ELSEVIER

Cardiovascular Research 63 (2004) 186–187

Cardiovascular Research

www.elsevier.com/locate/cardiores

Corrigendum

Corrigendum to "Relationships between preclinical cardiac electrophysiology, clinical QT interval prolongation and torsade de pointes for a broad range of drugs: evidence for a provisional safety margin in drug development" [Cardiovasc. Res. 58 (2003) 32–45]☆

W.S. Redfern[a], L. Carlsson[b], A.S. Davis[c], W.G. Lynch[d], I. MacKenzie[e], S. Palethorpe[a], P.K.S. Siegl[f], I. Strang[a], A.T. Sullivan[g], R. Wallis[h], A.J. Camm[i], T.G. Hammond[a,*]

[a] *Safety Assessment UK, AstraZeneca R&D Alderley Park, Macclesfield, Cheshire SK10 4TG, UK*
[b] *Cardiovascular Pharmacology, AstraZeneca R&D Mölndal, 431 83 Mölndal, Sweden*
[c] *Animal Welfare Group, AstraZeneca R&D Alderley Park, Macclesfield, Cheshire SK10 4TG, UK*
[d] *Drug Safety, AstraZeneca R&D Charnwood, Loughborough, Leicestershire LE11 5RH, UK*
[e] *Covance Laboratories Limited, Otley Road, Harrogate, North Yorks HG3 1PY, UK*
[f] *Merck Research Laboratories, P.O. Box 4, West Point, PA 19486-00047, USA*
[g] *GlaxoSmithKline Safety Assessment, The Frythe, Welwyn, Herts, AL6 9AR, UK*
[h] *Pfizer Global Research and Development, Sandwich Laboratories, Ramsgate Road, Sandwich, Kent CT13 9NJ, UK*
[i] *Department of Cardiological Sciences, St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, UK*

The following minor errors and potential ambiguities have been brought to our attention since publication of the article. None of these affect the interpretation of the data or overall conclusions.

1. The reference [36] cited for the single report of torsade de pointes with fluoxetine (p. 40) actually refers to the possible mechanism outlined in the sentence that follows in the text. The reference for the report of torsade de pointes is: Appleby M, Mbewu A, Clarke B. Fluoxetine and ventricular torsade—is there a link? Int. J. Cardiol. 1995; 49: 178–180.
2. The margin of hERG IC_{50} versus $ETPC_{unbound\ (max)}$ for amiodarone given in the results (p. 36) and discussion (p. 40) should be 2000-fold, not 1400-fold. A margin of 2000-fold was used (correctly) in Fig. 2.
3. In the full version of the paper (pdf link from journal website), Table 2 gives the range of values for hERG IC_{50} for ciprofloxacin as being '>100–966 μM'. The value of '>100 μM' should read '>300 μM'. However, this value was not used in calculating margins as the hERG IC_{50} was not determinable. The hERG IC_{50} of 966 μM was used for calculating margins. Therefore, the figures are unaffected.
4. The legend to Fig. 1 should read "...for 52 drugs" (not "49").
5. The only error which affects the figures relates to ebastine. The ETPC range for ebastine given in the full version of the paper (pdf link from journal website) is incorrect. The data originally used (90–120 ng/ml; source: Wiseman LR and Faulds D. Ebastine: A review of its pharmacological properties and clinical efficacy in the treatment of allergic disorders. Drug Evaluation 1996; 51: 260–277) were inadvertently the values for the metabolite, carebastine. The correct data are actually 0.19–3.75 ng/ml (Moss AJ and Morganroth J. Cardiac Effects of Ebastine and Other Antihistamines in Humans. Drug Safety 1999; 21 Suppl. 1: 69–80.), giving an $ETPC_{unbound\ (max)}$ value of 0.16 nM. This affects Figs. 1 and 2: in Fig. 1, the $ETPC_{unbound}$ range for ebastine is now to the left of where it was; in Fig. 2, the margin of hERG IC_{50} versus $ETPC_{unbound\ (max)}$ for ebastine is now increased (to 1875-fold), so ebastine is now positioned third from bottom of the list of drugs in Category 5.
6. The term 'lowest published value' (or 'lowest quoted value') used in the paper refers to hERG or I_{Kr} IC_{50}

☆ doi of original article 10.1016/S0008-6363(02)00846-5.

* Corresponding author. Tel.: +44-1625 514810; fax: +44-1625 513779.
E-mail address: tim.hammond@astrazeneca.com (T.G. Hammond).

doi:10.1016/j.cardiores.2004.04.016

values, concentrations eliciting a 10–20% increase in APD_{90}, or in QTc, which are 'lowest in magnitude' (i.e. most potent). For example, if a drug had a range of published hERG/I_{Kr} IC_{50} values from 65 to 250 nM, we would have used 65 nM when calculating margins.

7. In the abstract and discussion (p. 43), where we have used the term 'C_{max}', we are referring to the *unbound* C_{max} concentration.