Open access • Journal Article • DOI:10.1097/WCO.0B013E3283407EED

2010: neuro-oncology is moving! — Source link

Roger Stupp, Michael Weller

Institutions: University Hospital of Lausanne, University of Zurich

Published on: 01 Dec 2010 - Current Opinion in Neurology (Lippincott Williams and Wilkins)

Topics: Recurrent Glioma, Cilengitide, Glioma, Bevacizumab and Primary central nervous system lymphoma

ASCO 2010 – Neuro-Oncology is moving!

The 2010 ASCO meeting was one of the most exciting ASCO meetings for Neuro-Oncology ever, with first presentations of various large phase III trials as well as first reports on several novel treatment approaches.

Combined temozolomide-based radiochemotherapy using temozolomide is considered standard of care for glioblastoma patients aged 65-70. Radiotherapy alone is usually considered standard of care in the elderly. The results of two large phase III trials challenging this standard were presented. The *Nordic Brain Tumor Trial* compared conventional radiotherapy (30 x 2 Gy) with hypofractionated radiotherapy (10 x 3.4 Gy) and a conventional regimen of temozolomide (5 out of 28 days) in 342 patients with glioblastoma $\geq$ 60 years of age. The median survival times in the three arms were 6, 7.5 and 8 months, and these differences were not significant (#LBA2002). The German NOA-08 trial (*Methvsalem*) randomized 412 patients > 65 years of age with glioblastoma or anaplastic astrocytoma to conventional radiotherapy or dose-dense temozolomide chemotherapy (*one week on one week off*). The one year survival rate was 38% with radiotherapy compared with 30% with chemotherapy, and this difference was significant. Moreover, radiotherapy was overall better tolerated (#LBA2001). These discrepant results are difficult to interprete until full publications become available, but a prudent conclusion would be to state that radiotherapy using either fractionation schedule remains the standard of care at present. Whether combined chemoradiation is superior to radiotherapy alone, is addressed in an ongoing phase III trial of NCIC and EORTC.

The UK BR12 trial had randomized 447 chemonaive patients with recurrent malignant glioma to PCV polychemotherapy or temozolomide, with a subrandomization of the temozolomide patients to the conventional 5 out of 28 days regimen or a dose-dense 21 out of 28 days regimen. At the ASCO meeting, the investigators provided molecular analyses of this study: *IDH*1 mutations and *MGMT* promoter methylation were independent prognostic markers, independent of the applied treatment regimen (#2035).

Updated results for one of the registration trials for bevacizumab in recurrent glioblastoma, the BRAIN study, were also presented. BRAIN had randomized the patients to treatment with either bevacizumab alone (n=85) or bevacizumab plus irinotecan (n=82). No new safety signals were reported, median survival times in both arms remained at 9.3 and 8.9 months, and survival at 30 months was 11% and 16%, respectively. Altogether, one major conclusion remains: the addition of irinotecan increased toxicity, but did not demonstrate activity over that seen with bevacizumab alone (#2008). The results from the dose-finding study for the integrin antagonist, cilengitide, were also reported. That study had randomized patients with recurrent glioblastoma to flat doses of 500 mg (n=41) or 2000 mg (n=40). At a median follow-up of 53.3 and 48.3 months, respectively, survival rates were consistently higher with 2000 mg at 12, 24, 36, 48 and 54 months. Again, no new safety signals were reported (#2010). Both agents, bevacizumab and cilengitide, are now explored in the first-line setting and aim at concluding patient enrolment prior to ASCO 2011.

Perhaps most controversial were the lessons to be learnt from the German G-PCNSL-SG-1 trial which randomized 551 patients with primary CNS lymphoma to high-dose methotrexate (HDMTX) followed either by whole brain radiotherapy

(WBRT) alone or observation (for patients with complete remission (CR) after HDMTX) or WBRT or HD-Ara-C (for patients failing to achieve a CR after HDMTX). This study was criticized for several shortcomings, including high drop-out rate and high number of protocol violations. Nevertheless, the analysis of 318 patients treated per protocol demonstrated trends for longer progression-free survival, but shorter overall survival in patients treated with WBRT first-line. Neither of these differences were significant. Thus, the possible gain in event-free survival afforded by WBRT has to be weighed against the cognitive sequelae which appear to be inescapable in long-term survivors (#8008).

Roger Stupp, Lausanne, Switzerland
Michael Weller, Zurich, Switzerland