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In the midst of crisis, a great opportunity

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See article by Wen et al. in this issue, pp. 1073–1113.

Since the World Health Organization declared COVID-19 a pandemic on March 11, 2020, health care has transformed in ways that could not previously be imagined. Almost overnight, countries began to limit nonessential procedures, surgeries, and clinic visits, reducing health care utilization, conserving personal protective equipment, and combating the rapid spread of this novel coronavirus. In the United States, the Centers for Medicare and Medicaid Services quickly adjusted reimbursement guidelines to broaden coverage for telehealth services. Care rapidly shifted away from in-person delivery in clinics to video encounters and telephone visits. Inpatient hospital volumes declined, face masks became widespread, and physical distancing was ingrained in our everyday lives.

As health care providers faced with these challenges, we rapidly innovated to respond to changing times. Initial publications defined the spectrum of COVID-19 disease.[1] We then learned of the increased risk of neurological complications including cerebrovascular events, impaired consciousness, neuromuscular disorders, and others.[2,3] Cancer patients are at heightened risk for severe infection, intensive care unit admission, and mortality rates as high as 28%.[4,5] In neuro-oncology, international collaborations were readily formed, consensus built, and guidance published on how to approach care for brain tumor patients. These rapid publications provided guidance on the appropriate precautions to use when delivering standard treatments and identified methods that can help select appropriate patients who can delay, defer, or avoid potentially immunosuppressive treatments.[6–8] Many providers have now developed pathways for virtual preoperative assessments, remote interfaces to include family members virtually into rounds, use of e-consents for clinical trials, and telehealth visits for routine and even urgent patient evaluations. As providers, we have also identified what not to do—we should avoid large gatherings, limit droplet generating procedures, and coordinate inpatient care to reduce excess personnel entry into patient rooms.

As communities have moved to reopen, conversations are shifting to define what the new normal will be in the future. Where will we shop and eat? How will we watch sporting events? What will happen with grade and graduate schools? From the ashes of this crisis comes an opportunity for new growth in ways that we had not previously considered.

In this issue, Wen and colleagues provide a consensus review of the current management of isocitrate dehydrogenase (*IDH*) wildtype glioblastoma.[9] The authors are to be commended on their comprehensive review of this most common and vexing condition in neuro-oncology. The article, which is a collaboration between the Society for Neuro-Oncology (SNO) and the European Association of Neuro-Oncology (EANO), discusses molecular classification of glioblastoma, including the recategorization of *IDH*-mutant glioblastoma with other *IDH*-mutant gliomas. The review includes the latest approaches to imaging as well as standard and emerging therapies. Despite important progress in the field, few new therapeutic advances can be highlighted and are largely limited to publication of the phase III data on intensified lomustine and temozolomide in newly diagnosed *MGMT* promoter methylated glioblastoma and hypofractionated chemoradiotherapy for elderly patients.

These authors are left to review the many substantial challenges that define the current crisis that exists for patients with glioblastoma. To date, molecularly defined subtyping has not translated into the success of targeted therapies that has been seen with other cancers. Tumor metabolism has been the source of significant preclinical study but few translational advances have occurred. Efforts to overcome adaptive immunologic resistance to glioblastoma through viral therapies, vaccines, immune checkpoint blockade, and chimeric antigen receptor T cells have been underwhelming. Combining temozolomide with DNA damage response inhibitors (eg, PARP inhibitors) is

attractive but has been complicated by overlapping toxicity and unclear efficacy. New approaches to surgical resection and radiotherapy do not address the diffusely infiltrative drivers of recurrence. Major challenges abound, including:

1. Low rates of enrollment into clinical trials for glioblastoma particularly for patients with newly diagnosed glioblastoma
2. Obstacles to drug delivery in neuro-oncology that require dedicated study of methods that will overcome the blood–brain and blood–tumor barriers
3. Inter- and intrapatient heterogeneity which result in differential drug sensitivity, treatment resistance, and tumor recurrence
4. Complex immunologic mechanisms that will likely require use of the right type or combination of immune-based therapies delivered at the right time for the immune system

Patients with glioblastoma are in crisis. Only 3 therapies have ever received FDA approval for newly diagnosed glioblastoma. Five-year overall survival rates remain <10%. Corticosteroid use is frequent and impairs the effectiveness of immunotherapies. Comprehensive cancer centers frequently require that patients travel long distances for clinical trials. Neurologic disability often limits patient mobility and can restrict access to care. Solving these problems necessitates innovation in ways that have not previously been envisioned.

Albert Einstein said, "In the middle of difficulty lies opportunity."[10] The COVID-19 pandemic has breathed life into these words in ways that are now palpable. In neuro-oncology, great opportunities exist to innovate and advance the care of patients with glioblastoma but will require shifts in our thinking and approach. As our field moves to reopen clinical care and research, we must ask the questions that will shift us to a new normal. How can telemedicine be optimally expanded to enhance clinical trial access and patient enrollment in neuro-oncology? What opportunities exist to pool global resources and share data in real time that could promote broad collaboration or subgroup identification through expanded biobanking? Where can virtual care reduce disparities and overcome barriers to delivering high quality neuro-oncology in resource limited settings?

In the midst of every crisis lies great opportunity. We must see opportunity.

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