Quality of Evidence

"Quality of evidence" and why we introduced it to www.hiv-druginteractions.org

When making any treatment recommendation, it is important to make an informed decision based on the available evidence. Equally important is to assess the quality of that evidence. Whilst the drug interaction charts indicates a strength of recommendation for coadministration of an anti-HIV drug and a co-medication (i.e., red, amber, yellow, green), there was no indication of the quality of evidence behind that recommendation. We have introduced a system that categorises the quality of evidence from high to very low.

Systems to evaluate quality of evidence

Various systems exist to describe quality of evidence. For example, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) working group was set up to help resolve the confusion among the different systems of rating evidence and recommendations. The group has wide representation from many organisations including the Agency for Healthcare Research and Quality in the US, the National Institute for Clinical Excellence for England and Wales, and the World Health Organization. Since 2006 the BMJ has requested in its "Instructions to Authors" that authors should preferably use the GRADE system for grading evidence when submitting a clinical guidelines article and more recently the 2009 update of WHO's Antiretroviral Therapy for HIV Infection in Adults and Adolescents included GRADE profiles.

The following selected articles explain the background to and the workings of the GRADE system (links to the BMJ website for the pdf of the article are provided).

- What is "quality of evidence" and why is it important to clinicians?
  Guyatt GH, Oxman AD, Kunz R, et al. BMJ, 2008, 336(7651): 995-8.
- GRADE: an emerging consensus on rating quality of evidence and strength of recommendations.
  Guyatt GH, Oxman AD, Vist GE, et al. BMJ, 2008, 336(7650): 924-6.
- Grading quality of evidence and strength of recommendations.
  Atkins D, Best D, Briss PA, et al. BMJ, 2004, 328(7454): 1490.

Applying Quality of Evidence to www.hiv-druginteractions.org

The table on the following page gives examples of the criteria we used to determine Quality of Evidence when assessing interaction data on www.hiv-druginteractions.org.

Quality of Evidence

Example	Quality of Evidence	Upgrade	Downgrade
Editorial comment about metabolism	Very Low		
SPC/USPI statement about metabolism of the antiviral drug, metabolic effects of the co-med, efficacy/toxicity, in vitro studies, or extrapolation of data from a similar co-med	Very Low	• SPC/USPI contraindication due to serious and/or life threatening effects	
Animal studies or in vitro studies (not in SPC/USPI)	Very Low		
Single case report	Very Low		
Multiple case reports (published individually or as case series)	Low	• major clinical or laboratory abnormality	• abstract
Crossover, steady state PK study with AUCs	Moderate	• large* change in PK *and/or* clinical/laboratory abnormality	• abstract • <10 subjects[#] • dose/formulation not in clinical use
Crossover, steady state PK study without AUCs	Low	• large* change in PK *and/or* clinical/laboratory abnormality *and/or* PK estimates derived by population PK modelling	
Parallel, steady state PK study with AUCs	Moderate	• large* change in PK *and/or* clinical/laboratory abnormality	• abstract • <15 subjects[†] • dose/formulation not in clinical use
Parallel, steady state PK study without AUCs	Low	• large* change in PK *and/or* clinical/laboratory abnormality *and/or* PK estimates derived by population PK modelling	
Crossover, single dose PK study with AUCs	Low	• large* change in PK *and/or* clinical/laboratory abnormality	• abstract • <10 subjects[#] • dose/formulation not in clinical use
Crossover, single dose PK study without AUCs	Very Low	• large* change in PK *and/or* clinical/laboratory abnormality *and/or* PK estimates derived by population PK modelling	
Parallel, single dose PK study with AUCs	Low	• large* change in PK *and/or* clinical/laboratory abnormality	• abstract • <15 subjects[†] • dose/formulation not in clinical use
Parallel, single dose PK study without AUCs	Very Low	• large* change in PK *and/or* clinical/laboratory abnormality *and/or* PK estimates derived by population PK modelling	
PK data/study, steady state or single dose, *cf* historical data	Very Low		
PK data/study in HIV+ subjects *cf* data/study in healthy volunteers	Very Low		
Observational PK in HIV+ subjects (including non-specified population PK analysis)	Low		• abstract • significant source of bias
Data obtained from a randomised, controlled interaction trial with clinical or validated surrogate endpoints	High		• abstract • not specifically an interaction trial
Metabolism/interaction study using probe substrates	Low	• large* change in PK *and/or* clinical/laboratory abnormality	• abstract

Notes:

SPC Summary of Product Characteristics (European), USPI United States [of America] Prescribing Information.

PK trial Information described in the SPC/USPI may be classified as Very Low, Low or Moderate depending on the information provided.

Outcome upgrades (i.e. not population PK estimates) over ride downgrades – in such cases, down grades are not applied. Downgrades are cumulative or until "very low" is reached.

** 50% decrease or 2-fold (100%) increase in AUC (or Cmax, Cmin or Ctrough if AUC not studied).*

[#] e.g., N=10 required in order to have 80% power to show a 50% difference, assuming 50% variation in PK.

[†] e.g., N=15 required in order to have 80% power to show a 50% difference, assuming 50% variation in PK.