Opportunities to enhance our management, outcomes, and interventions for patients with CNS malignancy

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The current issue of *Neuro-Oncology Practice* collectively describes recent advances in and current standards for management, outcomes, and interventions for patients with CNS malignancy from experience in the clinic and results from our clinical trials. A systematic review and meta-analysis to identify management standards for the diverse population of patients with low-grade glioma (LGG) was performed by Brown et al. In addition to identifying areas where the practice standards appear to be reasonably agreed on, they bring to light numerous areas where we are still in need of well-designed, comprehensive, long-term trials to provide definitive, multidimensional guidance to patients and health care providers. Moreover, a clear gap still exists in contextualizing survival outcomes with rigorous data on critical patient outcomes, including cognitive function, and neurologic signs and symptoms.

Within the European LGG Network, Darlix and colleagues conducted a survey that revealed substantial heterogeneity in clinical management and infrequent patient participation in clinical trials. Additionally, they found that whereas the majority consider standardized neuropsychological assessment and quality of life (QOL) measurement necessary, only a minority actually do so despite most feeling the resources were available. As a neuropsychologist it is encouraging to hear of our colleagues' interest in our participation in the multidisciplinary care of these patients. The oncologic neuropsychological community has recently galvanized through our international and national organizations to increase awareness and educate our non-oncology-focused neuropsychology colleagues to help prepare our field for the increased demand for our services in this specialty area.

Leveraging prospective clinical trial data, Laack et al reported on the longitudinal patient-reported outcome (PRO) and neurocognitive function (NCF) outcome data from preplanned secondary analyses of RTOG 0614. Recent clinical trials that have incorporated these clinical outcome assessments have, perhaps arguably, enhanced the clinical interpretability and overall value of what are generally long and expensive controlled experiments designed to improve the way we care for patients. In this trial, NCF and PRO outcomes were weakly associated with each, and NCF testing captured patient decline

over time. The authors advise against using PRO measures to monitor NCF as a clinical trial end point.

Providing further evidence of the feasibility of integrating NCF testing as a clinical outcome assessment in multisite clinical trials, Cerhan and colleagues demonstrated that, with rigorous training, health care staff without experience in NCF testing produce very low error rates. Furthermore, most errors can be corrected with centralized expert review, thereby preventing invalid data from entering into analyses. Reinforcing the importance of including evaluation and management of NCF in everyday practice, Loughan et al summarized a single institution's experience with a multidomain NCF screening instrument (RBANS) in a heterogeneous group of treated patients with CNS lesions. Consistent with previously published neuropsychological literature, they observed that patients' worst performance was in the domain of episodic memory.

There is tremendous interest in the use of immunotherapies in patients with brain metastasis. However, one area of concern is the potential for increased toxicity if these therapies are used with radiation to the brain. Arscott and colleagues examined their institutional experience to determine the frequency of acute toxicities in patients with brain metastasis who received radiation to the brain and immune checkpoint blockade therapy. They report acute rates that were not markedly dissimilar to what has been previously reported with radiation alone, which is encouraging with regards to this therapeutic approach. As the investigation and use of combined immunoradiotherapy treatments grows, it will be important to evaluate side effect profiles in high-quality trials that may offer more robust level I evidence regarding the safety of combination treatment.

Screening for distress is critical to allow for tailored interventions to alleviate these symptoms. Patil et al summarized a practical and pragmatic clinical intervention for distress in patients with CNS malignancies. Using the National Comprehensive Cancer Network distress thermometer during treatment and follow-up, they found that nearly two-thirds of patients report symptoms of distress throughout treatment, with half of these due to emotional problems, most often worry.

Brief physician counseling reduced distress in almost every case, underscoring the critical importance of assessing distress and the responsiveness of such symptoms to intervention.

Interventions to improve QOL, mood, and fatigue as well as cognition are needed in our patient population. Milbury and colleagues shared results from a pilot randomized controlled trial of dyadic yoga vs wait list control in patients with glioma, and their partners, during radiation to the brain. They demonstrated that this intervention is feasible and showed encouraging efficacy signals for QOL, mood, fatigue, and cognition. This shows the promise of symptom management trials in this population, which will, it is hoped, lead to further efficacious interventions to actively enhance patients' QOL.

Standardization of care across clinical practice and research is important to generate optimal results. Skorupan et al have raised awareness of an opportunity for greater harmonization both in clinical practice and clinical research

protocols in the area of *Pneumocystis jiroveci* prophylaxis. Results of their survey of providers revealed variability in clinical practice in terms of choice of antibiotic, duration of therapy, clinical monitoring, and discontinuation criteria. The neuro-oncology community has been actively developing clinical and research harmonization, and this seems ripe for inclusion in these efforts.

Lastly, bringing attention to vigilant monitoring for associated symptoms that can confound the clinical picture, Yari and colleagues share a case study of a patient who developed herpes simplex encephalitis after resection of a craniopharyngioma. They note that this postoperative complication may be unrecognized, and delays in diagnosis and treatment can lead to marked morbidity and mortality. The authors raise the awareness of concurrent disease entities and the importance of early initiation of therapy while working up the etiology for these symptoms.