If drug interaction software does not alert, did a drug interaction happen?

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INTRODUCTION

Drug–drug interactions (DDIs) are a well-known cause of drug related problems (DRPs). A 1993 study already found that up to 2.8% of hospital admissions are caused by adverse effects resulting from DDIs [Drug Saf. 1993 Jul;9(1):51-9.]

Another study found that clinicians can recognize correctly only 44% (range 11–64%) of all DDI pairs [Med Care. 2002;40:1161–71.]. Drug interaction databases and software are used as a primary tool to alert clinicians of potential DDIs. But various software solutions provide different results to the same question, as there is no standard to define a DDI. Even more importantly, they may provide only partial results, as multiple studies [i.e J Am Pharm Assoc (Wash) 2001;41:200–4.] demonstrate that up to 33% of relevant DDIs are not detected by dedicated software. Therefore, improving clinicians' ability to detect DDIs by either further education or innovative tools providing the widest possible scope of accurate data, is bound to lead to reduction in ADEs, preserve patients' safety, and prevent drug related problems.

Ischemic heart disease is the leading cause of death according to the world health organization (WHO).

CASE ESSENTIALS

Age:	66
Gender:	Male
Medical Conditions:	Diabetes Mellitus Type 2, Hyperlipidemia, and Essential Hypertension

AN UNDETECTED DRUG INTERACTION LEADING TO A SERIOUS OUTCOME

A 66-year-old man was diagnosed with diabetes mellitus type 2, hyperlipidemia, and essential hypertension. Among his chronic medications are metformin 850mg BID, atorvastatin 20mg QD, and ramipril 5mg QD. He is clinically stable, as his LDL levels are constantly below 100 mg/dl, fasting blood glucose below 100 mg/dl and HbA1C of 6.8%. He stopped smoking 6 years ago when diagnosed with elevated fasting glucose, and he keeps a healthy Mediterranean diet and exercises for 30 minutes 3 times a week. His blood pressure is well controlled with values under 130/90 mmHg.

This patient was also diagnosed with a non-metastatic castration-resistant prostate cancer (CRPC). His oncologist decided to begin treatment with enzalutamide. The oncologist checked for possible drug interactions of enzalutamide with the patient's chronic medications using one of the most common legacy drug interaction systems and found no alerted DDIs. In the patient's next visit to his primary physician, for the patient's drug regimen was again checked for possible drug interactions with enzalutamide, using a different legacy drug interaction system. The review did not result in any alerts regarding the patient's usual drug combinations.

Five months later, the patient senses a pressure-like substernal pain in his chest, radiating to his arm. He calls the emergency services who decide to transfer him to the nearest hospital, where he was diagnosed with a myocardial infarction (MI).

After the patient was stable, the medical team further examined the case. They assume that the cause of this event is the enzalutamide treatment initiated a few months back, as the drug label and available published data suggest cardiovascular toxicity is possible [Clin Genitourin Cancer. 2018 Jun;16(3):e645-e653]. In addition, the medical staff were surprised to see his LDL levels were almost 150 mg/dl. This result was not consistent with this patient's "normal" LDL level and with the fact he is compliant with daily atorvastatin at bedtime.

After consulting with colleagues and investing more extensively, they realize there was an interaction between enzalutamide and atorvastatin, which could have significantly reduced atorvastatin's plasma concentration, leaving the patient without the cardiovascular protection atorvastatin provides, and with much higher than expected LDL levels. Studies demonstrate that lowering LDL cholesterol reduces the risk for coronary heart disease. The elevated LDL level in this patient is likely due to the drug interaction and could increase the risk to this patient of coronary heart disease. [Figure 1, Arteriosclerosis, Thrombosis, and Vascular Biology. 2000;20:830–835]

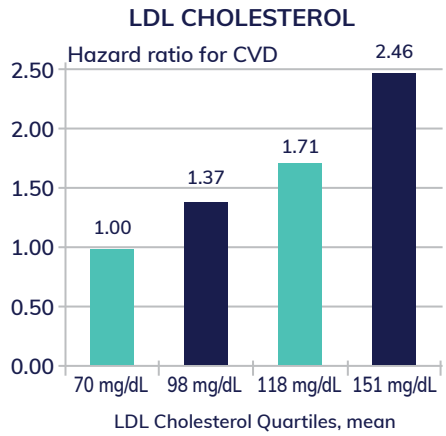

Figure 1 – hazard ratio for CVD according to LDL levels [Arteriosclerosis, Thrombosis, and Vascular Biology. 2000;20:830–835]

If the physicians would have used Seegnal, an evidenced-based, patient-specific off-the-shelf software to assess this patient's treatment, they would have been immediately informed of the important issues arising from the patient's drug therapy, and could have easily avoided this risky DRP.

HOW?

Seegnal's evidence-based data clearly shows that atorvastatin is a sensitive substrate of CYP3A and enzalutamide is a known potent inducer of CYP3A. This could lead to more than 80% decrease in the AUC of atorvastatin based on enzalutamide's effects on other CYP3A substrates. Seegnal's smart, comprehensive, and patented algorithms evaluate all available patient specific parameters, and in this case would have alerted the physician to the drug interaction. The physician could consider a different drug combination or monitor the patient's LDL levels.

The physicians decided to change patient's medication regimen by switching atorvastatin to a different statin which is not a substrate of CYP3A. The patient's LDL levels were lowered within few weeks.

This is an important example of the involvement of important DDIs in everyday patient care, which when left unnoticed and unmanaged can cause serious consequences. There is significant potential for enzalutamide to affect and interact with other CYP3A substrates which may have serious clinical consequences.

Seegnal is patient-specific, taking into consideration all relevant patient factors, such as prescription and over the counter drugs, laboratory values, genetic polymorphism, smoking, and diet that might contribute to the risk of a DRP. Seegnal then provides the most comprehensive pharmacokinetic data allowing healthcare providers to base their clinical decisions on the most accurate, evidence-based reference.

ABOUT SEEGNAL

Seegnal eHealth Ltd. was established with the goal of globally disrupting the clinician-medication-patient value chain by introducing revolutionary concepts, new knowledge, and advanced technologies, generating both value and safety.

Seegnal is a smart and intuitive clinical decision support platform that empowers clinicians to quickly and effectively manage and resolve patient-specific Drug-Related Problems (DRPs - the 4th leading cause of death in the US alone).

Seegnal interfaces with the EMR at the point of care and harnesses the widest scope of DRP-related information, generating an additional 50% of unique data (which legacy systems either don't recognize or address), while delivering groundbreaking accuracy (sensitivity and specificity) of about 95%.

The platform diminishes alert fatigue (~ 6% alert load vs. legacy systems) and is intuitive and easy to use, requiring only 5-10 seconds for DRP detection, prioritization, and resolution.

Seegnal
Patientivity, defined