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Survival Outcomes Associated With First-Line Procarbazine, CCNU, and Vincristine or Temozolomide in Combination With Radiotherapy in IDH-Mutant 1p/19q-Codeleted Grade 3 Oligodendroglioma

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Abstract

Purpose: Patients with IDH-mutant 1p/19q-codeleted grade 3 oligodendroglioma (O3^{IDHmt/Codelet}) benefit from adding alkylating agent chemotherapy to radiotherapy (RT). However, the optimal chemotherapy regimen between procarbazine, 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU), and vincristine (PCV) and temozolomide (TMZ) remains unclear given the lack of randomized trial data comparing both regimens.

Methods: The objective was to assess the overall survival (OS) and progression-free survival (PFS) associated with first-line PCV/RT versus TMZ/RT in patients newly diagnosed with O3^{IDHmt/Codelet}. We included patients with histologically proven O3^{IDHmt/Codelet} (according to WHO criteria) from the French national prospective cohort *Prise en charge des Oligodendrogliomes Anaplasiques* (POLA). All tumors underwent central pathological review. OS and PFS from surgery were estimated using the Kaplan-Meier method and Cox regression model.

Results: 305 newly diagnosed patients with O3^{IDHmt/Codelet} treated with RT and chemotherapy between 2008 and 2022 were included, of which 67.9% of patients (n = 207) were treated with PCV/RT and 32.1% with TMZ/RT (n = 98). The median follow-up was 78.4 months (IQR, 44.3-102.7). The median OS was not reached (95% CI, Not reached [NR] to NR) in the PCV/RT group and was 140 months (95% CI, 110 to NR) in the TMZ/RT group (log-rank *P* = .0033). On univariable analysis, there was a significant difference in favor of PCV/RT in both 5-year (PCV/RT: 89%, 95% CI, 85 to 94; TMZ/RT: 75%, 95% CI, 66

to 84) and 10-year OS (PCV/RT: 72%, 95% CI, 61 to 85; TMZ/RT: 60%, 95% CI, 49 to 73), which was confirmed using the multivariable Cox model adjusted for age, type of surgery, gender, Eastern Cooperative Oncology Group performance status, and *CDKN2A* homozygous deletion (hazard ratio, 0.53 for PCV/RT, 95% CI, 0.30 to 0.92, $P = .025$).

Conclusion: In patients with newly diagnosed O3^{IDHmt/Codel} from the POLA cohort, first-line PCV/RT was associated with better OS outcomes compared with TMZ/RT. Our data suggest that the improved safety profile associated with TMZ comes at the cost of inferior efficacy in this population. Further investigation using prospective randomized studies is warranted.

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