3 treatment groups. 134 patients received study medication (96 GBM, 38 AA). Trabedersen was administered intratumorally for up to 11 treatment cycles (7d on, 7d off).
Results: In both trabedersen groups, trabedersen treatment led to long-lasting remissions in AA and GBM patients with tumor remissions exceeding by far the treatment period.
In AA patients, 10 μM trabedersen was superior to standard chemotherapy for progression rate (PR, $p = 0.0032$) and overall response rate (CR+PR, $p = 0.034$) at 14 months. About twice as many AA patients from the 10 μM trabedersen group survived 2 years compared to standard chemotherapy (83.3% vs. 41.7%, $p = 0.09$). A median overall survival benefit of 17.4 months was found for 10 μM trabedersen-treated AA patients compared to standard chemotherapy.
In GBM patients, trabedersen was as efficacious as standard chemotherapy and patients showed a long-term reduction in the risk to die. In a subgroup of GBM patients with favorable prognostic factors (age $\leqslant$ 55yr, KPS>80%) the 24-month survival rate was favorable for the 10 μM trabedersen compared to the standard chemotherapy group (44.4% vs. 13.3%).
Conclusions: The Phase IIb study showed that trabedersen as monotherapy had a higher efficacy than standard chemotherapy in AA patients and was as efficacious or even better as standard chemotherapy in GBM patients. Based on these results, the Phase III study G005 SAPPHIRE was designed as a confirmatory, randomized, multinational, active-controlled study in patients with recurrent/refractory AA. Main objective is to evaluate progression and survival rates of 10 μM trabedersen compared to standard chemotherapy (TMZ or BCNU). The study has started and patient enrollment is ongoing. A Phase III study in GBM patients is in preparation.

8715 POSTER

Cisplatin and Temozolomide in heavily pretreated and poor performance status (PS) patients with temozolomide refractory glioblastoma

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Background: There is pre-clinical evidence of synergism between cisplatin and temozolomide due to higher inhibition of O^6-alkyl-guanine-alkyltransferase (*AGAT*), an enzyme involved in the mismatch repair system. In earlier clinical studies this combination, used as first-line treatment, appeared active against glioblastomas and so it is now regarded as second-line treatment. Considering heavily pretreated and poor status population, the primary end point of the present phase II study was response rate and toxicity evaluation while secondary end points included progression-free survival at 6 months (PFS-6).
Patients and Methods: we enrolled 19 heavily pretreated patients (PTS) with temozolomide refractory glioblastoma (most patients already treated with second surgery, Carmustine Wafer, first and second-line chemotherapy). Median age was 62 (range 18−79); male/female = 11/8; Median PS was 2 (PS = 1 in 2 PTS, PS = 2 in 13 PTS and PS = 3 in 4 PTS). Each patient received cisplatin at the dose of 75 mg/m^2 on day 1 and temozolomide at the dose of 150 mg/m^2 on days 1 to 5 every 21 days until progression or major toxicity.
Results: a total of 79 cycles were delivered (median for each patient = 4). Toxicity was manageable and mostly of grade 1−2: haematological, gastroenterological (nausea and vomiting) and fatigue. We obtained an overall response rate of 29.4% with no complete response. The disease control rate (responses plus stabilizations) was of 64.7%. The median time to progression was of 3.8+ (range 0.7−19+) months and the PFS-6 was of 32%, encouraging considering our heavily pretreated and poor PS population.
Conclusion: the combination of temozolomide and cisplatin is safe and effective in the treatment of refractory temozolomide glioblastomas even in heavily pretreated patients with poor PS.

8716 POSTER

The prognostic significance of volumetry in patients with glioblastoma multiforme (GBM)

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Background: The importance of tumor volume as a prognostic factor in GBM is highly controversial. In this study a computer-based application was used in order to assess several tumor-related volumes from hard copies and a survival analysis was conducted in order to evaluate the prognostic significance of pre- and postoperative volumetric data in patients with GBM.
Materials and Methods: We prospectively analyzed 65 patients suffering from GBM who underwent radiotherapy with concomitant and adjuvant temozolomide. For the purpose of volumetry T1 and T2-weighted MR sequences were used, acquired both pre- and post surgically. Since the MR scans were not available in electronic format, but only in hard copies, they were digitized, by means of a commercial high resolution scanner. Before determining tumor volume with our specialized software, images were converted to the widely used DICOM format with a different computer application. The volumes measured on preoperative MRIs were necrosis, enhancing tumor and edema (including the tumor) and on postoperative ones, net enhancing tumor and net edema. Age, performance status (PS) and type of operation were also included in the multivariate analysis. Overall survival (OS) and progression free survival (PFS) were measured from the time of operation.
Results: In the univariate Cox analysis, volume of postoperative enhancing tumor was significant for OS ($p = 0.001$) and volume of preoperative necrosis was significant for PFS ($p = 0.023$). In the multivariate analysis preoperative T2 abnormality was found significant for OS ($p = 0.023$), preoperative necrosis for PFS ($p = 0.020$) and postoperative enhancing tumor for both OS and PFS ($p < 0.001$ and $p = 0.042$, respectively). Furthermore, the multivariate analysis confirmed the importance of age and PS in PFS and OS of patients.
Conclusions: Our findings implicate that both pre- and postoperative volumetric data play a significant role in the prognosis of patients with GBM. Further studies are definitely required in order to clarify the importance of these factors.

8717 POSTER

Short course of hypofractionated radiotherapy and concomitant temozolomide in patients affected with glioblastoma with V-VI prognostic classes – a pilot study

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Purpose: To evaluate outcome and toxicity profile of glioblastoma (GB) patients treated with hypofractionated radiotherapy (HPF) (Roa 2004) and concomitant Temozolomide (TMZ) (Stupp 2005) in unfavorable V and VI prognostic classes (Mirimanoff 2006).
Materials and Methods: We are monitoring clinical outcome, survival, and acute and long term toxicities of patients treated with HPF scheme (40 Gy in 15 fractions, 2.66 Gy/fraction) concomitantly with TMZ (75 mg/m^2 for 2 patients and 85 mg/m^2 for 8 patients) for 21 days, followed by adjuvant TMZ (150−200 mg/m^2). Median progression free survival time (MPFST) and median survival time (MST) are calculated from surgical procedure.
Results: Eleven patients have been recruited till 4/2009, 10 of them are able to be validated (6 men and 4 women; median age of 69 years). Classification according to the RTOG/EORTC recursive partitioning analysis was as follows: class V for 4 patients and class VI for 6 patients. Surgery consisted of partial resection (n = 3) or only biopsy (n = 7). Gene promoter MGMT methylation was observed in 7 cases.
Median survival time was 19.8 weeks (r 4.8−69.3). MPFST was 12.9 weeks (r 4.8 to 45.14 w). Acute toxicity was mild. Only 4 patients had alopecia grade 2, and one case had pneumonitis grade 3. Three patients died during treatment because of progression disease. No long term neurological complications have been found. Steroid dependence was observed in 7 patients. After progression, 3 patients were entered in schedule of CPT-11 and bevacizumab, with MRI and SPECT monitoring.
Conclusions: Hypofractionated RT concomitantly with temozolomide can be used for selected poor prognostic GB patients to reduce the overall treatment time, without apparent increased toxicity. Improvement of overall survival in comparison with other series seems not be reached. This study reflects the bias of other trials which do not show the real daily clinical practice. Methylation of MGMT gene promoter is not related with PFS and OS, and poor medical conditions are more important than other factors.