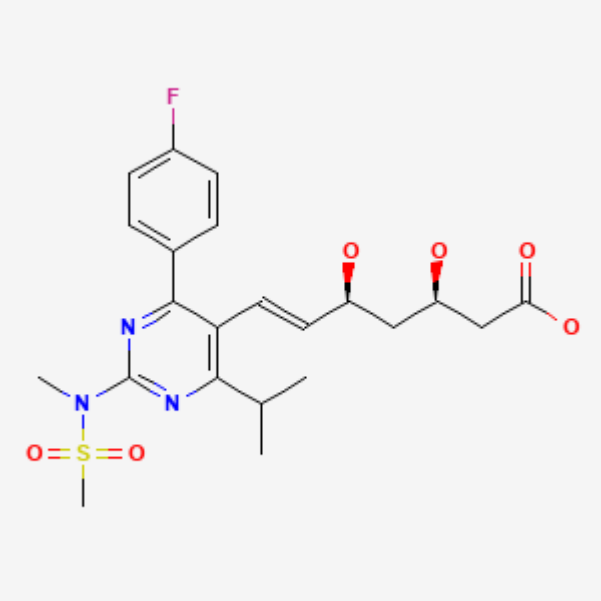
DRUG CLASS

Antilipemic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Rosuvastatin	287714-41-4	C22-H28-F-N3-O6-S	

CITED REFERENCE

1. Famularo G, Miele L, Minisola G, Grieco A. Liver toxicity of rosuvastatin therapy. World J Gastroenterol. 2007;13:1286–8. PubMed PMID: 17451217.

ANNOTATED BIBLIOGRAPHY

References updated: 01 December 2021

Abbreviations used: ANA, antinuclear antibody; HDL, high density lipoprotein; LDL, low density lipoprotein; OD, odds ratio.

Zimmerman HJ. Drugs used in the treatment of hypercholesterolemia and hyperlipidemia. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 660-2.

(Expert review of hepatotoxicity published in 1999; the statins have dose related hepatic effects in guinea pigs and rabbits, and transient elevations in aminotransferases occur in 1-5% of humans treated; several cases of clinically apparent liver injury from lovastatin and simvastatin have been published).

De Marzio DH, Navarro VJ. Hepatotoxicity of cardiovascular and antidiabetic medications. Lipid lowering agents. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 519-40.

(Review of hepatotoxicity of lipid lowering agents; asymptomatic elevations in aminotransferases are common in patients receiving statins, but clinically significant hepatotoxicity is rare).

Gurgle H, Blumenthal DK. Drug therapy for dyslipidemias. In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 605-618.

(Textbook of pharmacology and therapeutics; "Serious hepatotoxicity is rare and unpredictable, with a rate of about 1 case per million person-years of use." Multiple academic societies and the FDA recommend testing all patients for routine liver tests before starting statins but monitoring or retesting only if symptoms arise).

Brewer HB Jr. Benefit-risk assessment of rosuvastatin 10 to 40 milligrams. Am J Cardiol. 2003;92 Suppl:23K–29K. PubMed PMID: 12948873.

(Review of efficacy and safety of rosuvastatin in doses of up to 80 mg daily in 12,569 patients [14,231 patient years]: ALT elevations >3 times ULN occurred in 0.2% and similar rate in comparators: atorvastatin, simvastatin, and pravastatin).

Simonson SG, Martin PD, Mitchell P, Schneck DW, Lasseter KC, Warwick MJ. Pharmacokinetics and pharmacodynamics of rosuvastatin in subjects with hepatic impairment. Eur J Clin Pharmacol. 2003;58:669–75. PubMed PMID: 12610743.

(Pharmacokinetic studies of rosuvastatin [10 mg daily for 10 days] in 18 subjects, found normal peak and total area under the curve levels in 6 of 6 with Childs Class A and 4 of 6 with Childs Class B cirrhosis [alcoholic] compared to 6 of 6 subjects with normal liver function).

Shepherd J, Hunninghake DB, Stein EA, Kastelein JJ, Harris S, Pears J, Hutchinson HG. Safety of rosuvastatin. Am J Cardiol. 2004;94:882–8. PubMed PMID: 15464670.

(Overview of safety of rosuvastatin based upon data from 12,400 patients in clinical trials using 5-40 mg daily; rates of adverse events similar to those with placebo, rates of ALT elevations >3 times ULN were 0.5% with 5, 0.1% with 10, 0.1% with 20 and 0.3% with 40 mg, with overall rates 0.2% similar to comparator statins).

Wolters LMM, Van Buuren HR. Rosuvastatin-associated hepatitis with autoimmune features. Eur J Gastroenterol Hepatol. 2005;17:589–90. (letter). PubMed PMID: 15827453.

(46 year old developed jaundice 9 weeks after starting rosuvastatin [bilirubin 7.9 mg/dL, ALT 2539 U/L, Alk P 151 U/L, IgG 2.4 g/dL, SMA1:160], improved upon stopping rosuvastatin, but eventually required long term corticosteroid therapy [during follow up for more than 4 years after this publication]).

Alsheikh-Ali AA, Ambrose MS, Kuvin JT, Karas RH. The safety of rosuvastatin as used in common clinical practice: a postmarketing analysis. Circulation. 2005;111:3051–7. PubMed PMID: 15911706.

(Review of MedWatch adverse event reports on rosuvastatin over first year of marketing; rates of liver related reports were 25 per million prescriptions for rosuvastatin compared to 4-5 for simvastatin, pravastatin and atorvastatin and rates also higher for comparable marketing period of the other statins).

McKenney JM. An assessment of statin safety. Am J Manag Care. 2006;12:S310–7. PubMed PMID: 17042673.

(Review of the safety of the statins; liver failure reported at a rate of 1 per million, which is similar to nonstatin-taking population, recommends monitoring based upon symptoms rather than blood test abnormalities).

Conforti A, Magro L, Moretti U, Scotto S, Motola D, Salvo F, Ros B, et al. Fluvastatin and hepatic reactions: a signal from spontaneous reporting in Italy. Drug Safety. 2006;29:1163–72. PubMed PMID: 17147462.

(Italian Pharmacovigilance Group review of 35,757 adverse reaction reports; 1260 due to statins of which 178 were hepatic: 69 [36%] fluvastatin, 37 [21%] atorvastatin, 50 [28%] simvastatin, 16 [9%] pravastatin, 6 [3%] rosuvastatin; proportion reporting rate based on number of prescriptions was highest for fluvastatin [~9] compared to other agents [~2-3]).

Zipes DP, Zvaifler NJ, Glassock RJ, Gilman S, Muñoz A, Gogolak V, Gordis L, et al. Rosuvastatin: an independent analysis of risks and benefits. MedGenMed. 2006;8:73. PubMed PMID: 16926812.

(Expert review of the literature concludes that safety and tolerability of rosuvastatin is similar to other statins, and rates of liver injury are very low).

McAfee AT, Ming EE, Seeger JD, Quinn SG, Ng EW, Danielson JD, Cutone JA, et al. The comparative safety of rosuvastatin: a retrospective matched cohort study in over 48,000 initiators of statin therapy. Pharmacoepidemiol Drug Saf. 2006;15:444–53. PubMed PMID: 16761308.

(Analysis of electronic records on 11,249 patients starting rosuvastatin compared to 37,282 starting another statin; over the first 6 months of treatment, hepatic dysfunction reported in 2 [0.020%] starting rosuvastatin vs 8 [0.024%] starting other statins).

Goettsch WG, Heintjes EM, Kastelein JJ, Rabelink TJ, Johansson S, Herings RM. Results from a rosuvastatin historical cohort study in more than 45,000 Dutch statin users, a PHARMO study. Pharmacoepidemiol Drug Saf. 2006;15:435–43. PubMed PMID: 16761304.

(Analysis of electronic database on more than 2 million Dutch residents comparing those on rosuvastatin [10,147], other statins [37,396] and non-users [99,935]; hepatic impairment identified in none on rosuvastatin, 4 [0.011%] on statins and 7 [0.006%] controls).

Silva MA, Swanson AC, Gandhi PJ, Tataronis GR. Statin-related adverse events: a meta-analysis. Clin Ther. 2006;28:26–35. PubMed PMID: 16490577.

(Metaanalysis of adverse event rates in 18 placebo controlled trials of six statins in 71,108 patients; ALT elevations >3 times ULN in 1.7% of statin vs 1.4% placebo recipients; event rates highest with atorvastatin, lowest with fluvastatin).

Antonopoulos S, Mikros S, Mylonopoulou M, Kokkoris S, Giannoulis G. Rosuvastatin as a novel treatment of non-alcoholic fatty liver disease in hyperlipidemic patients. Atherosclerosis. 2006;184:233–4. PubMed PMID: 16168995.

(Open label study of rosuvastatin [10 mg/day] for 8 months in 23 patients with nonalcoholic fatty liver disease; ALT levels fell to normal in all patients and no instance of hepatotoxicity).

Clearfield MB, Amerena J, Bassand JP, Hernández García HR, Miller SS, Sosef FF, Palmer MK, et al. Comparison of the efficacy and safety of rosuvastatin 10 mg and atorvastatin 20 mg in high-risk patients with hypercholesterolemia--Prospective study to evaluate the Use of Low doses of the Statins Atorvastatin and Rosuvastatin (PULSAR). Trials. 2006;7:35. PubMed PMID: 17184550.

(Controlled trial comparing rosuvastatin [10 mg] vs atorvastatin [20 mg] daily for 6 weeks; one patient on atorvastatin had confirmed ALT elevations >3 times ULN; no clinically apparent liver injury).

Law M, Rudnicka AR. Statin safety: a systematic review. Am J Cardiol. 2006;97(8A):52C–60C. PubMed PMID: 16581329.

(Review of safety of statins; 38 cases of acute liver failure attributed to statins were submitted to MedWatch by end of 1999, which gives an estimated rate of 1 per million person years of use; rate of confirmed ALT elevations >3 times ULN is 0.1% with statins and 0.04% with placebo).

Guthrie RM, Martin DR. The safety of rosuvastatin: effects on renal and hepatic function. Expert Opin Drug Saf. 2007;6:573–81. PubMed PMID: 17877444.

(Review of hepatic adverse events due to rosuvastatin without new information; ALT elevations occur at a similar rate during rosuvastatin as with other statins and average ~0.4%; acute liver failure has not been definitely linked to statins, estimated rate being ~1 per million patient years, similar to background rate; authors argue against routine monitoring of liver enzymes during rosuvastatin therapy).

Kasliwal R, Wilton LV, Cornelius V, Aurich-Barrera B, Shakir SA. Safety profile of rosuvastatin: results of a prescription-event monitoring study of 11,680 patients. Drug Saf. 2007;30:157–70. PubMed PMID: 17253880.

(Postmarketing study of 11,680 patients on rosuvastatin; therapy stopped in 17.5% because of adverse events, myalgias being most frequent reason; ALT or AST elevations in 101 patients [~1%], but only 9 [~0.1%] had confirmed ALT values >3 times ULN, one patient developed an autoimmune hepatitis-like syndrome 4 months after starting rosuvastatin, resolving spontaneously with stopping, another patient had cholestatic jaundice).

Bhardwah SS, Chalasani N. Lipid-lowering agents that cause drug-induced hepatotoxicity. Clin Liver Dis. 2007;11:597–613. PubMed PMID: 17723922.

(Review of hepatotoxicity of statins; reported rates of ALT or AST elevations >3 times ULN: atorvastatin 0.7%, fluvastatin 1.2%, lovastatin 0.6%, pravastatin 1.4%, rosuvastatin 0% and simvastatin 1.8%. Usually asymptomatic, individual case reports of autoimmune hepatitis).

Stein EA, Amerena J, Ballantyne CM, Brice E, Farnier M, Guthrie RM, Harats D, et al. Long-term efficacy and safety of rosuvastatin 40 mg in patients with severe hypercholesterolemia. Am J Cardiol. 2007;100:1387–96. PubMed PMID: 17950795.

(Open label, extension study of rosuvastatin [40 mg daily] for 2 years in 1,380 patients with severe hypercholesterolemia; confirmed ALT elevations >3 times ULN occurred in 0.8%, half resolved despite continuing therapy, no clinically apparent hepatitis or jaundice and no deaths from liver disease).

Merz T, Fuller SH. Elevated serum transaminase levels resulting from concomitant use of rosuvastatin and amiodarone. Am J Health Syst Pharm. 2007;64:1818–21. PubMed PMID: 17724362.

(73 year old developed minimal ALT elevations on rosuvastatin which worsened two weeks after starting amiodarone [ALT 13→91→336 U/L], improving with stopping rosuvastatin despite continuing amiodarone, possibly demonstrating interaction between the two agents).

Famularo G, Miele L, Minisola G, Grieco A. Liver toxicity of rosuvastatin therapy. World J Gastroenterol. 2007;13:1286–8. PubMed PMID: 17451217.

(64 year old man developed jaundice ~3 months after starting rosuvastatin [bilirubin 2.6 mg/dL, ALT 775 U/L, normal GGT, ANA negative], resolving within 2 weeks of stopping: case 1).

Crouse JR 3rd, Raichlen JS, Riley WA, Evans GW, Palmer MK, O'Leary DH, Grobbee DE, et al; METEOR Study Group. Effect of rosuvastatin on progression of carotid intima-media thickness in low-risk individuals with subclinical atherosclerosis: the METEOR Trial. JAMA. 2007;297:1344–53. PubMed PMID: 17384434.

(Among 984 patients with hypercholesterolemia but no history of cardiovascular disease treated with rosuvastatin [40 mg] or placebo daily for a period of 2 years, LDL-cholesterol levels decreased by 49% in statin treated patients who had less progression of carotid intima-media thickening, while adverse event rates were similar to placebo treatment including myalgia [12.7% vs 12.1%] and ALT elevations above 3 times ULN [0.6% vs 0.4%], and there were no cases of clinically apparent hepatitis or rhabdomyolysis).

Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM Jr, Kastelein JJ, Koenig W, et al; JUPITER Study Group. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008;359:2195–207. PubMed PMID: 18997196.

(Among 17,802 healthy adults with low risk for cardiovascular events [LDL-C less than 130 mg/dL] but elevated C-reactive protein treated with rosuvastatin [20 mg] or placebo once daily for a median of 1.9 years, LDL-cholesterol levels decreased by 50% and major cardiovascular event rates were lower with statin therapy, while adverse event rates were similar, such as serious events [15.2% vs 15.5%], muscle symptoms [16% vs 15.4%], myopathy [0.1% vs 0.1%], ALT elevations above 3 times ULN [0.3% vs 0.2%], although new onset diabetes was more frequent with rosuvastatin [3.0% vs 2.4%]).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug-Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. Gastroenterology. 2008;135:1924–34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected from 2004 to 2008, 3 cases were attributed to atorvastatin, 3 to simvastatin/ezetimibe, and one each to pravastatin, fluvastatin, and simvastatin, but most cases were mild or not clearly attributable to the statin therapy; none related to rosuvastatin).

Oteri A, Catania MA, Russo A, Salvo F, Giacci L, Caputi AP, Polimeni G. Reversible acute hepatitis induced by rosuvastatin. South Med J. 2008;101:768. PubMed PMID: 19209117.

(62 year old man developed jaundice 2 months after switching from simvastatin to rosuvastatin [10 mg daily] [bilirubin 6.1 mg/dL, ALT 2317 U/L, Alk P levels and ANA not reported], resolving within 3 weeks of stopping drug).

García-Rodríguez LA, Massó-González EL, Wallander MA, Johansson S. The safety of rosuvastatin in comparison with other statins in over 100,000 statin users in UK primary care. Pharmacoepidemiol Drug Saf. 2008;17:943–52. PubMed PMID: 18425988.

(Analysis of electronic records on 10,289 patients starting rosuvastatin and 117,102 starting other statins [mostly simvastatin and atorvastatin] for adverse events; 4 cases [0.003%] of myopathy, 4 [0.003%] of rhabdomyolysis and 6 [0.05%] of acute liver injury identified, but none in rosuvastatin users).

García-Rodríguez LA, González-Pérez A, Stang MR, Wallander MA, Johansson S. The safety of rosuvastatin in comparison with other statins in over 25,000 statin users in the Saskatchewan Health Databases. Pharmacoepidemiol Drug Saf. 2008;17:953–61. PubMed PMID: 18425987.

(Analysis of electronic medical records on 25,238 first time statin users, 10,384 starting rosuvastatin; 2 cases each of myopathy, rhabdomyolysis and acute liver injury [all 0.008%], but both liver related adverse events occurred in atorvastatin treated patients).

Rubba P, Marotta G, Gentile M. Efficacy and safety of rosuvastatin in the management of dyslipidemia. Vasc Health Risk Manag. 2009;5:343–52. PubMed PMID: 19436657.

(Review of mechanism of action, pharmacology, safety and efficacy of rosuvastatin; elevations of ALT levels >3 times ULN during rosuvastatin therapy are uncommon [<0.2%]).

Hippisley-Cox J, Coupland C. Unintended effects of statins in men and women in England and Wales: population based cohort study using the QResearch database. BMJ. 2010;340:c2197. PubMed PMID: 20488911.

(Among 225,922 new users of statins in a UK health care database, there was an increased risk of moderate or severe liver dysfunction [ALT > 3 times ULN], usually within first 6 months and associated with higher doses of statins; relative risks were highest with fluvastatin [2.53 in women, 1.97 in men] and lowest with pravastatin [0.93 to 1.58], and intermediate for rosuvastatin [1.31 to 1.46]).

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology. 2010;52:2065–76. PubMed PMID: 20949552.

(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 were attributed to drug induced liver injury, including 2 due to atorvastatin, 2 simvastatin and 2 cerivastatin, but none to rosuvastatin).

Saku K, Zhang B, Noda K; The PATROL Trial Investigators. Randomized head-to-head comparison of pitavastatin, atorvastatin, and rosuvastatin for safety and efficacy (quantity and quality of LDL). Circ J. 2011;75:1493–1505. PubMed PMID: 21498906.

(Controlled trial comparing 3 potent statins in 302 patients for 16 weeks; ALT elevations above 3 times ULN occurred in 2 on atorvastatin, 2 on rosuvastatin and 1 on pitavastatin, but none developed clinically apparent liver injury).

Toth PP, Dayspring TD. Drug safety evaluation of rosuvastatin. Expert Opin Drug Saf. 2011;10:969–86. PubMed PMID: 21999163.

(Review of pharmacology, safety and efficacy of rosuvastatin; "compared to other statins, it has no excess signal for liver, skeletal muscle or renal toxicity").

Kato JD, Wang CT. Cardiac rehabilitation participant with sickle cell trait and statin-related hepatotoxicity: a case report. J Cardiopulm Rehabil Prev. 2012;32:182–6. PubMed PMID: 22595892.

(51 year old man developed marked aminotransferase elevations [ALT 2498 U/L, AST 1452 U/L; Alk P and bilirubin not given] 75 days after starting rosuvastatin, which fell to normal within 3 months of stopping, but rose again 1 month after restarting).

Björnsson E, Jacobsen EI, Kalaitzakis E. Hepatotoxicity associated with statins: reports of idiosyncratic liver injury post-marketing. J Hepatol. 2012;56:374–80. PubMed PMID: 21889469.

(Between 1988 and 2010, the Swedish registry received 217 adverse event reports possibly related to statins, 124 [57%] being liver related, 73 of which could be evaluated: 2 were fatal and one led to liver transplant; 3 had positive rechallenge; 43 [59%] were hepatocellular, 22 [30%] cholestatic and 8 [11%] mixed; 30 were due to atorvastatin, 28 simvastatin, 11 fluvastatin, 2 pravastatin and 2 rosuvastatin, arising after 30-248 days; atorvastatin injury was more likely to be cholestatic and was estimated to occur in 2.9 per 100,000 person years).

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology. 2010;52:2065–76. PubMed PMID: 20949552.

(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 [11%] were attributed to drug induced liver injury, of which 6 were attributed to statins: 2 atorvastatin, 2 simvastatin [one with ezetimibe] and 2 cerivastatin, but none to rosuvastatin).

Vaverkova H, Farnier M, Averna M, Missault L, Viigimaa M, Dong Q, Shah A, et al. Lipid-altering efficacy of ezetimibe/simvastatin 10/20 mg compared to rosuvastatin 10 mg in high-risk patients with and without type 2 diabetes mellitus inadequately controlled despite prior statin monotherapy. Cardiovasc Ther. 2012;30:61–74. PubMed PMID: 20626402.

(In a randomized trial in patients with hypercholesterolemia, ALT or AST elevations >3 times ULN occurred in none of 303 patients receiving rosuvastatin versus 0.7% of 312 on the combination of simvastatin and ezetimibe).

DeGorter MK, Tirona RG, Schwarz UI, Choi YH, Dresser GK, Suskin N, Myers K, et al. Clinical and pharmacogenetic predictors of circulating atorvastatin and rosuvastatin concentrations in routine clinical care. Circ Cardiovasc Genet. 2013;6:400–8. PubMed PMID: 23876492.

(Measurement of plasma levels of atorvastatin and rosuvastatin in two cohorts [299 and 576 patients] found levels varied 45-fold and were consistently higher in Chinese and Japanese compared to European subjects and that differences could not be completely explained by racial variation in frequencies of SLCO and ABCG2 polymorphisms known to affect peak drug levels).

Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology. 2013;144:1419–25. PubMed PMID: 23419359.

(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, including 2 cases due to atorvastatin and 1 to simvastatin, but none to rosuvastatin).

Hernández N, Bessone F, Sánchez A, di Pace M, Brahm J, Zapata R, A, Chirino R, et al. Profile of idiosyncratic drug induced liver injury in Latin America. An analysis of published reports. Ann Hepatol. 2014;13:231–9. PubMed PMID: 24552865.

(Systematic review of literature of drug induced liver injury in Latin American countries published from 1996 to 2012 identified 176 cases, none of which were attributed to statins or lipid lowering agents).

Russo MW, Hoofnagle JH, Gu J, Fontana RJ, Barnhart H, Kleiner DE, Chalasani N, et al. Spectrum of statin hepatotoxicity: Experience of the drug-induced liver injury network. Hepatology. 2014;60:679–86. PubMed PMID: 24700436.

(Among 1,188 cases of drug induced liver disease collected in the US between 2004 to 2012, 22 [2%] were attributed to statins, including atorvastatin [8], simvastatin [5], rosuvastatin [4], fluvastatin [2], pravastatin [2] and lovastatin [1]; median age was 60 years and 68% were women; 9 cases were cholestatic and 12 hepatocellular [6 with autoimmune features]; the latency ranged widely, from 1 month to 10 years; only one case was fatal [a man with preexisting cirrhosis presenting with acute-on-chronic liver failure]).

Bays H, Cohen DE, Chalasani N, Harrison SA. An assessment by the Statin Liver Safety Task Force: 2014 update. J Clin Lipidol. 2014;8(3 Suppl):S47–57. PubMed PMID: 24793441.

(Review of the safety of statins including their use in patients with liver disease recommending that liver tests be obtained before therapy, but that routine monitoring is not necessary and that statins can be safety used in patients with nonalcoholic liver disease, and are probably safe in other forms of chronic liver disease and after liver transplantation).

Ooba N, Sato T, Wakana A, Orii T, Kitamura M, Kokan A, Kurata H, et al. A prospective stratified case-cohort study on statins and multiple adverse events in Japan. PLoS One. 2014;9:e96919. PubMed PMID: 24810427.

(Among 6877 patients started on statins between 2008 and 2010, 139 developed an increase in ALT or AST deemed likely due to the drug with no significant differences among those treated with pra-, ator-, flu-, pita- or rosuvastatin).

Macedo AF, Taylor FC, Casas JP, Adler A, Prieto-Merino D, Ebrahim S. Unintended effects of statins from observational studies in the general population: systematic review and meta-analysis. BMC Med. 2014;12:51. PubMed PMID: 24655568.

(Systematic review of 90 studies of 48 different "unintended effects" of statins with evidence of an increased risk of myopathy [Odds Ratio: OR=2.6] and raised liver enzymes [OR=1.5]).

Drugs for lipids. Treat Guidel Med Lett. 2014;12(137):1–6. PubMed PMID: 24419209.

(Concise recommendations on management of hyperlipidemia mentions that 1-2% of patients on high doses of statins develop ALT elevations [above 3 times ULN], but that there is not always cross sensitivity to this side effect and that patients with mild-to-moderate ALT elevations can tolerate statins; no discussion of clinically apparent liver).

Vishwakarma P, Nehra R, Kumar A. Acute hepatic injury with atorvastatin: an unusual occurrence. Indian J Pharmacol. 2014;46:343–4. PubMed PMID: 24987187.

(63 year old man developed jaundice 2 months after starting 20 mg daily of atorvastatin [bilirubin 5.2 mg/dL, ALT 1124 U/L, Alk P 214 U/L], falling to normal within a month of switching to 10 mg daily of rosuvastatin).

Perdices EV, Medina-Cáliz I, Hernando S, Ortega A, Martín-Ocaña F, Navarro JM, Peláez G, et al. Hepatotoxicity associated with statin use: analysis of the cases included in the Spanish Hepatotoxicity Registry. Rev Esp Enferm Dig. 2014;106:246–54. PubMed PMID: 25075655.

(Among 858 cases of drug induced liver injury enrolled in a Spanish Registry between 1994 and 2012, 47 [5.5%] were attributed to statins [16 atorvastatin, 13 simvastatin, 12 fluvastatin, 4 lovastatin and 2 pravastatin], usually with a hepatocellular pattern of injury, 8.5% with autoimmune features, chronic injury in 19%, and no liver-related deaths).

Chen GL, Hsiao FY, Dong YH, Shen LJ, Wu FL. Statins and the risk of liver injury: a population-based case-control study. Pharmacoepidemiol Drug Saf. 2014;23:719–25. PubMed PMID: 24829162.

(Among 2165 Taiwanese patients hospitalized for liver injury between 2002 and 2009, use of statins was not more frequent than among 16,600 hospitalized controls, except for use of high doses of rosuvastatin [adjusted odds ratio of 2.29]).

Birmingham BK, Bujac SR, Elsby R, Azumaya CT, Zalikowski J, Chen Y, Kim K, et al. Rosuvastatin pharmacokinetics and pharmacogenetics in Caucasian and Asian subjects residing in the United States. Eur J Clin Pharmacol. 2015;71:329–40. PubMed PMID: 25630984.

(Pharmacokinetic studies using a single oral dose of rosuvastatin [20 mg] showed that East-Asian subjects [Chinese, Filipino, Korean, Vietnamese and Japanese] had greater area under the curve concentrations [64% to 84%higher] and higher maximum drug concentrations [70-98% higher] than Caucasians, while Asian-Indians demonstrated intermediate levels; higher values were also seen in subjects with polymorphisms in SLCO1B1 and ABCG2 hepatic transporter genes, which may have accounted for some of the differences).

Birmingham BK, Bujac SR, Elsby R, Azumaya CT, Wei C, Chen Y, Mosqueda-Garcia R, et al. Impact of ABCG2 and SLCO1B1 polymorphisms on pharmacokinetics of rosuvastatin, atorvastatin and simvastatin acid in Caucasian and Asian subjects: a class effect? Eur J Clin Pharmacol. 2015;71:341–55. PubMed PMID: 25673568.

*(Among 96 subjects treated in an open-label, 3-way crossover study of a single oral dose of rosuvastatin [20 mg], atorvastatin [40 mg], or simvastatin [40%], Chinese and Japanese subjects had higher plasma levels than European subjects, and the differences could not be attributed entirely to hepatic transporter polymorphisms {SLCO1B1*1a and ABCG2c.421] known to be associated with higher statin levels).*

Hwang NK, Park JS, Cha KS, Kang JS. Hepatotoxicity associated with a short course of rosuvastatin. Chin Med J (Engl). 2015;128:1693–4. PubMed PMID: 26063377.

(76 year old Korean man with coronary artery disease developed abdominal pain and jaundice 12 days after a percutaneous intervention and starting rosuvastatin [bilirubin 10.3 mg/dL, ALT 612 U/L, Alk P 174 U/L], which resolved rapidly [< 1 week] upon stopping).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology. 2015;148:1340–52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 31 cases [3.4%] were attributed to statins, including 8 to atorvastatin, 8 simvastatin, 7 rosuvastatin, 4 pravastatin, 2 fluvastatin and 2 lovastatin).

Chang CH, Chang YC, Lee YC, Liu YC, Chuang LM, Lin JW. Severe hepatic injury associated with different statins in patients with chronic liver disease: a nationwide population-based cohort study. J Gastroenterol Hepatol. 2015;30:155–62. PubMed PMID: 25041076.

(Among 37,929 Taiwanese persons with chronic liver disease started on statin therapy for hyperlipidemia between 2005 and 2009, there were 912 incident cases of hospitalization for liver injury, rates being similar for the 6 different statins used [1.94-2.95 per 100,000 person-days], but higher in those on high doses of atorvastatin [40 or 80 mg daily]).

Kim HS, Lee SH, Kim H, Lee SH, Cho JH, Lee H, Yim HW, et al. Statin-related aminotransferase elevation according to baseline aminotransferases level in real practice in Korea. J Clin Pharm Ther. 2016;41:266–72. PubMed PMID: 27015878.

(Among 21,233 Korean patients starting statin therapy between 2009 and 2013, abnormal ALT or AST values above 3 times ULN were more frequent among those with mild baseline elevations).

Yusuf S, Bosch J, Dagenais G, Zhu J, Xavier D, Liu L, Pais P, et al; HOPE-3 Investigators. cholesterol lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med. 2016;374:2021–31. PubMed PMID: 27040132.

(Among 12,705 adults with intermediate cardiovascular risk treated with rosuvastatin [10 mg] or placebo daily for a median period of 5.6 years, LDL-cholesterol levels were 26.5% lower and cardiovascular endpoints 24% lower with statin therapy, while muscle pain or weakness was more frequent with statins [5.8% vs 4.7%], myopathy and liver test abnormalities were rare [<1% in both groups]).

Wang LY, Huang YS, Perng CL, Huang B, Lin HC. Statin-induced liver injury in an area endemic for hepatitis B virus infection: risk factors and outcome analysis. Br J Clin Pharmacol. 2016;82:823–30. PubMed PMID: 27197051.

(Analysis of the Taipei Veterans Hospital database from 2008 to 2012 identified 108 patients with statin-associated liver injury [including 28 rosu-, 20 flu-, 17 sim-, 11 pra-, 8 lo-, and 8 pita-vastatin] most of which 75 [69%] were mild and only one fatal [80 year old on rosu-], and there were no differences in disease features or peak enzyme or bilirubin levels between HBsAg positive vs negative subjects [n=16 vs 92]).

Wu HF, Hristeva N, Chang J, Liang X, Li R, Frassetto L, Benet LZ. Rosuvastatin pharmacokinetics in Asian and White subjects wild type for both OATP1B1 and BCRP under control and inhibited conditions. J Pharm Sci. 2017;106:2751–2757. PubMed PMID: 28385543.

*(Pharmacokinetic studies of rosuvastatin in Asians and Whites subjects found differences in peak plasma levels that could not be attributed to differences in hepatic transporter alleges [SLCO1B1*1a or ABCG2c.421]).*

Björnsson ES. Hepatotoxicity of statins and other lipid-lowering agents. Liver Int. 2017;37:173–8. PubMed PMID: 27860156.

(Review of the hepatotoxicity of statins mentions that atorvastatin has been the most frequently implicated statin [accounting for 30-40% of cases] in drug induced liver injury estimated to arise in 1 in 17,000 users, cholestatic in 56% and with autoimmune features in 10% and rarely fatal).

Sánchez M, Castiella A, Zapata E, Zubiaurre L, Pérez-Yeboles J, Mendibil L, Iribarren A. Autoimmune hepatitis (immune-mediated liver injury) induced by rosuvastatin. Gastroenterol Hepatol. 2018;41:311–313. PubMed PMID: 28655408.

(47 year old man was found to have abnormal liver tests 10 months after switching from atorvastatin to rosuvastatin [bilirubin 0.7 mg/dL, ALT 201 U/L, Alk P 77 U/L, ANA 1:160], with worsening for several weeks after stopping but ultimate spontaneous complete resolution with normal liver tests and ANA negativity).

Hong SJ, Jeong HS, Ahn JC, Cha DH, Won KH, Kim W, Cho SK, et al. A phase III, multicenter, randomized, double-blind, active comparator clinical trial to compare the efficacy and safety of combination therapy with ezetimibe and rosuvastatin versus rosuvastatin monotherapy in patients with hypercholesterolemia: I-ROSETTE (Ildong Rosuvastatin & Ezetimibe for Hypercholesterolemia) randomized controlled trial. Clin Ther. 2018;40:226–241.e4. PubMed PMID: 29402522.

(Among 396 Korean patients with hypercholesterolemia treated with rosuvastatin [5, 10 or 20 mg daily] with or without ezetimibe [10 mg daily] for 8 weeks, the percent decrease in LDL-cholesterol was higher at each dose of rosuvastatin combined with ezetimibe [overall -57% vs -44%] and the proportion of patients achieving a targeted goal of LDL-cholesterol was also higher [92% vs 80%], while there were similar rates of total adverse events [11.2% vs 11.3%], serious adverse events [0.5% vs 0.5%] as well as ALT elevations above 3 times the ULN [0.6% vs 0]).

Tirona RG, Kassam Z, Strapp R, Ramu M, Zhu C, Liu M, Schwarz UI, et al. Apixaban and rosuvastatin pharmacokinetics in nonalcoholic fatty liver disease. Drug Metab Dispos. 2018;46:485–492. PubMed PMID: 29472495.

(Analysis of pharmacokinetics of rosuvastatin in patients with nonalcoholic fatty liver were not different from those in healthy volunteers but did vary by body weight).

Teschke R. Top-ranking drugs out of 3312 drug-induced liver injury cases evaluated by the Roussel Uclaf Causality Assessment Method. Expert Opin Drug Metab Toxicol. 2018;14:1169–1187. PubMed PMID: 30354694.

(A compilation of national and international databases on drug induced liver injury identified the ten top-ranking causes which included two statins, atorvastatin [ranking 3rd] and simvastatin [ranking 6th]).

Moore N, Duret S, Grolleau A, Lassalle R, Barbet V, Duong M, Thurin N, et al. Previous drug exposure in patients hospitalised for acute liver injury: a case-population study in the French National Healthcare Data System. Drug Saf. 2019;42:559–572. PubMed PMID: 30361989.

(Analysis of a French nationwide health database for medication use and hospitalizations for unexplained acute liver injury identified 4807 cases, 76% of which had been exposed to at least one medication in the previous 7-60 days, 263 cases [5.5%] had taken atorvastatin, but the exposed/case ratio was 15,742; 182 cases [3.8%} had taken rosuvastatin, the exposed/case ratio being 20,359; while only 10 cases had taken pyrazinamide but with an exposed/case ratio of 770).

Yebyo HG, Aschmann HE, Kaufmann M, Puhan MA. Comparative effectiveness and safety of statins as a class and of specific statins for primary prevention of cardiovascular disease: A systematic review, meta-analysis, and network meta-analysis of randomized trials with 94,283 participants. Am Heart J. 2019;210:18–28. PubMed PMID: 30716508.

(Metaanalyses of 40 trials of statins that enrolled 94,283 patients followed for a median of 1 year for efficacy and safety reported that statins as a class increased the risk of hepatic dysfunction by 6% with fluvastatin having the highest relative risk).

Lipid-lowering drugs. Med Lett Drugs Ther. 2019;61(1565):17–24. PubMed PMID: 30845106.

(Concise review of the mechanism of action, relative efficacy, safety and costs of lipid lowering drugs including statins, ezetimibe, PCSK9 inhibitors, bile acid sequestrants, fibric acid derivatives niacin and fish oil, mentions that statin therapy is associated with ALT elevations above 3 times ULN in 1-3% of patients but "whether statins actually cause liver damage is unclear").

Hung TH, Tsai CC, Lee HF. Statin use in cirrhotic patients with infectious diseases: A population-based study. PLoS One. 2019;14:e0215839. PubMed PMID: 31017946.

(Analysis of the Taiwan National Health Insurance Database identified 816 patients with cirrhosis receiving statins [including rosuvastatin] who were hospitalized for bacterial infections and similar number of cirrhotic controls not on statins, found a lower 30-day mortality with statins: 5.3% vs 9.8%).

Shah J, Lingiah V, Pyrsopoulos N, Galan M. Acute liver injury in a patient treated with rosuvastatin: a rare adverse effect. Gastroenterology Res. 2019;12:263–266. PubMed PMID: 31636777.

(47 year old Peruvian man developed jaundice 6 weeks after starting rosuvastatin [5 mg daily] [bilirubin 3.5 rising to 17.2 mg/dL, ALT 2260 U/L, Alk P 277 U/L, INR 1.1, ANA negative], liver biopsy with changes suggestive of autoimmune hepatitis, treated with methylprednisolone with gradual resolution of injury).

Courlet P, Livio F, Alves Saldanha S, Scherrer A, Battegay M, Cavassini M, Stoeckle M, et al; Swiss HIV Cohort Study. Real-life management of drug-drug interactions between antiretrovirals and statins. J Antimicrob Chemother. 2020;75:1972–1980. PubMed PMID: 32240298.

(Assessment of lipid levels in person living with HIV who were taking rosuvastatin found that one-third had suboptimal lipid control despite high doses, perhaps due to drug-drug interactions including inhibition of OATP1b1 causing poor hepatic uptake of statin).

Kawasaki E, Fukuyama T, Kuriyama E, Uchida A, Sagara Y, Tamai H, Nakano Y, et al. Statin-induced autoimmune hepatitis in patients with type 1 diabetes: A report of two cases and literature review. J Diabetes Investig. 2020;11:1673–1676. PubMed PMID: 32277861.

(Two men, ages 46 and 54, with type 1 diabetes developed hepatitis 6 and 8 months after starting atorvastatin and rosuvastatin [bilirubin 5.1 and unknown mg/dL, ALT 1632 and 709 U/L, Alk P not given and 2055 U/L, ANA 1:80 and negative, IgG 1495 and 1857 mg/dL], both with autoimmune hepatitis like features on liver biopsy and both with response to corticosteroid therapy).

Balasubramanian R, Maideen NMP. HMG-CoA reductase inhibitors (statins) and their drug interactions involving CYP enzymes, P-glycoprotein and OATP transporters-an overview. Curr Drug Metab. 2021;22:328–341. PubMed PMID: 33459228.

(Systematic review of literature on drug-drug interactions with statins and their clinical significance mentions that toxicity can be enhanced by inhibitors of CYP3A4 [atorva-, simva- and lova-statin] as well as by inhibitors of P glycoprotein and OATP1B1 [most statins including rosuvastatin], with specific recommendations for the most common inhibitors).

Sung S, Al-Karaghouli M, Kalainy S, Cabrera Garcia L, Abraldes JG. A systematic review on pharmacokinetics, cardiovascular outcomes and safety profiles of statins in cirrhosis. BMC Gastroenterol. 2021;21:120. PubMed PMID: 33726685.

(Systematic review of literature suggests that rosuvastatin and pitavastatin pharmacokinetics are unchanged in patients with Child's Class A cirrhosis as opposed to atorvastatin and pravastatin, although unlike rosuvastatin, simvastatin, atorvastatin and pravastatin have been assessed in clinical trials in cirrhotic patients).

Onfiani G, Nascimbeni F, Carubbi F. A case of statin-induced liver injury with positive rechallenge with a second statin. Is there a class effect? J Basic Clin Physiol Pharmacol. 2021 Apr 21. Epub ahead of print. PubMed PMID: 33882199.

(58 year old woman on long term simvastatin therapy developed ALT elevations 2 months after dose increase from 10 mg to 20 mg daily [ALT 314 U/L] without symptoms, Alk P or bilirubin elevations, which was normal 2 months after stopping but was elevated again without symptoms or jaundice 2 months after starting rosuvastatin in a dose of 5 mg daily [ALT 542 U/L], slowing falling to normal 5 months after stopping statins a second time).

Cai T, Abel L, Langford O, Monaghan G, Aronson JK, Stevens RJ, Lay-Flurrie S, et al. Associations between statins and adverse events in primary prevention of cardiovascular disease: systematic review with pairwise, network, and dose-response meta-analyses. BMJ. 2021;374(n1537) PubMed PMID: 34261627.

(Systematic review of placebo controlled trials of statins for cardiovascular disease prevention identified 62 publications with 120,456 patients and found an increased risk of muscle symptoms, liver test abnormalities, renal insufficiency and eye conditions for all 7 statins, but not muscle disorders or diabetes; rosuvastatin having relatively high risk for muscle symptoms and renal abnormalities and also was also associated with eye conditions and diabetes while atorvastatin and lovastatin had highest risk for liver abnormalities).

Vijayakanthi N, Felner EI, Romero R, Daley TC. Rhabdomyolysis due to rosuvastatin in a patient with ROHHAD syndrome. J Clin Lipidol. 2021 Sep 10:S1933-2874(21)00201-4. Epub ahead of print.

(13 year old with obesity, NASH and panhypopituitarism developed rhabdomyolysis two weeks after switching from lovastatin [40 mg/daily taken for 8 years] to rosuvastatin [40 mg daily] [bilirubin not given, ALT 298 U/L, AST 558 U/L, Alk P not given, CPK 53,000 U/L, creatinine 2.2 mg/dL, drug levels not given], with rapid improvement on stopping).