JOURNAL WATCH

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Our panel of experts highlight the most important research articles across the spectrum of topics relevant to the field of CNS oncology

Expert panel: **Larry Junck**, University of Michigan Health System, Department of Neurology, Ann Arbor, MI, USA; **Maura Massimino**, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milano, Italy

Haliasos N, Brew S, Robertson F, Hayward R, Thompson D, Chakraborty A. Preoperative embolisation of choroid plexus tumours in children: part I – does the reduction of perioperative blood loss affect the safety of subsequent surgery? *Childs Nerv. Syst.* doi:10.1007/s00381-012-1912-8 (2012) (Epub ahead of print).

Choroid plexus tumors are very rare, accounting for 1% of all intracranial tumors in children but making up 12% of brain tumors that occur in the first 3 years of life. Mortality rates of surgical excision can be as high as 12% owing to large tumor size and vascularity, which results in significant perioperative blood loss. The group from Interventional Neuroradiology and Neurosurgery at Great Ormond Street Hospital for Children (London, UK) have hypothesized that preoperative embolization could reduce blood loss during surgery with the advantage of the possibility to perform total tumor resections. The group report their experience with a series of 30 consecutive patients, in whom 13 out of 15 tumors were successfully embolized, and 15 were not embolized. Both the rate of complete resection and intraoperative blood loss compared favorably in the embolized cohort with the nonembolized one, with a rate of nonfatal morbidities of 20%. Owing to the prognostic impact of complete surgery in choroid plexus tumor management, the indications for this innovative procedure, which allows more

complete resections, need to be included in the context of a clinical trial.

– Written by Maura Massimino

Hashizume R, Smirnov I, Liu S et al. Characterization of a diffuse intrinsic pontine glioma cell line: implications for future investigations and treatment. *J. Neurooncol.* 110(3), 305–313 (2012).

A fundamental limitation felt by many clinicians in the development of efficacious therapies for diffuse intrinsic pontine glioma (DIPG) is that the diagnosis is usually confirmed by imaging studies, whereas surgical biopsy is rarely performed. Viable cells and tissue resources are, therefore, very limited. Recent results, moreover, have identified a number of *DIPG* gene and chromosomal alterations that clearly distinguish adult gliomas and DIPGs.

The research group at the University of California (CA, USA) has provided a fundamental contribution to research in this difficult field by obtaining both ethical committee approval and family consents for the use of a stereotactic biopsy. This procedure allowed the determination of both the histological subtype of the tumor and the establishment of a primary cell culture. They transduced cells with a retrovirus vector containing hTERT for cell immortalization and, subsequently, with a lentiviral vector containing firefly luciferase. These modified tumor cells were injected into the pontine tegmentum of

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athymic rats obtaining a diffuse infiltrating tumor similar to that observed in the surgical biopsy. The authors demonstrated the feasibility of developing sustainable and tumorigenic DIPG cell sources that can be applied to test therapies.

– Written by Maura Massimino

Cairncross G, Wang M, Shaw E *et al.* Phase III trial of chemoradiotherapy for anaplastic oligodendroglioma: long-term results of RTOG 9402. *J. Clin. Oncol.* doi:10.1200/JCO.2012.43.2674 (2012) (Epub ahead of print).

van den Bent MJ, Brandes AA, Taphoorn MJ *et al.* Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC Brain Tumor Group Study 26951. *J. Clin. Oncol.* doi:10.1200/JCO.2012.43.2229 (2012) (Epub ahead of print).

The study by Cairncross *et al.* is a late follow-up of the RTOG study 9402, in which 291 patients with anaplastic oligodendroglioma and anaplastic mixed oligoastrocytoma were randomly assigned to radiation therapy (RT) alone or four cycles of intensive procarbazine, lomustine and vincristine (PCV) followed by RT. For 126 patients with 1p/19q codeletion, median survival was 14.7 years for PCV plus RT versus 7.3 years for RT (hazard ratio: 0.36). For 137 patients without codeletions, median survival was 2.6 versus 2.7 years (hazard ratio: 0.85 favoring PCV plus RT).

The study by van den Bent *et al.* is a late follow-up of the EORTC study 26951, in which 368 patients with anaplastic

oligodendroglial tumors were randomly assigned to receive RT alone or RT followed by six cycles of standard-dose PCV. In the 80 patients with 1p/19q codeletion, median survival was not reached (but was apparently >14 years) in the RT plus PCV group versus 9.3 years in the RT group (hazard ratio: 0.56; 95% CI: 0.31–1.03). Among the 236 patients with noncodeleted tumors, median survival was 2.1 versus 1.8 years.

Together, these studies provide an important advance in our understanding and future treatment of anaplastic oligodendroglial tumors. Both studies show that 1p/19q deletions are strongly prognostic for survival and predictive of PCV benefit. The importance of deletions in 1p/19q was unknown at the conception of both studies, thus the analyses based on deletions were unplanned, but the similarity of the results of the two studies makes the findings highly convincing. The results are all the more remarkable considering that most patients in the RT arm of both studies received chemotherapy at progression, suggesting that chemotherapy must be given early, not at relapse, to be of full benefit. Taken together, these studies indicate that RT alone is not a preferred option for most patients with codeletions. Today, many physicians prefer the easier and less toxic option of temozolomide, either concomitant with RT followed by cyclic therapy or as adjuvant cyclic therapy alone, supported by the efficacy of temozolomide for glioblastoma and for recurrent anaplastic glioma. The CODEL study may determine whether temozolomide plus RT equals or surpasses PCV plus RT in efficacy, but results will be many years away.

– Written by Larry Junck

Boisselier B, Pérez-Larraya JG, Rossetto M *et al.* Detection of

***IDH1* mutation in the plasma of patients with glioma. *Neurology* 79, 1693–1698 (2012).**

The authors analyzed sera of 12 low-grade glioma (LGG) and 27 high-grade glioma (HGG) patients for the *IDH1* R132H mutation by a combination of co-amplification at a lower denaturation temperature and digital PCR. Among patients bearing the mutation in their tumors, the authors detected it in the sera of three out of eight LGG patients and 12 out of 17 HGG patients. Sensitivity of the serum assay was 60% and correlated with tumor volume, suggesting release from the tumor; specificity was 100%. The results suggest the possibility of noninvasive diagnosis in patients with mutated tumors.

They also extracted small-size DNA (150–250 base pairs) from the sera of 80 glioma patients and 31 controls, and correlated it with MRI data. The concentrations in LGG patients were not significantly different from controls, but concentrations were increased in HGG patients and correlated with enhancing tumor volume. Again, the results suggested release from tumor cells. The overlap between glioma and control patients was too great to support noninvasive diagnosis.

– Written by Larry Junck

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