Advances in neuro-oncology: stepping in the right direction

Antonio Omuro

In the midst of the current challenges faced worldwide, it is refreshing to learn that scientific advances in themes outside of COVID-19 are far from halting. Even in a challenging field such as Neuro-Oncology, admirable progress has been made, and this Neoplasm section of *Current Opinion in Neurology* proves our field is well alive, and clearly thriving.

Immuno-oncology is undoubtedly the 'talk of the town' in the cancer world, but given the recent failures of nivolumab in improving survival in glioblastoma, one is left wondering if Neuro-Oncology will ever join this party. Two articles in this issue give us hope that it will. In 'T Cell Dysfunction in Glioblastoma: A Barrier and an Opportunity for the Development of Successful Immunotherapies', Lucca *et al.* (pp. 000–000) provide us with an overview of the remarkable advances in the understanding of the ways the immune system operates in the brain, and how it differs from other organs. Dissecting the various elements of what constitutes the so-called 'sanctuary site', the article zooms in on recent discoveries related to T-cell dysfunction in this disease. From defective antigen presentation and meningeal lymphatic drainage to barriers to trafficking and re-activation of T cells, the article reviews what it takes to successfully mount antitumor immune responses in the central nervous system (CNS). In another article, Sun *et al.* (pp. 000–000) provide us further clues and alternative pathways for the successful use of immune-checkpoint inhibitors in gliomas. In 'Is there a role for neoadjuvant anti-PD-1 therapies in glioma?', authors discuss the recently described strategy based on priming and expanding exhausted T cells with neoadjuvant anti-PD-1 therapy, followed by removal of the immunosuppression triggered by the tumor microenvironment with surgical resection. The jury is still out on this intriguing new concept but if proven right, it will establish a new paradigm for efficacious usage of anti-PD-1 and other new up-and-coming immune checkpoint inhibitors.

Our field has also watched uplifting stories surrounding the application of genomic profiling leading to successful targeted therapies in other cancer types, while a series of failures were seen in gliomas. In 'Targeting gene fusions in glioma' (pp. 000–000), the author reviews the recent discoveries in the field of gene fusions and their oncogenetic role, highlighting that new tyrosine kinase inhibitors are now available to treat patients with gliomas harboring NTRAK-fusions. As NTRAK fusions are not always part of gene sequencing panels, actively evaluating all patients for the presence of these relatively rare fusions is imperative, hence the importance of raising awareness.

Another potential use of genomic data in Neuro-Oncology is highlighted in 'Targeting Bruton's tyrosine kinase in primary CNS lymphoma' (pp. 000–000). The high frequency of mutations activating the NFκB pathway in this disease, including mutations in *CD79B*, *CARD11*, and *MYD88* has sparked an interest in the use of Bruton's tyrosine kinase inhibitors (BTKi), such as ibrutinib. However, the article highlights this story is more complicated, and discusses the current experience with ibrutinib and second generation BTKi agents, such as tirabrutinib, acalabrutinib, orelabrutinib, and others. Genomic data is also leading to novel therapies for recurrent meningiomas, a disease for which there are no medical treatments available. As discussed by Graillon *et al.* (pp. 000–000) in 'Chemotherapy and Targeted Therapies for Meningiomas: What is the evidence?', novel regimens have been tested, particularly targeting mutations in NF2, by far the most common molecular abnormality in this disease.

Finally, the past two decades were dominated by the rise of cancer stem cell theories, and their role in hierarchical heterogeneity and treatment resistance in gliomas. However, that extensive body of work is yet to produce meaningful therapeutic

Department of Neurology and Yale Cancer Center, Yale School of Medicine, Connecticut, USA

Correspondence to Antonio Omuro, MD, Section Editor, Department of Neurology and Yale Cancer Center, Yale School of Medicine, 15 York Street, LLCI 920, PO Box 208028, New Haven, CT 06520, USA.
Tel: +1 203 737 7084; fax: +1 203 737 2591;
e-mail: Antonio.Omuro@Yale.edu

Curr Opin Neurol 2021, 33:000–000

DOI:10.1097/WCO.0000000000001000

developments. In 'Cancer stem cells in gliomas: Evolving concepts and therapeutic implications' (pp. 000–000), the authors provide us with a summary of the state of cancer stem cells research, and discuss how recent discoveries are resolving the high complexity of these cells' functions while unveiling new therapeutic avenues, perhaps priming the field for a triumphant comeback.

We are grateful to the authors who worked hard to contribute to this Section, especially during these challenging times. Their fine articles provide us readers with much needed moments of respite through fulfilment of scientific curiosity and learning needs, as well as renewed hope. I hope you will enjoy.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

Personal compensation: Consulting/Advisory Board (Merck, Ono Therapeutics, Kiyatec); research support to the institution: Arcus Biosciences. The drugs mentioned in this article are considered experimental and have not been approved by the FDA for the respective indications.