Letter to the Editor

Response to 'Communicating Information about Drug Interactions'

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The editorial in a recent issue of the Journal [1] commented on the comparative assessment of four drug interaction compendia [2] and was a timely reminder that (i) drug interactions are an essential aspect of clinical pharmacology and (ii) providing prescribers with clear and simple information is an imperative. One therapeutic area that has emerged as a real challenge for understanding drug interactions is antiretrovirals. With over 20 licensed drugs in four classes [nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs) and entry inhibitors] and HIV+ patients receiving at least triple combination therapy, there is the potential for drug interactions within an antiretroviral regimen. However, often of greater significance is the patient receiving multiple other therapies with consequent interactions between the antiretroviral and one or more drugs in the regimen.

Although HIV physicians and other HIV healthcare professionals are generally used to hearing about CYP450 induction and inhibition (PIs, an integral part of most regimens, are metabolized by and are inducers/inhibitors of CYP450 and other enzymes; NNRTIs are potent inducers) and even speak with some degree of understanding about transporters, there is still the challenge of having the relevant information to hand when it is needed – which is usually when the patient is sitting in front of you in the clinic!

Some years ago we attempted to meet what we considered to be a deficiency in accessible data by building a website (<http://www.hiv-druginteractions.org>) [3]. This is based on a traffic light system (road not rail) and is easy to access either from a computer with internet connection or from a downloadable version for hand-held devices [personal digital assistants (PDAs)]. The structure is illustrated in Figure 1, which displays the interactions of antiretroviral drugs and anticonvulsants. The antiretroviral drug is shown as the column and the anticonvulsant as the row. Clicking on the symbol (red/circle: these drugs should not be coad-

ministered; orange/square: potential drug interaction that may require close monitoring or dosage change; green/triangle: no clinically significant interaction expected) gives further information (where available) on all the published studies or case reports and a brief summary of the data. There is also the facility to download the charts to make posters for the clinic wall, which is particularly useful in developing world where the burden of HIV is so great.

This is by no means the only web-based resource for keeping abreast of drug interactions in HIV. Indeed, there has been a published evaluation of nine such sites [4], with three sites – <http://www.hiv-druginteractions.org>, <http://www.tthhivclinic.com> and <http://hivinsite.ucsf.edu> – rated of high quality.

Clearly having up-to-date drug interaction data available online or via PDA has to be the way forward in this and other therapy areas, but who is going to foot the bill in the long term to maintain such a resource? To maintain the Liverpool site requires a full-time research assistant with considerable experience of the underlying pharmacology, the ability to extract key data from published papers and abstracts, and to check Summaries of Product Characteristics and Prescribing Information for updates and differences between Europe and the USA. Currently, colleagues in the pharmaceutical industry support the site with unrestricted educational grants and, importantly, no editorial input. However, in the longer term this is shaky ground and there needs to be greater stability to enable planning and development. Of 1198 patients starting highly active antiretroviral therapy in the EUROSIDA study [5], only 70% remained on the original therapy at the end of 1 year, 24% had changed and 6% were off treatment. The most frequent reason for discontinuation was toxicities, and we know that it is often interactions that are responsible for adverse drug reactions [6]. Avoidance or at least effective management of drug interactions remains a priority, but we must have the tools and resources to meet this challenge.

Figure 1

Composite screen shot showing the structure of the web-based interaction resource

REFERENCES

- Aronson JK. Communicating information about drug interactions. *Br J Clin Pharmacol* 2007; 63: 637–9.
- Vitry AI. Comparative assessment of four drug interaction compendia. *Br J Clin Pharmacol* 2007; 63: 709–14.
- HIV Drug Interactions. Available at <http://www.hiv-druginteractions.org> (last accessed 3 August 2007).
- Sheehan NL, Kelly DV, Tseng AL, van Heeswijk RPG, Beique LC, Hughes CA. Evaluation of HIV drug interaction web sites. *Ann Pharmacother* 2003; 37: 1577–86.
- Mocroft A, Phillips AN, Soriano V, Rockstroh J, Blaxhult A, Katlama C, Boron-Kaczmarek A, Viksna L, Kirk O, Lundgren J for the EuroSIDA Group. Reasons for stopping antiretrovirals used in an initial highly active antiretroviral regimen: increased incidence of stopping due to toxicity or patient/physician choice in patients with hepatitis C coinfection. *AIDS Res Hum Retroviruses* 2005; 21: 743–52.
- Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ* 2004; 329: 15–9.

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