

Scientific programme – details

Tuesday 28 September

Opening Ceremony

Room ABC

13:10–13:15 Opening remarks
 A. Eggermont EORTC
 A. Barker NCI
 K. Antman AACR

Michel Clavel Lecture

Room ABC

13:15–14:00 How to develop a successful cancer drug – molecules to medicines or targets to treatments?
 H. Newell, UK p. 3

Keynote Lecture

Room ABC

14:00–14:45 Pitfalls in developing cancer chemoprevention agents p. 3
 A. Decensi, I

Plenary Session 1

Room ABC

15:15–17:20 **Applications of proteomics and genomics in drug discovery** p. 3
 Chairs: P. Workman (UK) and E.C. Kohn (USA)

15:15 Overview of proteomics with emphasis on diagnosis and monitoring
 E.C. Kohn, USA

15:40 High throughput genome sequencing for cancer gene discovery: BRAF and beyond
 R. Wooster, UK

16:05 Towards a high throughput platform for quantitative serum protein profiling
 R. Aebersold, USA

16:30 Genomics and proteomics in drug development
 P. Workman, UK

16:55 Mapping and targeting proteins at the endothelial cell surface and its caveolae for improved penetration, imaging and radiodestruction of solid tumors
 J.E. Schnitzer, USA

Wednesday 29 September

Workshop 1

Room A

- 08:00–09:45 **Marketing approval for anticancer agent – the perspective of a worldwide co-ordination!** p. 7
Chairs: S. Hirschfeld (USA) and P. Therasse (B)
- 08:00 The FDA perspective on marketing approval for anticancer agent
A. Farrell, USA
- 08:25 The EMEA perspective on marketing approval for anticancer agent
B. Jonsson, S
- 08:50 The Industry perspective on marketing approval for anticancer agent
G. Burke, USA
- 09:15 Discussion

Workshop 2

Room B

- 08:00–09:45 **Preclinical models** p. 7
Chairs: P. LoRusso (USA) and J. Tomaszewski (USA)
- 08:00 Overview of the models currently in development
C. Marks, USA
- 08:25 Linking cancer genetics to cancer therapy
S. Lowe, USA
- 08:50 Patient and cell line derived human tumor xenograft models – preclinical/clinical correlations
H.H. Fiebig, D
- 09:15 Discussion

Workshop 3

Room C

- 08:00–09:45 **Mechanistic combinations** p. 8
Chairs: J. Sebolt-Leopold (USA) and J. Dancey (USA)
- 08:00 Introduction
J. Dancey, USA
- 08:05 Combined targeted agents with cytotoxic chemotherapy
L. Gianni, I
- 08:25 Radiation with targeted agents
M. Brown, USA
- 08:50 Targeted agent with targeted agents
P. Houghton, USA
- 09:15 Discussion
Chair: J. Sebolt-Leopold, USA
- 09:45–10:15 Coffee Break

Workshop 4**Room A**

10:15–12:00	Practical issues in tissue research Chairs: F. Meunier (B) and A. Murgo (USA)	p. 9
10:15	Introduction <i>F. Meunier, B</i>	
10:20	US NCI perspective on tissue handling and banking <i>S.E. Taube, USA</i>	
10:40	US Cooperative Group perspective on tissue handling and banking <i>R. Schilsky, USA</i>	
11:00	Current challenges of national and pan European human tumour banking <i>M.M. Morente, S</i>	
11:20	Legal and ethical requirements of human tissue research <i>C. Trouet, B</i>	
11:40	Discussion	

Workshop 5**Room B**

10:15–12:00	Tumour vaccines Chairs: C.J.A. Punt (NL) and J.S. Weber (USA)	p. 10
10:20	Human dendritic cell subsets and their implications for clinical studies <i>C.G. Figdor, NL</i>	
10:40	Development of heat shock cancer vaccine strategies <i>G. Parmiani, I</i>	
11:00	Experimental strategies to enhance the potency of dendritic cell-based cancer vaccines for clinical use <i>J.J. Mulé, USA</i>	
11:30	Discussion	

Workshop 6**Room C**

10:15–12:00	Pharmaceutical industry, investigators and institutions: partners or tools? Practical issues in clinical cancer drug development Chairs: E.K. Rowinsky (USA) and J. Verweij (NL)	p. 11
10:00	Introduction <i>J. Verweij, NL</i>	
10:40	Pharmaceutical industry, investigators and institutions: partners or tools? Practical issues in clinical cancer drug development. Erosion of the principal investigator in a climate of industry dominance <i>E.K. Rowinsky, USA</i>	
11:05	The difficulties industry is experiencing with investigators <i>G.R.P. Blackledge, UK</i>	
11:30	Discussion	
12:00–14:40	Lunch/Poster sessions	

Keynote Lecture**Room ABC**

- 14:40–15:00 Highlights from the 3rd EORTC–NCI International Conference on Cancer
Molecular Markers: From Discovery to Clinical Practice
R. Schilsky, USA p. 12

Plenary Session 2**Room ABC**

- 15:00–16:00 **Proffered papers** p. 13
Chairs: A.M.M. Eggermont (NL) and E. Raymond (F)
- 15:00 Molecular and clinical analysis of response to Imatinib for locally advanced dermatofibrosarcoma protuberans
G. McArthur, AUS
FNAB Translational Research Grant Award winner
- 15:15 A phase I pharmacokinetic (PK) and pharmacodynamic (PD) study of OGX-011, a 2'-methoxyethyl phosphorothioate antisense to clusterin, in patients with prostate cancer prior to radical prostatectomy
K.N. Chi, CDN
- 15:30 A phase I clinical trial of HGS-ETR1, an agonist monoclonal antibody to TRAIL-R1, in patients with advanced solid tumors
R.B. Cohen, USA
- 15:45 Temozolomide (TMZ) targets only glioblastoma with a silenced MGMT-gene. Results of a translational companion study to EORTC 26981/NCIC CE.3 of radiotherapy±TMZ
M. Hegi, CH
- 16:00–16:30 Coffee Break

Plenary Session 3**Room ABC**

- 16:30–18:15 **AKT/PTEN/Survival pathways** p. 14
Chairs: E. Raymond (F) and P. Dennis (USA)
- 16:30 Functional analysis of PDK1 signalling pathway using knockout and knockin approaches; evaluation of PDK1 as a cancer target
D. Alessi, UK
- 16:55 Approaches to inhibit the Akt pathway
W.R. Sellers, USA
- 17:20 Novel targets that control protein translation downstream from Akt and PTEN
N. Sonneberg, CDN
- 17:45 Clinical experiences with mTOR inhibitors
S. Faivre, F

Poster Sessions**New drug targets**

p. 15

Abstract number

- 36 Transcriptional signature associated with sensitivity to ET-743 (Yondelis) in low passage sarcoma cell lines
M. Sanchez Beato, N. Martinez, I. Fernandez, M. Navarrete, P. de la Cueva, A. Carnero, J.C. Tercero, J. Jimeno, M.A. Piris

- 37 Sensitivity and resistance of human leukemic blasts to aplidin; molecular signature by gene expression profiling (GEP)
N. Martinez, M. Sanchez Beato, G. Kaspers, I. Fernandez, P. de la Cueva, J.C. Tercero, J. Jimeno, M.A. Piris
- 38 The role of sample preparation on gene expression profiling: impact on clinical use of microarray technology
S. Debey, U. Schoenbeck, T. Zander, J.L. Schultze
- 39 Discovery and development of multiplex angiogenesis inhibitors that target EphB4: validation with a novel chemical-genetics based in vivo model
D. Qian, S. Srinivasa, S. Mitchell, L. Elkin, D. Pippin, J. Darrow, J. Di Paolo, R. DeSimone, X. Qian, M. Velleca
- 40 RAD001 sensitizes tumor cells to cisplatin-induced apoptosis in an mTOR dependent manner by inhibition of p53-induced p21 protein expression
I. Beuwick, A. Boulay, S. Fumagalli, F. Zilbermann, S. Ruetz, T. O'Reilly, F. Natt, J. Hall, H. Lane, G. Thomas
- 41 A potential for combining the rapamycin derivative RAD001 (everolimus) with the EGF/ErbB2/VEGF receptor tyrosine kinase inhibitor AEE788 in human cancer
C. Stephan, S. Zumstein-Mecker, S. Gerboth, A. Boulay, S. Ruetz, N. Hynes, J. Baselga, H.A. Lane
- 42 Phase II study of BAY 43–9006 in patients with advanced hepatocellular carcinoma (HCC)
G.K. Abou-Alfa, S. Ricci, D. Amadori, A. Santoro, A. Figer, J. De Greve, J. Douillard, M. Moscovici, B. Schwartz, L.B. Saltz
- 43 Proteasome inhibition activates a p38 MAPK-dependent anti-apoptotic program involving MKP-1 and Akt
R. Orlowski, G. Small, Y. Shi
- 44 Selective small molecule inhibitors of ADAM metalloproteases as a novel approach for modulating ErbB pathways in cancer
P. Scherle, J. Fridman, X. Liu, E. Caulder, M. Hansbury, Y. Li, W. Yao, K. Vaddi, R. Newton, S. Friedman
- 45 Eukaryotic translation initiation factor eIF-4E is consistently upregulated with human prostate cancer progression: inhibition by siRNA or ASO therapy suppresses CaP xenograft growth
J. Graff, B. Konicek, R. Lynch, K. Hanna, S. Bailey, A. McNulty, R. Goode, T. Vincent, E. Marcusson, J. Carter
- 46 Biological testing of the tyrphostin tyrosine kinase inhibitor Adaphostin (NSC 680410) as a vascular endothelial growth factor secretion inhibitor in human and murine tumor cells and tumor-activated bone marrow stromal cells
E. Egilegor, L. Mendoza, N. Gallot, M. Valcárcel, M. Solaun, M. Hollingshead, E. Sausville, F. Vidal-Vanaclocha
- 47 CRx-026: discovery and clinical development of a syncretic anti-mitotic agent with significant anti-cancer activity
P.J. Elliott, M.S. Lee, M. Keegan, Y. Zhang, M.J. Nichols, A.A. Borisy, C.T. Keith
- 48 In vivo selection of vascular extravasating phage: novel means to isolate prostate tumor-homing peptides
S. Deutscher, M. Dickerson, L. Landon, C. Illy
- 49 DNA aptamers that recognize the MUC1 tumour marker
C. Ferreira, S. Missailidis
- 50 Inhibition of histone deacetylase 2 increases apoptosis and P21 expression
S.C. Hooi, M.L. Laban, B.H. Huang, L. Lee, G.C. Raju, C.K. Lee, M. Salto-Tellez
- 51 HSV-tk gene transduction enhances proliferation rate and COX-2 expression in rat gliosarcoma cells
K. Al-Athamen, A. Konson, G. Rimon, A. Danon, R. Agbaria
- 52 Attenuated immunogenicity and toxicity of PEGylated recombinant methioninase (PEG-rMETase) in primates
Z. Yang, J. Wang, Y. Kobayashi, C. Lian, S. Li, X. Sun, Y. Tan, S. Yagi, E.P. Frenkel, R.M. Hoffman
- 53 Pyrrolo[3,4-c]carbazole-1,3-dione inhibitors of the G2/M checkpoint kinase wee1
B.D. Palmer, R.J. Booth, W.A. Denny, K. Hook, A.J. Kraker, H.H. Lee, D. Ortwine, J.B. Smaill, C. Squire, A.M. Thompson
- 54 In vitro, in vivo and in silico examination of the activity of antitumor 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazoles
T. Bradshaw, C. Leong, M. Suggitt, D. Swaine, M. Bibby, M. Stevens
- 55 A phase I study of SB-715992, a novel kinesin spindle protein (KSP) inhibitor: pharmacokinetic (PK)/ pharmacodynamic (PD) modeling of absolute neutrophil counts (ANC)
D. Williams, S. Kathman, Q. Chu, K. Holen, E. Rowinsky, G. Wilding, P. Mudd, J. Herendeen, J. Orr, L. Pandite
- 56 Hsp90-targeted therapy for small cell lung cancer
G. Chiosis, N. Rosen, J. Kim, J. Aguirre, D. Solit, M. Vilenchik
- 57 The facilitative glucose transporter Glut-1 as a target for novel anti-cancer agents
A. Evans, S. Brittain-Dissont, K. Williams, I. Stratford, R. Airley

- 58 Pharmacodynamic responses to a novel histone deacetylase inhibitor, PXD101, in mice and humans
J.A. Plumb, N. Steele, T.R.J. Evans, P.W. Finn, P.B. Jensen, R. Kristeleit, J. DeBono, R. Brown
- 59 Comparison of the efficacy of MS-275, CI-994 and SAHA in vivo in various experimental tumor models after oral application
H. Hess-Stumpp, D. Grossbach, P. Lienau
- 60 Geldanamycin combined with bortezomib interferes with the ER-associated protein degradation function of valosin-containing protein
E. Mimnaugh, W. Xu, B. Scroggins, X. Yuan, T. Prince, S. Hartson, M. Vos, L. Neckers
- 61 Mutant-PTEN leads to constitutive integrin-linked kinase (ILK) activity that regulates PKB/Akt activity in glioblastoma cancer cells and targeting ILK results in tumor growth-delay in vivo
L. Edwards, B. Thiessen, V. Dragowska, T. Daynard, S. Dedhar, M. Bally
- 62 Isolation of pericytes from vasculature of human lung tumors
R. Bagley, C. Rouleau, S. Morgenbesser, B. Teicher
- 63 Identification of important genes for recurrence of gastric cancer by gene expression profiling
M. Motoori, I. Takemasa, M. Yano, H. Miyata, S. Takiguchi, Y. Fujiwara, T. Yasuda, Y. Kurokawa, K. Kato, M. Monden
- 64 Assessment of antitumor effects of erlotinib prior to first-line surgical treatment of head and neck squamous cell carcinoma
J.P. Delord, F. Thomas, I. Hennebelle, J. Sarini, A. Benlyazid, M. Rives, E. Chatelut, B. Allal, P. Rochoaix
- 65 Kinomic profiling identifies PKC/Akt and beta-catenin/TCF mediated signal transduction as important targets of celecoxib in colon cancer
J.B. Tuynman, M.P. Peppelenbosch, E.M.J. Boon, A.H. Zwinderman, D.J. Richel
- 66 Anti-proliferative activity of a PPAR gamma agonist is associated with changes in the expression of cell cycle and apoptosis related genes in human ovarian cancer cells
S. Vignati, V. Albertini, A. Rinaldi, F. Bertoni, G. Carbone, C. Catapano
- 67 Assessment of treatment efficacy in preclinical drug testing using magnetic resonance imaging
J.B. Moody, P. McConville, R.J. Lister, W.L. Elliott, B.A. Moffat, T.L. Chenevert, D.L. Dexter, A. Rehemtulla, B.D. Ross, W.R. Leopold, W.R. Leopold
- 68 Spermine/spermidine N1-acetyltransferase: a new target for prevention and/or therapy of colorectal cancer
F.G. Berger, C. Davis, J.M. Tucker, D.L. Kramer, C.W. Porter
- 69 Essential role of inducible 6-phosphofructo-2-kinase in ras transformation
S. Telang, A. Yalcin, A. Clem, J. Chesney
- 70 Therapeutic human monoclonal antibody targeting VEGFR-1 suppresses growth of human breast cancers
Y. Wu, Z. Zhong, H. Li, G. Makhoul, R. Bassi, P. Balderes, J. Tonra, D. Ludwig, P. Bohlen, D. Hicklin
- 71 In vivo efficacy of STI571 in xenografted human small cell cancer alone or combined with chemotherapy
D. Decaudin, P. de Cremoux, X. Sastre, F. Némati, C. Tran-Perennou, P. Fréneaux, A. Livartowski, P. Pouillart, M.F. Poupon
- 72 Restoration of wild-type p53 in malignant melanoma
D. Weber, J. Markowitz, A. MacKerell, F. Carrier
- 73 Inhibition of choline kinase is a highly specific and selective cytotoxic antitumoral strategy
M. Bañez-Coronel, A. Rodriguez-Gonzalez, A. Ramirez de Molina, A. Ramos, J.C. Lacal
- 74 Determinants of the synergistic interaction between TS inhibitors, IFN-gamma and Fas signaling in therapy of colon cancer
J.A. Houghton, D.M. Tillman, L.S. Schwartzberg, J.I. Geller
- 75 Conjugates of lytic peptides target and destroy prostate cancer metastases
C. Leuschner, W. Hansel, F. Enright
- 76 ZD4054: assessment of endothelin A receptor specificity following single dose administration in healthy volunteers
C. Morris, D. Wilson, A. Hughes, F. Le Maulf, S. Brahma, R. Fuhr
- 77 MKP-1/CL100 activity modulates cisplatin responses in non-small cell lung carcinoma
R. Perona, S. Chattopadhyay, C. Moratilla, C. Belda, P. Cejas, J. Fresno-Vara, R. Machado, M. Nistal, M. Gonzalez-Barón
- 78 ZD4054 specifically inhibits endothelin A receptor-mediated anti-apoptotic effects, but not endothelin B receptor-mediated pro-apoptotic effects
N. Curtis, Z. Howard, N. Brooks, J. Curwen

- 79 Characterization of novel therapeutic receptor target candidates for treatment of small cell lung cancer
H.S. Poulsen, T.T. Poulsen, M.W. Pedersen, N. Pedersen
- 80 Membrane gamma-glutamyltransferase as a target for intervention on several redox-modulated functions of the cancer cell
A. Pompella, A. Paolicchi, S. Dominici, A. Corti, M. Franzini, V. De Tata, E. Maellaro, R. Supino, F. Zunino, A. Casini
- 81 Synergistic effects of Apo-2L/TRAIL and ionizing irradiation in human tumor cell lines without relevant damage of normal tissue cells
P. Marini, A. Schmid, H. Faltin, V. Jendrossek, W. Budach, C. Belka
- 82 MS-275, a potent orally active inhibitor of histone deacetylases is highly active in experimental tumor models of melanoma and prostate cancer
H. Hess-Stumpp, J. Hoffmann, A. Schott
- 83 Antitumor activities of MGCD0103, a novel isotype-selective histone deacetylase inhibitor
Z. Li, N. Zhou, M. Fournel, G. Rahil, J. Wang, D. Delorme, O. Moradei, R. MacLeod, J. Besterman
- 84 Regulation of the oncogenic x-protein of hepatitis B by cellular chaperones
X. Yuan, W. Xu, L. Neckers
- 85 Progenitor cells derived from human bone marrow contribute to the growth of breast cancer cells
R. Bagley, A. Dash, X. Cao, T. Lodie, S. Madden, R. Tubo, B. Teicher
- 86 Preclinical pharmacokinetics (PK) and CNS distribution of RTA 203, a novel mammalian vacuolar H⁺-ATPase inhibitor
K. Culotta, N. Thapar, C. Meyer, D. Ferguson, J. Thapar, M. Johansen, T. Madden
- 87 Selection of pre-invasive lung cancer binding peptides using random phage display libraries
J.Y. Hung, A.J. Rebello, S. Lam, J.C. Ierliche
- 88 Substrate phage display: screening-approach for radiation-induced posttranslational peptide modifications in a complex proteome
A. Broggin-Tenzer, B. Hofstetter, C. Sauser, S. Bodis, P. Schubiger, C. Bonny, M. Pruschy
- 89 Gene expression profiling of cancer associated fibroblasts
P. Mücke, C. Sundquist, D. Hägerstrand, S. Scheidl, P. Lindahl, F. Pontén, C.H. Heldin, A. Ostman
- 90 AG879, a tyrphostin c-erbB-2 inhibitor, leads to transcriptional repression of cyclin D1 in pancreas cancer cells through a p27Kip1 independent pathway
A.N. Salesiotis, R. Samara, L. Laguinge, S. Ling, J.M. Jessup
- 91 17-allylamino-17-demethoxygeldanamycin overcomes trail resistance in colon cancer cell lines
I. Vasilevskaya, P. O'Dwyer
- 92 A phase I, pharmacological and biological study of Sarasar® (lonafarnib, SCH 66336), cisplatin and gemcitabine in patients with advanced solid tumors
L. Gore, M. Basche, S.N. Holden, C. O'Bryant, M.K. Schultz, S. Grolnic, M. Morrow, S.G. Eckhardt
- 93 Genetic validation of activated polyamine catabolism as a novel therapeutic strategy targeting prostate cancer
C.W. Porter, K. Kee, D.L. Kramer, F.G. Berger
- 94 The cytotoxic effects of 17-AAG, an inhibitor of Hsp90 are enhanced by combination with the PI-3-kinase inhibitor LY294002 in non-small cell lung cancer (NSCLC) cell lines
V. Papadimitrakopoulou, S. Angelaki, S. Lnu, E. Brown, G. Ayers
- 95 Expression of genes relevant for tumour aggressiveness in endometrial cancer
E. Steiner, J. Sagemüller, J. Brieger, C. Lindner, M. Werling, H. Kölbl
- 96 Characterization of carbonic anhydrase 9 (CA9) overexpression: endogenous hypoxia marker and potential tumor-specific target
D. Vordermark, A. Katzer, A. Kaffer, S. Riedel, M. Flentje
- 97 Eradication by induced apoptosis of chemoresistant infiltrating ductal carcinoma (IDC) characterised by HDAC2 overexpression and 5' CpG island hypermethylation of the FHIT, RARb2, BRCA1, APC, p16(CDKN2A), RASSF1A, CDH1(Ecadherin), stratifin, MDG1 and HIC1 oncosuppressor genes after combined treatment consisting of immunochemoconjugate of anti-DNMT1/HDAC2 bispecific F(ab)2-bsAb linked with cleavable disulfide onto vinorelbine (I-VRL)
J. Giannios, E. Michailakis, P. Lambrinos
- 98 The role of NAD(P)H: quinone oxidoreductase 1 (NQO1) in geldanamycin, 17AAG and 17AG metabolism
D. Siegel, W. Guo, D. Gustafson, J. Zirrolli, D. Ross

- 99 Para-amino benzoic acid (PABA) modulation of chemotherapy – evolution from preclinical work to a Phase I study. A report of early clinical activity including pharmacokinetic and pharmacodynamic studies
A. Paulick, L. Liebes, F. Muggia, K. Farrell, J. Goldberg, S. Mendoza, D. Fry, M. Caunt, J. Roth, P. Brooks
- 100 A peptide inhibitor of t(4;11) leukemia
J. Nesbit, C.S. Hemenway
- 101 Combinatorial cancer therapy using a pharmacological inhibitor of indoleamine 2,3-dioxygenase (IDO), a target of the cancer suppression gene Bin1
A.J. Muller, J.B. DuHadaway, E. Sutanto-Ward, P.S. Donover, G.C. Prendergast

Drug screening

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Abstract number

- 102 The synthetic lethal trap: a general approach for screening small-molecule protein inhibitors using genetic triangulation in the yeast *Saccharomyces cerevisiae*
D. Bellows, P. Jorgensen, M. Tyers, M. Tyers
- 103 High-throughput screening against intractable targets: the use of target disruption gene signatures for rapid cancer drug discovery
P.E. Young, J. Castaneda, M. Chakiath, K. Evans, S.K. Horrigan, S. Pikul, M.J. Shea, D.R. Soppet, J.W. Strovel, Q. Zong
- 104 Novel drug discovery strategies based on aptamer inhibitors which are especially useful for orphan targets
M. Blind, G. Mayer, B. Bandilla, K. Klenzke, P. Rudolph, S. Fesele, A. Girod, M. Grättinger
- 105 High throughput screening of a natural product library for telomerase inhibitory agents using target-defined model systems and bioinformatics
F. Dai, G. Kelter, S. Driever, T. Greiner, H.H. Fiebig, J.A. Double, A.M. Burger
- 106 A highly efficient approach to the anticancer drug discovery of potent small molecule kinase inhibitors
J. Mendoza, J. Dickson, I. Popa-Burke, R. Mohny, J. Murray, C. Toole, L. Cheatham, P. Bernasconi, K. Williams, N. Hodge
- 107 Screening the DTP Diversity Set for compounds that inhibit the growth of human melanoma cells with defined mutations
A.J. Sakko, V.J.N. Bykov, K.G. Wiman, J. Hansson
- 108 Profiling in vitro and in vivo of MS275, SAHA, LAQ824 and VPA as HDAC inhibitors currently tested in clinical trials
T. Beckers, C. Burkhardt, H. Wieland, J. Braunger, P. Gimmich, T. Maier
- 109 Identification of small molecule inhibitors of PKB/AKT in a high throughput screen
W. Aherne, S. Burns, J. Travers, Y. Newbatt, M. Rowlands, D. Barford, I. Collins, N. Thompson, M. Garrett, P. Workman
- 110 In vitro screening of anticancer drug penetration into tumour tissue
A.H. Kyle, L.A. Huxham, A.I. Minchinton
- 111 Development and validation of a mass spectrometric assay to evaluate drug–drug interaction in human liver microsomes. Application to anticancer agents
F.I. Raynaud, J. Moreno-Farre, P. Workman
- 112 Pharmacokinetic-pharmacodynamic (PK-PD) modeling of tumor growth inhibition in mice: a magnetic resonance imaging study
M. Rocchetti, A. De Grassi, M. Simeoni, E. Pesenti, M. Russo, I. Poggesi
- 113 Pharmacokinetic-pharmacodynamic (PK-PD) modeling of tumor growth inhibition in mice: the activity of brostallicin is enhanced in cells with high glutathione-S-transferase
M. Germani, M. Rocchetti, M. Simeoni, F. Del Bene, E. Pesenti, C. Geroni, T. Colombo, S. Marchini, I. Poggesi
- 114 Cell lysate arrays – High performance protein profiling and signaling pathway mapping
M. Pawlak, E. Schick, P. Oroszlan, M. Ehrat

Drug design and synthesis

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Abstract number

- 115 A radioiodinated meta-iodobenzylguanidine-octreotate conjugate
G. Vaidyanathan, M.S. O'Dorisio, D.J. Affleck, P.C. Welsh, M.R. Zalutsky

- 116 Inhibition of p53-MDM2 pathway by novel boronic-chalcones
A. Modzelewska, A. Geetha, M. Ghosh, C. Pettit, N.E. Davidson, T. Holak, P. Huang, S.R. Khan
- 117 Identification of novel cyclin dependent kinase 1/2 inhibitors using fragment based high-throughput X-ray crystallography and structure based drug design
P.G. Wyatt, V. Berdini, M.G. Carr, J.E. Curry, D.J. Davis, M. O'Reilly, G. Saxty, M.S. Squires, A.J. Woodhead, A.J.-A. Woolford
- 118 Substituted 7-amino-4-anilino-6-alkoxy-3-quinolinecarbonitriles as Src kinase inhibitors
H. Tsou, E. Overbeek-Klumpers, W. Hallett, J. Golas, F. Boschelli
- 119 A novel strategy to inhibit Stat3 for human cancer therapy
N. Jing, Y. Li, W. Sha, W. Xiong, D. Tweardy
- 120 Synthesis and cytotoxicity studies of platinum nucleobase adducts
A.R. Khokhar, M.S. Ali, Z.H. Siddik
- 121 Synthesis, anti-proliferative and anti-angiogenic effects of sulfamoylated 2-methoxyestradiol analogues
M.P. Leese, K. Gaukroger, J.J. Robinson, J.M. Day, S.P. Newman, S. Chander, A. Purohit, M.J. Reed, B.V.L. Potter
- 122 Identification of inhibitors of the MDM2–p53 interaction using a virtual screening approach with multiple binding modes
I.R. Hardcastle, S.U. Ahmed, S. Guyenne, C. Hutton, P. Kallblad, S. Kemp, J. Lunec, R. Reid, K. Saravanan, H.M.G. Willems
- 123 Chemical and structural studies on thioredoxin-inhibitory antitumour quinols
A.D. Westwell, A.J. McCarroll, J.M. Berry, R. Ren, D.L. Rathbone, P.R. Lowe, C.H. Schwalbe, M. Burke, C.A. Laughton, M.F.G. Stevens
- 124 Peptidomimetic inhibitors of Stat3: structure–activity relationships and cellular activity
J.S. McMurray, P.K. Mandal, D.R. Coleman, Z. Ren, X. Chen, W. Liao, N.J. Donato
- 125 Synthesis, biological evaluation and structure activity relationships of a novel series of aromatic hydroxamic acids as potent HDAC inhibitors
K. Van Emelen, J. Arts, P. Angibaud, H. De Winter, S. Van Brandt, M. Verdonck, J. Van Dun, T. Geerts, W. Floren, J. Van Gompel

Structure–activity relationships

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Abstract number

- 126 Development of a new series of tricyclic pyrimido-indole inhibitors targeting Aurora kinases
S.L. Warner, H. Vankayalapati, S. Bashyam, C.L. Grand, H. Han, D.D. Von Hoff, L.H. Hurley, D.J. Bearss
- 127 Integrin receptor binding and cytotoxicity of cyclopeptides and their Chlorambucil conjugates containing RGD or NGR sequence
H. Süli-Vargha, N. Mihala, R. Morandini, R.J. Kok, G. Ghanem
- 128 Sapphyrins: structure-activity relationships in a novel series of potential anti-cancer agents
L. Naumowski, M. Sirisawad, P. Lecane, Z. Wang, L. Fu, D. Magda, P. Thiemann, G. Boswell, J. Ramos, R. Miller
- 129 Biarylalanine inhibitors of histone deacetylase enhance radiation sensitivity in cancer cells
M. Jung, S. Schäfer, S. Wittich, M. Jung, A. Dritschilo
- 130 Structural features of texaphyrin metal complexes leading to altered metal cation response in cancer cells
D. Magda, P. Lecane, C. Lepp, Z. Wang, R. Miller

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- 131 Pharmacodynamic analysis of apoptosis and anti-vascular activity in GIST patients treated with Imatinib
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- 132 A phase I and pharmacokinetic clinical trial of subcutaneous (sc) VEGF Trap in advanced solid tumor patients
J. Dupont, L. Schwartz, J. Koutcher, D.R. Spriggs, M.S. Gordon, D. Mendelson, J. Murren, A. Lucarelli, J.M. Cedarbaum
- 134 In vitro and in vivo characterization of exel-7647, a novel spectrum selective receptor tyrosine kinase inhibitor that modulates angiogenesis and tumor cell proliferation
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- 133 A phase II study of oxaliplatin, capecitabine and bevacizumab in the treatment of metastatic colorectal cancer
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- 136 Regulation of tumour angiogenesis and cell survival by integrin-linked kinase (ILK): pre-clinical evaluation of novel small molecule inhibitors
S. Dedhar, A. Troussard, C. Tan
- 135 A clinical phase I dose escalation, pharmacokinetic (PK) and pharmacodynamic (PD) study of BIBF 1120 in advanced cancer patients
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- 137 A phase I study of an oral vascular endothelial growth factor receptor-2 (VEGFR-2) tyrosine kinase inhibitor, CP-547,632, in patients with advanced solid tumors
A. Tolcher, J.J. O'Leary, J. DeBono, K. Molpus, C. Woodard, M. Warnat, K. Liau, D. Noe, D. Healey, M. Huberman
- 138 Enhancement of the action of the antivascular drug 5,6-dimethylxanthenone-4-acetic acid (DMXAA) by co-administration of non-steroidal anti-inflammatory drugs
B. Baguley, L.C.S. Wang, L.-M. Ching, J. Paxton, Q. Ding, P. Kestell
- 139 BAY 57-9352: an inhibitor of VEGFR-2 and PDGFR receptor tyrosine kinases that demonstrates anti-angiogenic activity in vitro and in vivo
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- 140 A two-stage phase II study of the matrix metalloproteinase inhibitor (MMPI) Col-3 in patients with advanced soft tissue sarcoma (ASTS) – report of Stage I data
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- 141 The spectrum-selective kinase inhibitor EXEL-0999 inhibits mitogenic and angiogenic kinases, and causes rapid tumor vasculature destruction and regression in mouse xenograft models
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- 142 Impact of scheduling on combined ZD6474 and radiotherapy in head and neck tumor xenografts
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- 143 The interferon-inducible GTPase MxA is a metastasis suppressor
J.F. Mushinski, P. Nguyen, C. Khanna, S. Lee, W.M. Linehan, M.-J. Lee, M.A. Horrisberger, A. Mendoza, E.J. Chung, J. Trepel
- 144 Develop novel cancer drug that controls angiogenesis factor expression post-transcriptionally
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- 145 A mitogenic-independent mechanism for ErbB receptor-induced tumour cell invasion
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- 146 E7080, a novel multi-targeted tyrosine kinase inhibitor, exhibits anti-angiogenic activity via inhibition of KIT signalling in a small cell lung cancer xenograft model
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- 147 Phase I pharmacokinetic (PK) and safety study of the antiangiogenic peptide ATN-161 (Ac-PHSCN-NH₂) in patients with solid tumors
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- 148 BAY 57-9352: an inhibitor of VEGFR-2 and PDGFR receptor tyrosine kinases that demonstrates broad anti-tumor activity as a single agent in preclinical models
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- 149 Inhibition of vasculogenic mimicry in melanoma by the antivascular drug 5,6-dimethylxanthenone-4-acetic acid (DMXAA)
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- 150 Molecular tumor characteristics and response to bevacizumab plus irinotecan/5-fluorouracil/leucovorin in metastatic colorectal cancer
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- 152 A synthetic Resveratrol analog inhibits the proangiogenic response of liver sinusoidal cells to tumor-derived factors during hepatic melanoma metastasis formation
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- 153 Inhibition of cytosolic superoxide dismutase (SOD1) in endothelial cells: a possible mechanism for the antiangiogenic properties of the copper depleting drug ATN-224
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- 158 BIBF1120 a novel, small molecule triple angiokinase inhibitor: profiling as a clinical candidate for cancer therapy
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- 160 Antitumor therapy with VEGF receptor tyrosine kinase inhibitor ZD6474 in a mouse model of intestinal cancer
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- 161 Anticancer effects of ZD6474 in gefitinib (IressaTM)-resistant lung cancer cell lines in vitro
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- 166 A phase I dose-escalation study of anti- $\alpha 5\beta 1$ integrin monoclonal antibody (M200) in patients with refractory solid tumors
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- 168 PRL-3 promotes invasion in tumor epithelial cells and tube formation in normal endothelial cells
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- 170 Å6, a urokinase plasminogen activator (uPA)-derived peptide: a phase I trial in patients with advanced gynecologic cancer
A. Berkenblit, M.A. Gold, U.A. Matulonis, J.F. Kroener, B.J. Dezube, G.N. Lam, N. Brünner, T.R. Jones, M.H. Silverman
- 171 Unnatural small molecule mimic of VLA-4-binding VCAM-1 epitope inhibits the intravascular adhesion and proliferation of metastatic melanoma cells
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- 172 Preclinical profile of ABP309, a potent 2nd generation VEGF receptor tyrosine kinase inhibitor belonging to the class of aminonicotinamides
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- 173 Prostate specific membrane antigen (PSMA) expression in the neo-vasculature of non-prostate cancers: in vitro target validation and in vivo imaging
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- 175 Pseudolarix acid B inhibits angiogenesis and reduces hypoxia-inducible factor 1alpha by promoting proteasome-mediated degradation
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- 176 In vitro human metabolism of BAY 57-9352: a novel VEGFR-2/PDGFR kinase inhibitor
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- 177 Tyrosine kinase inhibition as a strategy to suppress growth of primitive endothelial cells
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- 178 Toxin-VEGF fusion protein inhibits tumor growth
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- 179 Augmentation of radiation response in upper aero-digestive tract tumors with the vascular targeting agent ZD6126
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- 180 Low-dose metronomic cyclophosphamide induces sustained hypoxia in human tumor xenografts, which can be exploited therapeutically by the combination with the hypoxic cell cytotoxin tirapazamine
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- 181 Suppression of neuroblastoma by targeted delivery of interleukin-12 to tumor vasculature
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- 182 Effect of chemotherapy on human tumor xenografts differently expressing vascular endothelial growth factor (VEGF) and fibroblast growth factor-2 (FGF-2).
M. Passiu, D. Coltrini, A. Garofalo, R. Dossi, M. Zucchetti, M. Presta, R. Giavazzi
- 183 Gene delivery of Escherichia coli nitroreductase into endothelial cells prolongs the survival of tumor-bearing mice after the treatment with the prodrug CB1954
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- 184 Pharmacokinetics of CNTO 328 in a three month intravenous dose toxicity study in cynomolgus monkeys with concomitant IL-2 therapy
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- 185 Phage display-derived peptides specific to the galectin-3 carbohydrate recognition domain inhibit metastasis-mediated cancer cell adhesion
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- 186 Potent analogues of the antiangiogenic agent NM-3 have enhanced antiproliferative activity in vitro
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- 187 Is hypoxia relevant in modulating the effects of the novel antiangiogenic agent, ZD6474, in head and neck cancer?
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- 188 Targeted delivery of endostatin using an antibody-endostatin fusion protein resulted in enhanced inhibition of tumor growth
S. Shin, H. Cho, M. Iruela-Arispe, S. Morrison, K. Webster, J. Rosenblatt
- 189 Rodent pharmacokinetics and antiangiogenic activity of a pyrimidopyrimidine dual KDR/FGFR antagonist
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- 190 Adaphostin (NSC680410) down regulates VEGF expression in human umbilical vein endothelial cells under hypoxia
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- 191 Recombinant endostatin prevents integrin alpha4, beta1-mediated adhesion and proliferation of vascular endothelial growth factor receptor-expressing B16 melanoma cells; antimetastatic implications
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- 192 Transplanted hair follicles give rise to blood vessels in skin visualized in nestin-driven GFP mice
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- 193 Histone deacetylase inhibitors LAQ824 and LBH589 inhibit proliferation and modulate angiogenesis-related genes in human endothelial cells
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- 195 Treatment of new cases of acute promyelocytic leukaemia by arsenic trioxide
A. Ghavamzadeh, K. Alimoghaddam, S. Rostami, H. Ghafari, M. Jahani, R. Hosseini, A. Mosavi, M. Irvani, B. Bahar, A. Khodabandeh
- 196 Nuclear survivin is a powerful novel prognostic marker in gastroenteropancreatic neuroendocrine tumour disease
P. Grabowski, S. Griß, C. Arnold, D. Hörsch, R. Göke, R. Arnold, B. Heine, H. Stein, M. Zeitz, H. Scherübl
- 197 A phase I and pharmacokinetic (PK) study of an agonistic, fully human monoclonal antibody, HGS-ETR2, to the TNF-alpha related apoptosis inducing ligand receptor 2 (TRAIL R2) in patients with advanced cancer
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- 198 BARD1 required for telomere maintenance and control of genomic stability
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- 199 Both RIP and c-FLIP are required for inhibition of caspase-8 cleavage in TRAIL-DISC in human cancer cells
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- 200 Mutant p53 reactivation by PRIMA-1: a novel strategy for cancer therapy
K. Wiman, V. Bykov, N. Issaeva, N. Zache, J. Bergman, G. Selivanova
- 201 Analysis of survivin splice variant transcripts in human breast tumor cells
S. Lizard-Nacol, F. Vegrar, R. Boidot, C. Oudin, B. Coudert
- 202 The proteasome inhibitor bortezomib (VELCADE™) sensitizes human tumor cells to TRAIL-mediated apoptosis by reduction of c-FLIP
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- 203 Modulation of DNA damage induced apoptosis by the proteasome inhibitor bortezomib (PS) in human colorectal and non-small cell lung cancer cells is p53-dependent and NF-kB-independent
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- 204 HGS-TR2J, a human, agonistic, TRAIL receptor 2 monoclonal antibody, induces apoptosis, tumor regression and growth inhibition as a single agent in diverse human solid tumor cell lines
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- 205 Erucylphosphocholine: molecular requirements for apoptosis induction by a membrane targeted drug
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- 206 Defective Bim induction, downstream of glucocorticoid receptor nuclear translocation, in dexamethasone-resistant childhood acute lymphoblastic leukemia xenografts
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- 207 Activation of the P73-P53AIP1 apoptotic pathway in leukemia cells by combining arsenic trioxide (ATO) with MEK1 inhibitor
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- 208 HGS-ETR1, a fully human monoclonal antibody to the tumor necrosis factor-related apoptosis-inducing ligand death receptor 1 (TRAIL-R1) in patients with advanced solid cancer: results of a phase I trial
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- 209 Phase I clinical trial in patients with refractory solid tumors: the weekly 24 hour intravenous infusion of aviscumine, a recombinant ribosome-inactivating protein
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- 210 Induction of apoptosis in chronic lymphocytic leukaemia by inhibition of NF-kB and novel sulfasalazine analogues
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- 214 Deregulated expression of BARD1 in human tumors; a novel diagnostic and prognostic marker
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- 215 High quality gene expression microarray data from the EORTC 10994/BIG 00–01 breast cancer study
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- 216 SPC-2004 – a potent locked nucleic acid drug against Bcl-2 in cancer
B. Hansen, M. Westergaard, C.A. Thruw, M. Asklund, H. Oerum, M. Frieden
- 217 Srp20, the first transcriptionally up-regulated gene by flavopiridol (flavo), is a pre-mRNA splicing factor that induces apoptosis in human colon cancer cells
M. Motwani, P. Sridhar, G.K. Schwartz
- 218 A phase I and pharmacokinetic trial ARQ 501, an Activated Checkpoint Therapy (TM) agent, in patients with advanced solid tumors
A. Craig, G. Shapiro, D. Ryan, J. Eder, J. Supko, A. Wolanski, S. Jones, E. Regan, T. Bell, C. Li
- 219 FasL, but not TRAIL, induces apoptosis in human hepatocytes in chimeric mice
C. HAO, J.H. Song, B. Hsi, J. Levis, D.K. Song, K.C. Petruk, D.L.J. Tyrrell, N.M. Kneteman
- 220 Identification of the molecular target for MX2167, a novel anticancer agent
S. Kasibhatla, K. Jessen, S. Maliartchouk, J. Wang, N. English, J. Drewe, H. Zhang, N. Sirisoma, S. Cai, B. Tseng
- 221 Ceramide promotes JNK translocation and Bim phosphorylation in lung cancer derived A549 cells
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- 222 P53-mediated apoptosis induced by NCX 4040, a nitric oxide-releasing aspirin derivative, in human colon cancer cell lines
A. Tesei, P. Ulivi, F. Fabbri, C. Leonetti, M. Scarsella, G. Zupi, D. Amadori, M. Bolla, W. Zoli
- 223 Evaluation of 2 new Rhodium ferrocene complexes for cytotoxicity, and apoptotic propensity to invoke alternative cell death pathways in prostate tumour cell lines
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- 224 Two distinct pathways regulate Bak function in apoptosis: a requirement for JNK1 in Bak 80–170 kDa complex formation but not in Bak activation
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- 225 Variable distribution of TRAIL Receptor 1 in primary human tumor and normal tissues
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- 226 Sulphamoylated 2-substituted oestrogens induce apoptosis through G2-M checkpoint arrest
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- 227 NF- κ B: a differential modulator of chemotherapy induced apoptosis
J.W. Purcell, C. Finnegan, M. Thomas, K.M.A. Rogers, P.G. Johnston, M. Boland
- 228 A phase I trial of LY573636 in patients with advanced solid tumors
G. Simon, M. Sovak, M. Wagner, E. Haura, S. Gerst, D. deAlwis, G. Bepler, D. Sullivan, A. Weitzman, D. Spriggs
- 229 Activation of caspases in human t-lineage leukemia cells treated with analogs of leflunomide metabolite
A. Vassilev, Y. Zheng, O.O. Grigoriants, S. Qazi, F.M. Uckun
- 230 Roles of N-cadherin in anoikis and invasion
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- 231 Significance of radiation apoptosis in cancer and its modification by beta carotene
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- 232 In vitro and in vivo antitumor efficacy of NCX-4040, a nitric oxide-releasing non-steroidal anti-inflammatory drug, in combination with antineoplastic drugs on human colon cancer lines
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- 233 Activation of NF κ B pathway in diffuse large B-cell lymphoma
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- 234 Induction of cell death by imidazoacridinone derivative C-1311 in T lymphoblastoid leukemia MOLT4 cells
A. Skwarska, E. Augustin, J. Konopa
- 235 Rapid activation of caspases involving microtubule stabilization and p53 upregulation by D501036, a novel selenophene derivative active against human renal cancer cells
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- 236 PTTG/securin induces and modulates p53 expression and function
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- 237 PTEN regulates differential Fas apoptosis in Type I and Type II cells
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Thursday 30 September

Plenary Session 4

Room ABC

- 08:00–09:45 **Proteasome inhibitors, antichaperone drugs, stress pathway inhibitors** p. 75
 Chairs: L. Neckers (USA) and R.Z. Orłowski (USA)
- 08:00 Oncogenic aberrations of SCF ubiquitin ligases
M. Pagano, USA
- 08:25 The proteasome and proteasome pathway inhibitors in cancer
A.J. Rivett, UK
- 08:50 Hsp90 and molecular chaperones as targets in cancer therapy
N. Rosen, USA
- 09:15 Targeting the myeloma cell in its bone marrow microenvironment
K.C. Anderson, USA
- 09:45–10:15 Coffee Break

Plenary Session 5

Room ABC

- 10:15–12:00 **Hypoxia as a target** p. 75
 Chairs: I. Stratford (UK) and M. Nordsmark (DK)
- 10:15 Imaging hypoxia in tumours
P.L. Olive, CDN
- 10:40 Clinical significance of tumour hypoxia
M. Nordsmark, DK
- 11:05 Kidney cancer and the von Hippel-Lindau tumor suppressor protein: implications for therapy
W.G. Kaelin Jr, USA
- 11:30 HIF-1, hypoxia inducible factor-1 as a therapeutic target
I. Stratford, UK
- 12:00–15:00 Lunch/Poster sessions

Plenary Session 6

Room ABC

- 15:00–16:00 **Proffered papers** p. 76
 Chairs: A. Barker (USA) and T. Tsuruo (J)
- 15:00 Novel ATP-competitive Akt inhibitors slow the progression of tumors in vivo
V. Giranda, USA
- 15:15 Silencing of survivin gene by small interfering RNAs (siRNAs) induces apoptosis in human prostate cancer cells and increases their sensitivity to 17-allylamino-17-demethoxygeldanamycin (17AAG)
N. Zaffaroni, I
- 15:30 Antitumor activity, pharmacodynamics and toxicity of PX-866 a novel inhibitor of phosphoinositide-3-kinase
L. Kirkpatrick, USA

- 15:45 Novel small molecule inhibitors of 3'-phosphoinositide-dependent kinase-1 (PDK-1)
R.I. Feldman, USA
- 16:00–16:30 Coffee Break

Plenary Session 7**Room ABC**

- 16:30–18:15 **Chromatin modifying agents** p. 78
Chairs: J.A. Zwiebel (USA) and G. Burke (USA)
- 16:30 Modification of the histone code: effects of DNA methylation
S. Clark, AUS
- 16:55 Histone deacetylase inhibition – a promising anticancer therapeutic strategy
P. Atadja, USA
- 17:20 Promising combinations of HDAC inhibitors and other agents
K.N. Bhalla, USA
- 17:45 Clinical development of histone deacetylase inhibitors
V. Richon

Poster Sessions**Cancer vaccines***p. 79*

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- 254 Frequencies of tetramer+ T cells specific for HPV16 E7 epitopes in the circulation of patients with squamous cell carcinoma of the oropharynx
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