

Scientific Programme – Overview

Tuesday 18 November		Wednesday 19 November	
Auditorium		Auditorium	Room 117
		08.00	Workshop 1
		09.45	Management of Toxicity of Molecular Targeted Agents
			Workshop 2
			Cancer Metabolism
			<i>Coffee Break</i>
		10.15	Workshop 3
			Liquid Biopsies in Solid Tumours
		12.00	Workshop 4
			Translational Research with Immunostimulatory Monoclonal Antibodies
		12.15	“Navigating Your Career with Confidence”
		12.00-13.15	A Professional Advancement Session Organized by the AACR-Women in Cancer Research (WICR) Council
		13.15	Plenary Session 2
			Proffered Paper Session
		15.20	<i>Coffee Break</i>
		16.00	Plenary Session 3
			Oncolytic Viruses
		17.50	
		18.00	Poster Viewing (Poster Area)
		19.30	
13.00	Opening Remarks		
13.15	Michel Clavel Lecture		
	Rational combination therapies for cancer		
14.00	Keynote Lecture		
	Immunecheckpoints - Gateway to Immunotherapy		
14.45	<i>Coffee Break</i>		
15.15	Plenary Session 1		
	Is the Genomic Landscape Changing the Outcome for Cancer Patients?		
17.30			
17:30 - 18:30	Welcome Reception (Exhibition Hall)		

Posters

Animal Models
 Cytotoxics
 Drug Resistance and Modifiers
 Drug Screening
 Immunotherapy (Immunecheckpoints, Vaccination,
 Oncolytic viruses, Cytokines)
 Preclinical Models
 Radiation Interactive Agents

Thursday 20 November		Friday 21 November	
	Auditorium		
08.00	Plenary Session 4	09.00	<i>Poster Viewing (Poster Area)</i>
10.00	Antibody-Based Therapies (ADC and others)	10.30	<i>Coffee Break</i>
	<i>Coffee Break</i>		Auditorium
10.30	Plenary session 5	11.00	Plenary session 8
12.30	Epigenetic Targets	13.00	Targeting RAS and Other Driver Oncogenes
	<i>Lunch 12.30-13.30</i> <i>Including Posters in the Spotlight Session</i>		
13.30	Plenary Session 6		
15.35	Proffered Paper Session		
	<i>Coffee Break</i>		
16.00	Plenary Session 7		
17.50	Novel Mechanisms for Drug Resistance		
18.00-19.30	<i>Poster Viewing (Poster Area)</i>		

Exhibition 09:45 - 16:00

- Posters
- Drug Synthesis
 - Molecular targeted agents II
 - New Therapies with Pleiotropic Activity

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

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

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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. Taberero (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**13:15–15:20 Proffered Paper Session****Auditorium**

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. Mileshekin, 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**16:00–17:50 Oncolytic Viruses****Auditorium**

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 3LBA synthase (FASN) inhibitor, TVB-2640
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 4LBA patients with hepatocellular carcinoma or advanced cancer with liver metastasis
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 <i>V. Vuaroqueaux, C. Gredy, S. Gorynia, S. Baltes, H.H. Fiebig, T. Metz</i>	7
P002 Imaging growth and anti-cancer activity in orthotopic patient derived tumors <i>M. Baugher, C. Bull, A. Cohen-Barnhouse, A. Flecha, M. Franklin, K. Guley, P. McConville, W.R. Leopold</i>	8
P003 Antineoplastic effects of auranofin in canine lymphoma <i>D. Thamm, B.J. Rose, J.K. Shoeneman</i>	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 <i>K. Klinghammer, J.D. Raguse, T. Plath, A.E. Albers, B. Brzezicha, A. Wulf-Goldenberg, U. Keilholz, J. Hoffmann, I. Fichtner</i>	10
P005 A panel of patient derived xenograft models of different haematological malignancies suitable for preclinical drug screening campaigns <i>E. Oswald, C. Tschuch, K. Klingner, B. Hammerich, D. Lehnhard, C. Rentsch, M. Lübbert, H.H. Fiebig, J. Schüler</i>	11
P006 Next generation sequencing (NGS) guided therapy prediction for the treatment of glioblastoma multiforme (GBM) <i>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</i>	12
P007 Whole exome sequence analysis of canine transitional cell carcinoma of the bladder <i>D.L. Duval, B. Hernandez, J. Brown, S.E. Lana, R. Page, K.L. Jones</i>	13
P008 Mixeno mouse models for in vivo evaluation of anti-human cancer immunotherapeutics <i>J. Zhang, J. Qiu, M. Qiao, Q. Shi</i>	14
P009 Genetic and molecular validation of uterine sarcoma patient-derived xenograft models <i>T. Cuppens, E. Hermans, J. Depreeuw, M. Moisse, T. Van Brussel, L. Coenegrachts, D. Lambrechts, F. Amant</i>	15

Poster board	Abstract number
P010 Allografting improves the feasibility of genetically engineered mouse models (GEMM) for anti-cancer drug development <i>K. Kukuk, K. Klingner, A.L. Peille, P. Müller, A. Zipelius, J. Schüler</i>	16
P011 Studies on glycoprotein expression differences between MCF-7 and MCF-7-Z <i>J. Ner-Kluza, A. Drabik, M. Kubbutat, A. Lingnau, J. Silberring</i>	17
P012 Establishment and characterization of a Merkel Cell carcinoma PDX panel: Screening for potentially useful therapies <i>M.J. Wick, J. Meade, M. Nehls, T. Vaught, J. Carlile, A.W. Tolcher, D.W. Rasco, A. Patnaik, K.P. Papadopoulos</i>	18
P013 Syngeneic models for developing cancer therapeutics targeting immune system <i>L. Zhang, J. Zhang, Q. Shi</i>	19
P014 miR-25 is a key regulator of prostate cancer invasiveness by modulation of the cross-talk between Notch and TGF- β signaling <i>E. Zoni, A.F. van de Merbel, G. van der Horst, J. Rane, T. Visakorpi, E.B. Snaar, N. Maitland, G. van der Pluijm</i>	20

Cytotoxics

Poster board	Abstract number
P015 Pharmacogenomics of mithramycin in thoracic malignancies <i>W. Figg, T.M. Sissung, C.J. Peer, D. Schrupp</i>	21
P016 Novel combination therapy, TAS-102 combined with the anti-EGFR antibody or the anti-VEGF antibody showed therapeutic benefit toward colorectal cancer xenografts <i>K. Ishida, K. Sakamoto, N. Tanaka, K. Oguchi, K. Yamamura, A. Fujioka, F. Nakagawa, K. Matsuo, T. Utsugi</i>	22
P017 Phase I study of lurbinectedin (PM01183) administered on days (D) 1 & 8 every 3 weeks (q3wk) in patients (pts) with solid tumors <i>M.J. Ratain, L. Gore, S. Szyldergemajn, J. Diamond, D. Geary, C. Fernandez-Teruel, A. Soto-Matos, M. Sharma, A. Jimeno</i>	23
P018 Androgen receptor (AR) expression in triple negative breast cancer (TNBC): results from a phase II neoadjuvant trial with carboplatin and eribulin mesylate in TNBC patients <i>K. Siziopikou, V. Parini, V. Kaklamani</i>	24
P019 An ING1b-derived peptide that inhibits cancer cell viability and promotes apoptosis <i>A. Boyko, K. Riabowol</i>	25
P020 NPD926, a small molecule inducer of reactive oxygen species, kills cancer cells via glutathione depletion <i>T. Kawamura, Y. Kondoh, M. Muroi, M. Kawatani, H. Osada</i>	26
P021 TAS-102 treatment results in high trifluridine incorporation into DNA with pyrimidine metabolic pathway markedly up-regulated in cancer <i>K. Oguchi, K. Sakamoto, H. Kazuno, H. Ueno, K. Ishida, T. Yokogawa, K. Yamamura, R. Kitamura, K. Matsuo, T. Utsugi</i>	27
P022 Characterization of the type of cell death induced by novel tambjamine analogs in lung cancer <i>A. Rodilla Martín, V. Soto-Cerrato, P. Manuel-Manresa, L. Korrodi-Gregório, R. Quesada, R. Pérez-Tomás</i>	28
P023 TAS-114 is a novel dUTPase/DPD inhibitor, its DPD inhibition reduces capecitabine dosage but does not diminish therapeutic window in human tumor xenografts <i>W. Yano, H. Kazuno, T. Yokogawa, K. Sakamoto, K. Yoshisue, T. Wakasa, M. Fukuoka, K. Matsuo, K. Noguchi, T. Utsugi</i>	29

Poster board	Abstract number
P024 The fungal-derived cyclohexadepsipeptide Destruxin E exerts multifaceted anticancer and antiangiogenic activities <i>R. Dorneishuber-Fleiss, P. Heffeter, T. Mohr, P. Hazemi, K. Kryeziu, C. Seger, W. Berger, R. Lemmens-Gruber</i>	30
P025 N-Myc amplification sensitizes tumor cells to inhibition by Danusertib, an Aurora kinase inhibitor <i>P. Carpinelli, R. Ceruti, R. Alzani, C. Re, D. Ballinari, S. Cribioli, M. Russo, A. Degrassi, G. Texido, M. Ciomei, E. Pesenti, A. Montagnoli, A. Galvani</i>	31
P026 Replication stress is a determinant of synergy between gemcitabine and Chk1 inhibition <i>S.B. Koh, A. Courtin, R. Boyce, B. Boyle, F.M. Richards, D.I. Jodrell</i>	32
P027 Combining the long-acting topoisomerase 1-inhibitor etirinotecan pegol with the PARP inhibitor rucaparib to provide anti-tumor synergy without increased toxicity <i>U. Hoch, D. Charych</i>	33
P028 Phase I, dose-escalation study of the investigational drug D07001-F4, an oral formulation of gemcitabine HCl, in patients (pts) with advanced solid tumors or lymphoma <i>C. Lin, W. Su, J. Lee, C. Hsu, A. Cheng, C. Lin, H. Ho, C. Huang, S. Hsueh, J. Yang</i>	34
P029 BRCA1 expression exploratory analysis in patients of the phase III trial of trabectedin vs. doxorubicin-based chemotherapy as first-line therapy in translocation-related sarcomas <i>M. Aracil, P. Lardelli, A. Nieto, C.M. Galmarini</i>	35
P030 Suppression of metastasis and improvement of drug distribution by eribulin mesylate <i>Y. Ozawa, K. Okamoto, Y. Adachi, M. Asano, K. Tabata, Y. Funahashi, J. Matsui</i>	36
P031 Effect of a microtubule-targeting drug on cell–cell contacts in bladder epithelial tumour cells <i>L.M. Antón-Aparicio, R. Castosa, M. Haz, M. Blanco, M. Rodriguez, M. Valladares, A. Figueroa</i>	37
P032 The indolyl-chalcone CDD-026 induces cancer cell death through targeting of STMN1 and mitotic catastrophe <i>B. Wegiel, Y. Wang, F. Jernigan, L. Sun</i>	38
P033 Phytochemical indole-3-carbinol synergizes strongly with fludarabine and induces p53-dependent and -independent cell death in chronic lymphocytic leukemia cells irrespective of their IGHV mutation state and treatment resistances <i>G. Perez-Chacon, C. Martinez-Laperche, N. Rebolleda, B. Somovilla-Crespo, C. Muñoz-Calleja, I. Buño, J.M. Zapata</i>	39
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P198 High-throughput functional screening identifies the flavoreductase POR as a principal determinant of sensitivity to the hypoxia-targeting prodrug SN30000 <i>F.W. Hunter, Z. Shalev, J. Wang, J. Moffat, T. Katella, M. Koritzinsky, W.R. Wilson, B.G. Wouters</i>	204
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P200 Identification of novel targets for radiosensitisation of non-small cell lung cancer by secretome analysis <i>A. Sharma, S. Bender, O. Riesterer, A. Broggini-Tenzer, M. Pruschy</i>	206
P201 The enhancement of radiotherapy efficacy with docetaxel-titanate nanotubes as a new nanohybrid for localized high risk prostate cancer <i>C. Mirjolet, J. Boudon, A. Loiseau, S. Chevrier, T. Gautier, R. Boidot, J. Paris, N. Millot, G. Crehange</i>	207
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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. Gökbüget (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. Gökbüget (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

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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

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P. LoRusso, T. LaVallee, L. Kimmel, C. Lubeski, R. Gedrich, C. Sidor

09:50 General discussion

A. Tolcher (USA)

Plenary Session 5**10:30–12:30 Epigenetic Targets***Chairs: K. Helin (Denmark) and T. Helleday (Sweden)***Auditorium**

Abstract number

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. Rezaei, 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. Ottosen, A. Italiano

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

12:45–13:15 Posters in the Spotlight Session*Moderator: E. Calvo (Spain)***Exhibition Hall**

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

Plenary Session 6**13:30–15:35 Proffered Paper Session***Chairs: E. Calvo (Spain) and J. Doroshov (USA)***Auditorium**

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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
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- 13:45 ORAL PRESENTATION: Homologous recombination deficiency (HRD) score and niraparib efficacy in high grade ovarian cancer 214
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- 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
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- 14:15 ORAL PRESENTATION: Phase I study of panobinostat and fractionated stereotactic re-irradiation therapy (FSRT) for recurrent high grade gliomas 216
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- 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
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- 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

16:00–17:50 Novel Mechanisms for Drug Resistance

Chairs: U. Banerji (United Kingdom) and S.A. Courtneidge (USA)

Auditorium

Abstract number

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.

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J. Turner, J. Dawson, S. Grant, K. Shain, C. Cubitt, Y. Dai, L. Zhoui, M. Kauffman, S. Shacham, D. Sullivan

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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**

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Chemoprevention

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| P002 | Estimating predictive values of short-term morphologic assays of cancer chemoprevention for efficacy in animal tumor assays | 222 |
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P187 Structural basis for inhibition of ligand-dependent and -independent ErbB3 activation by KTN3379 <i>D. Alvarado, S. Lee, E. Greenlee, G.F. Ligon, J.S. Lillquist, E.J. Natoli, J. Amick, Y. Hadari, J. Schlessinger</i>	407
P188 A potent and selective small molecule inhibitor of MCL-1 sensitizes DLBCL cell lines to the BCL-2 selective inhibitor ABT-199 <i>D.C. Phillips, Y. Xiao, L. Lam, E. Litinovic, L. Roberts-Rapp, A.J. Souers, J.D. Levenson</i>	408

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P193 Next-generation sequencing identifies the mechanism of tumorigenesis caused by loss of SMARCB1 in malignant rhabdoid tumours <i>M.A. Finetti, M. Selby, A. del Carpio Pons, J. Wood, B. Skalkoyannis, A. Smith, S. Crosier, S. Bailey, S. Clifford, D. Williamson</i>	413
P194 Genomic profiling using a clinical next generation sequencing (NGS) assay reveals genomic alterations to guide targeted therapy in advanced neuroblastoma patients <i>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</i>	414
P195 Comprehensive next generation sequencing of solid tumors from 669 adolescents and young adults reveals a distinct spectrum of targetable genomic alterations <i>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</i>	415
P196 Results of phase I study of bolus 5-fluorouracil in children and young adults with recurrent ependymoma <i>K.D. Wright, D.C. Turner, K.M. Haddock, M.O. Jacus, K.E. Harstead, S.L. Thom, V.M. Daryani, G.W. Robinson, G.T. Armstrong, A. Onar-Thomas, C.F. Stewart, A. Gajjar</i>	416
P197 Evaluating the activity of the p53–MDM2 inhibitor NDD0005 in Ewing sarcoma <i>J. Pecqueur, B. Vormoor, Y. Zhao, H. Newell</i>	417
P198 Population pharmacokinetics of intravenous bolus 5-fluorouracil in a phase I trial for children and young adults with recurrent ependymoma <i>D.C. Turner, K.M. Haddock, M.O. Jacus, K.E. Harstead, S.L. Thom, V.M. Daryani, C.F. Stewart, K.D. Wright</i>	418
P199 Targeted inhibition of casein kinase II (CK2) produces a strong therapeutic effect in pediatric leukemia <i>S. Dovat, C. Song, C. Gowda, K.J. Payne</i>	419
P200 Analysis of genomic alterations in Ewing sarcoma (German cohort) reveals cooperating mutations and novel therapy targets <i>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</i>	420
P201 Molecular profiling for factors predicting sensitivity or resistance to therapy in relapsed child cancer <i>F. Saletta, C. Wadham, J. Byrne, D. Ziegler, G. McCowage, M. Haber, G. Marshall, M. Norris</i>	421
P202 CBL0137, a novel NFκB suppressor and p53 activator, is highly effective in pre-clinical models of neuroblastoma <i>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. Burkhardt, A. Purmal, A.V. Gudkov, M.D. Norris</i>	422
P203 RNA helicase A is essential for 1p36 gene KIF1Bβ tumor suppression in neuroblastomas <i>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</i>	423

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- P204 Nonclinical safety assessment of a humanized anti-OX40 agonist antibody, MOXR0916 424
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- P205 Evaluation of drug reactions to anti-neoplastic agents in Phase I clinical trials 425
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- P206 Serum levels of CCL22 and CCL25 might predict skin rash induction the commonest adverse event 426
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Y. Terui, R. Kuniyoshi, Y. Mishima, K. Hatake
- P207 Hematotoxicity potential of new drug candidates measured in hematopoietic progenitors in 427
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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 <i>Chairs: J.A. Engelman (USA) and M. Barbacid (Spain)</i>	Abstract number
11:00	Targeting KRAS driven lung and pancreatic adenocarcinoma <i>M. Barbacid (Spain)</i>	
11:20	Systematic interrogation of vulnerabilities in KRAS driven cancers <i>W. Hahn (USA)</i>	
	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 <i>J. Luo (USA)</i>	
	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 <i>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</i>	428
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 <i>H. Murakami, H. Nokihara, T. Shimizu, T. Seto, A. Keating, A. Krivoshik, K. Uegaki, S. Morita, K. Nakagawa, M. Fukuoka</i>	9LBA
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 <i>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</i>	10LBA
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 <i>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</i>	11LBA
12:45	Discussion Late Breaking Abstracts <i>J.A. Engelman (USA)</i>	

Poster Sessions**Poster area****Drug Synthesis**

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P001 Development of extracellular signal-regulated kinase 5 (ERK5) inhibitors for anti-cancer therapy <i>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</i>	429
P002 Design and structure–activity relationships of highly potent and bioavailable imidazolinone FASN KR domain inhibitors <i>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</i>	430

Molecular Targeted Agents II

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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 <i>F. Lokiec, J. Bonnetterre, 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</i>	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 <i>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</i>	432
P005 Genomic predictors of therapeutic sensitivity to TAS-119, a selective inhibitor of Aurora-A kinase <i>H. Sootome, N. Fujita, A. Miura, T. Suzuki, H. Fukushima, S. Mizuarai, H. Hirai, T. Utsugi</i>	433
P006 Bipolar androgen therapy for men with castration sensitive and castration resistant prostate cancer: Reversing resistance and maintaining sensitivity to androgen ablative therapies <i>S.R. Denmeade, E.S. Antonarakis, M.A. Eisenberger, M.A. Carducci, H. Wang, C.J. Paller, J.T. Isaacs, M.T. Schweizer</i>	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 <i>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</i>	435
P008 Monitoring activity of RXDX-101 in Phase 1/2 patients using a pharmacodynamic assay for TrkA activation <i>D. Murphy, H. Ely, R. Patel, G. Wei, A. Diliberto, R. Shoemaker, J. Christiansen</i>	436
P009 PIM kinase inhibitor AZD1208 sensitises SCLC to BH3 mimetic AZD4320 <i>R. Sloane, B. Bola, M. Lancashire, C. Hodgkinson, C. Morrow, K. Simpson, C. Dive</i>	437
P010 MM-131: A bispecific antibody that inhibits c-Met signaling through avid binding to the EpCAM tumor antigen <i>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</i>	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 <i>V. Kolev, M. Padval, Q. Wright, J. Ricono, D. Weaver, J. Pachter, Q. Xu</i>	439
P012 Phenotypic alteration in a highly metastatic variant of the MDA-MB-231 cell line: role of Annexin A1 <i>Y. Tu, E. Fietz, J. Cameron, A. Stewart</i>	440

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P013 The role of methylation in metastasis of oral squamous cell carcinoma: understanding the OSCC methylome <i>M. Clausen, L.J. Melchers, T. De Meyer, S. Denil, W. Criekinge, G.B. Wisman, J.L.N. Roodenburg, E. Schuurin</i>	441
P014 Targeting urokinase plasminogen activator for radioimmunotherapy using an antagonistic internalizing human antibody <i>A. LeBeau, H.F. VanBrocklin</i>	442
P015 Notch3-targeted antibody drug conjugates have superior preclinical efficacy to Notch signaling inhibitors <i>K.G. Geles, Y. Gao, L. Sridharan, A. Giannakou, T.T. Yamin, J. Golas, M. Charati, J. Lucas, K. Wang, S. Pirie-Shepherd, M. Roy, M. Follettie, A. Maderna, X. Li, L. Tchistiakova, H.P. Gerber, P. Sapra</i>	443
P016 Debio 1143 in combination with carboplatin and paclitaxel in patients with non-small cell lung cancer (NSCLC), triple-negative breast cancer (TNBC) and platinum-refractory epithelial ovarian cancer (EOC). Preliminary results of a Phase I dose-escalation study <i>C. Le Tourneau, I. Ray-Coquard, N. Isambert, C.A. Gomez-Roca, P. Cassier, M.P. Sablin, E. Ruits, B. Gavillet, C. Zanna, P. Fumuleau, J.P. Delord</i>	444
P017 MEK inhibition enhances gemcitabine efficacy by increasing MDM2-mediated ubiquitination and degradation of RRM1 <i>F. Vena, E. Li Causi, T. Hagemann, J.A. Hartley, S. Goodstal, D. Hochhauser</i>	445
P018 The cancer stem cell inhibitors VS-6063 (defactinib) and VS-5584 exhibit synergistic anticancer activity in preclinical models of mesothelioma <i>Q. Xu, W.F. Tam, C.M. Vidal, V.N. Kolev, Y. Kadariya, C.W. Menges, J.R. Testa, J.A. Pachter</i>	446
P019 Novel, quantitative in vivo shRNA screening approach identifies new molecular targets to block cancer metastasis <i>L. Willetts, R. Paproski</i>	447
P020 Exposure to EGFR inhibitors influences release of extracellular vesicles by tumor cells <i>R. van der Meel, S.M. van Dommelen, P. de Corte, M. Coimbra, W.W. van Solinge, P. Vader, R.M. Schiffelers</i>	448
P021 Cytokine induces MIR-424 expression and modulates SOCS2/STAT5 signaling pathway in oral cancer <i>S.G. Shiah, H.Y. Peng, S.L.C. Jin, J.Y. Chang, C.C. Kuo</i>	449
P022 Precise gene editing of mutant NRAS using CRISPR to determine sensitivity to trametinib <i>C. Hose, N.D. Fer, M. Burkett, J. Connelly, E. Harris, J. Lih, M. Williams, D. Evans, T. Silvers, A. Monks, R. Parchment, B.A. Teicher, J.H. Doroshow, A. Rapisarda</i>	450
P023 Correlative and updated clinical endpoint analysis of a multicenter phase II trial of selumetinib (AZD6244) plus erlotinib in chemotherapy-refractory advanced pancreatic adenocarcinoma (PDAC) <i>A.H. Ko, A.H. Tempero, T.B. Bekaii-Saab, P. Kuhn, R. Courtin, S. Ziyeh, S. Tahiri, R.K. Kelley, E. Dito, A. Ong, R. Linetskaya, A. Talasz, A.P. Venook, W. Korn</i>	451
P024 eIF2alpha phosphorylation determines the adaptation of tuberous sclerosis complex mutant cells to stress and their response to anti-tumor therapies <i>A. Koromilas, C. Tenkerian, J. Krishnamoorthy, R. Kamindla, U. Kazimierczak, S. Wang</i>	452
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