IN THIS ISSUE
Highlighted research articles ....................... 1079

NEWS IN BRIEF
Important news stories affecting the community ............ 1084

NEWS IN DEPTH
Disparities Persist in Cancer Careers ....................... 1088

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ....................... 1089

ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/CDNews.

VIEWS
In The Spotlight
Same Name, Different Game: EGFR Drives Intrinsic KRASG12C Inhibitor Resistance in Colorectal Cancer .. 1094
M.K. Koleilat and L.N. Kwong
See article, p. 1129

Pegylated Engineered IL2 plus Anti–PD-1 Monoclonal Antibody: The Nectar Comes from the Combination ............... 1097
M. Rouanne, L. Zitvogel, and A. Marabelle
See article, p. 1158

All Myeloid-Derived Suppressor Cells Are Not Created Equal: How Gender Inequality Influences These Cells and Affects Cancer Therapy ................. 1100
D.I. Gabrilovich
See article, p. 1210

RESEARCH BRIEFS
Impact of PD-1 Blockade on Severity of COVID-19 in Patients with Lung Cancers ............... 1121
J. Luo, H. Rizvi, J.V. Egger, I.R. Preeshagul, J.D. Wolchok, and M.D. Hellmann
Précis: In 69 patients with lung cancer who developed COVID-19, disease severity and mortality were high, but prior PD-1 blockade was not a risk factor for poor outcomes in this group, suggesting the therapy should be used when indicated.

EGFR Blockade Reverts Resistance to KRASG12C Inhibition in Colorectal Cancer ............... 1129
Précis: KRASG12C inhibitor-resistant KRASG12C-mutant colorectal cancer cells, patient-derived organoids, and patient-derived xenografts responded to combination treatment with anti-EGFR, in part due to high upstream EGFR signaling.
See commentary, p. 1094

RESEARCH ARTICLES
Overcoming Genetically Based Resistance Mechanisms to PD-1 Blockade ............... 1140
Précis: Loss-of-function mutations in JAK1, JAK2, or B2M conferred resistance to anti–PD-1 treatment, but mechanism-informed treatment with a TLR9 agonist (for JAK1/2-mutant tumors) or an IL2 pathway agonist (for B2M-mutant tumors) could overcome resistance.

Bempegaldesleukin (NKTR-214) plus Nivolumab in Patients with Advanced Solid Tumors: Phase I Dose-Escalation Study of Safety,
Efficacy, and Immune Activation (PIVOT-02) ........................................ 1158
A. Diab, N.M. Tannir, S.-E. Bentebibel, P. Hwu,
V. Papadimitrakopoulou, C. Haymaker, H.M. Kluger,
S.N. Gettinger, M. Szol, S.S. Tykodi, B.D. Curti,
M.A. Tagliaferri, J. Zalesky, A.L. Hannah, U. Hoch,
S. Aung, C. Fanton, A. Rizwan, E. Iacucci, Y. Liao,
C. Bernatchez, M.E. Hurwitz, and D.C. Cho
Précis: In a phase I trial of 38 patients with advanced
melanoma, renal cell carcinoma, or non–small cell lung
cancer, the IL2 pathway agonist bempegaldesleukin
plus nivolumab was safe, and characteristics of
responders reflected bempegaldesleukin’s mechanism.
See commentary, p. 1097

The Genomic Landscape of Intrinsic and
Acquired Resistance to Cyclin-Dependent
Kinase 4/6 Inhibitors in Patients with
Hormone Receptor–Positive Metastatic
Breast Cancer ................................. 1174
S.A. Wander, O. Cohen, X. Gong, G.N. Johnson,
J.E. Buendia-Buendia, M.R. Lloyd, D. Kim, F. Luo,
P. Mao, K. Helvie, K.J. Kowalski, U. Nayar, A.G. Waks,
S.H. Parsons, R. Martinez, L.M. Litchfield, X.S. Ye,
C. Yu, VM. Jansen, J.R. Stille, PS. Smith, G.I. Oakley,
Q.S. Chu, G. Batist, M.E. Hughes, J.D. Kremer,
L.A. Garraway, E.P. Winer, S.M. Tolaney, N.U. Lin,
S.G. Buchanan, and N. Wagle
Précis: Genomic alterations in several genes were
associated with resistance to CDK4/6 inhibition
in patients with HR+HER2− breast cancer; for the
majority of tumors profiled, there is a targeted
therapy that could overcome or prevent resistance.

Antitumor Activity of Amivantamab
(JNJ-61186372), an EGFR–MET
Bispecific Antibody, in Diverse Models
of EGFR Exon 20 Insertion–Driven
NSCLC ............................................ 1194
J. Yun, S.-H. Lee, S.-Y. Kim, S.-Y. Jeong, J.-H. Kim,
K.-H. Pyo, C.-W. Park, S.G. Heo, M.R. Yum, S. Lim,
S.M. Lim, M.H. Hong, H.R. Kim, M. Thayu, J.C. Curtin,
R.E. Knoblauch, M.V. Lorenzi, A. Roshak, and B.C. Cho
Précis: The EGFR–cMET-targeted bispecific
antibody amivantamab inhibited growth of EGFR
exon 20 insertion–driven non–small cell lung
cancer cells, organoids, and xenografts as well as
showing hints of clinical efficacies.

Myeloid-Derived Suppressor Cell
Subsets Drive Glioblastoma Growth
in a Sex-Specific Manner .......... 1210
D. Bayik, Y. Zhou, C. Park, C. Hong, D. Vail, D.J. Silver,
A. Lauko, G. Roversi, D.C. Watson, A. Lo, T.I. Alban,
M. McGraw, M. Sorensen, M.M. Grabowski, B. Otvos,
M.A. Vogelbaum, C. Horbinski, B.W. Kristensen,
A.M. Khalii, T.H. Hwang, M.S. Ahluwalia, F. Cheng,
and J.D. Lathia
Précis: Sex-biased differences in myeloid-derived
suppressor cell subsets mediated treatment
responses in glioblastoma models; these differences
were also observed in patients and were predictive
of prognosis.
See commentary, p. 1100

The INPP4B Tumor Suppressor
Modulates EGFR Trafficking and
Promotes Triple-Negative
Breast Cancer ............................... 1226
H. Liu, M.N. Paddock, H. Wang, C.J. Murphy, R.C. Geck,
A.J. Navarro, G.M. Wulf, O. Elemento, V. Haucke,
L.C. Cantley, and A. Toker
Précis: In a model of triple-negative breast
cancer, the PI3K–AKT pathway member and lipid
phosphatase INPP4B functioned as a tumor
suppressor, and loss of INPP4B caused delayed
EGFR degradation and increased EGFR signaling.