

Neurocognitive Functioning and Quality of Life in Patients with Recurrent Glioblastoma Treated with Avelumab and Axitinib

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Introduction

Glioblastoma is the most frequent malignant tumor of the central nervous system. After surgery, temozolomide chemotherapy and radiation therapy, the cancer almost inevitably recurs. Patients with recurrent glioblastoma (recGB) have a median overall survival of 25 to 30 weeks. Up till now, randomized clinical trials have not demonstrated any treatment option to improve the overall survival expectancy of patients with recGB. In this study, axitinib, a small molecule tyrosine kinase inhibitor of the VEGFReceptor, and avelumab, a monoclonal antibody directed against PD-L1, are being combined to treat recGB. The primary objective is to assess the anti-tumor effect of this combination therapy and to document the percentage of patients who are alive and confirmed free from tumor progression at 24 weeks. An important secondary objective is to assess neuro-cognitive functioning (NCF), psycho-emotional wellbeing and quality of life (QoL) in the patients. Impairment of NCF in patients with recGB, is very common due to the tumor itself, tumor-related epilepsy, treatment and patient-related factors (e.g. age, psychological distress). NCF has been shown to be a predictor of survival in these patients and seems to affect QoL. As neurocognitive decline often precedes radiographic evidence of tumor progression, we want to assess whether systematic NCF testing is of additional clinical and predictive value. Moreover, outcome measures evaluating QoL and emotional burden can offer additional information to judge upon the potential clinical benefits of this therapy and if found necessary, help to offer adapted psycho-social care.

Methods

- Patients with recGBM after surgery, radiation therapy and temozolomide chemotherapy are stratified to:
 - Stratum A: no need for corticosteroids
 - Stratum B: baseline need for corticosteroids
- MRI to assess anti-tumor activity (week 1 (before start of treatment) and every 6 weeks thereafter)
- General questionnaire to evaluate history of personal and/or familial psychiatric disorders, sleep disturbances and subjective cognitive symptoms (week 1 (before start of treatment), week 9 and every 12 weeks thereafter).
- NCF testing with Cogstate (week 1 (before start of treatment), week 9 and every 12 weeks thereafter)
- A subjective wellbeing (SWB) index and the Anamnestic Comparative Self-Assessment (ACSA) (week 1 (before start of treatment), week 9 and every 12 weeks thereafter).
- Validated questionnaires (week 1 (before start of treatment), week 9 and every 12 weeks thereafter):
 - Hospital Anxiety and Depression Scale (HADS)
 - EORTC Quality of Life Questionnaire (QLQ-C30)
 - EORTC Brain Cancer module (QLQ-BN20)

Results

Baseline descriptives (week 1, before start of treatment)

General questionnaire: most disabling symptom

N = 29	n	%
Fatigue	20	68.97
Paralysis	8	27.59
Epilepsy	6	20.69
Concentration & memory	11	37.93
Other	5	17.24

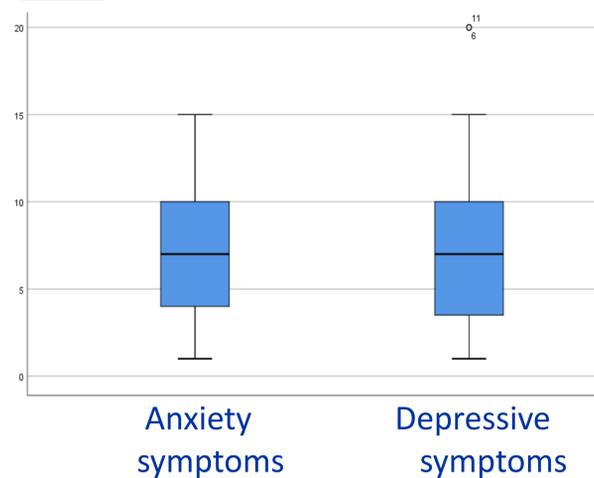
EORTC QLQ-C30

N = 29	M	SD
Global Health	48.77	23.54
Fatigue	55.56	26.19
Insomnia	29.63	33.76
Emotional functioning	65.18	31.35

Neurocognitive functioning

Results are not yet available

HADS



→ Cut-off score = 11

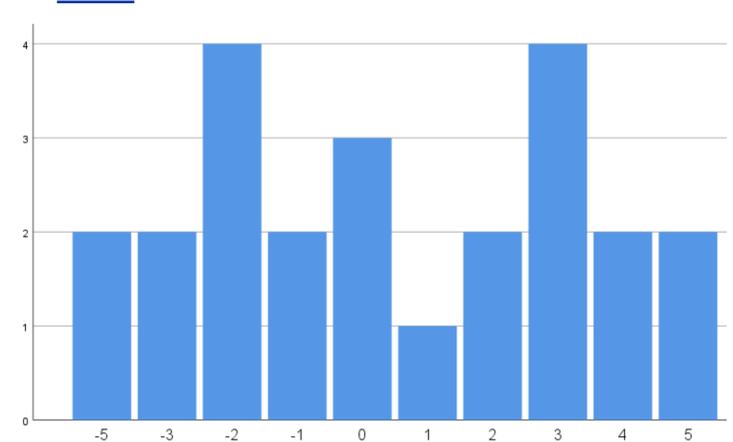
Anxiety symptoms: 24.14% of patients

(Mdn = 7, Q₁ = 4, Q₃ = 11)

Depressive symptoms: 27.59% of patients

(Mdn = 7, Q₁ = 3.25, Q₃ = 11.75)

ACSA



Indicate your SWB in the present period
+5 "as good as the best period in your life"
-5 "as bad as the worst period in your life"

→ **37.93%** of patients (n = 29) indicate that their SWB in the **present period** is **more alike** their SWB in their **best period** in life in comparison to their SWB in their **worst period** in life (M = 0.38, SD = 3.02)

Conclusion

Baseline evaluation of patients with recurrent glioblastoma participating in this prospective phase II clinical trial with axitinib and avelumab indicates that most patients report multiple disabling symptoms of which fatigue (68.97%) is the most common. The patients' emotional burden is increased in 25% of the patients. At the start of the study treatment 38% of the patients indicate that their SWB in the present period is more alike their SWB in their best period in life in comparison to their SWB in their worst period in life. Nevertheless, EORTC and ACSA results indicate that the patients' QoL is diminished. This clinical trial is currently ongoing and patients are longitudinally followed-up for Neurocognitive Functioning and Quality of Life.