Poster

[P27-10] P27-10: Pharmacokinetics and pharmacogenetics

Chair: Andrew Somogyi, Australia

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[P27-10-5] Pharmacogenetics-based personalized therapy: levels of evidence and recommendations from the French national network of pharmacogenetics (RNPGx) regarding 4 major therapeutic domains

Jean-Baptiste Woillard[1], Nicolas Picard[2], Laurent Becquemont[3], Chantal Barin-Le Guellec[4], Jean-Christophe Boyer[5], Laurent Chouchana[6], Thomas Duflot[7], Julien Dupouey[8], Marie-Christine Etienne-Grimaldi[9], Fabien Lamoureux[10], Sylvie Quaranta[11], Fabienne Thomas[12], Celine Verstuyft[13], Marie-Anne Loriot[14] (1.CHU Limoges, 2.CHU Limoges Univ Limoges, 3.Hopital Bicetre, Paris, 4.CHU Breteneau Tours, 5.CHU Caremeau, Nimes, 6.Hopital Cochin, Paris, 7.CHU Rouen, 8.Hopital Timone, Marseille, 9.Centre Antoine Lacassagne, Nice, 10.CHU Rouen, 11.Hopital Timone, Marseille, 12.Oncopole, Toulouse, 13.Hopital Bicetre, Paris, 14.Hopital Europeen Georges Pompidou)

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Background

Pharmacogenetic (PGx) testing is now available for a variety of drug-gene pairs. It helps to select the most appropriate drug option or to adjust drug dose, hence to prevent serious adverse reactions. The tests are rarely mentioned in drug information labels and the data provided is generally insufficient to know how they can be useful.

Methods

The French national network of pharmacogenetics (RNPGx) elaborated a classification with three levels of recommendations for PGx testing: ‘essential’, ‘advisable’ or ‘possibly useful’. The classification integrates (i) the functional impact of genetic variations, (ii) the nature of the phenotype concerned (e.g. drug efficacy, adverse effect or concentration), (iii) the clinical evidences available, and (iv) the existence of non-genetic options for treatment personalization.

Results

RNPGx considers testing ‘essential’ in the case of a clinical phenotype of major importance, which is unpredictable (or hardly predictable) by a non-genetic approach. Testing becomes ‘advisable’ in the case of (1) intermediary phenotypes (e.g. drug concentration) useful and important for therapeutic drug monitoring, or (2) for clinical phenotypes of major importance, but with non-genetic options readily available (e.g. enzyme phenotyping). The lowest level of recommendation is restricted to tests related to clinical or intermediary phenotypes, which have less robust evidences but are useful case-by-case. Following this classification, *TPMT* testing before azathioprine therapy appears ‘essential’ while *CYP3A5* testing to determine tacrolimus first-dose in renal transplantation is ‘advisable’. On the other hand, *SLCO1B1* rs4149056 before (or early after) starting a treatment with statins has a lower level of recommendation (‘possibly useful’).

Conclusions

This classification has been applied to drugs in 4 major therapeutic domains (i.e. transplantation, cardiology,

oncology, psychiatry) and it can be useful for other drug-gene pairs. It will help to reach consensual recommendations in order to rationalize and promote PGx testing.