Prospective Validation of Pooled Prognostic Factors in Women with Advanced Cervical Cancer Treated with Chemotherapy with/without Bevacizumab: NRG Oncology/GOG Study

Krishnansu S. Tewari1, Michael W. Sill2, Bradley J. Monk3, Richard T. Penson4, Harry J. Long III5, Andrés Poveda6, Lisa M. Landrum7, Mario M. Leitao8, Jubilee Brown9, Thomas J.A. Reid10, Helen E. Michael11, and David H. Moore12

Abstract

Purpose: In the randomized phase III trial, Gynecologic Oncology Group (GOG) protocol 240, the incorporation of bevacizumab with chemotherapy significantly increased overall survival (OS) in women with advanced cervical cancer. A major objective of GOG-240 was to prospectively analyze previously identified pooled clinical prognostic factors known as the Moore criteria.

Experimental Design: Potential negative factors included black race, performance status 1, pelvic disease, prior cisplatin, and progression-free interval <365 days. Risk categories included low-risk (0–1 factor), mid-risk (2–3 factors), and high-risk (4–5 factors). Each test of association was conducted at the 5% level of significance. Logistic regression and survival analysis was used to determine whether factors were prognostic or could be used to guide therapy.

Results: For the entire population (n = 452), high-risk patients had significantly worse OS (P < 0.0001). The HRs of death for treating with topotecan in low-risk, mid-risk, and high-risk subsets are 1.18 [95% confidence interval (CI), 0.63–2.24], 1.11 [95% CI, 0.82–1.5], and 0.84 [95% CI, 0.50–1.42], respectively. The HRs of death for treating with bevacizumab in low-risk, mid-risk, and high-risk subsets are 0.96 [95% CI, 0.51–1.83; P = 0.9087], 0.673 [95% CI, 0.5–0.91; P = 0.0094], and 0.536 [95% CI, 0.32–0.905; P = 0.0196], respectively.

Conclusions: This is the first prospectively validated scoring system in cervical cancer. The Moore criteria have real-world clinical applicability. Toxicity concerns may justify omission of bevacizumab in some low-risk patients where survival benefit is small. The benefit to receiving bevacizumab appears to be greatest in the moderate- and high-risk subgroups (5.8-month increase in median OS). Clin Cancer Res; 21(24):5480–7. ©2015 AACR.

Introduction

Women with recurrent and metastatic cervical cancer constitute a population for whom treatment options have been extremely limited (1). With sophisticated radiotherapy planning and concurrent chemotherapy for radiosensitization and sterilization of occult metastatic tumor foci, central control can be achieved, which indirectly eliminates candidacy for pelvic exenteration to clear recurrent tumor (2). In cases when central failure occurs, it is commonly accompanied by distant failure that also abrogates any curative intent of exenteration. Previously, chemotherapy using cisplatin plus paclitaxel in these settings had been palliative, with rapid clinical deterioration, worsened quality of life (QoL), and the median overall survival (OS) rate ranging from 7 to 12 months (3,4). Importantly, many patients with recurrent disease have been preirradiated with limited bone marrow reserves, and may be platinum resistant as a consequence of prior platinum exposure with radiotherapy and subsequent acquired drug resistance (5,6). In addition, many are medically infirm due to renal failure and malnutrition.

Gynecologic Oncology Group (GOG)-240 was developed to study the nonplatinum chemotherapy doublet, topotecan plus paclitaxel, as well as antiangiogenesis therapy (7). VEGF has emerged as an important therapeutic target, and the monoclonal anti-VEGF humanized antibody bevacizumab was found to be active in GOG-227C, a phase II trial in heavily pretreated patients with recurrent cervical cancer (8). The primary endpoint of GOG-240 was OS.

In February 2013, the NCI and the GOG issued a press release stating that compared with chemotherapy alone, the
incorporation of bevacizumab led to significantly improved OS (17 mo vs. 13.3 mo) and progression-free survival (PFS; 8.2 mo vs. 5.9 mo; ref. 9). The integration of bevacizumab also significantly improved response rate (RR; 48% vs. 36%) without a significant deterioration in health-related QoL (9, 10).

A major objective of GOG-240 was to prospectively study previously identified pooled prognostic factors known as the Moore criteria (12). If risk stratification were to be validated in the GOG-240 population, two important questions could be asked. First, could risk stratification be used to guide therapy, i.e., to select the optimal chemotherapy backbone? Second, does risk stratification identify a cohort that is unsuitable for “standard” therapy due to a low likelihood for response?

**Materials and Methods**

**Eligibility criteria, study design, and treatment**

GOG-240 was a phase III randomized trial conducted through the GOG and the Spanish cooperative group, Grupo Español de Investigación en Cancer de Ovario (GEICO) with NCI-supplied bevacizumab (NSC #704865 and IND #113912), with central Institutional Review Board approval and registration (NCT00803062), signed informed consent, and central pathology review (9). Primary endpoints were OS, and the frequency and severity of toxicity and secondary endpoints were PFS and RR (9). Prospectively validated of the Moore criteria of pooled poor prognostic factors and QoL were tertiary endpoints. Eligibility required primary stage IVB or recurrent/persistent cervical carcinoma with measurable disease and GOG performance status 0 to 1 (9). Using a 2 × 2 factorial design, participants were randomized to one of four intravenous regimens: paclitaxel (135 mg/m² over 24 hours or 175 mg/m² over 3 hours) with cisplatin (50 mg/m²) with or without bevacizumab 15 mg/kg, or paclitaxel 175 mg/m² over 3 hours on day 1 with topotecan 0.75 mg/m² over 30 minutes days 1 to 3 with or without bevacizumab 15 mg/kg (Supplementary Fig. S1A). Cycles were repeated every 21 days until disease progression, unacceptable toxicity, or complete response. Tumor measurements were made using RECIST v1, and safety was assessed by the NCI’s Common Terminology Criteria for Adverse Events. One interim analysis was scheduled at 173 events. A second analysis (271 deaths) occurred 11 months later.

**Prospectively Validated Scoring System in Cervical Cancer**

**Translational Relevance**

The phase III international, multicenter trial GOG-240 demonstrated a significant survival advantage among women treated with chemotherapy plus bevacizumab compared with chemotherapy alone, and directly led to U.S. FDA approval of the two triplet regimens administering bevacizumab. However, antiangiogenesis therapy in this population may be associated with significant toxicity. Clinical scoring systems may allow for risk stratification. The data presented are a prospective validation of the Moore clinical prognostic factor scoring system. This system may be used as a clinical instrument to counsel patients regarding their likelihood of response and estimated risk of progression and death by cervical cancer when considering adding antiangiogenesis therapy to systemic chemotherapy for recurrent/persistent or metastatic cervical cancer. Importantly, based on these data patients at mid- to high-risk may be expected to derive the greatest benefit from the integration of bevacizumab to chemotherapy, although the benefit conferred to low-risk patients appears to be low.
Results
Using GOG-240 data, the five risk factors were examined separately and in joint models to assess the strength of association with clinical outcome. All of the risk factors appeared to be detrimental as indicated by their OR estimates being less than 1 even when not statistically significant (Table 1).

Validation of Moore criteria in entire GOG-240 population (arms 1+2+3+4)
The total risk score integrated all of the risk factors into a single statistic, as was done in the original publication (12). Application of the Moore criteria to the entire GOG-240 study population (i.e., arms 1–4 combined) placed the majority of patients in the mid-risk class (n = 303, 67%; Fig. 1). Low-risk patients account for 19% (n = 84) and high-risk patients comprise 14% (n = 65) of the study population. The distribution of OS, PFS, and RR mirrors the low-, mid-, and high-risk subgroup stratification in the direction of statistically significant declination for all three endpoints as one moves from low risk to high risk (Fig. 1). For example, patients with 0 or 1 high-risk factor (i.e., low-risk cohort) experience 21.8 months OS and 57% RR, while those in the high-risk cohort (4 or 5 factors) are separated by the administration of bevacizumab, the median OS (P = 0.0017). The effect on PFS, although not statistically significant, also deteriorates with increasing risk stratification (P = 0.066).

Patients treated with the topotecan–paclitaxel backbone (arms 3+4)
Using the Moore criteria, analysis of the 223 patients randomized to the topotecan–paclitaxel backbone assigns the majority of patients to the mid-risk class (n = 151). As one moves from low-risk to high-risk classes, OS significantly decreases from 20.1 months to 8.2 months (P = 0.017). The effect on PFS, although not statistically significant, also deteriorates with increasing risk stratification (P = 0.066).

Patients treated with bevacizumab (arms 2+4)
Analysis of the 227 patients randomized to the regimens administering bevacizumab places the majority (n = 152) in the mid-risk class. From low-risk to high-risk subgroups, OS decreases from 22.9 months to 12.1 months, respectively (P = 0.0513). The declination of PFS from low-risk to high-risk is not significant (P = 0.1417).

Risk stratification of chemotherapy backbones (arms 1+2 vs. 3+4)
The Moore criteria and risk assignment were used to determine whether there exists a preferential benefit for patients to be treated with one or the other chemotherapy backbone. Treatment with the topotecan–paclitaxel chemotherapy backbone was not a significant predictor of OS, PFS, or RR. Although the Moore criteria themselves are highly prognostic for OS, PFS, and RR, there is no evidence of interaction between the topotecan–paclitaxel backbone and the Moore criteria for OS, PFS, or response (Table 2). The estimates of the HRs of death for treating with topotecan to cisplatin in the low-risk, mid-risk, and high-risk subsets are 1.18 (95% CI, 0.63–2.24), 1.11 (95% CI, 0.82–1.5), and 0.84 (95% CI, 0.50–1.42), respectively, suggesting perhaps a modest (but nonsignificant) benefit for high-risk patients being treated on the topotecan–paclitaxel backbone. The HRs for PFS were likewise 1.15 (95% CI, 0.71–1.85), 1.26 (95% CI, 0.98–1.62), and 1.00 (95% CI, 0.60–1.67) in the low-, mid-, and high-risk groups, respectively. The ORs for responding to therapy in topotecan to cisplatin therapy were 0.43 (95% CI, 0.18–1.04) in the low-risk group, 0.67 (95% CI, 0.43–1.07) in the mid-risk group, and 1.45 (95% CI, 0.41–5.16) in the high-risk group. None of the interaction terms were significant.

Risk stratification among women treated with chemotherapy alone versus chemotherapy plus bevacizumab
Eighty-four patients had 0 or 1 risk factor. When these patients are separated by the administration of bevacizumab, the median OS between the groups is very similar (21.8 months in the chemotherapy alone cohort and 22.9 months in the chemotherapy plus bevacizumab cohort; Fig. 2A), with a HR of death estimated at 0.96 (95% CI, 0.51–1.83; P = 0.9087). Median PFS was also not significantly different among low-risk patients treated with chemotherapy with and without bevacizumab (10.9 vs. 8.0 months; HR, 0.85; 95% CI, 0.53–1.37; P = 0.2903).

Table 1. Frequency and impact on progression-free survival and overall survival of each prognostic factor examined separately

<table>
<thead>
<tr>
<th>Factor</th>
<th>N (%)</th>
<th>OR</th>
<th>95% CI</th>
<th>HR PFS</th>
<th>95% CI</th>
<th>HR OS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>N</td>
<td>392 (86.7)</td>
<td>0.685</td>
<td>0.372–1.260</td>
<td>1.091</td>
<td>0.808–1.473</td>
<td>1.32</td>
</tr>
<tr>
<td>Performance status</td>
<td>0</td>
<td>263 (58.2)</td>
<td>0.560</td>
<td>0.371–0.845</td>
<td>1.330</td>
<td>1.069–1.655</td>
<td>1.657</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>189 (41.8)</td>
<td>0.801</td>
<td>0.529–1.215</td>
<td>0.946</td>
<td>0.755–1.186</td>
<td>1.068</td>
</tr>
<tr>
<td>Pelvic disease</td>
<td>N</td>
<td>210 (46.5)</td>
<td>0.801</td>
<td>0.529–1.215</td>
<td>0.946</td>
<td>0.755–1.186</td>
<td>1.068</td>
</tr>
<tr>
<td>Prior CDDP radiation</td>
<td>N</td>
<td>115 (25.4)</td>
<td>0.263</td>
<td>0.160–0.432</td>
<td>1.801</td>
<td>1.375–2.360</td>
<td>2.166</td>
</tr>
<tr>
<td>Progression-free interval</td>
<td>&lt;12 mo</td>
<td>203 (44.9)</td>
<td>0.599</td>
<td>0.395–0.909</td>
<td>1.484</td>
<td>1.189–1.854</td>
<td>1.950</td>
</tr>
<tr>
<td></td>
<td>≥12 mo</td>
<td>249 (55.1)</td>
<td>0.599</td>
<td>0.395–0.909</td>
<td>1.484</td>
<td>1.189–1.854</td>
<td>1.950</td>
</tr>
</tbody>
</table>
The mid-risk group (2 or 3 factors) contained 303 patients. As expected, the median OS declined when compared with the low-risk cohort, but in this subgroup the difference in median OS (12.1 months in the chemotherapy alone cohort and 17.9 months in the chemotherapy plus bevacizumab cohort) is highly significant with an estimated hazard of death of 0.673 (95% CI, 0.5–0.91; \( P = 0.0094 \); Fig. 2B). The estimated HR for the PFS endpoint was 0.694 (95% CI, 0.54–0.89; \( P = 0.0047 \)).

Among the 65 patients that had 4 or 5 risk factors, the Moore criteria and high-risk stratification class were highly prognostic between chemotherapy cohorts who did not receive and did receive bevacizumab. The bevacizumab group had better survival with an estimated HR of death of 0.536 (95% CI, 0.32–0.93; \( P = 0.0196 \); Fig. 2C) and an estimated HR of the PFS endpoint of 0.506 (95% CI, 0.277–0.926; \( P = 0.0272 \)).

The OR of response for those treated with bevacizumab to those who were not in the low-, mid-, and high-risk class patients was 1.52 (95% CI, 0.64–3.64), 1.84 (95% CI, 1.16–2.92), and 1.93 (95% CI, 0.52–7.18), respectively.

Discussion

The original impetus to study poor prognostic markers in advanced cervical cancer was to identify patients a priori who were unlikely to respond to conventional cytotoxic therapy in an effort to avoid administration of futile treatment (18,19). The prognostic model for tumor response was based on five similarly weighted factors that did not interact, allowing for an index based on the total number of risk factors to be derived (13–15).

The Moore criteria were identified in the platinum or cytotoxic era when antiangiogenic agents were not yet employed in randomized clinical trials for cervical cancer patients (20–22). One of the major conclusions of the original Moore criteria analysis was that because even limited toxicity in the face of nonresponse to treatment or disease progression is unacceptable, then high-risk patients should be spared the toxicity of ineffective therapy and instead be considered for best supportive care or investigational trials. Before GOG-240 was developed, some suggested using the Moore criteria to pull out high-risk patients from subsequent phase III studies. However, at that time, the Moore criteria had not been prospectively validated and, for this reason, the scoring system was not used to limit eligibility in GOG-240. In GOG-240, we have demonstrated that, compared with high-risk patients treated with chemotherapy alone, high-risk patients who received bevacizumab had a significantly lower hazard of death not only within the high-risk group but also compared with those at the mid-risk level.

Women with advanced cervical cancer are distinguished by often having been preirradiated, resulting in diminished marrow reserves and a vasculitis that limits adequate drug distribution and perfusion into irradiated tumor beds. Concurrent chemoradiation leads to acquired drug resistance, making cisplatin-based therapies less effective at recurrence. Finally, often poor and lacking access to healthcare, this population is marginalized by society, medically debilitated, malnourished, and with diminished renal function due to tumor- and radiation-related hydronephrosis and consequent renal insufficiency/failure. Women with recurrent cervical cancer often do not respond to multiple lines of chemotherapy as do patients with cancer of other types (e.g., ovary and breast). Additional not-yet-developed models that include factors such as income...
level, nutritional status, and/or renal function may also have clinical utility. It is not difficult to understand how performance status, short disease-free interval, pelvic disease, and prior cisplatin may impair prognosis. It is less clear how African-American ethnicity worsens outcome. African Americans may have limited access to care with comorbidities not reflected in performance status, or they may have biologically worse cervical cancers (23–27). Farley and colleagues reported that in an equal access, unbiased, nonracial environment, such as the military, race is not an independent predictor of survival for patients with cervical carcinoma (28). Interestingly, in a GOG ancillary data study in the recurrent cervical cancer population, Plaxe and colleagues found that cisplatin-based chemotherapy was better tolerated by African-American women (29). In the Moore criteria, African American ethnicity may be a surrogate for limited access to healthcare, suggesting that this scoring system may be applicable to populations in which African Americans may not be prevalent.

![Figure 2. Kaplan–Meier overall survival curves following risk stratification according to the Moore criteria among women with advanced cervical cancer treated with chemotherapy with and without bevacizumab. A, low-risk class (0–1 poor prognostic factor). B, mid-risk class (2–3 poor prognostic factors). C, high-risk class (4–5 poor prognostic factors). Bev, bevacizumab; Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; mo, months; OS, overall survival; PFS, progression-free survival; RR, response rate.](image)
Angiogenesis confers a poor prognosis in cervical cancer and a molecular cascade involving viral oncoproteins E6 and E7 and their interactions with cellular tumor suppressor gene products p53 and pRb leads to increased hypoxia inducible factor-1α and VEGF production and angiogenesis (30). Through ligand-binding, bevacizumab, sequesters VEGF and inhibits angiogenesis. Although the Moore criteria lack definitive predictive capabilities in chemotherapy guidance (i.e., backbone selection with which to integrate bevacizumab), there is evidence that the risk model can serve as a surrogate for personalized medicine in predicting outcomes among different cohorts treated with bevacizumab.

This risk model is a tool for office practice when counseling patients with advanced disease. Prognostic factors can be compiled and an estimation of RR (and median survival) using antiangiogenesis therapy can be provided to an individual patient and her family members. Patients with the highest risk stratification (i.e., 4–5 factors) derive the greatest relative benefit from bevacizumab (HR, 0.536) compared with those patients who are in the mid-risk (HR, 0.673) or low-risk (HR, 0.96) cohorts. Not all low-risk patients are the same, and anticipated toxicity should also be considered when counseling patients. For example, in GOG-240, fistula occurred in 8.6% of patients treated with bevacizumab, all of whom had been previously irradiated. Additional risk factors for fistula may also include recurrent disease in the irradiated pelvis (with or without distant metastases) and persistent disease following chemoradiation. In a low-risk patient (0–1 factors) treated with chemoradiation prior to recurrence, the Moore criteria can be used to argue against including bevacizumab as the fistula risk is 8.6% with very small survival benefit. We must acknowledge that despite a significantly improved OS and subsequent U.S. FDA regulatory approval, bevacizumab is not curing patients. Development of a fistula may preclude eligibility for participation in a promising immunotherapy clinical trial. When taken in this context, a previously irradiated low-risk patient who is carefully counseled may reasonably choose to not receive bevacizumab. Performance status is the one Moore factor that is modifiable through medical, nutritional, and possibly spiritual intervention. Eligibility criteria for GOG-240 were more stringent than in preceding trials. Previously, great expense and effort had been invested in patients with very low likelihood of response. Through optimization of medical comorbidities, correction of malnutrition, improved understanding of renal function with expeditious placement of ureteral stents and/or percutaneous nephrostomies, the GOG-240 population was “healthier” at enrollment than their predecessors in prior trials. To improve survival, we believed that resources (including expensive therapies) are best applied to those who stand the greatest chance of benefiting. The identification of a near-4-month window of improved OS without significant deterioration of QoL suggests that the disease may lend itself to chronicity. Patients deriving benefit (e.g., stable disease) but who are intolerable to chemotherapy may have the latter drugs peeled away and continue with bevacizumab monotherapy. Alternatively, those patients responding to antiangiogenesis therapy may be considered for incorporation of immunotherapy prior to progression. Bevacizumab does not signify the end of advanced cervical cancer, but hopefully represents a small step forward in the treatment of this devastating disease (Fig. 3).

This is the first prospectively validated prognostic scoring system in cervical cancer, a disease that is only second to lung and breast in cancer-related mortality worldwide. Advanced cervical cancer is not a disease in which “cure” is an issue. Studies such as this, which help to refine treatment selection in a manner that stratifies patients into risk groups for anticipated response to treatment and complications, are clinically important. Characterization of gene signatures that confer risk and blood-based predictive protein signatures obtained from women with durable responses to anti-VEGF therapy are needed. Mathematical modeling may be used to combine clinical (i.e., Moore-like) risk factors with molecular ones and through assignment of different weights, the predictive capabilities of the risk model can be refined further.

Figure 3.
Successive improvement in median overall survival among women with advanced cervical cancer. The phase III experience of the Gynecologic Oncology Group (now, part of NRG Oncology): BEV, bevacizumab; CIS, cisplatin; CTX, chemotherapy; IFO, ifosfamide; PAC, paclitaxel; TOP, topotecan. Used with permission from G.E. Konecny.
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): K.S. Tewari, A. Poveda, I.M. Landrum, M. Leitao, J. Brown, T.J. Reid, H.E. Michael

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): K.S. Tewari, M.W. Sill, B.J. Monk, R.T. Penson, A. Poveda, J. Brown, D.H. Moore

Writing, review, and/or revision of the manuscript: K.S. Tewari, M.W. Sill, B.J. Monk, R.T. Penson, A. Poveda, L.M. Landrum, M. Leitao, J. Brown, H.E. Michael, D.H. Moore

Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): K.S. Tewari, B.J. Monk

Study supervision: B.J. Monk, R.T. Penson

Acknowledgments

The following Gynecologic Oncology Group member institutions participated in the primary treatment studies: Roswell Park Cancer Institute, University of Alabama at Birmingham, Duke University Medical Center, Abington Memorial Hospital, Walter Reed Army Medical Center, Wayne State University, University of Minnesota Medical School, Northwestern Memorial Hospital, University of Mississippi Medical Center, Colorado Gynecologic Oncology Group P.C., University of Washington, University of Pennsylvania Cancer Center, Milton S. Hershey Medical Center, University of Cincinnati, University of North Carolina School of Medicine, University of Iowa Hospitals and Clinics, University of Texas Southwestern Medical Center at Dallas, Indiana University School of Medicine, Wake Forest University School of Medicine, University of California Medical Center at Irvine, Rush-Presbyterian-St. Luke's Medical Center, Magee Women's Hospital, SUNY Downstate Medical Center, University of Kentucky, University of New Mexico, The Cleveland Clinic Foundation, State University of New York at Stony Brook, Washington University School of Medicine, Memorial Sloan-Kettering Cancer Center, Cooper Hospital/University Medical Center, Columbus Cancer Council, MD Anderson Cancer Center, University of Massachusetts Medical School, Fox Chase Cancer Center, Women's Cancer Center, University of Oklahoma, University of Virginia Health Sciences Center, University of Chicago, Mayo Clinic, Case Western Reserve University, Tampa Bay Cancer Consortium, Yale University, University of Wisconsin Hospital, Cancer Trials Support Unit, University of Texas–Galveston, Women and Infants Hospital, The Hospital of Central Connecticut, Georgia Core, Aurora Women's Pavilion of West Allis Memorial Hospital, Grupo Espanol de Investigacion en Cancer de Ovario, University of California, San Francisco-Mt. Zion, St. Joseph's Hospital and Medical Center (Arizona), and Community Clinical Oncology Program.

Grant Support

This study was supported by National Cancer Institute grants to the Gynecologic Oncology Group Administrative Office (CA 27469) and the Gynecologic Oncology Group Statistical Office (CA 37517) and NRG Oncology Group Grant 1 U10 CA180822.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received June 8, 2015; revised July 28, 2015; accepted August 5, 2015; published online December 15, 2015.

References

Correction: Prospective Validation of Pooled Prognostic Factors in Women with Advanced Cervical Cancer Treated with Chemotherapy with/without Bevacizumab: NRG Oncology/GOG Study

In this article (Clin Cancer Res 2015;21:5480–7), which was published in the December 15, 2015, issue of Clinical Cancer Research (1), the grant support is listed incorrectly. It should read as follows: "This study was supported by National Cancer Institute grants to the Gynecologic Oncology Group Administrative Office (CA 27469) and the Gynecologic Oncology Group Statistical Office (CA 37517), NRG Oncology Group Grant 1 U10 CA180822, and by the NIH/NCI Cancer Center Grant P30 CA008748." The authors regret this error.

Reference

Published online August 1, 2016.
doi: 10.1158/1078-0432.CCR-16-1208
©2016 American Association for Cancer Research.