A number of important studies were presented at the Society for Neuro-Oncology annual meeting in Montréal, Canada, on 18–21 November 2010. Cediranib as monotherapy or in combination with lomustine did not show increased efficacy when compared with lomustine alone in patients with recurrent glioblastoma (GBM). Addition of temozolomide (TMZ) or irinotecan (CPT) to bevacizumab (BEV) in patients with recurrent GBM was well tolerated, with similar efficacy to BEV alone. The addition of BEV to radiation and TMZ in newly diagnosed GBM improved progression-free survival but did not improve overall survival. TMZ alone may be a reasonable approach in elderly GBM patients with poor performance status. Two Phase II trials with suntinib and vatalanib showed a hint of activity in patients with recurrent or progressive meningiomas.

The Society for Neuro-Oncology (SNO) was founded in 1995 in response to the need for coordinated activities in the neuro-oncology community that would promote multidisciplinary interactions in advancing research and the treatment of neurological malignancies. Membership is drawn from over 40 countries and is comprised of professionals from multiple specialties, including neurology/neuro-oncology, neurosurgery, medical oncology, radiation oncology, neuro-radiology and basic science. The SNO has come to be recognized as the premier organization for all specialties engaged in the research and treatment of CNS tumors. Since its inception, the SNO annual meeting has become a platform for disseminating state-of-the-art neuro-oncology research data and providing an opportunity for global exchange. The SNO 2010 meeting was well attended by nearly 1200 participants and approximately 600 abstracts were presented.

Glioblastoma (GBM) is the most common primary malignant CNS tumor, accounting for approximately 10,000 new cases diagnosed each year in the USA [1]. GBMs are extremely aggressive tumors and are associated with a dismal prognosis, with a median survival of 15 months [2]. Approximately 25% of patients survive for 2 years and fewer than 10% survive for 5 years. Hence, there is an urgent need for more promising agents. Since bevacizumab (BEV) was approved by the US FDA for recurrent GBM in 2009, a number of novel agents including antiangiogenic agents have undergone evaluation in both newly diagnosed as well as recurrent GBM [3,4]. Some of these trials were presented at the 2010 SNO annual meeting.

Tracy Batchelor (Massachusetts General Hospital, MA, USA) reported on the findings of Cediranib in Combination with Lomustine Chemotherapy in Recurrent Glioblastoma (REGAL; NCT00777153), a randomized, parallel-group, multicenter Phase III study comparing cediranib (as monotherapy and in combination with lomustine) with bevacizumab (BEV) in patients with recurrent GBM. The addition of BEV to radiation and TMZ in newly diagnosed GBM improved progression-free survival but did not improve overall survival. TMZ alone may be a reasonable approach in elderly GBM patients with poor performance status. Two Phase II trials with suntinib and vatalanib showed a hint of activity in patients with recurrent or progressive meningiomas.
oral cediranib 20 mg/day plus oral lomustine 110 mg/m² once every 6 weeks (n = 129), or a control group of oral lomustine 110 mg/m² every 6 weeks and oral cediranib-matched placebo (n = 65). The primary end point was progression-free survival (PFS) in order to determine the relative efficacy of cediranib (either as monotherapy or in combination with lomustine) compared with lomustine alone. The study found no statistically significant difference in the median PFS of 92 days in the cediranib arm (p = 0.889) or the median PFS of 125 days in the combination arm (p = 0.162) compared with a median PFS of 82 days in the control arm. PFS at 6 months (PFS-6) was 16% in the monotherapy arm compared with 34.5% in the combination arm, and 24.5% in the control arm. This PFS-6 of 16% in the cediranib arm was lower than the PFS-6 of 25.8% reported in the Phase II trial of cediranib carried out earlier by Batchelor and colleagues [6]. The initial study used a 45-mg/day dose of cediranib, and a dose–response property with the agent was observed which may be the likely reason for the difference in the PFS-6 seen in the two studies.

Mark Gilbert (University of Texas MD Anderson Cancer Center, TX, USA) presented the results of the Radiation Therapy Oncology Group (RTOG) 0625: A Randomized Phase II Trial of BEV with either Irinotecan (CPT) or Dose-Dense Temozolomide (TMZ) in Recurrent GBM trial [7]. Patients were treated with intravenous BEV 10 mg/kg, and either TMZ 75–100 mg/m² day 1–21 of a 28-day cycle or CPT 200 mg/m² every 2 weeks. In total, 60 patients were treated on the TMZ arm and 57 patients on the CPT arm. A PFS-6 rate of 40% was seen in the TMZ arm compared with 39% for the CPT arm. This is similar to the PFS-6 of 42.6% seen in the BEV-only arm in the Bevacizumab Alone or in Combination with Irinotecan for Treatment of Glioblastoma Multiforme (BRAIN) study [8], the randomized Phase II study of BEV versus BEV and CPT in recurrent GBMs that contributed to the accelerated approval of BEV in 2009. Objective responses of 21% in the TMZ arm and 28% in the CPT arm were again similar to 28.2% in the BEV-alone and 37.8% in BEV plus CPT groups reported previously in the BRAIN study [8]. A moderate to moderately high rate of toxicities were reported, and the frequency of selected adverse events was consistent with that previously reported for a similar regimen. A median overall survival (OS) of 9.4 months in the TMZ arm and 7.7 months in CPT arm was comparable to the 9.2 months reported in the BEV arm of the BRAIN study [8].

Annick Desjardins (Duke University Medical Center, NC, USA) presented the survival and toxicity update of a Phase II trial of BEV in combination with TMZ and radiation therapy (RT) followed by BEV, TMZ and CPT (CPT-11) for newly diagnosed GBM patients [9]. A total of 125 patients with newly diagnosed GBM were enrolled in the study and received standard RT and daily TMZ. A total of 113 patients (90%) proceeded with the consolidative TMZ, BEV and CPT therapy in the adjuvant part of this trial. The median follow-up for the 125 patients was 21 months. The median PFS was 13.8 months and median OS was 21.3 months. These results are similar to those reported by Albert Lai et al. in a Phase II trial of BEV plus TMZ and RT in patients with newly diagnosed GBM [10]. The median PFS and OS of 13.6 and 19.6 months, respectively, in the Lai study compared with 7.6 and 21.1 months respectively, in the University of California, Los Angeles/KPLA control cohort. These two studies demonstrate that patients treated with BEV and TMZ during and after RT may show improved PFS without improved OS compared with the University of California, Los Angeles/KPLA control group. The two ongoing Phase III studies; the Hoffmann-La Roche Study of BEV in combination with TMZ and radiotherapy in patients with newly diagnosed GBM (NCT00943826) and the RTOG 0825, a randomized Phase III trial of TMZ and RT with or without BEV in treating patients with newly diagnosed GBM (NCT00884741) will help answer the question of whether the addition of BEV to TMZ and radiotherapy will improve the survival of patients with GBM.

The incidence of high-grade gliomas in elderly patients is increasing. The optimal treatment for this group of patients is unknown, as they tend to respond less well to standard therapies and have a worse prognosis. There is no standard for the management of GBM in elderly patients with a poor Karnofsky Performance Status (KPS; KPS <70). Jamie Gállego Pérez-Larraya (Service de Neurologie Mazarin, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France) reported the results of the Association des Neuro-Oncologues d’Expression Française (ANOCEF) ‘TAG’ trial, a Phase II trial of TMZ in elderly patients with GBM and a poor performance status (KPS <70) [11]. In this multicenter, prospective Phase II trial, 70 patients (from ten centers) with a median age of 77 years were treated with TMZ (150–200 mg/m² every 4 weeks) for a maximum of 12 cycles or until progression between July 2007 and February 2009. A total of 91% of the patients underwent biopsy and the remaining 9% underwent either complete or partial resection. The postoperative KPS was 60 in 44 patients (63%) and below 60 in 26 patients (37%). After therapy, 18 patients (25.7%) achieved a KPS of 70 or more, and 21 patients (30%) improved their KPS by at least 10 points. An objective response was seen in 26% patients. The toxicity profile was acceptable, with grade 4 neutropenia and/or thrombocytopenia occurring in five patients. PFS-6 of 29% and a median OS of 25 weeks compared favorably with 12–16 weeks seen with supportive care. This represents a reasonable alternative for treating elderly patients with GBM and poor performance status.

Meningiomas are the most common type of primary brain tumors in adults, accounting for a third of the total brain tumors [12]. Currently, the management for meningiomas is surgery, RT and stereotactic radiosurgery. These approaches are effective in achieving tumor control for most patients with WHO grade I disease as well as a subset of patients with WHO grade II disease. However, treatment options for patients with inoperable or higher grade meningiomas who develop recurrent disease following surgery and RT is limited. Chemotherapy use in meningioma is mostly limited to patients who have exhausted all surgical and radiotherapy options [12]. Previous trials and retrospective reports have demonstrated minimal efficacy for chemotherapeutics against meningiomas. Jeffrey Raizer
(Northwestern University, Feinberg School of Medicine, IL, USA) presented the results of a Phase II trial of PTK787 (vatalanib) in recurrent or progressive meningiomas [13]. A total of 25 patients (two patients with grade I, 14 with grade II and eight with grade III meningiomas, respectively, as well as one patient with hemangiopericytoma) were treated with vatalanib, an antiangiogenic agent that results in VEGF/PDGF inhibition. Of the 21 evaluable patients, partial response was seen in one patient, stable disease was seen in 15 patients and progressive disease was reported in five patients. Overall, PFS-6 was 57.2% and median time to progression was 7.5 months (intent-to-treat). Median OS was 26.9 months. The authors concluded that combination VEGF/PDGF inhibition in patients with recurrent or progressive meningiomas can lead to disease stabilization. Thomas Kaley (Memorial Sloan–Kettering Cancer Center, NY, USA) reported on the Phase II trial of sunitinib (SU011248) for recurrent meningioma [14]. Sunitinib is a small-molecule multiple tyrosine kinase inhibitor that targets VEGF and PDGF receptors, which was abundant in meningiomas. The study included 36 heavily pretreated patients (30 had a diagnosis of atypical meningiomas and six had been diagnosed with malignant meningiomas). Median PFS was 5.1 months and a PFS-6 of 36% was seen in this group of patients.

While the data presented in these two studies did not have immediate practice-changing implications, overall these studies suggest that targeted therapy may have a better role than cytotoxic therapies. More studies using this approach are warranted as it is likely that these novel therapies will complement the traditional approaches such as surgery and RT, and lead to more effective treatments for patients with meningiomas.

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