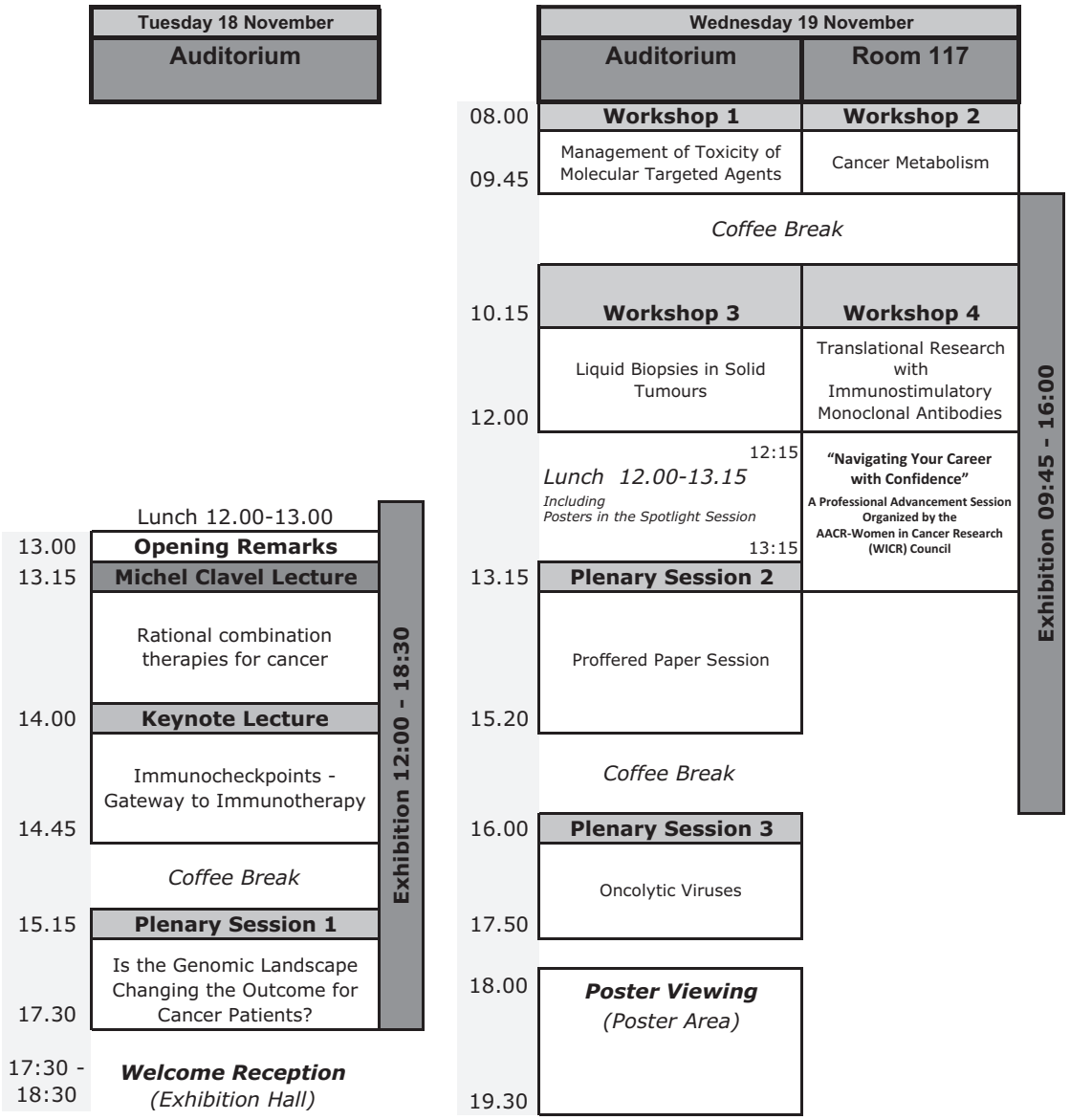
Scientific Programme – Overview



Posters

Animal Models

Cytotoxics

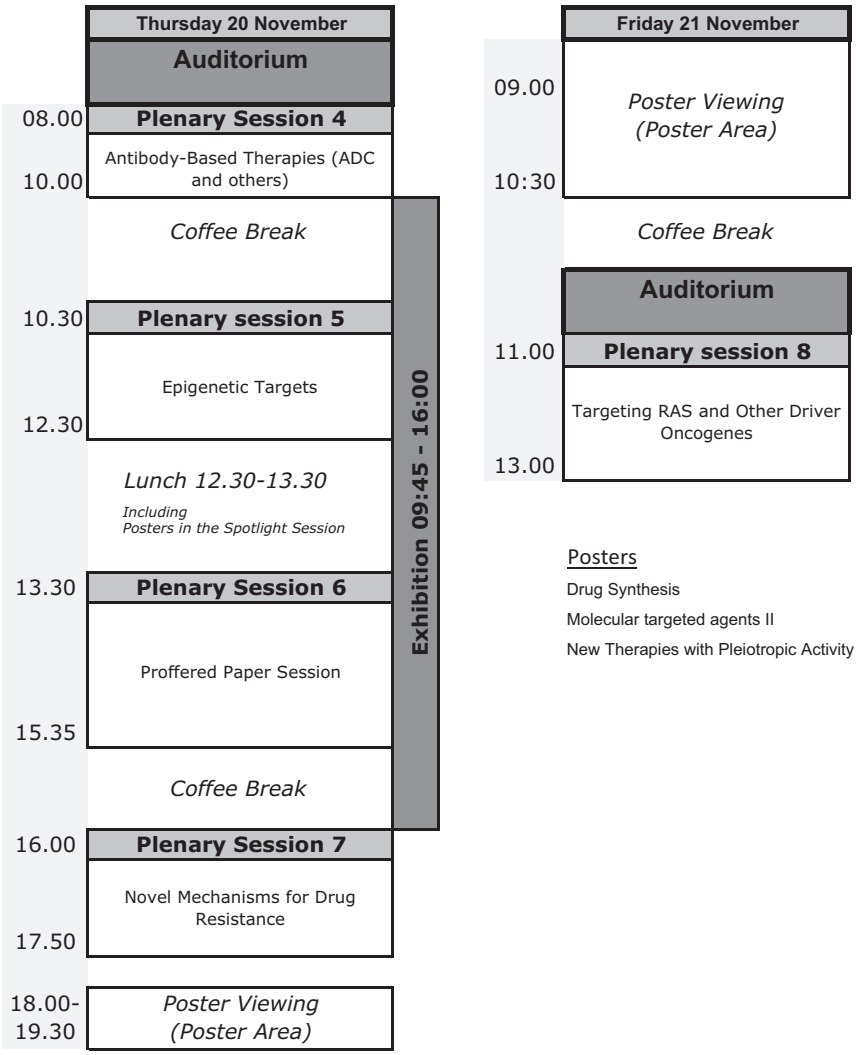
Drug Resistance and Modifiers

Drug Screening

Immunotherapy (Immunecheckpoints, Vaccination, Oncolytic viruses, Cytokines)

Preclinical Models

Radiation Interactive Agents



Networking Event

Posters

Chemoprevention

Clinical Methodology

DNA Repair Modulation (including PARP, CHK, ATR, ATM)

Drug Delivery

Drug Design

Molecular Targeted Agents I

Paediatric Oncology

Toxicology

Posters

Drug Synthesis

Molecular targeted agents II

New Therapies with Pleiotropic Activity

Scientific Programme – Details

Tuesday 18 November 2014

Opening Ceremony **Auditorium**

13:00–13:15 Opening Remarks

13:00	*J.C. Soria (France)*	EORTC
13:05	*L.J. Helman (USA)*	NCI
13:10	*J.A. Engelman (USA)*	AACR

13:15–14:00 **Michel Clavel Lecture** **Auditorium**
Chair: J.C. Soria (France)

13:15 Rational combination therapies for cancer
R. Bernards (Netherlands)

14:00–14:45 **Keynote Lecture** **Auditorium**
Chair: A.M.M. Eggermont (France)

14:00 Immunocheckpoints – Gateway to Immunotherapy
D. Chen (USA)

Objectives:
1. Understand how cancer immunotherapy works, the cancer-immunity cycle and what makes it different from other forms of cancer therapy.
2. Understand what rationale approaches can be taken to monotherapy and combination therapy involving cancer immunotherapy.
3. Understand the role for biomarkers in understanding emerging immune biology, interpreting clinical results and identifying optimal treatment decisions.

Key Messages:
1. Our understanding of how the immune system interacts with cancer is rapidly evolving.
2. Cancer immunotherapy approaches may be able to generate durable responses in patients with metastatic cancer.
3. Emerging biomarkers may be able to help us understand biology, define combination approaches and choose between therapeutic options.

Plenary Session 1 **Auditorium**

15:15–17:30 **Is the Genomic Landscape Changing the Outcome for Cancer Patients?** Abstract number
Chairs: R. Stupp (Switzerland) and J. Tabernero (Spain)

15:15 Overview of academic precision medicine trials
P. Bedard (Canada)

15:35 Lessons from SAFIR01 trial
F. Andre (France)

Main objectives:
1. Understand the pillars of personalised medicine.
2. Understand the main reasons of failures to deliver personalised medicine.
3. Understand what are the possible solutions to address these limitations.

Key messages:
1. There is a need for randomised trials before implementing multigene tools for personalised medicine.
2. Drug availability and rules to interpret genome data are mandatory.
3. Genome analysis will not provide all the informations needed to deliver personalised medicine.

15:55 Translating gene expression signatures into clinical practice: prospects and challenges in the context of 'next-generation medicine'
R. Dienstmann (USA)

Key messages:
1. There are unique issues with high-dimensional data that represent obstacles to generating performant genomic signature classifiers and translating initial research findings into robust diagnostics.
2. Better understanding of the intrinsic gene expression-based subtypes of a histopathologically defined cancer, independent of their prognostic and predictive values, may also lead to new biological insights and eventually to development of novel therapies directed toward homogeneous molecular subsets.
3. A rational and focused approach to the evaluation of genomic markers is needed, whereby analytically validated assays are prospectively investigated in clinical trials with adaptive designs that take into consideration primary–metastatic site tumour heterogeneity and clonal evolution in the decision-making process.

16:15 Genomic characterisation of cancer: Case studies
E.R. Mardis (USA)

Key objectives:
1. Provide detailed description of the molecular assays being used to characterise the cancer mutations and their expression in RNA for individual patients.
2. Describe the analytical approaches that permit integrated analysis of mutations and RNA expression toward two therapeutic ends: (1) identification of small molecule therapies that may provide relief of tumour burden, (2) identification of immunoepitopes that may contribute toward a personalised vaccine strategy for individual patients.
3. Illustrate the two aforementioned objectives by detailed descriptions of specific case studies from our work in this area of applied cancer genomics.

16:35 Screening Patients for Efficient Clinical Trial Access (SPECTA)
D. Lacombe (Belgium)

Key messages:
1. Cancer drug development is undergoing profound changes and the path to registration will be substantially altered due to challenges of big data (omics).
2. The forms and the methods of cancer clinical research are evolving with the need to integrate new technologies to understand biology early on in development. New efficient platforms for patient access (molecularly defined subgroups) are needed.
3. Clinical oncology will need to take into account new type of guidelines for treatment decision with an increased role played by molecular advisory boards.

16:55 ORAL PRESENTATION: Feasibility of large-scale genomic testing to facilitate enrollment on genomically-matched clinical trials 1
F. Meric-Bernstam, L. Brusco, S. Kopetz, M. Davies, M.J. Routbort, S.A. Piha-Paul, R. Alvarez, S. Khose, J. DeGroot, V. Ravi, F. Janku, D. Hong, Y. Li, R. Luthra, K.P. Patel, R. Broaddus, K. Shaw, J. Mendelsohn, G.B. Mills

17:10 General discussion
J. Tabernero (Spain)

17:15 Faster execution of clinical trials – has bioinformatics the solution?
G. McVie (Italy)

Wednesday 19 November 2014

Workshop 1 **Auditorium**

08:00–09:45 **Management of Toxicity of Molecular Targeted Agents**
Chairs: J.C. Soria (France) and P. Bedard (Canada)

08:00 Cardiac toxicities with MOA and TKI
S. Ederhy (France)

08:20 Digestive and endocrine toxicities of checkpoint inhibitors
N. Chaput (France)

Main objectives:
1. To describe digestive toxicities (clinic/endoscopic/histological) in patients treated with anti-CTLA4 and/or anti-PD1.
2. To describe immune disorders in patients developing digestive toxicities (blood and colonic biopsies).

Key messages:
1. Anti-CTLA-4 and/or anti-PD-1, monoclonal antibody treatment of cancer, are associated with several phenotypes of enterocolitis.
2. Intestinal inflammation observed in patients who were prescribed anti-CTLA-4, anti-PD1 or both, have distinct phenotypes: anti-CTLA-4 is associated with acute, often severe colitis, chronic duodenitis and less often with ileal and anal lesions. Anti-PD-1 seems to be associated with mild, chronic colitis. The combination of anti-CTLA-4 and anti-PD1 seems to lead to severe duodenal inflammation and severe colitis.
3. Anti-CTLA-4 colitis appears as a model of T-cell induced colitis in humans as suggested by the immune monitoring of patients.

08:40 Management of pulmonary toxicity due to targeted anticancer agents
J. Porter (United Kingdom)

09:00 Ocular toxicity of MEK inhibitors and other targeted therapies
J.P. Velazquez-Martin (Canada)

Main objectives:
1. Identify the key agents associated with ocular toxicities.
2. Identify symptoms and clinical findings associated with ocular toxicity.
3. Learn the management, follow up and prognosis of these patients.

Key messages:
1. Ocular toxicities from targeted therapies are frequent.
2. Symptoms range from none to moderate visual impairment.
3. Always consult with an ophthalmologist or retina specialist (preferable).

09:20 Discussion

Workshop 2 **Room 117**

08:00–09:45 **Cancer metabolism**
Chairs: C. Van Dang (USA) and G. Hardie (United Kingdom)

08:00 AMPK – opposing the metabolic changes in tumour cells
G. Hardie (United Kingdom)

Key messages:
1. The AMP-activated protein kinase (AMPK) is a highly conserved sensor of cellular energy status that is switched on by metabolic stresses causing depletion of cellular ATP, such as ischaemia (a frequent event within solid tumours).
2. Most tumour cells (and other rapidly proliferating cells) display elevated glucose uptake and glycolysis (the Warburg effect); this occurs in part because the TCA cycle is being used as an anabolic pathway providing precursors for biosynthesis, and can no longer satisfy the increased demand for ATP caused by activation of biosynthetic pathways.

3. By inactivating most biosynthetic pathways and promoting oxidative metabolism rather than glycolysis, AMPK opposes these metabolic changes; this explains why the pathway is often down-regulated in tumour cells, but also why AMPK-activating drugs have potential in the treatment or prevention of cancer.

08:20 IDH1/IDH2
D.P. Schenkein (USA)

Key messages:
1. Cancer metabolism, a newly validated area for oncology drug discovery.
2. Mutations in the metabolic enzyme IDH are present in a wide range of malignancies and increasingly recognised in pre-malignant conditions: the role of 2-HG as an oncometabolite.
3. Clinical trial results from the first IDH inhibitor, AG-221: significant single agent activity in AML, excellent safety profile, and a novel mechanism of action.

08:40 Targeting MYC-driven Glutaminolysis
C. Van Dang (USA)

09:00 Identification of novel inhibitors of GLUT1 as potent cancer cell-killing agents
A. Wise (United Kingdom)

Key objectives:
1. Demonstrate chemical tractability of the glucose transporter GLUT1 as a drug target by identifying a lead series of potent and selective small molecule inhibitors.
2. Demonstrate in vitro validation of GLUT1 as a therapeutic target in cancer by utilising our novel GLUT1 inhibitors as tool compounds.
3. Demonstrate in vivo validation of GLUT1 as a therapeutic target in cancer by utilising our novel GLUT1 inhibitors as tool compounds.

09:20 Discussion

Workshop 3 **Auditorium**

10:15–12:00 **"Liquid Biopsies" in Solid Tumours**
Chairs: K. Dhingra (USA) and A. Bardelli (Italy)

10:15 Application of CTC detection technologies in oncology clinical trials
J.S. De Bono (United Kingdom)

Key objectives:
Showing that circulating blood biomarkers can have clinical utility as multi-purpose biomarkers as
1. Prognostic biomarkers.
2. Predictive biomarkers
3. Response and surrogate biomarkers.

10:35 Cancer mutation and transcriptome analysis in exosomes
J. Skog (USA)

Key objectives:
1. What is an exosome and what do they contain?
2. What is the benefit of analyzing exosome nucleic acids?
3. What do you need for successful analysis of exosomal RNA, and what types of analysis are possible?

10:55 cfDNA for detection of actionable cancer mutations
C. Caldas (United Kingdom)

11:15 Precision medicine for colorectal cancers: liquid biopsies and preclinical models
A. Bardelli (Italy)

Key objectives:
1. Understanding the molecular bases of secondary resistance to EGFR blockade in CRC is necessary to design additional therapeutic options.
2. Molecular alterations in KRAS, NRAS, and MET are causally associated with the onset of acquired resistance to anti-EGFR antibodies in colorectal cancers.

3. Development of a diagnostic platform to detect 'molecular resistance' in the blood (liquid biopsy) months before clinical or radiographic evidences of disease progression.

11:35 Discussion

Workshop 4 **Room 117**

10:15–12:00 **Translational Research with Immunostimulatory Monoclonal Antibodies**
Chairs: J. Tabernero (Spain) and I. Melero (Spain)

10:15 The making of new immunotherapy agents
A. Korman (USA)

10:35 Translational research of combined immunotherapies
I. Melero (Spain)

11:05 Biomarkers for new immunotherapies
M. Calahan (USA)

11:25 The interface of immunomodulation and vaccines
A. Van Elsas (NL)

Key messages:
1. Cancer vaccines enhance anti-tumour immune responses when used prophylactically, but lack robust efficacy in therapeutic setting.
2. Several immunomodulatory receptor-ligand pathways regulate T cell responses to cancer and vaccines.
3. Experimental combinations of cancer vaccines and immunomodulatory antibodies display efficacy in preclinical models of established cancer.

11:45 Discussion

12:15–12:45 **Posters in the Spotlight Session** **Exhibition Hall**
Moderator: R. Plummer (United Kingdom)

The following abstracts will be discussed: 364 (poster board P144), 161 (P155), 422 (P155).

Professional Advancement Session **Room 117**

12:15–13:15 **"Navigating Your Career with Confidence" – A Professional Advancement Session Organized by the AACR-Women in Cancer Research (WICR) Council**
Chair: P. LoRusso (USA)

Feel and project more confidence when seeking new career opportunities. This session will include an inspirational Keynote Lecture from Susan M. Galbraith, MBBCh, PhD, Vice President of Oncology, AstraZeneca, as well as a panel of professionals discussing the ways that women scientists in particular can bolster their confidence and overcome insecurities in order to embrace new opportunities. The panel will address topics such as assessing which career opportunities are a good fit, improving a resume or portfolio in order to secure an interview, blending personal and career life once on the job, and more.

Although all conference attendees are invited to attend this session, it is geared toward early-career female investigators.

Welcome
P. LoRusso (USA)

Keynote
S.M. Galbraith (United Kingdom)

Panel Discussion
Susan M. Galbraith (United Kingdom), M. Foti (USA), F. Meunier (Belgium)

Audience Engagement (Q&A)

Closing Remarks and Evaluation
P. LoRusso (USA)

Plenary Session 2 **Auditorium**

13:15–15:20 **Proffered Paper Session** Abstract number

Chairs: C. Arteaga (USA) and R. Plummer (United Kingdom)

13:15 Target validation as a crucial bottleneck in cancer drug discovery
P. Workman (United Kingdom)

Key objectives:
1. To illustrate the challenges of identifying and prioritising new cancer targets in the multiomics era and to show how target validation is a critical bottleneck in cancer drug discovery.
2. To exemplify the above with case histories from our recent research discoveries concerning potential molecular targets in the areas of oncogenic kinases and the HSP90 molecular chaperone pathway.
3. To set out criteria for robust target validation, including the use of genetic techniques and chemical probes, so as to give the best chance of clinical impact.

13:35 ORAL PRESENTATION: Safety and early evidence of activity of a first-in-human phase I study of the novel cancer stem cell (CSC) targeting antibody OMP-52M51 (anti-Notch1) administered intravenously to patients with certain advanced solid tumors 2
A. Patnaik, P. LoRusso, P. Munster, A.W. Tolcher, S.L. Davis, J. Heymach, R. Ferraroto, L. Xu, A.M. Kapoun, L. Faoro, J.A. Lewicki, J. Dupont, S.G. Eckhardt

13:50 ORAL PRESENTATION: Afuresertib (GSK2110183), an oral AKT kinase inhibitor, in combination with carboplatin and paclitaxel in recurrent ovarian cancer 3
S. Blagden, A. Hamilton, L. Mileshkin, M. Hall, T. Meniawy, S. Wong, S. Anandra, M. Buck, D. McAleer, B.A. Reedy, R.B. Noble, D.A. Smith, S.R. Morris, H. Gabra

14:05 ORAL PRESENTATION: Activity of galeterone in castrate-resistant prostate cancer (CRPC) with C-terminal AR loss: Results from ARMOR2 4
M.E. Taplin, K.N. Chi, F. Chu, J. Cochran, W.J. Edenfield, E.S. Antonarakis, U. Emmenegger, E.I. Heath, A. Hussain, V.C. Njar, A. Koletsky, D. Lipsitz, L. Nordquist, R. Pili, M. Rettig, O. Sartor, N.D. Shore, D. Marrinucci, K. Mamlouk, B. Montgomery

14:20 ORAL PRESENTATION: Mechanism based targeted therapy for hereditary leiomyomatosis and renal cell cancer (HLRCC) and sporadic papillary renal cell carcinoma: interim results from a phase 2 study of bevacizumab and erlotinib 5
R. Srinivasan, D. Su, L. Stamatakis, M.M. Siddiqui, E. Singer, B. Shuch, J. Nix, J. Friend, G. Hawks, J. Shih, P. Choyke, W.M. Linehan

14:35 ORAL PRESENTATION: Imaging in cancer immunology: Phenotyping of multiple immune cell subsets in-situ in FFPE tissue sections 6
J.R. Mansfield, C. Slater, C. Wang, K. Roman, C.C. Hoyt, R.J. Byers

14:50 LATE BREAKING ABSTRACT: Clinical safety and activity in a phase I trial of AG-120, a first in class, selective, potent inhibitor of the IDH1-mutant protein, in patients with IDH1 mutant positive advanced hematologic malignancies 1LBA
D.A. Pollyea, S. de Botton, A.T. Fathi, E.M. Stein, M.S. Tallman, S. Agresta, C. Bowden, B. Fan, M. Prah, H. Yang, K. Yen, R.M. Stone

15:00 LATE BREAKING ABSTRACT: The identification of potent and selective inhibitors of oncogenes in medullary thyroid carcinoma and lung adenocarcinoma disease models 2LBA
S. Fritzl, H. Small, B. Acton, S. Holt, G. Hopkins, S. Jones, A. Jordan, N. March, R. Newton, I. Waddell, B. Waszkowycz, M. Watson, D. Ogilvie

15:10 Discussion Late Breaking Abstracts
C.L. Arteaga (USA)

Plenary Session 3 **Auditorium**

16:00–17:50 **Oncolytic Viruses** Abstract number

Chairs: K. Harrington (United Kingdom) and L.J. Helman (USA)

16:00 T-VEC for the treatment of melanoma: Are we ready for prime time?
H. Kaufman (USA)

16:20 Poliovirus oncolytic immunotherapy of glioblastoma
M. Gromeier (USA)

Key objectives:
1. Discuss the role of mechanisms of viral tumour cell killing in oncolytic immunotherapy.
2. Define principles of efficacious oncolytic immunotherapy: explain the role of the innate antiviral response to oncolytic poliovirus.
3. Communicate the major clinical/radiographic findings from oncolytic immunotherapy of recurrent glioblastoma with recombinant poliovirus.

16:40 Measles and vesicular stomatitis virus strains as novel oncolytic platforms
E. Galanis (USA)

17:00 Challenges in clinical development of oncolytic viruses
K. Harrington (United Kingdom)

17:20 LATE BREAKING ABSTRACT: Initial report of a first-in-human study of the first-in-class fatty acid synthase (FASN) inhibitor, TVB-2640 3LBA
J. Infante, M. Patel, D. Von Hoff, A. Brenner, C. Rubino, W. McCulloch, V. Zhukova-Harrill, M. Parsey

17:30 LATE BREAKING ABSTRACT: A phase 1 study of first-in-class microRNA-34 mimic, MRX34, in patients with hepatocellular carcinoma or advanced cancer with liver metastasis 4LBA
M. Beg, A. Brenner, J. Sachdev, M. Borad, J. Cortes, R. Tibes, Y. Kang, A. Bader, J. Stoudemire, S. Smith, S. Kim, D. Hong

17:40 Discussion Late Breaking Abstracts
L.J. Helman (USA)

18:00–19:30 **Poster Viewing** **Poster area**

Animal Models

Poster board		Abstract number
P001	Mouse clinical trial – A new preclinical study concept using patient-derived xenografts *V. Vuaroqueaux, C. Gredy, S. Gorynia, S. Baltes, H.H. Fiebig, T. Metz*	7
P002	Imaging growth and anti-cancer activity in orthotopic patient derived tumors *M. Baugher, C. Bull, A. Cohen-Barnhouse, A. Flecha, M. Franklin, K. Guley, P. McConville, W.R. Leopold*	8
P003	Antineoplastic effects of auranofin in canine lymphoma *D. Thamm, B.J. Rose, J.K. Shoeneman*	9
P004	mTOR inhibition with everolimus – a novel treatment option for head and neck cancer identified in a translational research study using patient-derived xenografts *K. Klinghammer, J.D. Raguse, T. Plath, A.E. Albers, B. Brzezicha, A. Wulf-Goldenberg, U. Keilholz, J. Hoffmann, I. Fichtner*	10
P005	A panel of patient derived xenograft models of different haematological malignancies suitable for preclinical drug screening campaigns *E. Oswald, C. Tschuch, K. Klingner, B. Hammerich, D. Lehnhard, C. Rentsch, M. Lübbert, H.H. Fiebig, J. Schüler*	11
P006	Next generation sequencing (NGS) guided therapy prediction for the treatment of glioblastoma multiforme (GBM) *J. Sarkaria, D.M. Ma, S.P. Peng, S.B. Byron, D.C. Craig, J.C. Carpten, M.B. Berens, B.O. O'Neill, N.T. Tran*	12
P007	Whole exome sequence analysis of canine transitional cell carcinoma of the bladder *D.L. Duval, B. Hernandez, J. Brown, S.E. Lana, R. Page, K.L. Jones*	13
P008	Mixeno mouse models for in vivo evaluation of anti-human cancer immunotherapeutics *J. Zhang, J. Qiu, M. Qiao, Q. Shi*	14
P009	Genetic and molecular validation of uterine sarcoma patient-derived xenograft models *T. Cuppens, E. Hermans, J. Depreeuw, M. Moisse, T. Van Brussel, L. Coenegrachts, D. Lambrechts, F. Amant*	15

Cytotoxics

Poster board Abstract number

Poster board Abstract number

Drug Resistance and Modifiers

Poster board Abstract number

Drug Screening

Poster board Abstract number

Immunotherapy (Immunecheckpoints, Vaccination, Oncolytic viruses, Cytokines)

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

P132 Preclinical activity and safety of MGD006, a CD123xCD3 Bispecific DART® molecule for the treatment of hematological malignancies 138
P. Moore, G.R. Chichili, L. Huang, H. Li, S. Burke, F. Chen, L. He, Q. Tang, L. Jin, S. Gorlatov, V. Ciccarone, S. Koenig, M. Shannon, R. Alderson, S. Johnson, E. Bonvini

P133 GBR1302: a BEAT® bispecific antibody for the treatment of HER2 positive cancers 139
A. Croset, J. Macoin, R. Ollier, M. Pluess, C. Delon, D. Skegro, S. Blein, S. Hou, J. Back

P134 Relationship between programmed death ligand 1 (PD-L1) expression and clinical outcome in patients (pts) with melanoma (MEL) treated with pembrolizumab (pembro; MK-3475) 140
A. Daud, O. Hamid, C. Robert, F.S. Hodi, J.D. Wolchok, W.J. Hwu, J.S. Weber, R. Kefford, P. Hersey, A.M. Joshua, R. Joseph, T.C. Gangadhar, R. Dronca, A. Patnaik, H. Zarour, K. Gerigich, J. Lunceford, K. Emancipator, M. Dolled-Filhart, X. Li, P. Kang, S. Ebbinghaus, A. Ribas

P135 Phase I study of ipilimumab with stereotactic radiosurgery for melanoma patients with brain metastases 141
W. Shi, E. Wuthrick, K. Feeney, M. Werner-Wasik, D.W. Andrews, J.J. Evans, K. Judy, C. Farrell, A.P. Dicker

P136 IL-17 as a novel molecular target for prostate cancer prevention 142
A. De Angulo, R. Faris, C. Jolly, L. deGraffenried

Preclinical Models

Poster board Abstract number

P137 Regional bias of intratumoral genetic heterogeneity of nucleotide repeats in colon cancers with microsatellite instability 143
C. An, Y. Choi, M. Kim, J. Lee, N. Yoo, S. Lee

P138 Association between interleukin 17/interleukin 17 receptor gene polymorphism and papillary thyroid cancer 144
Y. Eun, H. Chung, Y.C. Lee

P139 ARQ 087, a novel pan FGFR-inhibitor crosses the BBB (blood–brain barrier) and distributes to the brain of rats 145
R. Savage, T. Hall, B. Schwartz

P140 Establishment of patient-derived xenografts (PDX) models for triple negative breast cancer (TNBC) as a pre-clinical platform for drug development 146
J. Thatte, M. Meza, J. Ricono, T. Broudy, C. Mirsaidi, P. Nair

P141 An integrated approach for identifying E-cadherin synthetic lethality networks 147
I. Bajrami, S.J. Pettitt, R. Brough, H. Pemberton, D. Kastrev, Y. Fontebasso, J. Frankum, J. Campbell, A. Ashworth, C.J. Lord

P142 RAS synthetic lethal interactions from yeast to human cells 148
S. van Wageningen, A. Prahallad, G. Heynen, R. Rothstein, R. Bernards

P143 Quantitative mutational assessment of circulating tumor DNA using massively parallel deep sequencing in plasma and urine from advanced colorectal cancer patients 149
J.C. Poole, C.R.T. Vibat, L. Benesova, B. Belsanova, S. Hancock, T.L. Lu, M.G. Erlander, M. Minarik

P144 Pirin downregulates E-cadherin gene expression and contributes to EMT 150
K. Komai, Y. Niwa, Y. Sasazawa, S. Simizu

P145 Impact of EGFR amplification pattern on the expression of miRNA-200c in primary glioblastoma multiforme 151
L. Muñoz Hidalgo, C. López Gines, E. Serna, D. Monleon, R. Callaghan, R. Gil Benso, H. Martinetto, A. Gregori Romero, J. Gonzalez Darder, M. Cerda Nicolas

P146 Preclinical characterization of MM-151, an oligoclonal antibody therapeutic that targets EGFR by three distinct mechanisms of action 152
A. King, M. Sevecka, N. Gerami-Moayed, O. Burenkova, J. Kearns, G. Tan, C. Sloss, R. Bukhalid, U. Nielsen, B. Wolf

Poster board Abstract number

Poster board Abstract number

Radiation Interactive Agents

Thursday 20 November 2014

Plenary Session 4 **Auditorium**

08:00–10:00 **Antibody-Based Therapies (ADC and others)** Abstract number

Chairs: A. Tolcher (USA) and N. Gökbuget (Germany)

08:00 Antibody mediated payload delivery: Cautionary lessons from 20 years of clinical trials
A. Tolcher (USA)

Key objectives:
1. Understand the disconnect between activity with antibody drug conjugates (ADC) in preclinical models versus clinical results.
2. Understand the multiple challenges associated with ADCs as a drug from the 3 components: antibody, linker and payload.
3. Understand patient selection based on target and potential mitigation strategies when the target is also expressed on normal tissues.

08:20 Challenging the dogmas: Clinical efficacy of SN38 conjugated antibodies in solid tumours
D.A. Goldenberg (USA)

Key objectives:
1. Discuss current status and challenges of antibody-drug conjugates (ADC) in solid cancer therapy.
2. Supertoxic drugs used in ADC may compromise therapeutic index.
3. A moderate cytotoxic drug in an ADC may allow higher doses and a higher therapeutic index.

08:40 Targeted alpha particle therapy for haematologic malignancies
J. Jurcic (USA)

Key objectives:
1. List the advantages and disadvantages of targeted alpha-particle therapy.
2. Summarise the results of recent clinical trials using targeted alpha-particle therapy for the treatment for haematologic malignancies.
3. Describe the results of recent preclinical studies using alternative radioisotopes and pre-targeting strategies.

09:00 Bispecific T-cell engaging antibodies in acute leukaemia – Recent advances and future challenges
Speaker: N. Gökbuget (Germany)

Key messages:
1. Relapsed and refractory ALL has a very poor outcome and there is an urgent medical need for new, alternative treatment options.
2. Blinatumomab is a bispecific antibody which represents a new treatment principle based redirected cell kill of CD19 positive target cells by T-cells.
3. Reponse rates are promising and the compound is currently studied in a randomised trial.

09:20 ORAL PRESENTATION: Pre-clinical and translational pharmacology, pharmacokinetics and pharmacodynamics for a humanized anti-OX40 antibody MOXR0916, a T-cell agonist in the treatment of solid tumors 209
S. Sukumaran, J.M. Kim, M. Huseni, J. Ruppel, H. Taylor, K. Totpal, J. Zhu, C. Zhang, H. Chiu, E.G. Stefanich

09:35 ORAL PRESENTATION: A phase 1 study of KTN3379, a human anti-ErbB3 monoclonal antibody in patients with advanced cancers 210
P. LoRusso, T. LaVallee, L. Kimmel, C. Lubeski, R. Gedrich, C. Sidor

09:50 General discussion
A. Tolcher (USA)

Plenary Session 5 **Auditorium**

10:30–12:30 **Epigenetic Targets** Abstract number

Chairs: K. Helin (Denmark) and T. Helleday (Sweden)

10:30 Histone demethylases and methyltransferases as novel targets for cancer therapeutics
K. Helin (Denmark)

10:50 DOT1 and EZH2 targeted therapies
R. Copeland (USA)

Key messages:
1. EZH2 plays a critical role in normal B-cell maturation and is frequently dysregulated in germinal center-derived lymphomas.
2. EPZ-6438 is a potent and selective inhibitor of EZH2 that demonstrates robust and durable anti-lymphoma activity in preclinical animal models both as a single agent and in combination with standards of care.
3. EPZ-6438 is the first EZH2 inhibitor to enter human clinical studies and early observations from this clinical trial will be discussed.

11:10 Targeting non-oncogene addiction with MTH1 inhibitors
T. Helleday (Sweden)

11:30 ORAL PRESENTATION: A novel synthetic lethal interaction between the histone mark H3K36me3 and checkpoint kinases 211
S.X. Pfister, E. Markkanen, Y. Jiang, S. Sarkar, V. D'Angiolella, G. Dianov, A.J. Ryan, T.C. Humphrey

11:45 ORAL PRESENTATION: Novel anti-tumor activity of targeted LSD1 inhibition by GSK2879552 212
H. Mohammad, K. Smitheman, G. Van Aller, M. Cusan, S. Kamat, Y. Liu, N. Johnson, C. Hann, S. Armstrong, R. Kruger

12:00 LATE BREAKING ABSTRACT: Results of a first-in-man phase I trial assessing OTX015, an orally available BET-bromodomain (BRD) inhibitor, in advanced hematologic malignancies 5LBA
A. Stathis, B. Quesnel, S. Amorim, C. Thieblemont, E. Zucca, E. Raffoux, H. Dombret, Y. Peng, A. Palumbo, N. Vey, X. Thomas, M. Michallet, C. Gomez-Roca, C. Recher, L. Karlin, K. Yee, K. Rezai, C. Preudhomme, T. Facon, P. Herait

12:10 LATE BREAKING ABSTRACT: Phase 1 first-in-human study of the enhancer of zeste-homolog 2 (EZH2) histone methyl transferase inhibitor E7438 as a single agent in patients with advanced solid tumors or B cell lymphoma 6LBA
V. Ribrag, J.C. Soria, L. Reyderman, R. Chen, P. Salazar, N. Kumar, G. Kuznetsov, H. Keilhack, L.H. Ottesen, A. Italiano

12:20 Discussion Late Breaking Abstracts
T. Helleday (Sweden)

12:45–13:15 **Posters in the Spotlight Session** **Exhibition Hall**

Moderator: E. Calvo (Spain)

The following abstracts will be discussed: 41 (poster board P035), 195 (P189) and one to be announced.

Plenary Session 6 **Auditorium**

13:30–15:35 **Proffered Paper Session** Abstract number

Chairs: E. Calvo (Spain) and J. Doroshow (USA)

13:30 ORAL PRESENTATION: A phase I dose-finding study of BI 853520, a potent and selective inhibitor of focal adhesion kinase (FAK), in Japanese and Taiwanese patients with advanced or metastatic solid tumors 213
T. Doi, C.C. Lin, A. Ohtsu, J.C.H. Yang, K. Shitara, L.C. Pronk, A. Sarashina, A.L. Cheng

13:45 ORAL PRESENTATION: Homologous recombination deficiency (HRD) score and niraparib efficacy in high grade ovarian cancer 214
P. Haluska, K.M. Timms, M. AlHilli, Y. Wang, A.M. Hartman, J. Jones, A. Gutin, Z. Sangale, C. Neff, J. Lynchbury, L. Rudolph-Owen, M.A. Becker, S. Agarwal, K.M. Wilcoxen

14:00 ORAL PRESENTATION: Updated clinical and preliminary correlative results of ARIEL2, a Phase 2 study to identify ovarian cancer patients likely to respond to rucaparib 215
E. Swisher, J. Brenton, S. Kaufmann, A. Oza, R.L. Coleman, D. O'Malley, G. Konecny, L. Ma, M. Harrell, D. Visscher, A.W. Hendrickson, K. Lin, M. Raponi, E. Mann, H. Giordano, L. Maloney, L. Rolfe, I. McNeish

14:15 ORAL PRESENTATION: Phase I study of panobinostat and fractionated stereotactic re-irradiation therapy (FSRT) for recurrent high grade gliomas 216
W. Shi, Y.R. Lawrence, M. Werner-Wasik, D.W. Andrews, J.J. Evans, J. Glass, L. Kim, V. Bar Ad, Y. Moshel, K. Judy, C. Farrell, N.L. Simon, A.P. Dicker

14:30 ORAL PRESENTATION: Results of a phase I, open-label, multicentre study to assess the safety, tolerability, pharmacokinetics and preliminary anti-tumour activity of AZD9150 in patients with advanced/metastatic hepatocellular carcinoma 217
Y.K. Kang, B.Y. Ryoo, T.Y. Kim, K.H. Lee, H.Y. Lim, S.J. Lee, M. Ikeda, T. Okusaka, S. Nadano, C.C. Lin, T.P. Poon, C.J. Yen, P. McCoon, F. Neumann, K. Vishwantahan, R. DuPont, P. Lyne

14:45 ORAL PRESENTATION: Genomic analysis identifies novel drivers and targetable pathways in inflammatory breast cancer patient samples 218
D.M. Moran, K. Rao, P. Bacon-Trusk, K. Pry, V. Weigman, V. Velculescu, M. Cristofanilli, S. Bacus

15:00 ORAL PRESENTATION: Phase I trial evaluating the antiviral agent Cidofovir in combination with chemoradiation in cervical cancer patients: A novel approach to treat HPV related malignancies? 219
E. Deutsch, A. Levy, R. Mazeron, A. Gazzah, E.A. Angevin, V. Ribrag, R. Balheda, A. Varga, C. Lhomme, C. Haie-Meder, J.C. Soria

15:15 LATE BREAKING ABSTRACT: Phase 1 dose-expansion study of AMG 900, a pan-Aurora kinase inhibitor, in adult patients with advanced taxane-resistant solid tumors 7LBA
B. Markman, D. Mahadevan, S. Hurvitz, D. Kotasek, M. Shaheen, M. Carducci, O. Goodman, X. Jiang, V. Chow, G. Juan, G. Friberg, E. Gamelin, J. Desai

15:25 Discussion Late Breaking Abstract
J. Doroshow (USA)

Plenary Session 7 **Auditorium**

16:00–17:50 **Novel Mechanisms for Drug Resistance** Abstract number
Chairs: U. Banerji (United Kingdom) and S.A. Courtneidge (USA)

16:00 Genomic instability, diversity and resistance during cancer evolution
N. McGranahan (United Kingdom)

Key messages:
1. Driver mutations are often subclonal in non-small cell lung cancer (NSCLC), potentially comprising the efficacy of targeted therapy approaches.
2. A single NSCLC tumour may follow multiple distinct evolutionary trajectories simultaneously, with mutational processes varying over space and time.
3. NSCLCs have a long period of tumour latency prior to clinical detection.

16:20 Immune-scape to PD1/PDL1 blockade
D. Chen (USA)

Key objectives:
1. Understand what responses and durability of responses looks like for cancer immunotherapy and PD-L1/PD-1 inhibitors to date.
2. Understand potential reasons for primary resistance.
3. Understand potential reasons for secondary resistance.

Messages:
1. Responses to PD-L1/PD-1 inhibitors appear highly durable, but not every patient responds and not every responding patient is "cured".
2. Primary resistance may be driven by lack of adequate active anti-cancer T cell immune responses in tumours.
3. It is too early to tell what might account for secondary resistance, but it could involve factors that lead to fluctuations in immunity and a break in the cancer-immunity cycle.

16:40 EMT as mechanism of resistance to TKI
J.P. Thiery (Singapore)

Key objectives:
1. Malignant cells harbor numerous genetic alterations at the time of clinical detection. The mutational landscape is extraordinarily complex, exhibiting considerable heterogeneity within the primary tumour, in circulating tumour cells and in metastases.
2. These findings are in support of the original hypothesis of clonal evolution, and suggest that the current therapeutics strategies must be revisited to delay the onset of tumour refractoriness.
3. It is imperative to develop treatment strategies that do not strictly rely on specific activating mutations. In particular, one can leverage on the Epithelial–Mesenchymal Transition (EMT) status of a tumour, as it has an impact on the tumour's potential to progress and resist treatment. This can be achieved by establishing an EMT score for each tumour along the EMT spectrum. Targeted therapeutics can then be used to move the tumour along the EMT spectrum rather than inhibiting its growth in order to improve its response to conventional therapeutics and to restore the body's immune response.

17:00 The landscape of kinase fusions in cancer
C. Lengauer (USA)

Key messages:
1. We have performed a pan-cancer analysis of kinase fusions across all TCGA RNA-seq data (>7,000 samples).
2. Our analysis unveiled several new and recurrent kinase fusions. Overall, kinase fusions are a driver event in at least 3% of solid tumours.
3. These discoveries have profound and immediate implications for the diagnosis and treatment of cancer patients, as well as potential avenues for new drug discovery programmes.

17:20 ORAL PRESENTATION: Overcoming drug-resistance in multiple myeloma by XPO1 inhibitor combination therapy 220
J. Turner, J. Dawson, S. Grant, K. Shain, C. Cubitt, Y. Dai, L. Zhoui, M. Kauffman, S. Shacham, D. Sullivan

17:35 LATE BREAKING ABSTRACT: Activity of the PARP inhibitor olaparib in ATM-deficient gastric cancer: from preclinical models to the clinic 8LBA
D. Hodgson, H. Mason, L. Oplustilova, C. Harbron, X. Yin, S.A. Im, H. Jones, L. Zhongwu, B. Dougherty, M. McLoughlin, A. Dickinson, A. Fielding, J. Robertson, W.H. Kim, C. Womack, Y. Gu, Y.J. Bang, A. Lau, J.C. Barrett, M.J. O'Connor

17:45 Discussion Late Breaking Abstract
U. Banerji (United Kingdom)

18:00–19:30 **Poster Viewing** **Poster area**

Chemoprevention

Poster board — Abstract number

P001 Docosahexaenoic acid along with modulation of actin binding proteins reduces cancer cell migration 221
M. Ali, L.K. Rogers

P002 Estimating predictive values of short-term morphologic assays of cancer chemoprevention for efficacy in animal tumor assays 222
B. Dunn, V.E. Steele, R.M. Fagerstrom, C.F. Topp, D. Ransohoff, C. Cunningham, R. Lubet, L.G. Ford, B.S. Kramer

Poster board Abstract number

Clinical Methodology

Poster board Abstract number

Poster board Abstract number

P017 Impact of phase 1 expansion cohorts on probability of success in phase 2 and time-to-drug-approval: analysis of 385 new drugs in oncology 237
D. Bugano, K. Hess, L.L. Siu, F. Meric-Bernstam, A.R.A. Razak, D.S. Hong

DNA Repair Modulation (including PARP, CHK, ATR, ATM)

Poster board Abstract number

P018 Reversal of primary and acquired PARP-inhibitor resistance in BRCA-mutated triple-negative breast cancers by inhibition of transcriptional cyclin-dependent kinases (CDKs) 238
S. Johnson, N. Johnson, D. Chi, B. Primack, C. Cruz, D. Stover, A.K. Greifenberg, S. Cao, K. O'Connor, J. Baselga, J. Balmaña, V. Serra, M. Geyer, A. D'Andrea, E. Lim, G.I. Shapiro

P019 Niraparib, a selective PARP 1/2 inhibitor, is efficacious in pre-clinical models of small-cell lung cancer 239
Y. Wang, J. Ricono, K. Admunson, S. Agarwal, R.J. Fram, T. Broudy, K.M. Wilcoxen

P020 The combination of Chk-1 and ATR inhibitor synergistically kills cancer cells 240
K. Sanjiv, A. Hagenkort, P.M. Reaper, T. Koolmeister, O. Mortusewicz, N. Schultz, M. Scobie, U.W. Berglund, P.A. Charlton, J.R. Pollard, T. Helleday

P021 Epigenetic loss-of-function BRCA1 mediates tumor cure by single dose radiotherapy 241
C. Campagne, T.H. Thin, J.D. Fuller, K. Manova-Todorova, A. Haimovitz-Friedman, S.N. Powell, R.N. Kolesnick, Z. Fuks

P022 BMN 673 as single agent and in combination with temozolomide or PI3K pathway inhibitors in small cell lung cancer and gastric cancer models 242
Y. Feng, L.E. Post, R. Cardnell, L.A. Byers, B. Wang, Y. Shen

P023 Modulation of PI3K/mTOR pathway following PARP inhibition in small cell lung cancer 243
R.J. Cardnell, Y. Feng, L. Diao, Y. Fan, F. Masrorpour, S. Mukherjee, J. Shen, J. Wang, L.A. Byers

P024 Development of xenoimplants from germline BRCA1/2 mutant breast cancer (BC) for the identification of predictive biomarkers, mechanisms of resistance against poly(ADP-ribose) polymerase (PARP) inhibitors and evaluation of novel therapies 244
C. Cruz, Y. Ibrahim, B. Morancho, P. Anton, J. Grueso, P. Cozar, M. GuzmÁn, P.M. Avilés, M.J. Guillén, C. Galmarini, J. Arribas, J. Baselga, J. Balmaña, V. Serra

P025 Chk1 is a potential novel therapeutic target that regulates cell survival and potentiates chemotherapy in osteosarcoma (OS) models 245
S.J. Strauss, P. Mistry, A. Mendoza, M. Robson, H. Holme, P. Nandabhiwat, B. Kwok, M. Qadir, R.B. Pedley, J.S. Whelan, P.H.B. Sorensen

P026 PARP inhibitors trap PARP1 onto damaged DNA via catalytic inhibition and not by an allosteric mechanism 246
T. Hopkins, L. Solomon, Y. Shi, L. Rodriguez, C. Donawho, E. DiGiammarino, S. Panchal, A. Olson, D. Stolarik, D. Osterling, W. Gao, E. Johnson, D. Maag

P027 Selective inhibitors of nuclear export (SINE) block the expression of DNA damage repair proteins and sensitize cancer cells to DNA damage therapeutic agents 247
T. Kashyap, M. Crochiere, S. Friedlander, B. Klebanov, W. Senapedis, E. Baloglu, D. del Alamo, S. Tamir, T. Rashal, D. McCauley, R. Carlson, M. Kauffman, S. Shacham, Y. Landesman

P028 Use of ATR inhibitor in combination with topoisomerase I inhibitor kills cancer cells by disabling DNA replication initiation and fork elongation 248
R. Jossé, S.E. Martin, R. Guha, P. Ormanoglu, T. Pfister, J. Morris, J. Doroshow, Y. Pommier

P029 Preclinical efficacy of the PARP inhibitor rucaparib (CO-338/AG014699/PF-01367338) in pancreatic cancer models with homologous recombination deficiencies (HRD) 249
L. Robillard, K. Lin, P.P. Lopez-Casas, M. Hidalgo, T.C. Harding

Poster board Abstract number

P030 Comprehensive genomic profiling of pancreatic acinar cell carcinomas identifies recurrent RAF fusions and frequent inactivation of DNA repair genes 250
J. Chmielecki, K.E. Hutchinson, G.M. Frampton, Z.R. Chalmers, A. Johnson, C. Shi, J. Elvin, S.M. Ali, J.S. Ross, O. Basturk, S. Balsubramanian, D. Lipson, R. Yelensky, W. Pao, V.A. Miller, D.S. Klimstra, P.J. Stephens

P031 A combined in vitro and mathematical modelling approach for understanding the impact of an inhibitor of ATR on DNA damage and repair after ionising radiation 251
J. Yates, S. Checkley, L. MacCallum, R. Odedra, J. Barnes, A. Lau

P032 The DNA damage response gene Schlafen 11 (SLFN11) is a transcriptional target of ETS transcription factors in Ewing's sarcoma and other cancers 252
Y. Pommier, S.W. Bilke, F. Sousa, M. Yamade, J. Murai, V. Rajapakse, L. Helman, P. Meltzer

P033 Phase 1 correlative study of ARQ761, a β-lapachone analogue that promotes NQ01-mediated programmed cancer cell necrosis 253
D. Gerber, Y. Arriaga, M.S. Beg, J.E. Dowell, J.H. Schiller, A.E. Frankel, R. Leff, C. Meek, J. Bolluyt, O. Fatunde, R.T. Martinez, P. Vo, F. Fattah, V. Sarode, Y. Zhou, Y. Xie, M. McLeod, B. Schwartz, D.A. Boothman

P034 Molecular analysis in breast cancer: correlation with immunohistochemical classification and pathologic complete response (pCR) to neoadjuvant chemotherapy (NAC) 254
S. Baulies, M. Gonzalez-Cao, N. Karachaliou, A. Rodriguez Capitan, M.A. Molina-Vila, M.T. Cusido, C. Teixido, S. Viteri, R. Fabregas, X. Gonzalez, R. Rosell

Drug Delivery

Poster board Abstract number

P035 Pre-clinical in vivo characterization of MLN7243, an investigational ubiquitin activating enzyme inhibitor, in solid tumor models 255
T. Traore, J.H. Huck, J.S. Shi, D.S. Sappal, J.D. Duffey, Y.Y. Yang, E.K. Kadakia, A.C. Chakravarty, B.S. Stringer, Y.I. Ishii, R.G. Griffin, C.X. Xia, M.M. Milhollen, J.C. Ciavarri, P.F. Fleming, N.B. Bence, M.H. Hyer

P036 Minicell packaged targeted delivery of shRNA to cancer cells 256
M. Jivrajani, N. Shrivastava, M. Nivsarkar

P037 Development of peptide-mediated drug delivery systems for colon cancer targeted imaging and therapy 257
H.C. Wu, C.H. Wu, Y.H. Kuo

P038 Pancreatic cancer cells expressing the OATP1B3 transporter show promising sensitivity to the highly cytotoxic microcystin-LR molecule 258
V. Kounnis, G. Chondrogiannis, M.D. Mantzaris, D. Fokas, N.A. Papanikolaou, I. Sainis, E. Briasoulis

P039 Factors that limit delivery of Cdk4/6 inhibitor palbociclib to GBM 259
K. Parrish, J. Pokorny, R. Mittapalli, K. Bakken, J. Sarkaria, W. Elmquist

P040 Hsp90 Inhibitor Drug Conjugates (HDC): Payloads and possibilities 260
D. Chimmanamada, W. Ying, J. Zhang, D. Proia, T. Przewloka, J. Jiang, D. Vutukuri, G. Lu, S. Osman, S. Chen, J. Chu, P. Rao, D. Zhou, T. Inoue, L. Shin Ogawa, R. Singh, N. Tatsuta, A. Sonderfan, C. Cortis

P041 Lesion characterization with ferumoxytol MRI in patients with advanced solid tumors and correlation with treatment response to MM-398, nanoliposomal irinotecan (nal-IRI) 261
R.K. Ramanathan, R.L. Korn, J.C. Sachdev, G.J. Fetterly, G. Jameson, K. Marceau, V. Marsh, N. Raghunand, J. Prey, S.G. Klinz, J. Kim, E. Bayever, J.B. Fitzgerald

P042 Improved cytotoxic activity of Nor-β-lapachone-loaded PLGA microcapsules in PC3M prostate cancer cell line 262
C. Pessoa, A.C.S. Feitosa, M.P. Costa, F.C. Evangelista, F.A.M. Sales, I.S. Bomfim, E.N. Silva Júnior, G.G. Dias, V.N. Freire, W.S. Caetano

Drug Design

Molecular Targeted Agents I

Poster board Abstract number

Poster board Abstract number

P090 Inhibition of Trk-driven tumors by the pan-Trk inhibitor RXDX-101 310
D. Anderson, M. Ciomei, P. Banfi, S. Cribioli, E. Ardini, A. Galvani, G. Li

P091 IGF-1R inhibition induced activation of Yes/SFK acts as a by-pass resistance pathway in rhabdomyosarcoma 311
X. Wan, C. Yeung, C. Heske, A. Mendoza, L.J. Hlman

P092 The prognostic role of mesothelin expression and its association with KRAS mutation in advanced lung adenocarcinoma 312
A. Thomas, Y. Chen, S. Steinberg, J. Luo, G. Giaccone, I. Pastan, M. Miettinen, R. Hassan

P093 Development of a one-step isolation platform for exosomal RNA and circulating cell-free DNA from cancer plasma samples 313
D. Enderle, K. Brinkmann, T. Koestler, S. Bentink, C. Berking, J. Skog, M. Noerholm

P094 Optimal sequencing schedules for combining BRAF inhibition with BCL-2 inhibition 314
A. Schalck, D.T. Frederick, M.R. Hammond, I. Ferreiro-Neira, Z.A. Cooper, J.C. Cusack, D.P. Lawrence, K.T. Flaherty, J.A. Wargo, R.J. Sullivan

P095 Biological characterization of TAS3681, a new type of androgen receptor antagonist with androgen receptor downregulating activity 315
K. Minamiguchi, M. Seki, H. Aoyagi, T. Mori, D. Kajiwara, N. Masuko, R. Fujita, S. Okajima, Y. Hayashi, E. Sasaki, T. Utsugi

P096 Potent, partial agonists at ERalpha as selective estrogen mimics for treatment of tamoxifen-resistant breast cancer 316
G. Thatcher, R. Xiong, H.K. Patel, J. Zhao, X. Liang, Y. Wang, M.E. Molloy, D. Tonetti

P097 IKKβ inhibition suppresses sphere formation and self-renewal of lung cancer initiating cells 317
T. Carneiro-Lobo, A.C.P. Salviatto, A.S. Baldwin, D.S. Basseres

P098 Novel therapeutic targets for ARID1A mutant ovarian clear cell carcinoma (OCCC) 318
R.E. Miller, I. Bajrami, R. Brough, A. Konde, J. Campbell, R. Rafiq, A. Ashworth, C.J. Lord

P099 Genomic profiling of uterine leiomyosarcomas reveal frequent alterations in Akt/mammalian target of rapamycin (mTOR) pathway genes and other actionable genomic abnormalities linked to targeted therapies 319
J.A. Elvin, Z.R. Chalmers, J. Chiemlicki, K.A.I. Wang, N. Palma, S.M. Ali, A. Huho, C.E. Sheehan, V.A. Miller, P.J. Stephens, J.S. Ross

P100 First-in-human study with ARQ 092, a novel pan AKT-inhibitor, in subjects with advanced solid tumors or recurrent malignant lymphoma 320
M. Saleh, K. Papadpoulos, A. Arabnia, A. Patnaik, R.M. Stein, F. Chai, M. Lamar, R. Savage, G. Abbadessa, A. Tolcher

P101 Potent and selective inhibition of EZH2 by AU-2121 leads to significant tumor growth inhibition in mutant EZH2 dependent non-Hodgkin lymphoma 321
S. Ahmed, K. Narayanan, A. Gadakh, S. Dodheri, S. Surendranath, S. Nathan, S. Mukherjee, S. Marappan, R. Sushmita, S. Dhadunia, K.M. Obilisetti, J. Anil, J. Reddy, K. Reddy, A. Basavaraju, C. Naik, C. Pandit, M. Ramachandra

P102 Novel alternative splice variants as potential biomarkers and therapeutic targets in aggressive prostate cancer in men of African descent 322
S. Patierno, J. Freedman, B. Wang, N. Lee, D. George

P103 The development of short form of mimic microRNA for lung cancer therapy 323
S. Ohno, K. Sudo, M. Kuroda

P104 Clinical pharmacokinetics (PK), translational PK/pharmacodynamics (PD), and exposure–adverse events (AEs) relationship of MLN2480, an oral investigational pan-RAF kinase inhibitor 324
X. Zhou, A.J. Olszanski, M. Middleton, R. Gonzalez, M.J. Bargfrede, M. Kneissl, V. Bozón, E. Gangolli, K. Venkatakrishnan, M. Patel, C. Zopf, D.W. Rasco

Poster board Abstract number

Poster board Abstract number

P120 Preclinical activity of the VEGFR, FGFR and PDGFR inhibitor lucitanib in FGFR2 aberrant endometrial and gastric cancer models 340
F. Guffanti, R. Chilà, E. Bello, L. Ceriani, M. Zangarini, M. Zucchetti, C. Saba, A. Jacquet-Bescond, M. Pierrat, G. Damia

P121 Dinaciclib alters cell cycle dynamics and induces cell death in Soft Tissue Sarcomas 341
N. Mulet Margalef, S. Rello-Varona, S. Garcia-Monclús, M. Fuentes-Guirado, O.M. Tirado, X. Garcia del Muro

P122 A phase 1/2 study evaluating the safety, pharmacokinetics and efficacy of ABT-414 in subjects with advanced solid tumors likely to over-express the epidermal growth factor receptor (EGFR) 342
A. Tolcher, G. Goss, M. Gordon, L. Gandhi, K.P. Papadopoulos, D. Rasco, M. Pedersen, J. Fischer, W. Ames, H. Xiong, M. Dudley, W. Munasinghe, P. Ansell, K. Holen, E. Vokes

P123 *Salmonella typhimurium* A1-R effectively targets experimental breast cancer brain metastasis 343
Y. Zhang, S. Miwa, N. Zhang, R.M. Hoffman, M. Zhao

P124 Search for new blood biomarkers for response to antiangiogenic therapy in non-small cell lung cancer patients 344
A. Rodríguez-Garzotto, M.T. Agulló-Ortuño, S. Ponce, C.V. Díaz-García, A. Agudo-López, C. Pérez, E. Prieto-García, H. Cortés-Funes, L. Iglesias

P125 Interaction of plitidepsin with eEF1A in living tumor cells 345
C. García, A. Losada, J.M. Molina-Guijarro, M.A. Sacristán, J. Martinez, C.M. Galmarini, M.P. Lillo

P126 Inhibition of Wnt pathway by novel thiazole-based Traf2- and Nck-interacting kinase (TNIK) inhibitor 346
Y. Uno, H. Moriyama, S. Kashimoto, M. Masuda, M. Sawa, T. Yamada

P127 Can a link between the EGFR and cMET pathway in non-small cell lung cancer explain resistance against targeted therapies and open new therapeutic opportunities? 347
N. Van Der Steen, K. Van Der Steen, K. Zwaenepoel, E. Giovannetti, M. Castiglia, A.P. Carreca, P. Pauwels, C. Rolfo

P128 Two NSCLC-PDXs with different EGFR exon 20-insertions respond differently to different TKIs 348
H. Li, M. Yang, J. Cai

P129 Synergistic drug combinations that target beta-catenin-driven and MYC-driven cancers 349
J.C.M. Uitdehaag, J.A.P. Spijkers-Hagelstein, J.A.D.M. de Roos, A.M. van Doornmalen, M.B.W. Prinsen, J. de Man, R.C. Buijsman, G.J.R. Zaman

P130 Oncogenic Ras mutants differentially utilize PLC-dependent calcium flux and PKC activation for MAPK signaling 350
C. Pitt, F. McCormick

P131 hz515H7, a humanized antibody exerts its antitumor activity via antagonism of the CXCR4/SDF-1 axis, and through effector functions 351
C. Klinguer-Hamour, M. Broussas, B. Akla, S. Berger, N. Boute, C. Beau-Larvor, A. Robert, J.F. Haeuw, L. Goetsch, C. Bailly, N. Corvaia

P132 UNC2025, a novel small molecule MerTK and Flt3 tyrosine kinase inhibitor, has therapeutic activity and promotes sensitivity to chemotherapy in animal models of acute leukemia 352
D. Graham, D. DeRyckere, X. Wang, A.A. Hill, W. Zhang, S.V. Frye, H.S. Earp

P133 Protein expression for receptor activator of NFkB (RANK) and its ligand (RANKL) in non-small cell lung cancer (NSCLC) 353
M. D'Arcangelo, S. Ekman, W. Dougall, D. Branstetter, M. Bergqvist, P. Liv, D. Chan, J. Botling, F. Hirsch

P134 PCR-based assay for BRAFV600 mutation analysis in ctDNA: clinical results from plasma and serum samples 354
M. Gonzalez-Cao, C. Mayo de las Casas, M.A. Molina-Vila, L. De Mattos-Arruda, J.L. Manzano, E. Muñoz, J. Cortes, J.P. Berros, M. Sanmamed, A. Gonzalez, C. Alvarez, N. Karachaliou, N. Jordana-Ariza, S. Martin Algarra, R. Rosell

Poster board Abstract number

Poster board		Abstract number
P149	Diagnosis and molecular targeting for individualized treatment of patients with pre-neoplastic lesions and locally advanced cervical cancer *P.M.A. Moreno-Acosta, A.R.R. Alfredo Romero-Rojas, A.H.S. Antonio Huertas Salgado, D.M. Diana Mayorga, N.M. Nicolas Morales, J.A. Jinneth Acosta, O.G. Oscar Gamboa, N.M. Nicolas Magne, M.M. Monica Molano*	369
P150	Discovery of the genes that underpin the transition to malignant phenotype of breast tissues in a highly consanguineous region *I. Gupta, S. Shanmuganathan, A. Ouhtit*	370
P151	Selective targeting of head and neck cancer cells by perturbing reactive oxygen species homeostasis *M. Kwon, J.W. Kim, E.H. Kim, J.Y. Park, S.Y. Kim, J.L. Roh*	371
P152	Specific inhibition of hTERT expression by targeting common promoter mutations which cause quadruplex DNA instability *D. Miller, A. Sokolova, S. Thomas, F. Rezzoug, J. Chaires, W. Dean, R. Buscaglia, J. Trent*	372
P153	AKT2 gene amplification is a marker for sensitivity to allosteric but not ATP-competitive AKT inhibitors *T. Abe, K. Ichikawa, R. Fujita, M. Okada, K. Tanaka, M. Ohkubo, K. Yonekura, T. Shimomura, T. Utsugi*	373
P154	Neuregulin 1 (NRG1) expression is a predictive biomarker for response to AV-203, an ERBB3 inhibitory antibody, in human tumor models *K. Meetze, S. Vincent, S. Tyler, E. Mazsa, A. Delpero, S. Bottega, D. McIntosh, J. Gyuris, Z. Weng*	374
P155	MER as a novel therapeutic target in colorectal cancer *K. Wong, A.C. Tan, T. Pitts, P. Klauck, S. Earp, S. Frye, X. Wang, D.K. Graham, S.G. Eckhardt*	375
P156	Tumor-targeting *Salmonella typhimurium* A1-R enhances gemcitabine–bevacizumab efficacy on a patient-derived orthotopic xenograft (PDOX) pancreatic cancer nude mouse model *Y. Hiroshima, M. Zhao, M.H.G. Katz, J.B. Fleming, S. Sato, T. Murakami, M. Yamamoto, F. Uehara, S. Miwa, S. Yano, M. Momiyama, Y. Zhang, A. Maawy, T. Chishima, K. Tanaka, M. Bouvet, I. Endo, R.M. Hoffman*	376
P157	Plucked hair as a platform for monitoring pharmacodynamic and mechanistic consequences of clinical exposure to the Wnt/beta-catenin inhibitor PRI-724 *G. Miele, B. Reed, E. Harrison, T. Mefo, J. Read, T. Senba, T. Odagami*	377
P158	A first-in-human (FIH) safety and pharmacological study of SAR405838, a novel HDM2 antagonist, in patients with solid malignancies *V. de Weger, M.P. Lolkema, M. Dickson, A. Le Cesne, A. Wagner, M. Merqui-Roelvink, A. Varga, W. Tap, G. Schwartz, G. Demetri, W. Zheng, G. Tuffal, S. Macé, H. Miao, J.H.M. Schellens, M. de Jonge*	378
P159	Identification and rational in silico-based targeting of a novel mediator of metastatic breast cancer *R. Clarkson, J. Soukupova, A. Wakefield, D. Turnham, W. Yang, C. Bordoni, A. Westwell, A. Brancale*	379
P160	Induction of apoptosis with a novel dual cIAP1/XIAP antagonist in models of melanoma *G. Ward, G. Chessari, C.N. Johnson, J. Lewis, S. Rich, N. Thompson*	380
P161	Efficacy of specific FGFR inhibitors against gatekeeper resistance mutations and shared mechanism of cell death in FGFR2-dependent endometrial cancer cell lines *L. Packer, S. Byron, S. Stehbens, D. Loch, F. Dehkhoda, S. Stephenson, P. Pollock*	381
P162	Phase Ib study of oral dual-PI3K/mTOR inhibitor GDC-0980 in combination with capecitabine and mFOLFOX6 + bevacizumab in patients with advanced solid tumors and colorectal cancer *L. Rosen, J. Goldman, J.M. Hubbard, M. Roos, J. Capdevila, J. Maynes, W. Lin, B. O'Keeffe, M. Lackner, J. Spoerke, J. Ware, B. Arnieri, E. Freas, S. Leong*	382
P163	Identification of potent and selective tankyrase 1/2 inhibitors with activity in a subset of APC mutant colorectal cancer *S.M. Guichard, Y. Zhang, D. Ferguson, A. Mazzola, H. Wang, L. Bao, S. Grosskurth, J. Johannes, M. Wagoner, M. Zinda, S. Fawell, E.J.E. Pease, A. Schuller*	383

Poster board Abstract number

Poster board Abstract number

Paediatric Oncology

Poster board Abstract number

Poster board Abstract number

P191 Druggability of p16 deleted pediatric leukemia: The novel cell line POETIC3 identifies potential agents and drug combinations for mechanism based targeted therapeutics 411
J. Reimer, A. Kovulchuk, Y. Ruan, R. Shah, A. Jayanthan, M. Perinpanayagam, T. Truong, I. Auer-Grzesiak, J. Luider, O. Kovulchuk, T. Trippett, A. Narendran

P192 The Pediatric Preclinical Testing Program (PPTP): Analysis of the first 10 years in vivo testing 412
P. Houghton, R. Lock, H. Carol, R. Gorlick, A. Kolb, J. Maris, S. Keir, J. Wu, M. Kang, P. Reynolds, R. Kurmasheva, M. Smith

P193 Next-generation sequencing identifies the mechanism of tumourigenesis caused by loss of SMARCB1 in malignant rhabdoid tumours 413
M.A. Finetti, M. Selby, A. del Carpio Pons, J. Wood, B. Skalkoyannis, A. Smith, S. Crosier, S. Bailey, S. Clifford, D. Williamson

P194 Genomic profiling using a clinical next generation sequencing (NGS) assay reveals genomic alterations to guide targeted therapy in advanced neuroblastoma patients 414
S. Ali, E.M. Sanford, M.J. Hawryluk, J. Chmielecki, K. Wang, G.A. Palmer, N.A. Palma, D. Morosini, R. Erlich, R. Yelensky, D. Lipson, J.S. Ross, Y. Mosse, P.J. Stephens, J.M. Maris, V.A. Miller

P195 Comprehensive next generation sequencing of solid tumors from 669 adolescents and young adults reveals a distinct spectrum of targetable genomic alterations 415
D. Morosini, K. Wang, K. Wagner, B. Gershenhorn, R. Yelensky, D. Lipson, J. Chmielecki, S.M. Ali, J.S. Ross, P.J. Stephens, V.A. Miller

P196 Results of phase I study of bolus 5-fluorouracil in children and young adults with recurrent ependymoma 416
K.D. Wright, D.C. Turner, K.M. Haddock, M.O. Jacus, K.E. Harstead, S.L. Throm, V.M. Daryani, G.W. Robinson, G.T. Armstrong, A. Onar-Thomas, C.F. Stewart, A. Gajjar

P197 Evaluating the activity of the p53–MDM2 inhibitor NDD0005 in Ewing sarcoma 417
J. Pecqueur, B. Vormoor, Y. Zhao, H. Newell

P198 Population pharmacokinetics of intravenous bolus 5-fluorouracil in a phase I trial for children and young adults with recurrent ependymoma 418
D.C. Turner, K.M. Haddock, M.O. Jacus, K.E. Harstead, S.L. Throm, V.M. Daryani, C.F. Stewart, K.D. Wright

P199 Targeted inhibition of casein kinase II (CK2) produces a strong therapeutic effect in pediatric leukemia 419
S. Dovat, C. Song, C. Gowda, K.J. Payne

P200 Analysis of genomic alterations in Ewing sarcoma (German cohort) reveals cooperating mutations and novel therapy targets 420
G.H.S. Richter, K. Agelopoulos, E. Schmidt, K. von Heyking, B. Moser, H.U. Klein, U. Kontny, M. Dugas, K. Poos, E. Korsching, T. Buch, G. Köhler, C. Rössig, D. Baumhoer, H. Jürgens, S. Burdach, W.E. Berdel, C. Müller-Tidow, U. Dirksen

P201 Molecular profiling for factors predicting sensitivity or resistance to therapy in relapsed child cancer 421
F. Saletta, C. Wadham, J. Byrne, D. Ziegler, G. McCowage, M. Haber, G. Marshall, M. Norris

P202 CBL0137, a novel NFkB suppressor and p53 activator, is highly effective in pre-clinical models of neuroblastoma 422
M. Haber, J. Murray, L. Gamble, A. Carnegie-Clark, H. Webber, M. Ruhle, D. Carter, A. Oberthur, M. Fischer, D. Ziegler, G.M. Marshall, K. Gurova, C. Burkhart, A. Purmal, A.V. Gudkov, M.D. Norris

P203 RNA helicase A is essential for 1p36 gene KIF1Bβ tumor suppression in neuroblastomas 423
Z.X. Chen, K. Wallis, S.M. Fell, V.R. Sobrado, M.C. Hemmer, D. Ramsköld, Z. Choo, U. Hellman, R. Sandberg, R.S. Kenchappa, T. Martinsson, J.I. Johnsen, P. Kogner, S. Schlisio

Poster board Abstract number

Toxicology

Poster board Abstract number

Friday 21 November 2014

09:00–10:30 **Poster Viewing** **Poster area**

Plenary Session 8 **Auditorium**

11:00–13:00 **Targeting RAS and Other Driver Oncogenes** Abstract number

Chairs: J.A. Engelman (USA) and M. Barbacid (Spain)

11:00 Targeting KRAS driven lung and pancreatic adenocarcinoma
M. Barbacid (Spain)

11:20 Systematic interrogation of vulnerabilities in KRAS driven cancers
W. Hahn (USA)

Key objectives:
1. Understand the concept of synthetic lethality.
2. Understand systematic genetic screens to identify targets.
3. Understand the role of innate immune regulators in KRAS induced tumorigenesis.

11:40 Targeting synthetic lethal partners of KRAS
J. Luo (USA)

Main objectives:
1. To inform the participants about therapeutic strategies in targeting KRAS mutant cancer.
2. To inform the participants about the concept of synthetic lethality and its therapeutic utilities.
3. To provide the participants examples of synthetic lethal interactions with the KRAS oncogene.

Take home messages:
1. Current difficulties in treating KRAS mutant tumours warrant exploration of new therapeutic strategies.
2. Synthetic lethality is a powerful approach for identifying functional vulnerabilities in cancer cells.
3. Synthetic lethal partners of the KRAS oncogene could be potential targets for drug discovery.

12:00 ORAL PRESENTATION: Clinical acquired resistance to combined RAF/EGFR or RAF/MEK inhibition in BRAF mutant colorectal cancer (CRC) patients through MAPK pathway alterations 428
R. Corcoran, E.M. Coffee, E. Van Allen, L.G. Ahronian, N. Wagle, E.L. Kwak, J.E. Faris, A.J. Iafrate, L.A. Garraway, J.A. Engelman

12:15 LATE BREAKING ABSTRACT: Antitumor activity of ASP8273, an irreversible mutant selective EGFR-TKI, in NSCLC patients with tumors harboring EGFR activating mutations and T790M resistance mutation 9LBA
H. Murakami, H. Nokihara, T. Shimizu, T. Seto, A. Keating, A. Krivoshik, K. Uegaki, S. Morita, K. Nakagawa, M. Fukuoka

12:25 LATE BREAKING ABSTRACT: Interim phase 2 results of study CO-1686-008: A phase 1/2 study of the irreversible, mutant selective, EGFR inhibitor rociletinib (CO-1686) in patients with advanced non small cell lung cancer 10LBA
J. Soria, L.V. Sequist, J.W. Goldman, H.A. Wakelee, S.M. Gadgeel, A. Varga, H.A. Yu, B.J. Solomon, S.H. Ou, V. Papadimitrakopoulou, G.R. Oxnard, L. Horn, R. Dziadziuszko, B. Chao, A.I. Spira, S. Liu, T. Mekhail, S. Matheny, J. Litten, R.D. Camidge

12:35 LATE BREAKING ABSTRACT: Phase I study of the selective BRAFV600 inhibitor encorafenib (LGX818) combined with cetuximab and with or without the α-specific PI3K inhibitor alpelisib (BYL719) in patients with advanced BRAF mutant colorectal cancer 11LBA
J. Tabernero, R. van Geel, J.C. Bendell, A. Spreafico, M. Schuler, T. Yoshino, J.P. Delord, Y. Yamada, M.P. Lolkema, J.E. Faris, F.A.L.M. Eskens, S. Sharma, R. Yaeger, H.J. Lenz, Z. Wainberg, E. Avsar, A. Chatterjee, S. Jaeger, T. Demuth, J.H.M. Schellens

12:45 Discussion Late Breaking Abstracts
J.A. Engelman (USA)

Poster Sessions **Poster area**

Drug Synthesis

Poster board		Abstract number
P001	Development of extracellular signal-regulated kinase 5 (ERK5) inhibitors for anti-cancer therapy *S. Myers, N. Martin, R. Bawn, T. Blackburn, L. Barrett, T. Reuillon, B. Golding, R. Griffin, T. Hammonds, I. Hardcastle, H. Leung, D. Newell, L. Rigoreau, A. Wong, C. Cano*	429
P002	Design and structure–activity relationships of highly potent and bioavailable imidazolinone FASN KR domain inhibitors *G. Bignan, R. Alexander, J. Bischoff, P. Connolly, M. Cummings, S. De Breucker, N. Esser, E. Fraiponts, R. Gilissen, B. Grasberger, B. Janssens, T. Lu, D. Ludovici, L. Meerpoel, C. Meyer, M. Parker, D. Peeters, C. Rocaboy, C. Schubert, K. Smans*	430

Molecular Targeted Agents II

Poster board		Abstract number
P003	Real-time pharmacokinetic (PK) results from an ongoing randomized, parallel-dose phase 1 study of onapristone in patients (pts) with progesterone receptor (PR)-expressing cancers *F. Lokiec, J. Bonneterre, A. Italiano, A. Varga, M. Campone, T. LeSimple, A. Leary, V. Dieras, K. Rezai, S. Giacchetti, S. Proniuk, A. Bexon, E. Gilles, J. Bisaha, A. Zukiwski, P. Cottu*	431
P004	ODM-203, a novel, selective and balanced FGFR and VEGFR inhibitor with strong anti-tumor activity in FGFR- and VEGFR-dependent cancer models *T. Holmström, A. Moilanen, T. Linnanen, G. Wohlfahrt, S. Karlsson, R. Oksala, T. Korjamo, M. Björkman, S. Samajadar, S. Rajagopalan, S. Chelur, K. Narayan, R. Ramachandra, T. Anthony, S. Ds, M. Ramachandra, P. Kallio*	432
P005	Genomic predictors of therapeutic sensitivity to TAS-119, a selective inhibitor of Aurora-A kinase *H. Sootome, N. Fujita, A. Miura, T. Suzuki, H. Fukushima, S. Mizuarai, H. Hirai, T. Utsugi*	433
P006	Bipolar androgen therapy for men with castration sensitive and castration resistant prostate cancer: Reversing resistance and maintaining sensitivity to androgen ablative therapies *S.R. Denmeade, E.S. Antonarakis, M.A. Eisenberger, M.A. Carducci, H. Wang, C.J. Paller, J.T. Isaacs, M.T. Schweizer*	434
P007	A pan-cancer tumor-derived epithelial-to–mesenchymal transition (EMT) signature determines patterns of drug sensitivity and enrichment in immune target expression following EMT *M.P. Mak, P. Tong, L. Diao, P.K.S. Ng, Y. Fan, R.J. Cardnell, D.L. Gibbons, W.N. William, J.V. Heymach, K.R. Coombes, L.A. Byers, J. Wang*	435
P008	Monitoring activity of RXDX-101 in Phase 1/2 patients using a pharmacodynamic assay for TrkA activation *D. Murphy, H. Ely, R. Patel, G. Wei, A. Diliberto, R. Shoemaker, J. Christiansen*	436
P009	PIM kinase inhibitor AZD1208 sensitises SCLC to BH3 mimetic AZD4320 *R. Sloane, B. Bola, M. Lancashire, C. Hodgkinson, C. Morrow, K. Simpson, C. Dive*	437
P010	MM-131: A bispecific antibody that inhibits c-Met signaling through avid binding to the EpCAM tumor antigen *B.D. Harms, A. Lugovskoy, A. Abu-Yousif, A. Fulgham, M. Geddie, S.V. Su, N. Kohli, B. Johnson, K. Masson, U.B. Nielsen, B. Schoeberl, G. MacBeath*	438
P011	PI3K/mTOR inhibitor VS-5584 targets cancer stem cells and prevents tumor regrowth after chemotherapy in preclinical models of small cell lung cancer *V. Kolev, M. Padval, Q. Wright, J. Ricono, D. Weaver, J. Pachter, Q. Xu*	439
P012	Phenotypic alteration in a highly metastatic variant of the MDA-MB-231 cell line: role of Annexin A1 *Y. Tu, E. Fietz, J. Cameron, A. Stewart*	440

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

New Therapies with Pleiotropic Activity

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number

Poster board Abstract number