

## editorials

- PARP inhibitor receives FDA breakthrough therapy designation in castration resistant prostate cancer: beyond germline BRCA mutations  
*T. Helleday* 755

- Reporting incidental germline variants in the context of day-to-day somatic genomic profiling  
*G. Mak, M. Moschetta & H.-T. Arkenau* 758

## special article

- Statistical controversies in clinical research: statistical significance—too much of a good thing ...  
*M. Buyse, S. A. Hurvitz, F. Andre, Z. Jiang, H. A. Burris, M. Toi, W. Eiermann, M.-A. Lindsay & D. Slamon* 760

## reviews

- Molecular classification of gastric cancer  
*N.-Y. Chia & P. Tan* 763

- New drugs in acute myeloid leukemia  
*T. M. Kadia, F. Ravandi, J. Cortes & H. Kantarjian* 770

- Breakthrough therapies in B-cell non-Hodgkin lymphoma  
*C. Y. Cheah, N. H. Fowler & M. L. Wang* 778

- Phosphoproteomics in translational research: a sarcoma perspective  
*J. Noujaim, L. S. Payne, I. Judson, R. L. Jones & P. H. Huang* 787

## original articles

### precision medicine

- Incidental germline variants in 1000 advanced cancers on a prospective somatic genomic profiling protocol  
*F. Meric-Bernstam, L. Brusco, M. Daniels, C. Wathoo, A. M. Bailey, L. Strong, K. Shaw, K. Lu, Y. Qi, H. Zhao, H. Lara-Guerra, J. Litton, B. Arun, A. K. Eterovic, U. Aytac, M. Routbort, V. Subbiah, F. Janku, M. A. Davies, S. Kopetz, J. Mendelsohn, G. B. Mills & K. Chen* 795

### Response to angiotensin blockade with irbesartan in a patient with metastatic colorectal cancer

- M. R. Jones, K. A. Schrader, Y. Shen, E. Pleasance, C. Ch'ng, N. Dar, S. Yip, D. J. Renouf, J. E. Schein, A. J. Mungall, Y. Zhao, R. Moore, Y. Ma, B. S. Sheffield, T. Ng, S. J. M. Jones, M. A. Marra, J. Laskin & H. J. Lim* 801

### breast tumors

#### Observation versus late reintroduction of letrozole as adjuvant endocrine therapy for hormone receptor-positive breast cancer (ANZ0501 LATER): an open-label randomised, controlled trial

- N. Zdenkowski, J. F. Forbes, F. M. Boyle, G. Kannourakis, P. G. Gill, E. Bayliss, C. Saunders, S. Della-Fiorentina, N. Kling, I. Campbell, G. B. Mann, A. S. Coates, V. Gebski, L. Davies, R. Thornton, L. Reaby, J. Cuzick & M. Green on behalf of the Australia and New Zealand Breast Cancer Trials Group* 806

- A phase II trial of abiraterone acetate plus prednisone in patients with triple-negative androgen receptor positive locally advanced or metastatic breast cancer (UCBG 12-1)  
*H. Bonnefoi, T. Grellety, O. Tredan, M. Saghatelian, F. Dalenc, A. Mailliez, T. L'Haridon, P. Cottu, S. Abadie-Lacourtoisie, B. You, M. Mousseau, J. Dauba, F. Del Piano, I. Desmoulins, F. Coussy, N. Madranges, J. Grenier, F. C. Bidard, C. Proudhon, G. MacGrogan, C. Orsini, M. Pulido & A. Gonçalves* 812

- The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis  
*C. G. Rusthoven, R. A. Rabinovitch, B. L. Jones, M. Koshy, A. Amini, N. Yeh, M. W. Jackson & C. M. Fisher* 818

#### Identifying the potential long-term survivors among breast cancer patients with distant metastasis

- E. S. Lee, S. Y. Jung, J. Y. Kim, J. J. Kim, T. K. Yoo, Y. G. Kim, K. S. Lee, E. S. Lee, E. K. Kim, J. W. Min, W. Han, D. Y. Noh & H. G. Moon* 828

Continued overleaf

## *gastrointestinal tumors*

Long-course oxaliplatin-based preoperative chemoradiation versus  $5 \times 5$  Gy and consolidation chemotherapy for cT4 or fixed cT3 rectal cancer: results of a randomized phase III study

K. Bujko, L. Wyrwicz, A. Rutkowski, M. Malinowska, L. Pietrzak, J. Kryński, W. Michalski, J. Olędzki, J. Kuśnierz, L. Zająć, M. Bednarczyk, M. Szczepkowski, W. Tarnowski, E. Kosakowska, J. Zwoliński, M. Winiarek, K. Wiśniowska, M. Partycki, K. Bęczkowska, W. Polkowski, R. Styliński, R. Wierzbicki, P. Bury, M. Jankiewicz, K. Paprota, M. Lewicka, B. Cisel, M. Skórzewska, J. Mielko, M. Bębenek, A. Maciejczyk, B. Kapturkiewicz, A. Dybko, Ł. Hajac, A. Wojnar, T. Leśniak, J. Zygułska, D. Jantner, E. Chudyba, W. Zegarski, M. Las-Jankowska, M. Jankowski, L. Kołodziejski, A. Radkowski, U. Żelazowska-Omiotek, B. Czeremszynska, L. Kępka, J. Kolb-Sielecki, Z. Toczek, Z. Fedorowicz, A. Dzik, A. Danek, G. Nawrocki, R. Sopyło, W. Markiewicz, P. Kędzierski & J. Wydmański for the Polish Colorectal Study Group

834

FOLFOXIRI or FOLFOXIRI plus bevacizumab as first-line treatment of metastatic colorectal cancer: a propensity score-adjusted analysis from two randomized clinical trials  
C. Cremolini, F. Loupakis, G. Masi, S. Lonardi, C. Granetto, M. L. Mancini, S. Chiara, R. Moretto, D. Rossini, S. Vitello, G. Allegrini, G. Tonini, F. Bergamo, G. Tomasello, M. Ronzoni, A. Buonadonna, S. Bustreo, C. Barbara, L. Boni & A. Falcone

843

Role of major resection in pulmonary metastasectomy for colorectal cancer in the Spanish prospective multicenter study (GECMP-CCR)

J. Hernández, L. Molins, J. J. Fibla, F. Heras, R. Embún & J. J. Rivas on behalf of the Grupo Español de Metástasis Pulmonares de Carcinoma Colo-Rectal (GECMP-CCR) de la Sociedad Española de Neumología y Cirugía Torácica (SEPAR)

850

Sorafenib with or without everolimus in patients with advanced hepatocellular carcinoma (HCC): a randomized multicenter, multinational phase II trial (SAKK 77/08 and SASL 29)

D. Koeberle, J.-F. Dufour, G. Demeter, Q. Li, K. Ribi, P. Samaras, P. Saletti, A. D. Roth, D. Horber, M. Buehlmann, A. D. Wagner, M. Montemurro, G. Lakatos, J. Feilchenfeldt, M. Peck-Radosavljevic, D. Rauch, B. Tschanz & G. Bodoky for the Swiss Group for Clinical Cancer Research (SAKK)

856

## *thoracic tumors*

Detection of ubiquitous and heterogeneous mutations in cell-free DNA from patients with early-stage non-small-cell lung cancer

M. Jamal-Hanjani, G. A. Wilson, S. Horswell, R. Mitter, O. Sakarya, T. Constantin, R. Salari, E. Kirkizlar, S. Sigurjonsson, R. Pelham, S. Kareht, B. Zimmermann & C. Swanton

862

## *urogenital tumors*

Patient-reported quality-of-life analysis of radium-223 dichloride from the phase III ALSYMPCA study

S. Nilsson, P. Cislo, O. Sartor, N. J. Vogelzang, R. E. Coleman, J. M. O'Sullivan, J. Reuning-Scherer, M. Shan, L. Zhan & C. Parker

868

Prognostic factors in patients with poor-risk germ-cell tumors: a retrospective analysis of the Indiana University experience from 1990 to 2014

N. Adra, S. K. Althouse, H. Liu, M. J. Brames, N. H. Hanna, L. H. Einhorn & C. Albany

875

A randomized, double-blind phase II study evaluating cediranib versus cediranib and saracatinib in patients with relapsed metastatic clear-cell renal cancer (COSAK)

T. Powles, J. Brown, J. Larkin, R. Jones, C. Ralph, R. Hawkins, S. Chowdhury, E. Boleti, A. Bhal, K. Fife, A. Webb, S. Crabb, T. Geldart, R. Hill, J. Dunlop, P. E. Hall, D. McLaren, C. Ackerman, L. Beltran & P. Nathan

880

## *hematologic malignancies*

Spectrum of clinical and genetic features of patients with inherited platelet disorder with suspected predisposition to hematological malignancies: a nationwide survey in Japan

A. Yoshimi, T. Toya, Y. Nannya, K. Takaoka, K. Kirito, E. Ito, H. Nakajima, Y. Hayashi, T. Takahashi, A. Moriya-Saito, K. Suzuki, H. Harada, N. Komatsu, K. Usuki, M. Ichikawa & M. Kurokawa

887

Factors influencing outcome in advanced stage, low-grade follicular lymphoma treated at MD Anderson Cancer Center in the rituximab era

C. Y. Cheah, D. Chihara, M. Ahmed, R. E. Davis, L. J. Nastoupil, K. Phansalkar, F. B. Hagemeister, L. E. Fayad, J. R. Westin, Y. Oki, M. A. Fanale, J. E. Romaguera, M. L. Wang, H. Lee, F. Turturro, F. Samaniego, M. A. Rodriguez, S. S. Neelapu & N. H. Fowler

895

Safe and prolonged survival with long-term exposure to pomalidomide in relapsed/refractory myeloma

G. Fouquet, B. Pegourie, M. Macro, M. O. Petillon, L. Karlin, D. Caillot, M. Roussel, B. Arnulf, C. Mathiot, G. Marit, B. Kolb, A. M. Stoppa, S. Brechinac, V. Richez, P. Rodon, A. Banos, M. Wetterwald, L. Garderet, B. Royer, C. Hulin, L. Benbouker, O. Decaux, M. Escoffre-Barbe, J. P. Fermand, M. Attal, H. Avet-Loiseau, P. Moreau, T. Facon & X. Leleu on behalf of IFM (Intergroupe Francophone du Myélome)

902

Continued overleaf

## head and neck tumors

Response-adapted volume de-escalation (RAVD) in locally advanced head and neck cancer  
V. M. Villaflor, J. M. Melotek, T. G. Garrison, R. J. Brisson, E. A. Blair, L. Portugal, J. A. De Souza, D. T. Ginat, K. M. Stenson, A. Langerman, M. Kocherginsky, M. T. Spiotto, N. Hannigan, T. Y. Seiwert, E. E. W. Cohen, E. E. Vokes & D. J. Haraf 908

## miscellaneous tumors

Merkel cell carcinoma: value of sentinel lymph-node status and adjuvant radiation therapy  
A. Servy, E. Maubec, P. E. Sugier, F. Grange, S. Mansard, T. Lesimple, E. Marinho, B. Couturaud, A. Girod, S. Albert, R. Dendale, E. Calitchi, L. Sarda, J. Chanal, L. Deschamps, X. Sastre-Garau, L. Laroche, B. Crickx & M. F. Avril 914

## early drug development

What hides behind the MASC: clinical response and acquired resistance to entrectinib after *ETV6-NTRK3* identification in a mammary analogue secretory carcinoma (MASC)  
A. Drilon, G. Li, S. Dogan, M. Gounder, R. Shen, M. Arcila, L. Wang, D. M. Hyman, J. Hechtman, G. Wei, N. R. Cam, J. Christiansen, D. Luo, E. C. Maneval, T. Bauer, M. Patel, S. V. Liu, S. H. I. Ou, A. Farago, A. Shaw, R. F. Shoemaker, J. Lim, Z. Hornby, P. Multani, M. Ladanyi, M. Berger, N. Katabi, R. Ghossein & A. L. Ho 920

## epidemiology

The global decrease in cancer mortality: trends and disparities  
D. Hashim, P. Boffetta, C. La Vecchia, M. Rota, P. Bertuccio, M. Malvezzi & E. Negri 926

Cancer mortality in cohorts of workers in the European rubber manufacturing industry first employed since 1975  
M. Boniol, A. Koechlin, B. Świątkowska, T. Sorahan, J. Wellmann, D. Taeger, K. Jakobsson, E. Pira, P. Boffetta, C. La Vecchia, C. Pizot & P. Boyle 933

Periodontal disease and risk of all cancers among male never smokers: an updated analysis of the Health Professionals Follow-up Study  
D. S. Michaud, K. T. Kelsey, E. Papathanasiou, C. A. Genco & E. Giovannucci 941

## sarcoma

A phase I trial of panobinostat and epirubicin in solid tumors with a dose expansion in patients with sarcoma  
S. Thomas, R. Aggarwal, T. Jahan, C. Ryan, T. Troung, A. M. Cripps, P. Raha, K. T. Thurn, S. Chen, J. A. Grabowsky, J. Park, J. Hwang, A. Daud & P. N. Munster 947

## letters to the editor

Ovarian suppression during chemotherapy increases pregnancy rate in survivors  
Z. Blumenfeld 953

Transformation of *ALK* rearrangement-positive adenocarcinoma to small-cell lung cancer in association with acquired resistance to alectinib  
N. Takegawa, H. Hayashi, N. Iizuka, T. Takahama, H. Ueda, K. Tanaka, M. Takeda & K. Nakagawa 953

Prognostic impact of extracapsular lymph node involvement in colorectal cancer  
Q. Huang & X. Qin 955

Extranodal extension is an important prognostic parameter for both colonic and rectal cancer  
C. Luchini, A. Nottegar, A. Pea, M. Solmi, B. Stubbs, P. Capelli, G. Sergi, E. Manzato, M. Fassan, L. D. Wood, A. Scarpa & N. Veronese 955

Prognostic impact of extra-nodal extension on colon and rectal cancer should be investigated separately  
Q. Huang & H. Yang 956

Reply to the letter to the editor 'A randomized trial of intensive versus minimal surveillance of patients with resected Dukes B2-C colorectal carcinoma' by Rosati et al.  
R. B. Hines & R. Al-Rajabi 957

Reply to the letter to the editor 'Number-Needed-To-Treat for pricing costly anti-cancer drugs. The example of Regorafenib in metastatic colorectal cancer' by Graziano et al.  
F. Pignatti, J. Martinalbo, B. Jonsson & P. Foggi 958

Dendritic cells stimulated by MUC1 antigen could induce lymphocytes' anergy through PD-L2 but not through PD-L1 pathway  
K. Wojas-Krawczyk, I. Homa-Mlak, P. Krawczyk, T. Kucharczyk & J. Milanowski 958