361P Efficacy of chemotherapy plus bevacizumab in recurrent multiforme glioblastoma: A real-life study

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Background: Bevacizumab and chemotherapy are frequently used to treat recurrence of glioblastoma (GBM). However, the selection of the concomitant chemotherapeutic agent remains an open question.

Methods: All patients treated with at least one cycle of chemotherapy plus bevacizumab for recurrent GBM at the Georges-François Leclerc Cancer Centre in Dijon, France between June 2005 and August 2019 were included in this retrospective study. The primary and secondary objectives were progression-free survival (PFS) and overall survival (OS), respectively. As fotemustine is preponderant in the treatment of GBM, as recommended by the survival criteria, we compared this with other chemotherapy agent groups.

Results: A total of 160 patient files were analysed. One hundred patients received fotemustine (62.5%), 18 temozolomide (11.2%), seven lomustine (4.4%), and 35 irinotecan (21.9%). The majority were male (63.7%), and the mean age was 59.8 years. Further, 81% of patients had a Karnofsky performance status $\geq$90, and 43% had undergone initial surgical resection. All patients received the first-line Stupp regimen. In the whole cohort, the median PFS was 4.5 months [2.7-8.5] and median OS was 9 months [4.5-23]. Only MGMT (methyl guanine methyltransferase) unmethylated status was associated with poor PFS upon univariate analysis. For OS, fotemustine treatment was associated with poor survival: 7.3 mo vs 19.9 mo (HR=2.13[1.23-3.7], p=0.006). In the fotemustine group, steroid usage at baseline was associated with poor survival: median OS of 6.7 mo vs not reached (HR=2.9 [1.1-7.3], p=0.03). Similarly, in the low Karnofsky performance status subgroup, fotemustine treatment was associated with poor OS: median OS of 4.3 mo vs not reached, (HR=4.5 [1.3-16.7], p=0.02).

Conclusions: Using real-life data, this study shows the worst efficacy of the addition of fotemustine to bevacizumab compared with other added chemotherapeutic agents. We find that in patients with low-performance status, a concomitant steroid treatment other than an alkylating agent or irinotecan is a better choice for combotherapy.

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362P Influence of the expression of ABCG2 transporters on the results of photodynamic therapy in malignant gliomas

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Background: The analysis of the effect of ABCG2 transporters on the effects of photodynamic therapy in malignant gliomas was carried out.

Methods: A total of 98 patients with a glial tumor of supratentorial localization, a high degree of tumor anaplasia according to Grade (III-IV), were treated at the RNSI prof. A.L. Polenov. The analysis of the expression level of ABCG2 transporters and the effect on median survival during PDT was carried out. Chlorin e6 was used for PDT; the source of laser radiation was Latus 2.5 with a wavelength of 662 nm and a maximum power of 2.5 W.

Results: Data are presented that glioma malignant cells are characterized by high expression of several ABCG2 transporters. It is also presented that gene expression of these transporters can correlate with the effects of ongoing photodynamic therapy and chemotherapy and affect the survival rate in patients with gliomas, and can be used as a prognostic biomarker. Median survival of patients with Grade III gliomas up to 42.1 $\pm$ 4.1 months with low expression of ABCG2 transporter (with high expression of ABCG2 - 18.3 $\pm$ 3.9 months), for patients with Grade IV gliomas up to 22.7 $\pm$ 3.5 months with low expression of ABCG2 carrier (with high expression of ABCG2 - 11.6 $\pm$ 1.9 months) (P = 0.0001).

Conclusions: Malignant gliomas are characterized by various genetic and epigenetic aberrations, the influence of the microenvironment on the tumor, and the presence of cancer stem cells (CSCs), which make the tumor more aggressive, invasive, and resistant to treatment methods. A significant role in this complex process is played by ABCG2 transporters localized in tumor cells.

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363P Clinical significance of telomerase reverse transcriptase (TERT) promoter mutations, telomere length and MGMT promoter methylation status in newly diagnosed and recurrent IDHwildtype glioblastoma (GBM) patients (PTS): A large mono-institutional study

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Background: The clinical significance of TERT promoter mutations, telomere length and their interactions with MGMT status in patients with IDHwt GBM PTS is unclear. We performed a large study to investigate their impact on clinical outcomes.

Methods: TERT promoter mutations (C228T, C250T), relative telomere length (RTL) and MGMT status were assessed in 278 newly diagnosed (ND) and in 65 recurrent (REC) IDHwt GBM PTS which were treated from Dec 2016 to Jan 2020. We retrospectively explored association between gene characteristics and radiological response, progression free survival (PFS), overall survival (OS). Telomere length was measured by monochrome multiplex PCR and RTL values were calculated as a telomere/single-copy gene ratio.

Results: Characteristics of ND GBM PTS were median age 63, ECOG PS 0-1 in 71%, radical surgery in 38%, 78% received radiotherapy plus TMZ, MGMTmet in 53%, TERT promoter was mutated in 80% (75% C228T, 25% C250T), median RTL was 1.57 (range 0.4-11.37). ORR was reported in 15% of PTS, mOS was 15ms (95%CI 13-18), mPFS was 8ms (95%CI 7-9). At multivariable analysis TERT mutations and RTL were not associated with clinical outcomes and about OS, reported a HR of 1.05 (95% CI 0.64-1.64) and 0.99 (95% CI 0.89-1.10), respectively; MGMTmet tumors showed significant improved PFS and OS with a HR of 0.54 (95% CI 0.40-0.71) and 0.47 (95% CI 0.34-0.64), respectively. All interactions among MGMT, TERT mutation and RTL were not significant. Characteristics of REC GBM PTS were median age 55, ECOG PS 0-1 in 60%, MGMTmet in 37%, TERT mutations in 75% (75% C228T, 25% C250T), RTL was 1.67 (0.68-8.87). At multivariable analysis only MGMTmet tumors resulted significantly associated to prolonged OS (HR 0.16 95% CI 0.07-0.40). No gene interaction was significant.

Conclusions: We analyzed the impact of TERT mutations, RTL and MGMT status in both nd and rec IDHwt GBM PTS. TERT status and RTL were not associated with clinical outcomes at both diagnosis and relapse. MGMT status was the only prognostic factor in both cases. No significant interaction was demonstrated between TERT mutations, RTL and MGMT status.

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364P Implementation of a comprehensive streamlined next generation sequencing (NGS) test for glioma including detection of the 1p/19q codeletion

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Background: In 2016 the World Health Organization updated the classification of central nervous system tumours to incorporate molecular analysis alongside histopathological evaluation. Under the revised system, diagnosis of oligodendroglioma requires presence of both an IDH mutation and codeletion of chromosomal regions 1p and 19q. In 2019, the All Wales Medical Genomics Service (AWMGS) introduced a bespoke multi-gene NGS panel for a range of tumour types, which included 10 genes/regions implicated in the diagnosis, prognosis and treatment of gliomas. The NGS panel was designed to detect 1p/19q codeletion to streamline glioma testing, also demonstrating the ability to successfully identify different driver mutations in tumours efficiently using a single test.

Methods: Validation involved evaluation of the panel for determining 1p/19q codeletion status in FFPE-extracted DNA from samples previously tested by FISH. The