Phase II Trial of Continuous Dose-Intense Temozolomide in Recurrent Malignant Glioma: RESCUE Study

James R. Perry, Karl Bélanger, Warren P. Mason, Dorcas Fulton, Petr Kavan, Jacob Easaw, Claude Shields, Sarah Kirby, David R. Macdonald, David D. Eisenstat, Brian Thiessen, Peter Forsyth, and Jean-François Pouliot

See accompanying editorial on page 1977

ABSTRACT

Purpose
Concomitant temozolomide (TMZ)/radiotherapy followed by adjuvant TMZ has increased survival in patients with glioblastoma multiforme (GBM). However, few options are effective for patients who experience treatment failure. We conducted a multicenter, phase II study to assess the efficacy and safety of continuous dose-intense TMZ for recurrent GBM.

Patients and Methods
Patients with malignant glioma at progression after standard TMZ 150 to 200 mg/m² × 5 days in a 28-day cycle for three or more cycles were stratified by tumor type (anaplastic glioma group A, GBM, group B). Ninety-one patients with GBM were prospectively divided into three groups (early [B1], extended [B2], and rechallenge [B3]) according to the timing of progression during adjuvant therapy. All patients received continuous dose-intense TMZ 50 mg/m²/d for up to 1 year or until progression occurred. Response was assessed by using RECIST (Response Evaluation Criteria in Solid Tumors).

Results
A total of 116 of 120 patients were evaluated for efficacy. For patients with GBM, 6-month progression-free survival (PFS) was 23.9% (B1, 27.3%; B2, 7.4%; B3, 35.7%). One-year survival from time of study entry was 27.3%, 14.8%, and 28.6% for the B1, B2 and B3 groups, respectively. For patients with anaplastic glioma, 6-month PFS was 35.7%; 1-year survival was 60.7%. The most common grades 3 and 4 nonhematologic toxicities were nausea/vomiting (6.7%) and fatigue (5.8%). Grades 3 and 4 hematologic toxicities were uncommon.

Conclusion
Rechallenge with continuous dose-intense TMZ 50 mg/m²/d is a valuable therapeutic option for patients with recurrent GBM. Patients who experience progression during the first six cycles of conventional adjuvant TMZ therapy or after a treatment-free interval get the most benefit from therapy.

INTRODUCTION

Temozolomide (TMZ; Temodar/Temodal, Schering Corporation, Kenilworth, NJ) is an alkylating chemotherapeutic agent that is the standard of care for newly diagnosed glioblastoma multiforme (GBM). The EORTC (European Organisation for Research and Treatment of Cancer) 26981/22981–NCIC-CTG (National Cancer Institute of Canada Clinical Trials Group) CE.3 phase III trial showed that concomitant radiotherapy and TMZ (75 mg/m²/d for 6 weeks) plus six cycles of adjuvant TMZ (150 or 200 mg/m² for 5 days per 28-day cycle; ie, 5/28 dosing schedule) improves 2-year survival versus radiotherapy alone from 10.4% to 26.5%. A later analysis showed that the clinical benefit is sustained for some patients beyond 5 years.

The cytotoxic effects of TMZ and its active metabolite, 5-(3-methyltriazen-1-yl)imidazole-4-carboxamide (MTIC), are attributed to the formation of DNA adducts by the methylation of DNA at the O6 position of guanine. Resistance to TMZ may be conferred by expression of the O6-methylguanine DNA methyltransferase (MGMT) repair enzyme, which removes methyl or alkyl adducts and restores normal guanine. Methylation of the promoter region of the MGMT gene attenuates MGMT function and may be an independent predictor of 6-month progression-free survival (PFS) and overall survival.
There is no consensus on the optimal approach for patients with recurrent GBM, especially in the new era, in which recurrence occurs after exposure to TMZ used in the upfront setting, with many patients treated with 12 or more cycles of adjuvant therapy. Phase II trials have demonstrated prolonged time to progression and improved survival in high-grade glioma with TMZ at the conventional dose schedule of 150 or 200 mg/m² given on 5 of every 28 days in patients who are TMZ naive and have recurrent disease.

Protracted drug exposure may reduce MGMT activity. Several dose-intensive schedules (eg, 75 mg/m²/d for 42 of 70 days; 75 mg/m² for 21 of 28 days; 75 mg/m²/d, 7 weeks on/4 weeks off) have been investigated in recurrent GBM, anaplastic astrocytoma (AA), and low-grade glioma.

In addition to suppression of MGMT activity and increased dose-intensity, protracted TMZ dosing may have antiangiogenic effects. Metronomic chemotherapy (ie, continuous or near-continuous treatment below the maximum-tolerated dose) may limit endothelial cell recovery, inhibit the activity of circulating endothelial precursors, and upregulate thrombospondin-1, leading to an antiangiogenic effect. In vitro studies have indicated that low-dose TMZ at a concentration equivalent to 20 mg/m² every 8 hours inhibits angiogenesis. A preliminary study reported that continuous low-dose TMZ plus rofecoxib had antiangiogenic effects and was well tolerated.

For patients on TMZ with recurrence or progression on the conventional 150 or 200 mg/m² 5/28 dosing schedule, rechallenge with TMZ may be effective. Perry et al used continuous TMZ 50 mg/m² in patients with recurrent malignant glioma. Six-month PFS in patients with GBM who experienced progression on the TMZ 5/28 schedule was 17%; the overall clinical benefit (complete response, partial response, or stable disease) was 47%. In patients who experienced recurrence after completing standard concomitant and adjuvant TMZ, the 6-month PFS was 57%.

Thus, an alternative dosing schedule of TMZ may be a reasonable option in patients with GBM who experience progression after standard upfront therapy. It was hypothesized in the RESCUE study, that continuous dose-intensive TMZ 50 mg/m²/d might be effective in patients at the time of first progression after exposure to the conventional TMZ schedule.

### Study Design and Patient Selection

This was a nonrandomized, multicenter, two-stage, phase II trial designed to test the efficacy and safety of continuous (ie, 28 of 28 days) dose-intensive (50 mg/m²/d) TMZ rechallenge in adult patients with malignant glioma with recurrence or progression while receiving standard TMZ on a 5/28 dosing schedule. The study was conducted at 11 Canadian Brain Tumor Consortium (CBTC) centers. The protocol was approved by the institutional review boards at all centers, and each patient provided written informed consent before study entry.

Patients were included if they were adults (age 18 years or older) with a surgically confirmed diagnosis of malignant glioma (GBM, AA, anaplastic oligodendroglioma [AO], or anaplastic oligoastrocytoma [AOA]). All patients had to have completed radiotherapy, be 3 or more months away from the end of chemoradiation, and have radiologic evidence of progression (ie, magnetic resonance imaging [MRI] or computed tomography [CT]). Patients were enrolled within 2 weeks of radiologic confirmation of progression or, in the case of patients undergoing surgical resection, within 2 weeks of a postsurgical scan. An Eastern Cooperative Oncology Group (ECOG) score ≤ 1 was required (ECOG of 0 required if older than age 70 years). Steroid dosing should have stabilized or decreased in the 2 weeks before study enrollment. Patients with no residual disease were permitted.

Patients were excluded if they had received prior chemotherapy or radiotherapy for recurrent disease, if they had more than one prior course of TMZ, if they had disease that evolved from anaplastic glioma to GBM after the initial therapy, or if they had inadequate laboratory values (absolute neutrophil count ≥ 1.5 × 10⁹/L; platelets ≤ 100 × 10⁹/L; hemoglobin < 90 g/L; serum creatinine ≥ 1.5 times upper limit of laboratory normal [ULN]; total serum bilirubin ≥ 1.5 times ULN; AST or ALT > 2.0 times ULN; or alkaline phosphatase > 2.5 times ULN). The concomitant use of corticosteroids, antimetics, and antibiotics was permitted at the discretion of the investigator.

### Patient Stratification, Treatment and Response Criteria

Patients were stratified into four groups according to tumor diagnosis, prior duration of treatment with TMZ, and time of progression. Group A. Anaplastic glioma (ie, AA, AO, AOA) with progression after treatment with TMZ on a 5/28 regimen.

Group B1 (early). GBM with progression while receiving adjuvant TMZ before completion of six cycles of adjuvant TMZ.

Group B2 (extended). GBM with progression while receiving extended adjuvant TMZ beyond the standard six cycles but before completion of adjuvant treatment.

Group B3 (rechallenge). GBM with progression after completion of adjuvant treatment and a treatment-free interval of greater than 2 months. All patients received TMZ 50 mg/m²/d on a continuous (28/28) basis for a maximum of 12 months or until progression occurred. Treatment beyond 12 cycles could be given outside the protocol at the investigator’s discretion. There was no dose escalation. Dosing was interrupted if a patient developed hemato logic (ie, absolute neutrophil count < 1.0 × 10⁹/L; platelets < 100 × 10⁹/L) or nonhematologic (except for alopecia, nausea/vomiting) toxicities; dosing could be resumed on resolution of the toxicity. Treatment was discontinued if grade 3 or 4 toxicity recurred or persisted for more than 6 weeks.

Response was assessed clinically and radiologically by using RECIST (Response Evaluation Criteria in Solid Tumors). Safety was assessed by using National Cancer Institute Common Toxicity Criteria (version 3). MGMT promoter methylation status was determined by OncoMethylome Sciences (Durham, NC) by using a polymerase chain reaction–based method.

### Study End Points and Statistical Analysis

The primary end point was 6-month PFS, as determined from the start of the continuous dose-intensive regimen. Secondary end points included objective response rate (complete plus partial), overall clinical benefit (complete response, plus partial response, plus stable disease), overall survival at 12 months, and safety.

The Kaplan-Meier survival function was used to estimate 6-month PFS. Ninety-five percent CIs were used to assess the precision of this estimate and to test the hypothesis that the observed PFS rate was higher than the minimum clinically relevant value of 20%. In addition, the statistical significance of the difference between the observed PFS rate and 20% was assessed with the nonparametric test or the z test depending on the overall distribution of the survival function in each cohort.

Overall survival at 12 months from study entry was determined as a proportion of the patients achieving this end point. The Kaplan-Meier function was used to describe the duration of survival and to produce estimates of the survival rates at 3, 6, 9, and 12 months after the start of treatment. Cox proportional models were used for overall survival.

Statistical analyses of the primary and secondary end points were conducted for each study subgroup and for the overall cohort of 120 patients as a whole, as specified in the protocol (CONSORT diagram, Fig 1).

It was assumed that the results of treatment would be of clinical importance if the 6-month PFS rate was ≥ 20% and of lesser importance if ≤ 10%. The study was powered to obtain a lower bound 95% confidence limit of greater than 10% for a point estimate of 20%. For this requirement, 30 patients per group were needed, for a total of 120 patients in the study. This estimate was based on 80% power and two-tailed significance of 5%.
The study had a two-stage design. An interim analysis was conducted when the first 15 patients in each group were enrolled. If at least one of the first 15 patients in each group demonstrated a partial response or was free of progression at 6 months, the regimen was considered active, and the full target cohort of 30 patients was enrolled.

**RESULTS**

A total of 120 patients were enrolled at 11 centers across Canada between July 2006 and January 2008. Demographic data are listed in Table 1. Four patients (one in group A, one in group B2, and two in group B3) were excluded from the efficacy analysis because of evolution from low-grade glioma, unacceptable dose delay, increasing corticosteroids at baseline, and prior chemotherapy with irinotecan. All 120 patients were included in the safety analysis. Sixty-nine patients (58%) were receiving corticosteroids at study entry, at a median dose of 6 mg/d of dexamethasone. An interim analysis for futility was performed for the four subgroups of the trial. The prespecified minimal activity of at least one response was observed in the first 15 patients in each of the subgroups.

The median time on TMZ 50 mg/m²/d was 2.7 months (range, 0.3 to 24 months). A total of 15 patients (12.5%) completed 12 months of continuous therapy: six patients in group A, five in group B1, one in group B2, and three in group B3.

The median duration of follow-up was 19.1 months (range, 0.6 to 29.9 months). According to the preplanned subgroup analysis, median PFS was 3.6, 1.8, and 3.7 months for the B1 (early, n = 33), B2 (extended, n = 27) and B3 (rechallenge n = 28) groups, respectively (Fig 2). The overall 6-month PFS for patients with GBM (groups B1, B2, and B3) was 23.9%; the 6-month PFS rates were 27.3% in group B1, 7.4% in group B2, and 35.7% in group B3. The extended group had a shorter time to progression than the other GBM groups (P = .0027 by log-rank test). For patients with anaplastic glioma (group A, n = 28), the 6-month PFS was 35.7%.

Overall survival at 1 year was calculated as one of the secondary end points. Survivals from the time of study entry to 1 year of follow-up were 27.3% in group B1, 14.8% in group B2, and 28.6% in group B3 (Fig 3). Overall survival at 1 year for group A was 60.7%.

Determining the MGMT promoter methylation status was included as part of the protocol, but obtaining tissue samples for analysis was not a study requirement. MGMT promoter methylation status could be determined in 50 (43%) of 120 patients; an additional 10 samples were indeterminate. A sensitivity analysis found equal distribution of age, performance status, degree of surgery, and sex between the 50 patients in whom MGMT status was determined and the 120 patients as a whole. In patients for whom MGMT methylation could be determined, the overall promoter methylation rate was 42%. For the overall study population, the 6-month PFS was 42.9% for patients...
with a methylated MGMT promoter (mMGMT) compared with 37.9% for patients with an unmethylated promoter (umMGMT). For the GBM subgroup, 6-month PFS was 40.0% for patients with mMGMT and 36.4% for patients with umMGMT. Median time to progression was comparable in patients with mMGMT and umMGMT (3.8 vs 2.9 months, respectively; Fig 4). The time from initial surgery to study start was almost two times longer in the mMGMT group at 20.5 months (95% CI, 14.0 to 27.1 months) compared with the umMGMT group at 12.1 months (95% CI, 10.1 to 14.1 months).

The anaplastic glioma subgroup was heterogeneous and had a variety of prior therapies, including chemotherapy, radiation therapy, and radiotherapy followed by TMZ, or TMZ only. The 6-month PFS and 1-year overall survival rates for patients with anaplastic glioma were 35.7% and 60.7%, respectively.

Response evaluation was performed on all patients who had at least two visits; objective response required one additional confirmatory scan at least 4 weeks later. Four patients were excluded from this analysis because of early death but were included in the progression analysis. The objective response rates were 15.4%, 3%, 0%, and 11.1% in the anaplastic, early, extended, and rechallenge groups, respectively. Additionally, for each of the aforementioned subgroups, 23.1%, 24.2%, 7.7%, and 25.9% and achieved stable disease for more than 6 months, for an overall clinical benefit of 38.5%, 27.3%, 7.7%, and 7.0%, respectively.

Continuous dose-intense treatment was generally well tolerated. Minor hematologic abnormalities were present in 50% of patients at study entry. Hematologic toxicities primarily affected lymphocyte and total leukocyte but not platelet counts (Fig 5). Apart from a 15.8% incidence of grade 3 lymphopenia, other grade 3 and 4 hematologic toxicities were uncommon. Opportunistic infections were rare; grade 1 and 2 oral thrush was observed in 14% of patients, but the majority was grade 1. We observed one occurrence of herpes zoster reactivation and one occurrence of low-grade fungal infection. Seventeen patients (14%) received prophylaxis with trimethoprim/sulfamethoxazole during the study. Pneumocystis pneumonia was not observed.

Nonhematologic toxicities that could be attributed to the study medication were generally grades 1 to 2 and included nausea/vomiting, fatigue, peripheral edema, and cough (Table 2). A total of 48 patients (40%) received antiemetics during the study.

The RESCUE study hypothesized that a continuous regimen of 50 mg/m² TMZ could overcome resistance to standard therapy. Overall, the 6-month PFS rate for recurrent/progressive GBM was 23.9%, and it was 35.7% for recurrent anaplastic glioma. These results are superior to those of a pooled analysis by Wong et al³ of eight consecutive phase II trials of cytostatic and cytotoxic agents, in which the 6-month PFS was 15% for recurrent GBM and 31% for recurrent AA. Thus, continuous-dose-intense TMZ 50 mg/m²/d is clinically active and is effective in malignant glioma at recurrence or progression after adjuvant TMZ.

As expected, median survival was longer for patients with recurrent anaplastic glioma (14.6 months; 95% CI, 11.8 to 17.3 months) compared with patients who had GBM (9.3 months; 95% CI, 8.1 to 10.5 months). However, the anaplastic glioma group was highly heterogeneous with respect to duration of disease, prior radiotherapy, chemotherapy, and other factors. The number of patients with anaplastic disease was too small to permit a subgroup analysis (AA vs AO vs AOA).

For patients with GBM, the best response was obtained by those who had completed a prior course of adjuvant TMZ/radiotherapy plus adjuvant TMZ followed by a drug-free period of at least 2 months (ie, rechallenge group). Those who experienced progression early on standard therapy also obtained a similar benefit (ie, early group). However, those who experienced progression while on extended adjuvant (ie, beyond six cycles) treatment did significantly worse with a median time to progression of 1.8 months (95% CI, 1.7 to 1.9 months) compared with 3.7 months (95% CI, 2.1 to 5.2 months) for the two other GBM subgroups. A large proportion of patients in the extended group (46%) received adjuvant TMZ for 12 cycles or more and may have been more likely to develop resistance to TMZ.

We considered the possibility that the 6-month PFS in the early subgroup may be in part attributable to pseudoprogression. Therefore, to minimize the influence of pseudoprogression, we excluded patients who experienced progression within 3 months of radiotherapy. In fact, the median time from the end of radiotherapy to disease progression in the early group was 5.2 months, suggesting that the majority of patients entered onto the study had true disease progression.

It is unclear why changing the dosing regimen led to an improved response in relapsed patients. The continuous-dose RESCUE regimen represented a dose intensification from 750 to 1,000 mg/m² per 28-day cycle with the conventional dosing to 1,400 mg/m² per 28-day cycle.

---

**Fig 3.** Six-month progression-free survival (PFS) and 1-year survival in patients with glioblastoma multiforme by subgroup.

**Fig 4.** Median progression and survival in patients with glioblastoma multiforme according to O6-methylguanine DNA methyltransferase promoter methylation status.
The continuous regimen may lead to a depletion of MGMT and restoration of TMZ sensitivity. In addition, continuous therapy may provide an antiangiogenic effect associated with metronomic regimens. Controlled studies with molecular companion analyses are needed to clarify these issues.

An important finding in this trial was that 6-month PFS and time to progression were comparable in patients with and without MGMT promoter methylation. Numerous studies have reported that epigenetic silencing of the MGMT gene by promoter methylation is associated with benefit from alkylating agents, including TMZ, and represents a favorable prognostic factor for improved PFS and long-term survival in both patients with GBM and AA. One explanation of the similar outcome seen in patients with umMGMT and mMGMT promoter is MGMT depletion associated with the continuous TMZ regimen. Alternatively, we recognize that the MGMT analysis was performed on archival tissue from the time of initial diagnosis and that MGMT expression may be altered during treatment. Moreover, it is unclear whether MGMT status at the time of progression has the same prognostic and therapeutic significance as it does early in the disease. As expected, patients in this study with promoter methylation had a longer treatment-free interval from the initial surgery and longer survival overall. Additional studies are needed to determine if continuous dosing overcomes the disadvantage of nonmethylation status in patients with GBM.

Continuous dose-intense TMZ is active in patients relapsing after standard therapy, notably in those patients with early or late progression after standard therapy. The present results are comparable to those seen with targeted therapies such as bevacizumab and cediranib, for which 6-month PFS is 25% to 46%. An important advantage of this regimen is its tolerability, with minimal hematologic toxicity and nausea/vomiting compared with other chemotherapies, including nitrosoureas or other TMZ schedules. Preliminary data suggest that the combination of daily TMZ 50 mg/m² plus bevacizumab is clinically active and has an acceptable safety profile.

The RESCUE study showed differences in prognosis depending on the duration of adjuvant therapy and treatment-free interval at the time of relapse. These parameters should be taken into consideration during the design and analysis of clinical trials evaluating the benefit of treatment for recurrent GBM. Our experience suggests that patients who progress early versus late or after a treatment-free interval may respond differently to re-treatment.

Table 2. Grades 3 to 4 Nonhematologic Toxicities That May Be Attributed to Continuous Dose-Intense Temozolomide

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>3</th>
<th>4</th>
<th>3 and 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
<td>No. %</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>6.0 5.0</td>
<td>2.0 1.7</td>
<td>8.0 6.7</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7.0 5.8</td>
<td>— —</td>
<td>7.0 5.8</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>1.0 0.8</td>
<td>2.0 1.7</td>
<td>3.0 2.5</td>
</tr>
<tr>
<td>Liver enzymes</td>
<td>— —</td>
<td>1.0 0.8</td>
<td>1.0 0.8</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>1.0 0.8</td>
<td>— —</td>
<td>1.0 0.8</td>
</tr>
<tr>
<td>Edema (peripheral)</td>
<td>1.0 0.8</td>
<td>— —</td>
<td>1.0 0.8</td>
</tr>
</tbody>
</table>

NOTE. No. of patients = 120.
Continuous dose-intense TMZ may serve as a useful platform for combination strategies. It might be a reasonable comparator arm in future trials of novel agents in patients with recurrent GBM previously exposed to TMZ. Randomized, comparative trials are needed to determine the optimal regimen for patients with malignant glioma who experience progression after adjuvant therapy.

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a “U” are those for which no compensation was received; those relationships marked with a “C” were compensated. For a detailed description of the disclosure categories, or for more information about ASCO’s conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: Jean-François Pouliot, Schering-Plough Canada (C)

Consultant or Advisory Role: James R. Perry, Schering-Plough Canada (C); Karl Bélanger, Schering-Plough Canada (C); Warren P. Mason, Schering-Plough Canada (C); Dorcas Fulton, Schering-Plough Canada (C); David R. Macdonald, Schering-Plough Canada (C); Brian Thiessen, Schering-Plough Canada (C)

Stock Ownership: None

Honoraria: James R. Perry, Schering-Plough Canada; Karl Bélanger, Schering-Plough Canada; Warren P. Mason, Schering-Plough; Dorcas Fulton, Schering-Plough Canada; Jacob Easaw, Schering-Plough Canada; David R. Macdonald, Schering-Plough; David D. Eisenstat, Schering-Plough Canada; Brian Thiessen, Schering-Plough Canada

Research Funding: Jean-François Pouliot, Schering-Plough Canada (C); Brian Thiessen, Schering-Plough Canada (C); Warren P. Mason, Schering-Plough Canada (C); Perry, Schering-Plough Canada (C); Karl Bélanger, Schering-Plough Canada; Warren P. Mason, Schering-Plough; Dorcas Fulton, Schering-Plough Canada; Jacob Easaw, Schering-Plough Canada; David R. Macdonald, Schering-Plough; David D. Eisenstat, Schering-Plough Canada; Brian Thiessen, Schering-Plough Canada

Other Remuneration: None

REFERENCES


AUTHOR CONTRIBUTIONS

Conception and design: James R. Perry, Karl Bélanger, Warren P. Mason, Dorcas Fulton, David R. Macdonald, Peter Forsyth, Jean-François Pouliot

Administrative support: Warren P. Mason, Jean-François Pouliot

Provision of study materials or patients: James R. Perry, Karl Bélanger, Warren P. Mason, Dorcas Fulton, Petr Kavan, Jacob Easaw, Claude Shields, Sarah Kirby, David R. Macdonald, David D. Eisenstat, Brian Thiessen, Peter Forsyth

Collection and assembly of data: Karl Bélanger, Warren P. Mason, Claude Shields, Sarah Kirby, David R. Macdonald, Jean-François Pouliot

Data analysis and interpretation: James R. Perry, Karl Bélanger, Warren P. Mason, Petr Kavan, Jacob Easaw, Claude Shields, David R. Macdonald, Brian Thiessen, Jean-François Pouliot


Final approval of manuscript: James R. Perry, Karl Bélanger, Warren P. Mason, Dorcas Fulton, Petr Kavan, Jacob Easaw, Claude Shields, Sarah Kirby, David R. Macdonald, David D. Eisenstat, Peter Forsyth, Jean-François Pouliot

Perry et al

Sign up for Alerts About Your Topic of Interest
Learn about new research in your field as it becomes available. Subscribe to a JCO e-mail alert to be notified immediately when new articles within your area of interest are posted.

Receive notification when:
- JCO releases a new issue’s Table of Contents.
- A new issue of JCO is posted online.
- New articles are published online ahead of print publication.
- New content in your subspecialty is published.
- An article is published online from an author of interest.

Go to jco.org/alerts to sign up.
ERRATA

Author Correction

The June 1, 2010, review article by Sideras et al, entitled “Coprescription of Tamoxifen and Medications That Inhibit CYP2D6” (J Clin Oncol 28:2768-2776, 2010), contained an error.

In Table 3, under the column “Moderate-to-Potent Inhibitors With Clearly Demonstrated or Expected In Vivo Inhibi-
tion,” the first medication for infectious diseases was given as “Terfenadine,” whereas it should have been “Terbinafine.”

The online version has been corrected in departure from the print. The authors apologize to the readers for the mistake.

DOI: 10.1200/JCO.2010.31.0896

Journal Corrections

The March 1, 2010, article by Barlogie et al, entitled “Long-Term Follow-Up of Autotransplantation Trials for Multiple Myeloma: Update of Protocols Conducted by the Intergroupe Francophone du Myelome, Southwest Oncology Group, and University of Arkansas for Medical Sciences” (J Clin Oncol 28:1209-1214, 2010), contained errors.

In Figures 1-3, the first plot on the x-axes was given as 10, whereas it should have been 4, as follows: 0, 4, 8, 12, 16, 20.

Journal of Clinical Oncology apologizes to the authors and readers for the mistakes.

DOI: 10.1200/JCO.2010.31.0862


In the Results section, the last sentence of the third to last paragraph was given as: “Additionally, for each of the afore-
mentioned subgroups, 23.1%, 24.2%, 7.7%, and 25.9% and achieved stable disease for more than 6 months, for an overall clinical benefit of 38.5%, 27.3%, 7.7%, and 7.0%, respectively.”

While it should have been: “Additionally, for each of the aforementioned subgroups, 23.1%, 24.2%, 7.7%, and 25.9% and achieved stable disease for more than 6 months, for an overall clinical benefit of 38.5%, 27.3%, 7.7%, and 37.0%, respectively.”

Journal of Clinical Oncology apologizes to the authors and readers for the mistake.

DOI: 10.1200/JCO.2010.31.0870


In the Recommendations section, under the heading “What Are the Clinically Validated Methods That Can Be Used in This Assessment?” and subheading “Laboratory concordance with standards,” references 71 and 60 were cited in the sixth and seventh sentences of the first paragraph, whereas references 11 and 12 should have been cited, respectively.

In the same section, under the heading “What Are the Preanalytic, Analytic, and Postanalytic Variables That Must Be Controlled to Ensure That the Assays Reflect the Tumor ER and PgR Status?” and subheading “Analytic standardization: antibody selection for ER testing,” the antibody 1A6 was inadvertently omitted from the third sentence, which should have read: “The Panel determined that the antibodies for ER that have met these criteria are clones 1D5, 6F11, SP1, and 1D5+ER.2.123, whereas the antibodies for PgR include clones 1A6, 1294, and 312 (Table 3).”

The online version has been corrected in departure from the print. Journal of Clinical Oncology and the authors apologize to the readers for the mistakes.

DOI: 10.1200/JCO.2010.31.0888