Fotemustine chemotherapy in elderly patients with recurrent malignant gliomas

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The interest for the treatment of cancer in elderly patients has recently raise due to the gradual increase in life expectancy. Evidence on the treatment of malignant gliomas in elderly patients are scarce. Indeed, the definition of patient 'elderly' varies in the literature. In medicine, a limit of 65 is often considered for elderly patients, while in the European literature on cancer in the elderly an age limit of 70 years is often used. However, the aging process varies from individual to individual and is scarcely reflected on a chronological basis. The use of chemotherapy in elderly patients is a widely debated issue. The pharmacokinetics of the drugs to be used should always be considered administering chemotherapy for elderly patients and some general considerations should be made. Elderly patients, have both a reduction in gastrointestinal motility and secretion of digestive enzymes, with mucosal atrophy and consequently reduced absorption of oral chemotherapy. In addition, hematologic toxicity seems to be more common and associated with a higher risk of infectious complications. There are no data in the literature on salvage treatment after relapse in patients with GBM elderly.

Fotemustine (FTM) is a third-generation nitrosourea. Recently, several groups have studied the use of FTM in high grade glioma (HGG) patients recurring after standard treatment. Accordingly, in a prospective single-institution study, we addressed the toxicity of a modified FTM schedule in patients with HGG at 1st and 2nd progression after failure of RT and TMZ.

Between January 2011 and October 2012, 41 elderly patients (17F, 24M) (median age 69 range 65-75) with a diagnosis of HGG at first or second recurrence after standard treatment were treated with an outpatient regimen with a non conventional schedule of FT as proposed by Addeo et al. In this setting, clinical, radiological and laboratory data of all patients treated were collected. In particular complete blood count (CBC) with differential, biochemistry panel (BUN, creatinine, liver enzymes, glucose), erythrocyte sedimentation rate (VES), C-reactive protein (CRP) and CD4 count were assessed every cycle. Toxicity was evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE; version 3.0). Median progression-free survival at 6 months (PFS-6) and median overall survival (m-OS) were calculated for the whole group of patients, as secondary study endpoints. Descriptive statistics were used to summarize relevant study information. PFS and OS were calculated by the Kaplan–Meier method.

Results: the 41 patients received a total of 194 chemotherapy cycles: the median number of cycles was 7 (range, 1–12). In no patients were observed grade IV toxicity concerning : WBC, PLT, RBC. In all patients, CD4 + lymphocytes counts were monitored: 21.7 % of patients developed grade 3–4 CD4 + lymphopenia (<200 cell/μL). All patients with grade 3/4 CD4 + lymphopenia received prophylactic cotrimoxazol. None of these patients developed Pneumocystis carinii pneumonia. Moreover, no death was considered to be closely related to chemotherapy toxicity. Major non

haematological toxicities (grade 3–4) concerned mainly hepatic enzymes, particularly GGT that increased in 8.9 % of cases Minor toxicities (grade I–II) were anemia (57.1 %), thrombocytopenia (16.9 %), leukopenia (8.2 %), AST/ALT increase (approximately 33 %), worsening of renal function (2.8 %), and gastrointestinal toxicity (6.2 %). Infections were observed in 3 cases (2 pulmonary, 1 urinary trait) and deep venous thrombosis in 3 cases. Two patients developed a pulmonary embolism, and one patient died for this.