Neuro-Oncology Practice
7(5), 569–570, 2020 | doi:10.1093/nop/npaa019 | Advance Access date 16 July 2020

Letter to the Editor

Letter to the Editor regarding clinical debate concerning treatment of pediatric LGG by Cooney et al

We read with great interest the recent clinical debate paper by Cooney et al on molecular targeted therapy vs conventional chemotherapy in pediatric low-grade glioma patients.[1] The authors provide an excellent and comprehensive review of the available safety, toxicity, and clinical outcome data for both types of treatment regimens, but we believe that the discussion merits consideration of other issues that were not addressed, including indications for biopsy, alternative regimens, and treatment costs:

- To consider upfront molecular targeted therapy, tissue sampling is generally required. When the surgical objective is to alleviate or restore function, as in the illustrated case, then molecular profiling is logical. However, in the vast majority of patients with optic pathway glioma who present with characteristic clinical and imaging findings, surgical intervention is seldom indicated. Whether tissue sampling should be performed in these patients for the sole purpose of molecular profiling is not clear given the ongoing debate relating to "optimal" medical therapy and inherent risks of surgery.[2]
- Although weekly carboplatin and vincristine is considered one of the standard upfront treatment regimens, as the authors point out, it is associated with significant toxicities including myelosuppression, allergic reactions, infectious and central-line complications, as well as neurotoxicity (neuropathy), and the weekly clinic visits are a burden on the patient and family. This regimen remains by far the most widely used, despite the lack of evidence to indicate that vincristine as a single agent has any clinical activity against low-grade glioma in children. In fact, carboplatin-only–containing regimens such as monthly carboplatin ("Duke regimen") have shown very similar response and disease control rates, including in single-arm prospective trials[3,4] and large retrospective studies.[5] A prospective, randomized clinical trial directly comparing the 2 regimens is ongoing (ClinicalTrials.gov identifier NCT02455245). Given the available data and the substantial practical, economical, and quality-of-life advantages of monthly carboplatin, including substantially fewer clinic visits, no requirement for a central line, avoidance of vincristine-related toxicities, as well a much lower incidence of carboplatin-related hypersensitivity,[5] we have defaulted to monthly carboplatin as our recommended first-line therapy for patients at our center who are ineligible for clinical trials. In patients who subsequently progress, we strongly consider biopsy and, if eligible, targeted therapy.
- The enormous financial consequences of targeted therapy when prescribed off-label are not addressed by Cooney and colleagues, but merit reflection. In view of an estimated retail cost of approximately $2500 for a 1-year supply of monthly carboplatin compared to approximately $150 000 for trametinib, the economic impact on families and society needs to be considered.

Conflict of interest statement. Dr Karajannis reports active consultant agreements with CereXis and QED Therapeutics (personal fees received). Dr Souweidane has nothing to declare. Dr Dunkel reports active consultant agreements with Apexigen (unpaid) and Astra Zeneca, Celgene and Roche (personal fees received).

Matthias A. Karajannis, Mark M. Souweidane, and Ira J. Dunkel

Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, New York (M.A.K., I.D.); Department of Neurosurgery, Memorial Sloan Kettering Cancer Center, New York, NY (M.M.S.)

Corresponding Author: Matthias A. Karajannis, MD, MS, Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, New York, NY 10065, US (karajanm@mskcc.org).

References

1. Cooney T, Yeo KK, Kline C, et al. Neuro-Oncology Practice Clinical Debate: targeted therapy vs conventional chemotherapy in pediatric low-grade glioma. *Neurooncol Pract.* 2020;7(1):4-10.

2. Revere KE, Katowitz WR, Katowitz JA, Rorke-Adams L, Fisher MJ, Liu GT. Childhood optic nerve glioma: vision loss due to biopsy. *Ophthalmic Plast Reconstr Surg.* 2017;33(3S Suppl 1):S107-S109.
3. Gururangan S, Cavazos CM, Ashley D, et al. Phase II study of carboplatin in children with progressive low-grade gliomas. *J Clin Oncol.* 2002;20(13):2951-2958.
4. Aquino VM, Fort DW, Kamen BA. Carboplatin for the treatment of children with newly diagnosed optic chiasm gliomas: a phase II study. *J Neurooncol.* 1999;41(3):255-259.
5. Dodgshun AJ, Maixner WJ, Heath JA, Sullivan MJ, Hansford JR. Single agent carboplatin for pediatric low-grade glioma: a retrospective analysis shows equivalent efficacy to multiagent chemotherapy. *Int J Cancer.* 2016;138(2):481-488.