Use of a Cocktail to Reduce the Need for Drug Interaction Studies During Drug Development.

Joseph S. Bertino Jr., Pharm.D., Scientific Director, Ordway Research Institute Drug Development Center, Albany, NY

The concept of using a multidrug cocktail to assess drug metabolizing enzyme (DME) activity and drug interactions has been discussed for decades. The use of a cocktail containing multiple probes for multiple DMEs has been used more commonly in recent years. Some problems with the cocktail approach include but are not limited to: 1) Use of unvalidated probes; 2) Use of unvalidated or invalid biomarkers; 3) Failure to assure that the study drug does not affect the assay for the probe; 4) Use of genotypic intermediate or poor metabolizers or the lack of genotype screening for the study. For validated cocktails, data has been generated in registration and Phase IV studies showing the utility of this approach. The use of the cocktail approach raises the question as to whether this type of drug interaction screening can be used for drug labeling and eliminate the need for specific drug-drug interaction studies. Unfortunately, some drug labels as well as medical drug reference sources provide inaccurate information on dosage adjustment for certain drugs when a significant drug interaction potential exists. This lecture will review and discuss probe, cocktail and biomarker validation and review the serious issues in some current product labeling as it applies to drug interactions and how the cocktail approach could be applied to drug labeling in the future. These approaches have the potential to improve and speed up the drug development process while providing clearer guidance to clinicians in the area of drug interactions.