Preface

This is truly an exciting time in the field of neuro-oncology, particularly in the area of high-grade gliomas. The management of patients with high-grade gliomas has historically been one of the most challenging and disheartening fields in medicine, where failure is the rule and longevity is the exception. The jaded often state that despite purported advances in surgical and radiotherapeutic techniques and a myriad of clinical trials of medical therapies, the survival statistics for glioblastoma have not changed in the last three decades. The nihilism associated with these tumors is such that some practitioners still advise against treatment or even biopsy, recommending palliative care with the diagnosis based only on history and an MRI scan. If the current state-of-the-art in the diagnosis and management of high-grade gliomas was truly so bleak, there would be no reason to compile and publish a monograph on the subject. The fact is that we have recently entered an era where real progress is being made in our understanding and treatment of high-grade gliomas that is directly benefiting some patients.

We are slowly but surely chipping away at this problem. One approach has exploited correlations between particular molecular markers and therapeutic response. The first such "breakthrough" in high-grade glioma was the observation that loss of chromosomes 1p and 19q uniformly predict chemosensitivity in anaplastic oligodendrogliomas *(1)*. Subsequent work has refined this relationship using additional markers to forecast longevity in patients with these tumors *(2)*. More recently we have seen similar observations in glioblastoma where methylation of the methyl-guanine-methyl transferase (MGMT) gene promoter is associated with better response to temozolomide (TMZ) *(3)*. Similarly, co-expression of the vIII mutation of epidermal growth factor receptor (EGFR) and the PTEN tumor suppressor gene predicts response to EGFR inhibitors *(4)*.

Another approach has been large multi-center clinical trials using conventional and unconventional agents. Stupp et al have shown that radiotherapy with concurrent low dose temozolomide and subsequent high dose TMZ leads to longer survival than radiotherapy alone for newly diagnosed glioblastoma *(5)*. Presently a large multicenter trial is comparing the use of an immuotoxin (IL13-PE39QQR) delivered by convection enhanced delivery against carmustine-impregnated biodegradable wafers in patients with operable glioblastoma at first recurrence. Yet another avenue of investigation is to use preclinical animal testing to improve response by refining traditional therapeutic delivery schedules, combining agents and investigating various modes of delivery and concentrations of agents achieved in tumor, brain and CSF.

So in this volume we present the spectrum of issues pertaining to high-grade gliomas from the basics of clinical characteristics and management to the state-of-the-art in diagnosis and therapeutics, as well as current areas of investigation that may lead to the treatments of tomorrow. We explore whether molecular diagnosis complements histology or is likely to supercede it, the most current information in imaging techniques to assist us in diagnosing and monitoring treatment, and the latest in "conventional" treatments such as surgery, radiation, and cytotoxic chemotherapy.

After decades of uniformly poor outcomes, we have entered an era where meaningful advances are being made in our understanding of the biology of high-grade gliomas that is leading to better, more rational, patient-specific treatments. I hope you find this book informative and useful.

Gene Barnett, MD, FACS

REFERENCES

1. Cairncross JG, Ueki K, Zlatescu MC, et al. Specific genetic predictors of chemotherapeutic response and survival in patients with anaplastic oligodendrogliomas. J Natl Cancer Inst 1998;90(19):1473–1479.
2. Ino Y, Betensky RA, Zlatescu MC, et al. Molecular subtypes of anaplastic oligodendroglioma: implications for patient management at diagnosis. Clin Cancer Res 2001;7(4):839–845.
3. Hegi M E, Diserens A-C, Gorlia T, et al. MGMT gene silencing and benefit from temozolomide in glioblastoma. N Engl J Med 2005;352:997–1003.
4. Mellinghoff IK, Wang MY, Vivanco I, et al. Molecular determinants of the response of glioblastomas to EGFR kinase inhibitors. N Engl J Med 2005;353:2012–2024.
5. Stupp R., Mason W P, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352:987–996.

http://www.springer.com/978-1-58829-511-8

High-Grade Gliomas
Diagnosis and Treatment
Barnett, G.H. (Ed.)
2007, XIII, 495 p., Hardcover
ISBN: 978-1-58829-511-8
A product of Humana Press