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CURRICULUM VITAE: Charlie Brindley, PhD.

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Education

PhD, Studies on the Metabolism of N-Methyl Containing Agents with Anti-neoplastic Activity Cancer Research Campaign Laboratories University of Aston in Birmingham, UK (1983)

BSc, (Hons) Physiology and Biochemistry, University of Southampton, UK (1977)

Company Details

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Professional Experience

Oct 1982-Dec 1985	Post-Doctoral Research, Charing Cross Hospital, London, UK
Jan 1986-Sep 1989	Senior Clinical Pharmacokineticist Hoffman-La Roche, Basel, Switzerland
Oct 1989-Oct 1993	Senior Pharmacokineticist, Huntingdon Research Centre, Cambridgeshire, UK
Oct 1993 – 2005:	Director of Pharmacokinetics, Drug Metabolism and Pharmacokinetics, Quintiles Ltd, Edinburgh, UK (formerly Syntex Research Centre)
2005-March 2006	Director of Pharmacokinetics, Drug Metabolism and Pharmacokinetics, Aptuit (Edinburgh) Ltd, UK (formerly Quintiles Limited). Managing Pharmacokinetic & Pharmacodynamics Group of 9 Pharmacokineticists/Biostatisticians
April 2006-Present	Director of KinetAssist Limited. Pharmacokinetic Consultation and Services

Capabilities

Design, data analysis, interpretation of pharmacokinetic results and report writing on non-clinical and clinical studies within a Quality Managed System, compatible with GLP, GCLP and GCP. My Facility is a member of the MHRA UK GLP Compliance Programme.

Experience with all aspects of preclinical and clinical drug development including toxicokinetics, radiolabelled studies, first time in man, dose dependency, single- and multiple-dose pharmacokinetics, bioavailability, bioequivalence, drug interaction and renal-impairment studies.

Pharmacokinetic techniques includes compartmental and non-compartmental analysis, PK/PD modelling, deconvolution analysis, *in vitro-in vivo* (dissolution) correlations, allometric scaling, *in-vitro-in vivo* (clearance) scaling.

Received training in GLP for Study Directors (6 August 2003), GCLP (19 January 2006) and GCP (27 July 2005) during employment with Quintiles and Aptuit. Further GLP and GCP training received from Tower Mains QA; 2008, 2011 and 2013.

Software: WinNonlin Phoenix, Word, Excel, PowerPoint

Membership of Professional Bodies

Organisation	**Type of Membership**
Toxicokinetic Discussion Group (TKDG)	Chairman
Pharmacokinetics (UK) (PKUK)	Ordinary Member
Academy of Pharmaceutical Sciences of Great Britain (UKaps)	Ordinary Member
MHRA UK GLP Compliance Programme	Member

Publications

1. BRINDLEY, C J, GESCHER, A, LANGDON, S, BROGGINI, M, COLUMBO, T and D'INCALCI, M (1982)
'Studies of the Mode of Action of Antitumour Triazenes and Triazines III: Metabolism Studies on Hexamethylmelamine'
Biochem Pharmacol, 31, 625-631

2. BRINDLEY, C J, GESCHER, A, HARPUR, E, ROSS, D, SLACK, J, THREADGILL, M and WHITBY, H (1982)
'Studies on the Pharmacology of N-Methylformamide in Mice'
Cancer Treat Rep, 66, 1957-1965

3. BRINDLEY, C J, GESCHER, A and ROSS, D (1982)
'Studies on the Metabolism of Dimethylformamide in Mice'
Chem Biol Interac, 45, 387-392

4. BRINDLEY, C J, ANTONIW, P, NEWLANDS, E and BAGSHAWE, K (1985)
'Pharmacokinetics and Toxicity of the Epipodophylotoxin Derivative (VP16-213) in Patients with Gestational Choriocarcinoma and Malignant Teratoma'
Cancer Chemother Pharmacol, 15, 66-72

5. NEWLANDS, E, BLACKLEDGE, G, SLACK, J, GODDARD, C, BRINDLEY, C J, HOLDEN, L and STEVENS, M (1985)
'Phase I Clinical Trial of Mitozolomide (CCRG 81010, M&B 39565 NSC 353451)'
Cancer Treat Rep, 69, 801-805, 39565

6. BRINDLEY, C J, ANTONIW, P and NEWLANDS, E (1986)
'Plasma and Tissue Distribution of Mitozolomide in Tumour Bearing Mice'
Br J Cancer, 53, 91-97

7. BRINDLEY, C J, PEDLEY, R, ANTONIW, P and NEWLANDS, E (1987)
'Activity and Distribution Studies of Etoposide and Mitozolomide *In Vivo* and *In Vitro* Against Human Choriocarcinoma Cell Lines'
Cancer Chemother Pharmacol, 19, 221-225

8. GOLLNICK, H, BAUER, R, BRINDLEY, C J, ORFANOS, C, PLEWIG, G, WOLKALEK, H and HOTING, E (1988)
'Acitretin Versus Etretinate in Psoriasis: Clinical and Pharmacokinetic Results of a German Multicenter Study'J Am Acad Dermatol, 19, 458-468

9. McNAMARA, P, JENSEN, B and BRINDLEY, C J (1988)
'Food Increases the Bioavailability of Acitretin'
J Clin Pharmacol, 28, 1051-1055

10. STUCK, A, BRINDLEY, C J, BUSSLINGER, A and FREY, F (1988)
'Pharmacokinetics of Acitretin and Its 13-Cis Metabolite in Patients on Haemodialysis'
Br J Clin Pharmacol, 27, 301-304

Publications (continued)

11. BRINDLEY, C J (1988)
'Comparative Pharmacokinetics of Acitretin and Etretinate'
Retinoids Today and Tomorrow, Mediscript Press, vol 13, ed W Griffiths *et al*, pp 4-7

12. CZARNETZKI, B, GEIGER, J-M and BRINDLEY, C J (1988)
'Acitretin'
In: Dermatosen der Haende und Fuesse, Altmeyer (ed), Editiones Roche Basel 1988, pp 219-231

13. GEIGER, J-M and BRINDLEY, C J (1988)
'Cis-Trans Intercoversion of Acitretin in Man'
Skin Pharmacol, 1, 230-236

14. LAUGIER, J-P, BERBIS, P, BRINDLEY, C J, BUN, H, GEIGER, J-M, DURAND, A and PRIVAT, Y (1989)
'Quantification of acitretin and cis-acitretin in skin'
Skin Pharmacol, 2. 181-186

15. AL-MALLAH, N, BRINDLEY, C J, BUN, H, BERBIS, P, DURAND, D, GEIGER, J-M and PRIVAT, Y (1989)
'Pharmacokinetics of Acitretin (Ro 10-1670) Following Multiple Oral Dosing'
In: Reichert and Shroot (eds), Pharmacol Skin Basel, Karger 1989, vol 3, pp 181-187

16. BRINDLEY, C J, DUBACK, U and FORGO, I (1989)
'Absolute Bioavailability of Acitretin (Ro 10-1670)'
In: Reichert and Shroot (eds), Pharmacol Skin Basel, Karger 1989, vol 3, pp 207-210

17. LAMBERT, W, DeBERSAQUE, J, BRINDLEY, C J, WIEGAND, U and DeLEENHEER, A (1989)
'Comparison of the Pharmacokinetics of Acitretin (Ro 10-1670) in Young and Elderly Subjects'In: Reichert and Shroot (eds), Pharmacol Skin Basel, Karger 1989, vol 3, pp 211-214

18. BRINDLEY, C J (1989)
'An Overview of Recent Clinical Pharmacokinetics Studies with Acitretin (Etretin, Ro 10-1670)'
Dermatologica, 178, 79-87

19. BRINDLEY, C J, BRODIE, R R, COOK, S, OLDFIELD, P R, CHASSEAUD, L F, and BARBHAIYA, R (1991)
'Dose-Proportional Pharmacokinetics of Cefepime in Rats'
Eur J Drug Metab Pharmacokin, Special Issue No.111, 9-14

20. MIDGLEY, I, HOOD, A J, CHAUSSEAUD, L F, BRINDLEY, C J, BAUGHMAN, S and ALLAN, G (1992)
'Percutaneous Absorption of Co-Administered N-Methyl-2-[^{14}C] Pyrrolidinone and 2-[^{14}C] Pyrrolidinone in the Rat'
Fd Chem Toxicol, 30, 57-64

Publications (continued)

21. BRINDLEY, C J, TAYLOR, T, DINESS, V, OESTERGAARD, P B and CHASSEAUD, L F (1993)
'Relationship Between Pharmacokinetics and Pharmacodynamics of Tinzaparin (Logiparin), A Low Molecular Weight Heparin, in Dogs'
Xenobiotica, 23, 575-588

22. MIDGLEY, I, HOOD, A , PROCTOR, P, CHASSEAUD, L F, IRONS, S, CHENG, K, BRINDLEY, C J and BONN, R (1994)
'Metabolic Fate of ^{14}C-Camostat Mesylate in Man, Rat and Dog After Intravenous Administration'
Xenobiotica, 24, 79-92

23. CHASSEAUD, L F and BRINDLEY, C J (1995)
'Design and Interpretation of Toxicokinetic Studies'
Current Issues in Drug Development II.
Information Press UK pp 53-65

24. BRINDLEY, C J, SCHWARTZ, S (1997)
Practical Implementation of Toxicokinetics in Drug Development
Int. J Pharm Med, 11, 269-272

25. BRINDLEY, C (1997)
Toxicokinetics in Drug Development J Eur Soc Regulatory Affairs, 4, 12-15

26. DE BONO J S, DALGLEISH A G, CARMICHAEL J, DIFFLEY J, LOFTS F, FYFFE D, ELLARD S, GORDON R J, BRINDLEY C J, EVANS T R J.
Phase I study of ONO-4007, a synthetic analogue of the lipid moiety of bacterial lipopolysaccharide.
Clin. Cancer Res. 2000, 6: 297 - 405

27. BRINDLEY C J, MORRISON R, GORDON R J, DEVLIN A J, VERWEIJ J, VAN DER GAAST A.
Clinical Pharmacokinetics of DMDC : A novel deoxycytidine analogue antineoplastic agent.
Clin. Pharmacokinet. 2000, 38: 475-491

28. BRINDLEY C, FALCOZ C, McKIE A, BYE A.
Absorption Kinetics after inhaled flucticasone propionate delivered via the diskhaler®, diskus® and metered-dose inhaler in healthy subjects.
Clin. Pharmacokinet. 2000, 39 suppl 1, 1-8

29. FRIBERG L E, BRINDLEY C J, KARLSSON M O, DEVLIN A J.
Models of schedule dependent haematological toxicity of DMDC
Eur. J. Clin. Pharmacol. 2000, 56: 567-574

30. ESKENS F, DUMEZ H, HOEKSTRA R, PERSCHL A, BRINDLEY C, BOETTCHER S, WYNENDAELE W, DREVS J, VERWEIJ J, VAN OOSTEROM A. Phase I and pharmacokinetic study of continuous twice weekly intravenous administration of Cilengitide (EMD 121974), a novel inhibitor of the integrins αvβ3 and αvβ5 in patients with advanced solid tumours Eur. J. Cancer 2003, 39:917-926

Publications (continued)

31. MARTIN, P, WARWICK M, DANE A, BRINDLEY C, SHORT T. Absolute oral bioavailability of rosuvastatin in healthy white adult male volunteers. Clin Ther. 2003, 25:2553-2563

32. BRINDLEY CJ. Practical aspects of deconvolution. Pharmacokinetics in Drug Development (Ed: Bonate PL and Howard D). AAPS Press, Alexandria, VA, 2004.pp 479-499

33. DE JONG M, KAYE S, VERWEIJ J, BROCK C, READE S, SCURR M, VAN DOOM L, LOOS W, BRINDLEY C, MISTRY P, COOPER M, JUDSON I. Phase I and pharmacokinetic study of XR11576, an oral topoisomerase I and II inhibitor, administered on days 1-5 of a 3-weekly cycle in patients with advanced solid tumours. Br. J. Cancer 2004, 91: 1459-1465

34. HUMMEL J, MCKENDRICK S, BRINDLEY C, FRENCH R. Exploratory Assessment of Dose Proportionality: Review of Current Approaches and Proposal for a Practical Criterion. Pharmaceutical Statistics, 2008, http://www3.interscience.wiley.com/cgi-bin/fulltext/117952595/PDFSTART DOI: 10.1002/pst.326) DOI: 10.1002/pst.326

35. TAN T, FIELD B, MINNION S, CUENCO-SHILLITO J, CHAMBERS E, ZAC-VARGHESE S, BRINDLEY C, MT-ISA S, FLORENTINO F, ASHBY D, WARD I, GHATEL M, BLOOD S. Pharmacokinetics, adverse effects and tolerability of a novel analogue of human pancreatic polypeptide, PP 1420. Br. J. Clin. Pharmacol. 2011, 73:232-239 http://www.ncbi.nlm.nih.gov/pubmed/21834938

Presentations

1. Comparative kinetic evaluation of the metabolic N-demethylation of hexamethylmelamine (HMM) and its metabolites in vitro (BACR, London, 1980)

2. Plasma levels of N-methyl formamide following intravenous and oral administration in man (BACR, York, 1983)

3. Pharmacokinetics of High-Dose Etoposide in Patients with Choriocarcinoma (World Congress on Cancer Therapy, Brighton, 1985)

4. Cis-Trans Interconversion of Acitretin (DMDG, Cambridge, 1987)

5. Indices of Rate, Extent and Duration of Exposure in Toxicokinetics (Toxicokinetic Discussion group, Gatwick, 1992)

6. Rates of Absorption (PSI, Pharmacokinetics Interest group, May, 1993)

7. Practical Problems for the Toxicologist (UKAPS Symposium on Toxicokinetics, Milton Keynes, 1993)

8. In Vitro Dissolution of Ranalozine from Sustained-release Formulations by Linear Compartmental Deconvolution (PKUK, Glasgow, 1994)

9. Significance of interspecies variations in absorption, distribution, metabolism and excretion
Modular Training Programme in Applied Toxicology
(University of Surrey, Guilford, October 1997)

10. Assessment of starting dose and pharmacokinetic-guided dose escalation in Phase I using preclinical pharmacokinetic data
(TKDG, Leicester, September 1998)

11. Toxicokinetics in drug development
(PKUK, Manchester, November 1998)

12. 'Use of toxicokinetics in drug development'
Conference on Role of DMPK in both discovery and exploratory development: principles and practice, Nice, 24-27 Feb 1999

13. Toxicokinetics. Modular Training Programme in Applied Toxicology
(University of Surrey, Guildford, October 1999)

14. Use of statistics in toxicokinetic analysis: results of a survey conducted in the UK.
(TKDG; Bishops Stortford, November 2000).

15. Toxicokinetics. Modular Training Programme in Applied Toxicology
(University of Surrey, Guildford, October 2003)

16. BRINDLEY C, LOCKER J. HOWSON P, WARD C.
Pharmacokinetic modeling of PYM50028 (Cogane™) predicts once daily dosing can achieve plasma levels in PD patients associated with preclinical efficacy. 18th International Congress on PD and Related Disorders. 13-16 December 2009, Miami Beach, FL, USA.

Presentations (continued)

17. Predicting exposure in man from animal PK. Toxicokinetic Discussion Group Meeting. Cambridge (Clare College 25th January 2012)

18. CASS L, WOODWARD K, BRINDLEY C, WARRINGTON S, RAPEPORT G. Tolerability and pharmacokinetic profile of RV568, a narrow spectrum kinase inhibitor, following single and repeat inhaled dosing in healthy volunteers. ATS, Philedelphia 17-22 May 2013.

19. CASS L, WOODWARD K, BRINDLEY C, WARRINGTON S, RAPEPORT G. Tolerability and pharmacokinetic profile of RV568, a narrow spectrum kinase inhibitor, following single and repeat intransal dosing in healthy volunteers. ATS, Philedelphia 17-22 May 2013.

20. WNUK-LIPINSKA K, GAUSDAL G, SANDAL T, FRINK R, HINZ S, LIANG X, MILDE E, MATULANIEC P, BONIECKA A, MICKLEM D, TIRON C, BRINDLEY C ET AL. BGB324, a selective small molecule Axl kinase inhibitor to overcome EMT-associated drug resistance in carcinomas: Therapeutic rationale and early clinical outcomes. AACR, San Diego, CA 5-9 April 2014.

21. PLUMMER R, ANTHONEY A, EVANS J, [BRINDLEY C] ET AL. A Phase I Dose Escalation Study to Assess the Safety Tolerability and Pharmacokinetics of ETS2101 in Patients With Advanced Solid Tumours. ECCO/ESMO, Vienna, Austria, 27 September 2015

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Approved: JB Lindsay

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