# Cancer



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### **NEWS**

3265 CancerScope: Oncology Issues in Focus

Carrie Printz

This news section offers *Cancer* readers timely information on events, public policy analysis, topical issues, and personalities. This edition looks at 2 nationwide studies that seek answers in the use of targeted therapy for patients with lung cancer, results of a new study that conclude race is a factor in incidence of triple negative breast cancer, and a report showing that obesity is associated with mortality rates in women with ER-positive breast cancer.

Published online 20 October 2014

### **EDITORIALS**

3268 Translational Immunotherapeutics: Chemoimmunotherapy for Malignant Pleural Mesothelioma

Prasad S. Adusumilli

Recent data indicate that chemotherapy treats cancer, at least in part, by facilitating an immune response to the tumor. The study results outlined in this issue highlight the potential benefits in devising an optimal strategy for integrating new immune-based therapies into the standard of care for various cancers.

See also pages 3311-9.

Published online 2 July 2014

3272 Cancer-Related Inflammation: An Emerging Prognostic Domain in Metastatic Castration-Resistant Prostate
Carcinoma

David J. Pinato

The neutrophil-to-lymphocyte ratio effectively integrates into a novel prognostic model for castration-resistant prostate cancer according to the study by Templeton et al. Systemic inflammation may provide novel insight into the pathophysiology of the disease as well as new targets for therapy and useful surrogates to optimize clinical management.

See also pages 3346-52.

Published online 3 July 2014

3275 Quality Lung Cancer Screening Protects Quality of Life: No Harm, No Foul

Jamie S. Ostroff

This ancillary paper from the National Lung Screening Trial (NLST) dataset examines the impact of undergoing low-dose spiral computed tomography (LDCT) for early detection of lung cancer on health related quality of life and state anxiety assessed at 1 and 6 months following lung screening. Outcomes are compared by screening results. Overall, the findings provide reassurance that undergoing lung cancer screening in the context of a well-designed screening and follow-up protocol poses little or no psychological harm or quality of life impairment to screening participants.

See also pages 3401-9.

Published online 25 July 2014



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### **REVIEW ARTICLES**

3277 Oncolytic Polio Virotherapy of Cancer

Michael C. Brown, Elena Y. Dobrikova, Mikhail I. Dobrikov, Ross W. Walton, Sarah L. Gemberling, Smita K. Nair, Annick Desjardins, John H. Sampson, Henry S. Friedman, Allan H. Friedman, Douglas S. Tyler, Darell D. Bigner, and Matthias Gromeier

Oncolytic poliovirus immunotherapy is demonstrating early promise in phase 1 clinical trials against recurrent glioblastoma. Clinical use of oncolytic polioviruses is supported by uniquely suitable target tropism, safety and tumor specificity, tumor cytotoxicity, robust viral cytotoxicity in the presence of innate defenses and pre-existing neutralizing antibodies, and immunogenicity.

Published online 17 June 2014

3287 Medical Management of Metastatic Medullary Thyroid Cancer

Jessica E. Maxwell, Scott K. Sherman, Thomas M. D'Dorisio, and James R. Howe

Despite significant progress in our understanding of the molecular basis of medullary thyroid cancer, the treatment of patients with metastatic disease remains problematic. In this article, the authors review the evolution of medical therapy for medullary thyroid cancer from the early 1970s to the present.

Published online 18 June 2014

## **ORIGINAL ARTICLES**

#### **Disease Site**

### **Chest and Lung Disease**

- 3302 Exercise-Induced Lung Cancer Regression: Mechanistic Findings From a Mouse Model

  \*\*Kristin A. Higgins, Dongkyoo Park, Gee Young Lee, Walter J. Curran, and Xingming Deng

  This study demonstrates that daily cardiovascular exercise reduces lung tumor growth in mice, and tumor apoptosis is increased. Exercise should therefore be further explored as a potential anti-cancer therapy.

  \*\*Published online 2 July 2014\*\*
- 3311 Phase 1 Study of the Antimesothelin Immunotoxin SS1P in Combination With Pemetrexed and Cisplatin for Front-Line Therapy of Pleural Mesothelioma and Correlation of Tumor Response With Serum Mesothelin, Megakaryocyte Potentiating Factor, and Cancer Antigen 125

Raffit Hassan, Elad Sharon, Anish Thomas, Jingli Zhang, Alexander Ling, Markku Miettinen, Robert J. Kreitman, Seth M. Steinberg, Kevin Hollevoet, and Ira Pastan

In this first clinical evaluation of the combination of an immunotoxin with chemotherapy, SS1P, an antimesothelin immunotoxin, was combined with pemetrexed and cisplatin in chemotherapy-naive patients who had advanced malignant pleural mesothelioma. The results from this phase 1 trial demonstrate that SS1P and chemotherapy can be safely combined with no overlapping toxicity. In addition, the objective tumor response rate for the combination is higher than expected with chemotherapy alone and provides a strong rationale for a randomized trial to confirm this finding. See also pages 3268-71.

Published online 2 July 2014 (Continued)



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#### **Gastrointestinal Disease**

3320 Gastric Juice Long Noncoding RNA Used as a Tumor Marker for Screening Gastric Cancer

Yongfu Shao, Meng Ye, Xiaoming Jiang, Weiliang Sun, Xiaoyun Ding, Zhong Liu, Guoliang Ye, Xinjun Zhang, Bingxiu Xiao, and Junming Guo

Long noncoding RNAs (lncRNAs) stably exist in gastric juice and can be detected using real-time quantitative reverse transcription-polymerase chain reaction analysis. Some lncRNAs, such as AA174084 in gastric juice, can be used as biomarkers for the detection of gastric cancer with satisfactory specificity and sensitivity.

Published online 1 July 2014

Polymorphisms in Folate-Metabolizing Enzymes and Response to 5-Fluorouracil Among Patients With Stage II or III

Rectal Cancer (INT-0144; SW0G 9304)

Cornelia M. Ulrich, Cathryn Rankin, Adetunji T. Toriola, Karen W. Makar, Özge Altug-Teber, Jacqueline K. Benedetti, Rebecca S. Holmes, Stephen R. Smalley, Charles D. Blanke, and Heinz-Josef Lenz

There were no statistically significant associations noted between 8 functionally significant polymorphisms in 6 genes (MTHFR [C677T, A1298C], SLC19A1 [G80A], SHMT1 [C1420T], DHFR [Del19bp], TS 1494del, and TSER) involved in folate metabolism and overall survival, disease-free survival, and toxicity in the overall analyses. Nevertheless, there was a trend toward worse disease-free survival and reduced hematological and gastrointestinal toxicities among patients with variant alleles in MTHFR C677T, SLC19A1 G80A, and TSER, respectively.

Published online 15 July 2014

## **Genitourinary Disease**

3338 Substance Use Disorder and its Effects on Outcomes in Men With Advanced-Stage Prostate Cancer

Sumedha Chhatre, David S. Metzger, S. Bruce Malkowicz, George Woody, and Ravishankar Jayadevappa

The intersection of advanced prostate cancer and substance use disorder appears to adversely affect outcomes. Thus, incorporating substance use screening and treatments into prostate cancer care guidelines and care coordination is desirable.

Published online 9 July 2014

3346 Simple Prognostic Score for Metastatic Castration-Resistant Prostate Cancer With Incorporation of Neutrophil-to-Lymphocyte Ratio

Arnoud J. Templeton, Carmel Pezaro, Aurelius Dmlin, Mairéad G. McNamara, Raya Leibowitz-Amit,
Francisco E. Vera-Badillo, Gerhardt Attard, Johann S. de Bono, Ian F. Tannock, and Eitan Amir
A high neutrophil-to-lymphocyte ratio (NLR) is a marker of host inflammation, indicating poor prognosis in many solid tumors including castration-resistant prostate cancer (CRPC). Incorporation of NLR in a simple risk score improves prognostic accuracy for chemotherapy-naive men with CRPC.
See also pages 3272-4.

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#### **Head and Neck Disease**

3353 Trends and Variations in the Use of Adjuvant Therapy for Patients With Head and Neck Cancer

Michelle M. Chen, Sanziana A. Roman, Wendell G. Yarbrough, Barbara A. Burtness, Julie A. Sosa, and Benjamin L. Judson

Approximately one-quarter of patients are not receiving National Comprehensive Cancer Network

guideline-directed adjuvant therapy. Patient-level and hospital-level factors are associated with

variation in the receipt of adjuvant therapy.

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#### Soft Tissue and Bone Sarcoma

Prognostic Factors and Impact of Adjuvant Treatments on Local and Metastatic Relapse of Soft-Tissue Sarcoma
Patients in the Competing Risks Setting

Antoine Italiano, Axel Le Cesne, Jean Mendiboure, Jean-Yves Blay, Sophie Piperno-Neumann, Christine Chevreau, Corinne Delcambre, Nicolas Penel, Philippe Terrier, Dominique Ranchere-Vince, Marick Lae, Sophie Le Guellec, Jean-Jacques Michels, Yves Marie Robin, Carine Bellera, and Sylvie Bonvalot

In the setting of competing risks, tumor biology reflected by histological grade is a crucial predictor of local relapse of soft-tissue sarcomas, whereas tumor depth and size have poor if any influence. Grade could also predict the benefit of adjuvant chemotherapy in patients with soft-tissue sarcoma.

Published online 10 July 2014

## **Discipline**

### **Epidemiology**

3370 Interferon-γ-Induced Inflammatory Markers and the Risk of Cancer: The Hordaland Health Study

Hui Zuo, Grethe S. Tell, Stein E. Vollset, Per M. Ueland, Ottar Nygård, Øivind Midttun, Klaus Meyer, Arve Ulvik,

and Simone J.P.M. Eussen

Interferon- $\gamma$  (IFN- $\gamma$ )-induced inflammatory markers were associated with an increased cancer risk in a cohort of 6594 adults followed for a median of 12 years, revealing evidence for the role of IFN- $\gamma$  induced inflammation in human carcinogenesis.

Published online 19 June 2014

#### **Outcomes Research**

3378 Impact of Medicare Part D on Out-of-Pocket Drug Costs and Medical Use for Patients With Cancer

Sheetal M. Kircher, Michael E. Johansen, Halla S. Nimeiri, Caroline R. Richardson, and Matthew M. Davis

Medicare D has reduced out-of-pocket prescription drug costs and outpatient visits for seniors with

cancer beyond trends observed for younger patients with no major impact noted on use of other

medical services.

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3385 Racial Disparities in Urologist Visits Among Elderly Men With Prostate Cancer: A Cohort Analysis of Patient-Related and County of Residence-Related Factors

Eberechukwu Onukwugha, Phillip Osteen, Jinani Jayasekera, C. Daniel Mullins, Christine A. Mair, and Arif Hussain. The current study investigated novel social environment factors including crime, housing, and household characteristics. The results indicate that social environment characteristics and their relationship with urologist visits differed between African American and white men.

Published online 24 June 2014

### **Psychosocial Oncology**

3393 Suicidal Ideation in Prostate Cancer Survivors: Understanding the Role of Physical and Psychological Health
Outcomes

Christopher J. Recklitis, Eric S. Zhou, Eric K. Zwemer, Jim C. Hu, and Philip W. Kantoff

The results of the current study indicate that a significant percentage of prostate cancer survivors report recent suicidal ideation and, more importantly, demonstrate that both physical disability and prostate-associated symptoms are strongly associated with suicide ideation. These are novel findings that have important implications for both clinical care and outcomes research.

Published online 24 June 2014

### **Quality of Life**

3401 Impact of Lung Cancer Screening Results on Participant Health-Related Quality of Life and State Anxiety in the National Lung Screening Trial

Ilana F. Gareen, Fenghai Duan, Erin M. Greco, Bradley S. Snyder, Phillip M. Boiselle, Elyse R. Park, Dennis Fryback, and Constantine Gatsonis

In a large multi-center lung screening trial, participants receiving a false positive or significant incidental finding screen result experienced no significant difference in health related quality of life or state anxiety at 1 or at 6 months after screening relative to those receiving a negative result. See also pages 3275-6.

Published online 25 July 2014

### **Radiation Oncology**

3410 Highly Effective Treatment of Skull Base Chordoma With Carbon Ion Irradiation Using a Raster Scan Technique in 155 Patients: First Long-Term Results

Matthias Uhl, Matthias Mattke, Thomas Welzel, Falk Roeder, Jan Oelmann, Gregor Habl, Alexandra Jensen, Malte Ellerbrock, Oliver Jäkel, Thomas Haberer, Klaus Herfarth, and Jürgen Debus

Carbon ion therapy is a safe and effective treatment for skull base chordoma, resulting in high local control and overall survival rates.

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#### Translational Research

3418 Noninvasive Radiofrequency Treatment Effect on Mitochondria in Pancreatic Cancer Cells

Steven A. Curley, Flavio Palalon, Xiaolin Lu, and Nadezhda V. Koshkina

Anticancer efficacy of innovative non-invasive method of cancer treatment based on the use of electromagnetic radiofrequency fields (RF) treatment had been reported in our previous studies, however its mechanism of action remains poorly understood. Here we demonstrated the ability of RF treatment to affect mitochondria in cancer cells.

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### **INFORMATION ITEM**

3426 Erratum