

Clinically significant drug interactions of Eltrombopag: a retrospective study from the clinical pharmacist perspective

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Introduction

Thrombopoetin is the main cytokine involved in regulation of megakaryopoiesis and platelet production, and is the endogenous ligand for the thrombopoetin receptors. Eltrombopag interacts with the transmembrane domain of the human thrombopoetin receptors and initiates signaling cascades similar but not identical to that of endogenous thrombopoetin, inducing proliferation and differentiation from bone marrow progenitor cells.^[2] The aim of the study was to monitor administration of eltrombopag tablet in real life setting, and consolidate the clinical and pharmacologic aspects of drug interaction in patients that are receiving eltrombopag along with other medications with aim to develop a compendium of information, provide prescribers with information to mitigate the risk of interactions.

Materials & Methods

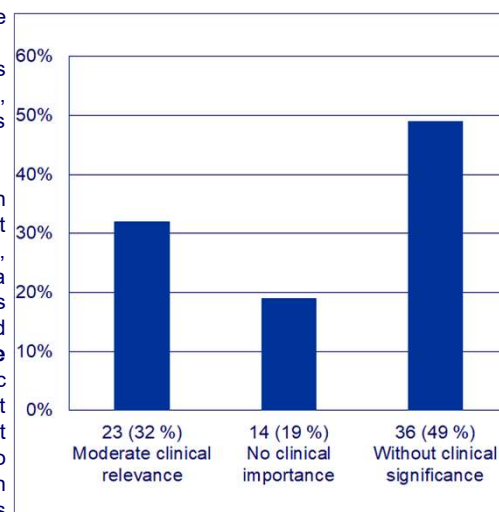
A retrospective, longitudinal study was conducted at the Hematology Clinic in Skopje, North Macedonia. A clinical pharmacist, focusing on eltrombopag and concomitant medications interactions, reviewed a total number of 16 patient's records for the period of 6 months (January-June 2023). Anamnestic data on additional drugs, herbal supplements, vitamins, minerals were also taken. The results of the evaluation were communicated to the hematology specialists. The potential drug- interactions were identified using Stockley's Drug Interactions manual, subsequently categorized according to the severity of the interaction and sub-classified into: co-administered drugs that alter the pharmacokinetics of eltrombopag and that interfere with the pharmacokinetics of co-administered drugs.^[1]

Results and discussion

A total number of 73 interactions were identified, of which 23 (31.51%) were with moderate clinical relevance. 14 (19.18%) may not be of clinical relevance, but require counseling about possible adverse effects and additional monitoring. The rest of 36 (49.32%) interactions were without clinical significance. Additionally, we determined that 7 (9.59%) of the total interactions were directly related to patients receiving eltrombopag in combination with one of the following agents: ciclosporin, atorvastatin, rosuvastatin, dexamethasone, prednisolone, valsartan, and magnesium. They were categorized as moderate and need close monitoring.^[1]

The identified side effects and recommendation for their management are as follows:

1) ciclosporin, in this interaction a small decrease in eltrombopag exposure was observed when eltrombopag was administered concomitantly with ciclosporin. Advice for monitoring platelet count at least weekly for up to 2 to 3 weeks, and adjustment of the dose as needed.^[1,3] **2) atorvastatin**, eltrombopag is known to increase atorvastatin exposure and **3) rosuvastatin**- eltrombopag causes a small increase in rosuvastatin exposure. Therefore in the case of 2) and 3) the dose of the statins should be reduced by as much as 50%. Patients should be warned of the risk of rhabdomyolysis and myopathy (e.g. report any unexplained muscle pain, tenderness or weakness).^[1,4] **4) dexamethasone** and **5) prednisolone**-the concurrent use of eltrombopag and other drugs for the treatment of idiopathic thrombocytopenic purpura (corticosteroids) might result in platelet counts increase above the referent levels. Close monitoring of platelet count is needed.^[1,5] **6) magnesium**- oral- magnesium is polyvalent cation, and known to reduce the absorption of eltrombopag. Eltrombopag should be taken at least two hours before of four hours after administration of polyvalent cations.^[1] **7) valsartan**- eltrombopag can increase the concentration of valsartan. Close monitoring of adverse effects related to valsartan use is required, as well as appropriate dose adjustment if necessary.^[1]



Conclusion

This study demonstrates toxicity and interactions potential of Eltrombopag associated with concomitant use of other medicines. Close collaboration of physicians and clinical pharmacists is necessary in all cases where patients are receiving Eltrombopag along with other medications in order to identify, prevent and manage in timely manner all significant interactions.

References

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