Supplemental Figure 1A

Genomic Prescribing System™ [GPS]

Patient Name :
Sex :
DOB :

Print Page

Patient Home/Current Medications | Search Drugs/Diseases | Search Results

Drug Search Results for : Pravastatin

Your patient carries a genotype that may confer an elevated risk of developing statin-induced adverse events (including myopathy) and also a lower relative cholesterol response, compared to individuals with no risk alleles.

The strongest data implicating an adverse event relationship were specifically derived from studies of patients taking higher-dose simvastatin. Another study of 509 patients taking one of three different statins (simvastatin, pravastatin, or atorvastatin) found that adverse statin-related outcomes (drug discontinuation, myalgias, and CK elevations) were significantly more common in those with your patient's genotype. However, sub-group analysis of the 143 patients specifically taking pravastatin did not demonstrate a relationship between this genotype and increased risk, except in females, although the sub-analyses were likely underpowered.

Separately, in a study of 5,411 Caucasian individuals randomized to 40 mg/d pravastatin or placebo, those patients with your patient's genotype had a relatively smaller decrease in LDL cholesterol levels at 6 and 12 months (31.8% +/- 12.8% decrease for patients with your patient's genotype versus 37.0 +/- 10.8% for those with favorable alelles, p<0.022). In a smaller study of 462 Caucasians receiving 20 mg pravastatin, this relationship was not found between genotype and changes in LDL.

Evidence
Level 3

Primary Literature Sources
J Am Coll Cardiol (2009)
Pharmacogenomics J (2005)
Atherosclerosis (2012)
Br J Clin Pharmacol (2007)

Supplemental Figure 1B

Genomic Prescribing System™ [GPS]

Patient Name :
Sex :
DOB :

Print Page

Patient Home/Current Medications | Search Drugs/Diseases | Search Results

Drug Search Results for : Carvedilol

Your patient has a genotype in the beta-2 adrenergic receptor (ADRB2) gene that is associated with the strongest improvements in left ventricular ejection fraction (LVEF) on carvedilol therapy.

In a study of 183 patients with chronic heart failure due to ischemic or nonischemic cardiomyopathy and a left ventricular ejection fraction (LVEF) at or below 35%, patients were treated with 12 months of carvedilol therapy (mean dose 36 mg/day (range 12.5 to 100 mg/daily). Patients with the same genotype as your patient (two favorable alleles) experienced stronger improvements in LVEF (increase by 13±12.2%) as compared to patients with one copy of the favorable allele (+8.3±11.4%) and those with no favorable alleles (+7.1±8,1%; p=0.022). No significant differences were found between the genotype groups at baseline (prior to carvedilol treatment).

The response findings were recapitulated in a study of 80 patients treated with carvedilol. Investigators defined a clinically significant improvement in left ventricular function as an absolute improvement of at least 10% in LVEF or 5% in LV fractional shortening. Patients with the same genotype as your patient were more likely to have clinical improvement (62% of those treated improved) compared to those who lacked the favorable allele (26% of those treated improved; p=0.003). There was no difference by genotype in LV function at baseline.

Finally, 33 stable chronic heart failure patients were treated with 6 months of 50 mg/day carvedilol therapy in another study. In patients with your patient's genotype, LVEF improved from 23.6±7.5% to 30.6±11.0% (p<0.01) with carvedilol, while carvedilol treatment had no effect on LV function in those lacking the favorable allele.

Evidence
Level 2

Primary Literature Sources
Pharmacogenetics (2003)
Cardiovasc Drugs The (2010)
Basic Clin Pharmacol (2009)

Supplemental Figure 1C

Genomic Prescribing System™ [GPS]

Patient Name :
Sex :
DOB :

Print Page

Patient Home/Current Medications | Search Drugs/Diseases | Search Results

Drug Search Results for : Atorvastatin

Your patient has a genotype in KIF6 that predicts a greater benefit from intensive atorvastatin therapy as compared to moderate pravastatin therapy for prevention of death or major cardiovascular events.

In a study of 1,778 Caucasian acute coronary syndrome patients, individuals who carried the favorable allele (like your patient does) had a significant benefit from intensive statin therapy with 80mg/day atorvastatin as compared to moderate treatment with 40mg/day pravastatin on prevention of death or major cardiovascular events (HR 0.59 [95% CI 0.44 - 0.77], p=0.018 for interaction between genotype and treatment approach). The absolute risk reduction for carriers like your patient receiving intensive therapy was 10.0% at 2 years, compared to no absolute benefit in noncarriers.

The effect appeared to be independent of a lipid or CRP mechanism, as there was no association of genotype on LDL cholesterol, triglyceride, or CRP levels during therapy in either treatment group.

Evidence
Level 2

Primary Literature Sources
J Am Coll Cardiol (2008)

Supplemental Figure 1D

Genomic Prescribing System™ [GPS]

Patient Name :
Sex :
DOB :

Print Page

Patient Home/Current Medications | Search Drugs/Diseases | Search Results

Drug Search Results for : Atenolol

Your patient's genotype in the beta(1)-adrenergic receptor gene predicts a protective role against death with use of the beta-blocker atenolol.

In the INVEST-GENES study, 5,895 coronary artery disease patients were randomized to verapamil SR vs atenolol-based antihypertensive therapy and followed for an average of 2.8 years. Individuals with the same genotype as your patient who took verapamil had a significantly increased risk (HR=8.58 [95% CI=2.06-35.8], p=0.003) of all-cause mortality compared to individuals without this genotype. Importantly, however, patients with this same "risk" genotype as your patient who were assigned atenolol did not have a statistically increased mortality risk (HR=2.31 [95% CI=0.82-6.55], p=NS). Blood pressure control did not differ between the treatment groups and therefore is unlikely to explain this treatment-risk difference.

These data suggest a protective role for use of the beta-blocker atenolol in patients with the same genotype as your patient.

Evidence
Level 2

Primary Literature Sources
Clin Pharmacol Ther (2008)

Supplemental Figure 1E

Genomic Prescribing System™ [GPS]

Patient Name :
Sex :
DOB :

Print Page

Patient Home/Current Medications | Search Drugs/Diseases | Search Results

Drug Search Results for : Verapamil

Your patient's genotype in the beta(1)-adrenergic receptor gene predicts a significantly increased risk of death if verapamil is chosen for antihypertensive therapy rather than atenolol.

In the INVEST-GENES study, 5,895 coronary artery disease patients were randomized to verapamil SR vs atenolol-based antihypertensive therapy and followed for an average of 2.8 years. Individuals with the same genotype as your patient who took verapamil had a significantly increased risk (HR=8.58 [95% CI=2.06-35.8], p=0.003) of all-cause mortality compared to individuals without this genotype. Importantly, however, patients with this same "risk" genotype as your patient who were assigned atenolol did not have a statistically increased mortality risk (HR=2.31 [95% CI=0.82-6.55], p=NS). Blood pressure control did not differ between the treatment groups and therefore is unlikely to explain this treatment-risk difference.

These data suggest a protective role for use of the beta-blocker atenolol in patients with the same genotype as your patient.

Evidence
Level 2

Primary Literature Sources
Clin Pharmacol Ther (2008)