# Procarbazine, CCNU and Vincristine (PCV) Versus Temozolomide Chemotherapy for Patients with Low-Grade Glioma: A Systematic Review

Karim Hafazalla BS; Arjun Sahgal; Blessing N.R Jaja MBBS, MSc; James R Perry; Sunit Das MD PhD
1. Sidney Kimmel Medical College at Thomas Jefferson University 2. University of Toronto

CNS 2018 ANNUAL MEETING
HOUSTON, TEXAS
OCTOBER 6–10, 2018

## Introduction

Low-grade glioma (LGG) encompasses a heterogeneous group of tumors that is clinically, histologically and molecularly diverse. They are relatively uncommon, constituting 5 to 10% of all primary brain tumors(1). Despite this, they are significant in that they typically progress and lead to premature death. Over the last five years, our understanding of LGG has evolved significantly, with a shift from classification of these tumors based on histology towards stratification of risk based on molecular subtype (Figure 1). Not only does this reduce subjective error, but allows for more targeted therapy.

Treatment decisions are directed toward improving upon natural history while limiting treatment-associated toxic effects. Recent evidence has documented a utility for adjuvant chemotherapy with procarbazine/lomustine/vincristine (PCV) or temozolomide (TMZ) in the management of LGG. Treatment efficacy with PCV has been well documented in treating these gliomas, but comes at the cost of severe adverse effects. TMZ is a relatively newer treatment that allows for the combination of prolonged exposure and minor adverse effects, making it a promising alternative. However, with no prospective trials comparing the two, it is difficult to say if one is an adequate substitute for the other. In addition, tumor response to chemotherapy based on molecular profile is a primary focus going forward.

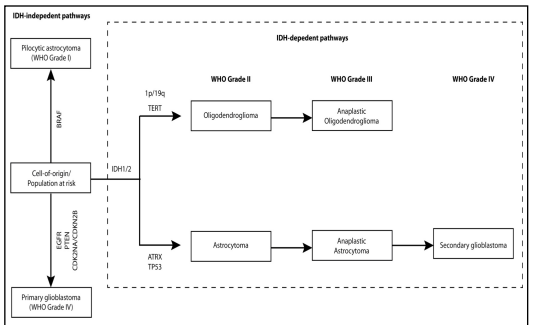


**FIGURE 1. Classification of glioma based on molecular subtype.**
Progression of a cell from WHO Grade I to Grade IV glioma based on molecular subtypes. *IDH* and *1p/19q* status are of primary focus in classification, survival, and treatment.

## Methods

A literature review was conducted to identify studies reporting patient response to PCV, TMZ, or a combination of chemotherapy and radiation therapy (RT). References for this review were identified by searches of PubMed between January 1, 2017 and May 1, 2017 (Figure 2). Eligibility criteria included: patients greater than 16 years of age; notation of LGG subtype; report of overall survival (OS); report of progression-free survival (PFS); treatment course. Class I, II, and III data were included. Figures including superimposed Kaplan-Meier curves were generated using Digitizelt (Bormisoft, Braunschweig, Germany).

## Learning Objectives

By the conclusion of this session, participants should have a well-rounded understanding of what the literature has shown in terms of survival outcomes in the use of chemotherapy in treating low-grade glioma.

## Results

Adjuvant therapy with PCV resulted in prolonged PFS and OS in patients with newly diagnosed high-risk LGG. This benefit was accrued most significantly by patients with tumors harboring 1p/19q codeletion and IDH1 mutation. Adjuvant therapy with temozolomide was associated with lower toxicity than therapy with PCV.

## Conclusions

In patients with LGG with an unfavorable natural history, such as with intact 1p/19q and wild-type IDH1, RT/TMZ plus adjuvant TMZ may be the best option. Patients with biologically favorable high-risk LGG are likely to derive the most benefit from RT and adjuvant PCV.

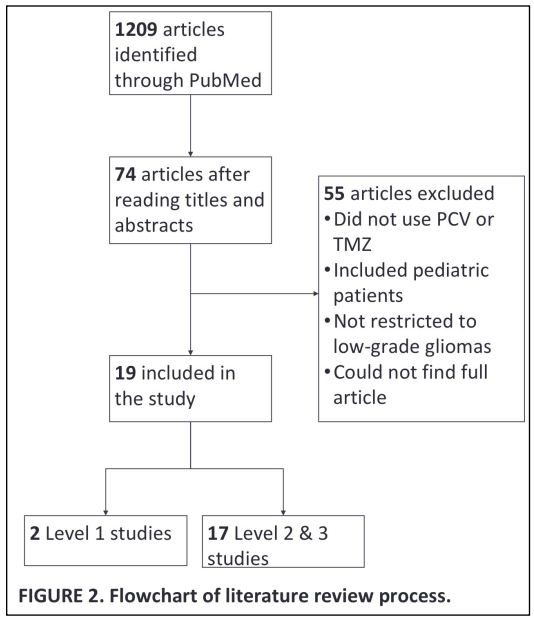


**FIGURE 2. Flowchart of literature review process.**

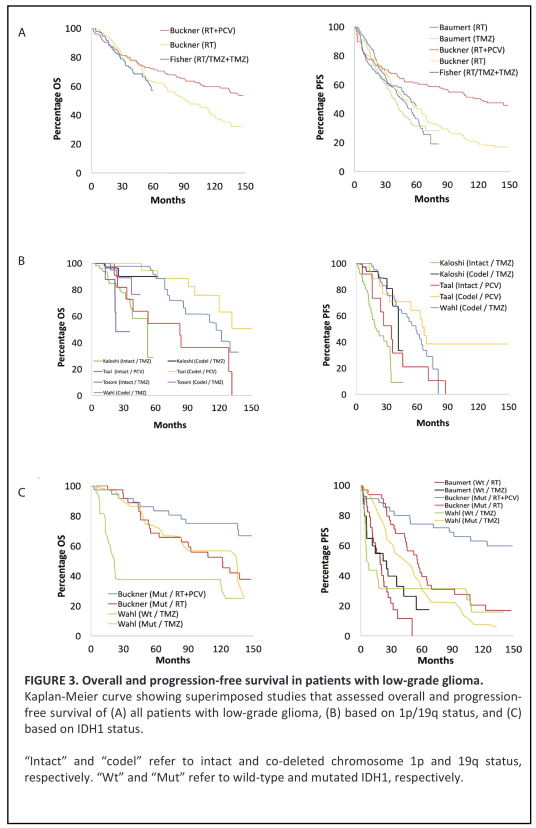


**FIGURE 3. Overall and progression-free survival in patients with low-grade glioma.**
Kaplan-Meier curve showing superimposed studies that assessed overall and progression-free survival of (A) all patients with low-grade glioma, (B) based on 1p/19q status, and (C) based on IDH1 status.

"Intact" and "codel" refer to intact and co-deleted chromosome 1p and 19q status, respectively. "Wt" and "Mut" refer to wild-type and mutated IDH1, respectively.

## References

1. Buckner JC, Shaw EG, Pugh SL, et al. Radiation plus procarbazine, CCNU, and vincristine in low-grade glioma. N Engl J Med. 2016;374:1344-55.
2. Schaff LR & Lassman AB. Indications for treatment: Is observation or chemotherapy alone a reasonable approach in the management of low-grade gliomas? Semin Radiat Oncol. 2015;25:203-09.
3. Baumert BG, Hegi ME, van den Bent MJ, et al. Temozolomide chemotherapy versus radiotherapy in high-risk low-grade glioma (EORTC 22033-26033): A randomised, open-label, phase 3 intergroup study. Lancet Oncol 2016;17:1521–32.