decrease the likelihood of discovering unknown toxic effects in larger populations and costly phase 2 and 3 studies. That (2) prospectively delineating therapeutic intent with prespecified clinical end points should be adopted because it may facilitate early identification of efficacy and improve insurance coverage of and patient access to early-phase trials.[2] The ability to directly attribute late toxic effects to specific drug radiation combinations is complicated by early patient mortality and confounding treatments. However, because investigators are obligated to their patients and peers to evaluate toxic effects from investigational treatments, we propose that (3) assessment and reporting of late toxic effects be included in phase 1 trials.

Limitations of this study include the time period evaluated, that it is a single database query, and that it only includes published trials and toxic effects. ClinicalTrials.gov was not included because trial registration is not mandated as a condition of publication for phase 1 trials.[6] However, these data identify 3 important measures, which if addressed, will improve the quality, availability, and interpretability of phase 1 trials.

Hyun Kim, MD
Tu D. Dan, MD
Joshua D. Palmer, MD
Benjamin E. Leiby, PhD
Yaacov R. Lawrence, MRCP
Adam P. Dicker, MD, PhD

Author Affiliations: Department of Radiation Oncology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania (Kim, Dan, Palmer, Dicker); Division of Biostatistics, Department of Pharmacology and Experimental Therapeutics, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania (Leiby); Department of Radiation Oncology, Sheba Medical Center, Tel HaShomer, Israel (Lawrence).

Corresponding Author: Hyun Kim, MD, Department of Radiation Oncology, Sidney Kimmel Medical College and Cancer Center, Thomas Jefferson University, 111 S 11th St, Philadelphia, PA 19107 (hyun.kim@jefferson.edu).

Published Online: December 17, 2015. doi:10.1001/jamaoncol.2015.4833.

Author Contributions: Dr Kim had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Kim, Dan, Palmer, Lawrence, Dicker.
Acquisition, analysis, or interpretation of data: Kim, Dan, Palmer, Leiby, Dicker.
Drafting of the manuscript: Kim, Dan.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Dan, Leiby, Lawrence.
Administrative, technical, or material support: Kim, Dicker.
Study supervision: Kim, Palmer.

Conflict of Interest Disclosures: None reported.

Funding/Support: Dr Leiby is supported in part by award No. P30 CA056036-16 from the National Cancer Institute (NCI). Dr Lawrence is supported in part by EU FP7 Marie-Curie funding (CIG PCIG10-GA-2011-303795).

Role of the Funder/Sponsor: The NCI and Marie-Curie funding had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Previous Presentation: Data were presented in part at the American Association for Cancer Research Radiation Oncology Think Tank, Inaugural Meeting; January 11-13, 2015; Fort Myers, Florida.

1. Shaw AT, Kim D-W, Mehra R, et al. Ceritinib in ALK-rearranged non-small-cell lung cancer. *N Engl J Med*. 2014;370(13):1189-1197. doi:10.1056/NEJMoa1311107.

2. Weber JS, Levit LA, Adamson PC, et al American society of clinical oncology policy statement update: the critical role of phase i trials in cancer research and treatment. *J Clin Oncol*. 2014 ;33(3):278-284.doi:10.1200/JCO.2014.58.2635.

3. Paller CJ, Bradbury PA, Ivy SP, et al. Design of phase I combination trials: recommendations of the Clinical Trial Design Task Force of the NCI Investigational Drug Steering Committee. *Clin Cancer Res*. 2014;20(16):4210-4217. doi:10.1158/1078-0432.CCR-14-0521.

4. Darby SC, Ewertz M, McGale P, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. *N Engl J Med*. 2013;368(11):987-998. doi:10.1056/NEJMoa1209825.

5. Elliott AC, Hynan LSA. A SAS(®) macro implementation of a multiple comparison post hoc test for a Kruskal-Wallis analysis. *Comput Methods Programs Biomed*. 2011;102(1):75-80. doi:10.1016/j.cmpb.2010.11.002.

6. Anderson ML, Chiswell K, Peterson ED, Tasneem A, Topping J, Califf RM. Compliance with results reporting at ClinicalTrials.gov. *N Engl J Med*. 2015;372(11):1031-1039. doi:10.1056/NEJMsa1409364.

Chemotherapy-Related Chronic Myelogenous Leukemia: A Case Series of Patients With Germ Cell Tumor

Germ cell tumors (GCTs) are the most common cancer in young men ages 15 to 35 years and are uniquely responsive to chemotherapy, with cure rates approaching 80%. Late adverse effects of treatment can manifest throughout the lifetime of a cured patient who will be at increased risk of solid and hematologic malignant neoplasms.[1,2] Etoposide has become one of the cornerstones of platinum-containing regimens for GCT. Treatment with etoposide entails a known risk of secondary leukemia that typically exhibits a short latency period, a chromosomal translocation (11q23 and 21q22), and rearrangement of the mixed-lineage leukemia gene.

Methods | We observed 3 patients with Philadelphia chromosome-positive chronic myelogenous leukemia (CML) following therapy for GCT.

Results | *Case 1.* In 1999, a man in his mid-30s with nonseminomatous GCT (NSGCT) was treated with orchiectomy followed by 4 courses of bleomycin, etoposide, and cisplatin. In September 2011, he was noted to have a white blood cell count (WBC) of 111 700/μL (111.7 × 10^9/L). Bone marrow examination showed morphologic findings of chronic-phase CML, and a t(9;22)(q34;q11) was identified. The patient started treatment with imatinib and achieved a complete molecular remission. Unfortunately, in 2014, he developed malignant transformation of teratoma to an undifferentiated neuroendocrine carcinoma with unresectable hepatic metastases and died of his disease.

Case 2. In 2006, a man in his early 30s had orchiectomy for clinical stage I NSGCT and elected to receive a single cycle of BEP. In November 2006, the disease relapsed, and he was treated with 3 cycles of etoposide, ifosfamide, and cisplatin (VIP). In 2007, the patient experienced a second relapse and was treated with 2 cycles of high-dose carboplatin and etoposide followed by peripheral blood stem cell rescue. In 2011, he was found to have leukocytosis (WBC, 91 700/μL [91.7 × 10^9/L]). Bone marrow examination confirmed chronic-phase CML with t(9;22)(q34;q11). The patient was treated with dasatinib and achieved a molecular remission . To date, he continues to be in remission for his CML and recurrent GCT.

Case 3. In 2012, a young adult man with history of Klinefelter syndrome presented with intermittent chest pain and was found to have a 15-cm primary mediastinal NSGCT. He was treated with 4 cycles of VIP followed by resection of residual mediastinal mass, which revealed teratoma. In 2014, he was found to have leukocytosis (WBC, 44 000/μL [44.0 × 10^9/L]). Bone marrow examination confirmed chronic-phase CML by morphologic characteristics, and a t(9;22)(q34;q11) was identified by chromosome analysis. The patient started treatment with dasatinib and achieved a hematologic response. To date, his *BCR/ABL* transcript declined appropriately from 55% to 9%. He continues to be in remission for his GCT.

Discussion | There have been reports of chemotherapy-related Philadelphia-chromosome leukemias in patients with antecedent malignant neoplasms.[3] Past treatments for GCT with cisplatin-etoposide–containing regimens or HDCT with carboplatin-etoposide have been linked to an increased risk of secondary acute leukemia[1,4] and solid tumors.[5] A review of the literature reveals 7 cases of GCT with subsequent development of CML.[1,3,6] In this series, we present 3 cases of patients with GCT who achieved remission with chemotherapy and later developed *BCR/ABL*-positive CML. These findings raise the question of a causal relationship between etoposide and/or platinum-containing chemotherapy and the development of CML with t(9;22)(q34;q11).

Etoposide-based chemotherapy in patients with GCT is leukemogenic. It is not clear whether combination chemotherapy with cisplatin and bleomycin contribute to this result. While its association with AML is well established, questions regarding the connection of etoposide and cisplatin-containing combination chemotherapy and secondary CML are posed herein. The relatively low risk of secondary leukemia in patients treated with potentially curative combination chemotherapy for GCT continues to be reassuring.[1] However, physicians should be aware of possible late toxic effects of these treatment regimens and the need for diligent follow-up in these patients.

Nabil Adra, MD
Hamid Sayar, MD
Lawrence H. Einhorn, MD

Author Affiliations: Indiana University, Indianapolis, Melvin & Bren Simon Cancer Center, Division of Hematology/Oncology, Indiana University School of Medicine, Indianapolis.

Corresponding Author: Nabil Adra, MD, Indiana University, 535 Barnhill Dr, RT 400, Indianapolis, IN 46202 (nadra@iu.edu).

Published Online: December 3, 2015. doi:10.1001/jamaoncol.2015.4837.

Author Contributions: Dr Adra had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Adra, Einhorn.
Critical revision of the manuscript for important intellectual content: All authors.
Administrative, technical, or material support: Adra.
Study supervision: Sayar.

Conflict of Interest Disclosures: None reported.

Funding/Support: Dr Einhorn supported in part by the National Cancer Institute (NCI) (1 RO1 CA157823-)1A1.

Role of the Funder/Sponsor: The NCI had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank the patients for granting permission to publish this information.

1. Travis LB, Andersson M, Gospodarowicz M, et al. Treatment-associated leukemia following testicular cancer. *J Natl Cancer Inst*. 2000;92(14):1165-1171.

2. Travis LB, Fosså SD, Schonfeld SJ, et al. Second cancers among 40,576 testicular cancer patients: focus on long-term survivors. *J Natl Cancer Inst*. 2005;97(18):1354-1365.

3. Pedersen-Bjergaard J, Brøndum-Nielsen K, Karle H, Johansson B. Chemotherapy-related - late occurring - Philadelphia chromosome in AML, ALL and CML: similar events related to treatment with DNA topoisomerase II inhibitors? *Leukemia*. 1997;11(9):1571-1574.

4. Houck W, Abonour R, Vance G, Einhorn LH. Secondary leukemias in refractory germ cell tumor patients undergoing autologous stem-cell transplantation using high-dose etoposide. *J Clin Oncol*. 2004;22(11):2155-2158.

5. Fung C, Fossa SD, Milano MT, Oldenburg J, Travis LB. Solid tumors after chemotherapy or surgery for testicular nonseminoma: a population-based study. *J Clin Oncol*. 2013;31(30):3807-3814.

6. Iurlo A, Foa P, Maiolo AT, Polli EE. Chronic myelogenous leukemia following radiation therapy for testicular seminoma. *Blut*. 1989;59(6):503-504.

Disease-Specific Hashtags for Online Communication About Cancer Care

Increasingly, patients, caregivers, and health care professionals (HCPs) go online to learn about and discuss cancer care.[1] However, finding other people or organizations with similar interests can be difficult without some structure.

Hashtags are user-generated tags that can organize and aggregate content on social networks. In July 2011, 2 patient advocates started a breast cancer chat on Twitter using the tag #bcsm (breast cancer social media); one of us (D.J.A.) joined as a comoderator. This same model but with hashtag #btsm was used to discuss brain tumors in January 2012. Both tags are now regularly used on Twitter by patients, caregivers, and HCPs.

Dedicated hashtags may make it easier to engage in relevant conversations online for other types of cancer. In this study, we describe a way to use disease-specific hashtags similar to #bcsm and #btsm to organize and increase online discussion of cancer care.

Methods | Based on the models using the #bcsm and #btsm hashtags, 2 of us (M.S.K. and P.F.A.) developed a set of 23 new cancer-specific tags that met the following criteria: disease specific, short, unique or minimally used on Twitter, and ending in "sm" for "social media" (as a prompt that online use is public). We selected this design to balance practical use with the ability to organize content. Initially proposed in July 2013, this cancer tag ontology (CTO) was posted on Symplur in November 2013 after public commentary and engagement (**Table**).[2]

We analyzed the number of tweets and users of the tags quarterly from April 2011 through June 2015 using Symplur