8744 POSTER

Extended Use of Adjuvant TMZ in Newly Diagnosed GBM Patients is Safe − Results From the Safety Analysis of the PATSGO Trial

F. Hammouch[1], T. Boterberg[2], P. Clement[3], E. Joosens[4], N. Whenham[5], V. Verschaeve[6], D. Devriendt[7], L. Renard[8], J.F.R. Baurain[9]. *[1]UCL Cliniques Universitaires St. Luc, Oncology, Brussels, Belgium; [2]Ghent University Hospital, Radiation Oncology, Ghent, Belgium; [3]Catholic University Leuven, Medical Oncology, Leuven, Belgium; [4]Virga Jesse Hospital, Oncology, Hasselt, Belgium; [5]Cliniques Saint-Pierre d'Ottignies, Oncology, Ottignies, Belgium; [6]Grand Hopital de Charleroi, Medical Oncology, Charleroi, Belgium; [7]Institut Jules Bordet, Radiotherapy, Brussels, Belgium; [8]UCL Cliniques Universitaires St. Luc, Radiotherapy, Brussels, Belgium; [9]UCL Cliniques Universitaires St. Luc, Medical Oncology, Brussels, Belgium*

We have performed a Belgian multicentric phase II study in newly diagnosed GBM patients to analyse the safety and clinical efficacy of the extended use of adjuvant Temozolomide (TMZ) beyond 6 cycles. We included 64 patients from end January 2008 to September 2010. They were randomised at the end of the adjuvant therapy between continuing TMZ and rechallenge with TMZ only at progression. MGMT status (y/n/uk) and presence of residual tumour were used as stratification factors.
No mature data on OS or PFS are available since only 33 progressed of whom 18 died. With a median follow-up of 12 months, the median PFS and OS are 15 and 24 months respectively. This is higher than what has been reported in other trials. This can be explained by the good performance index of the included patients (median KPS of 90%) and by the timing of inclusion at the end of the adjuvant treatment. The multivariate analysis on PD testing gender, RPA class and presence of residual tumour, shows only an impact of the absence of residual tumour ($n = 18$) with a $p = 0.028$ (HR = 3; 1.1−8.4).
We analysed the toxicity of TMZ treatment. In the 34 patients who pursued adjuvant TMZ, a total of 268 cycles have been administered. Only 10 grade 3 toxicities have been reported amongst these patients, all of them hematological. Grade 1 and 2 hematological and gastro-intestinal toxicities were reported in 90% and 30% of the patients, respectively. Interestingly, the frequency of toxicity didn't increase with the number of cycles received. Amongst the 30 patients in the observation arm, 14 have been rechallenged with TMZ (5d/28d). No response has been observed and the median time of PFS following rechallenge was only of 2.5 months. A total of 51 cycles of TMZ have been prescribed. Only 2 grade 3 toxicities have been reported, but half of the patients presented with grade 1/2 hematological toxicities. Globally, this suggests a better toxicity profile of TMZ in these patients.
Our study shows that the absence of residual tumour is predictive for PFS. We can't state that pursuing adjuvant TMZ increases survival of GBM patients, since mature data on OS and PFS are not yet available. However, our results suggest that this approach is safe. Interestingly, GBM patients who are free of progression at the end of the 6 months adjuvant TMZ have a survival reaching 2 years. Molecular subanalysis is ongoing in order to identify a potential subgroup that may benefit from longer TMZ treatment.

8745 POSTER

When May Temozolomide Be Completed? The Role of [11-C]-Methionine Positron Emission Tomography in the Treatment of Patients With Gliomas

Y. Hasegawa[1], T. Iuchi[1], F. Uchino[2], S. Hirono[3], K. Kawasaki[1], T. Sakaida[1]. *[1]Chiba Cancer Center, Neurological Surgery, Chiba, Japan; [2]Chiba Ryogo Center, Neurological Surgery, Chiba, Japan; [3]Chiba University Graduate School of Medicine, Neurological Surgery, Chiba, Japan*

Background: Recent innovations in treatments, including surgery, irradiation (RT) and chemotherapy (CHT) have provided better survival of pts with gliomas. Systemic CHT with Temozlomide (TMZ) is one of these treatments and we have experienced considerable cases without recurrence on MRI for more than one year after surgery. In these cases, the need for continued treatment with TMZ is unclear. We initiated the evaluation of amino-acid metabolism in such cases by [11C]-methionine positron emission tomography (MET-PET) in 2007, and completed the TMZ for pts with low MET-uptake. The aim of this study is to clarify the role of MET-PET on the decision to complete TMZ.
Material and Methods: Consecutive 103 glioma pts treated with TMZ were enrolled. TMZ was orally administrated until tumour progression. If no recurrence was observed on MRI after 12 cycles of TMZ, MET-PET was performed. In the cases with high MET-uptake ($T/N \geqslant 1.8$), second-look surgery or continued TMZ were performed. However, in some cases with high MET-uptake after high-dose RT which indicated radiation necrosis, TMZ was completed. Tumours with low MET-uptake ($T/N < 1.8$) were followed closely without treatment until tumour progression. The outcomes of these pts were analyzed.
Results: Out of 103 pts, 26 finished 12 cycles of TMZ without recurrence. Among these cases, 24 pts underwent MET-PET and were classified into high (11) and low (13) MET-uptake groups. Among the pts with high MET-uptake (6 astrocytic and 5 oligodendroglial tumours), second-look surgery was performed in 2 (both defined recurrence), additional cycles of TMZ were administrated in 4 (tumour progressed in 3 of 4), and TMZ was completed in 5 (only 1 recurred). Among the pts with low MET-uptake (6 astrocytic and 7 oligodendroglial tumours), only 5 demonstrated tumour progression (1 astrocytic and 4 oligodendroglial tumours) with a follow-up period of 9 to 40 months (median: 25.4 months). After all, MET-PET had negative predictive value of 88% in astrocytic and 43% in oligodendroglial tumours. Progression free and overall survivals of pts with low MET-uptake were significantly longer than those with high ($p = 0.0359$, 0.0256) although the pts with low MET-uptake were followed without treatment.
Conclusions: Even though high MET-uptake not always indicated the existence of viable tumour, low MET-uptake after 12 cycles of TMZ indicated a low risk for recurrence especially in astrocytic tumours. Completion of TMZ was acceptable for these pts.

8746 POSTER

Could Hypertension Be a Potential Biomarker in Patients With Recurrent Glioblastoma Treated With Antiangiogenic Drugs? − a Retrospective Analysis

G. Lombardi[1], F. Zustovich[1], P. Fiduccia[1], P. Farina[1], A. Della Puppa[2], E. Orvieto[3], M.P. Gardiman[4], F. Berti[5], V. Zagonel[6]. *[1]Istituto Oncologico Veneto Iov-irccs, Oncologia Medica 1, Padova, Italy; [2]Azienda Ospedaliera di Padova, Neurosurgery Department, Padova, Italy; [3]Azienda Ospedaliera di Padova, Pathology Department, Padova, Italy; [4]Istituto Oncologico Veneto-IRCCS, Pathology Department, Padova, Italy; [5]Istituto Oncologico Veneto-IRCCS, Radiotherapy and Nuclear Medicine Unit, Padova, Italy; [6]Istituto Oncologico Veneto-IRCCS, Oncologia Medica 1, Padova, Italy*

Background: Numerous antiangiogenic drugs (AD) have been using to treat recurrent glioblastoma (GBM). An important adverse effect of AD is hypertension. The aim of this study was to identify a potential use of blood pressure increase as a biomarker and a predictive factor for response, time to progression and survival from antiangiogenic treatment in patients (PTS) with recurrent GBM treated with AD.
Material and Methods: Retrospectively, we examined 48 PTS with recurrent GBM treated with AD: bevacizumab (21 PTS) and sorafenib (27 PTS). All patients underwent MRI assessments according to Macdonald criteria every two months or when clinically indicated. Fisher's exact test, univariate and multivariate analyses were performed.
Results: 13 (27.1%) and 35 PTS (72.9%) performed an AD as third or second line chemotherapy, respectively. Median age was 55.1, performance status (PS) was 0 in 8 PTS, 1 in 19 PTS, 2 in 18 PTS and 3 in 3 PTS. After two months of treatment 25 PTS (52.1%) obtained a disease control (DC): stable disease (22 PTS) or partial response (3 PTS). The median overall survival (OS) from AD was 6.2 months (CI 95% 4.9−7.6); the median time-to-progression (TTP) was 2.5 months.
21 PTS (43.8%) developed grade 2−4 hypertension within two months of treatment. No significant association was found between hypertension and response to treatment ($p > 0.05$). According to univariate analysis hypertension was not related to a longer TTP and OS ($p > 0.05$). On multivariate analysis, adjusted for age and AD (avastin vs sorafenib), hypertension was found to be an independent favourable predictor for OS (HR = 0.38, CI 95% 0.16–0.92).
Conclusions: Hypertension may be a valid biomarkers in PTS with recurrent glioblastoma treated with AD. Thus, PTS developing grade 2−4 hypertension within two months of treatment may have a better chance of prolonged OS.

	P	HR	CI 95%
Hypertension	*0.032*		
Yes (grade 2−4)		0.38	0.16–0.92
No		Ref.	
Age	*0.017*	1.04	1.008–1.085
Antiangiogenic	*0.014*	3.5	1.2−1.9
Sorafenib		0.28	0.10–0.77
Bevacizumab		Ref.	