A phase III double-blind placebo-controlled randomized study of dexamphetamine sulfate for fatigue in patients suffering from primary brain tumors

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Many primary brain tumor (PBT) patients complain of severe fatigue, which contributes to decreased quality of life (QOL).

Objective:

We hypothesized that **dexamphetamine sulfate**, a psychostimulating drug, could result in reduced fatigue in PBT patients.

Methods:

A **phase III, multi-institutional, placebo-controlled randomized trial** assessed the efficacy and tolerance of dexamphetamine administered up to 30 mg/day during **3 months** in PBT patients with non progressive disease.

Patients should complain of **severe fatigue**, defined by a **Multidimensional Fatigue Inventory (MFI) score ≥ 60** , and should not suffer from depression. Evaluation included treatment effect on **fatigue (primary outcome)**.

We also studied as **secondary outcomes anxiety and depression** (*Hospital Anxiety and Depression Scale*), **affectivity and fatigue** (*Norris Analogic Visual scale*), **Quality Of Life** (*EORTC QLQ C30 and Brain Module 20*), **cognitive functions**, such as memory, speech, executive functions and apathy (*Mattis dementia rating scale, Verbal Fluency Category, Trail Making Test Parts A and B, Wisconsin Card Sorting Test, Marin apathy scale*), as well as **tolerance**.

Conclusion: Dexamphetamine up to 30 mg/day, is well tolerated in non progressive PBT patients suffering from severe fatigue, but does not provide a significant benefit on fatigue, anxiety, depression, cognition, and QOL.

Results:

From April 2013 to November 2016, a total of **fourty-six** patients from **7 different French centers** were enrolled and randomized (**23** in the intervention arm (IA) and **23** in the placebo arm (PA)), with 41 (89%) retained for analysis:

Mean age: **57** years (IA)/**51** years (PA)

Histology:

- mainly **gliomas 17/22 (77%)(IA)/17/19 (89%) (PA)**;
- others : CNS lymphomas (4 cases (3IA+1PA)), medulloblastomas (3 cases (2IA+1PA))

Treatment: a maximal dose of **30 mg/day** of dexamphetamine sulfate, reached after 2 steps of 10 days of escalating dose (10 and 20 mg) in case of good tolerance.

Toxicity: Tolerance was generally **good**, with no treatment related death and no grade 4 toxicities. However, patients in the IA complained more frequently about **psychiatric side effects** (mostly hyperactivity, anxiety, sleep disorder, irritability...) than the patients in the PA (**$p=0,018$**).

Efficacy: There were **no statistically significant differences** at 3 months between the dexamphetamine and placebo subgroups in the MFI 20 score (Figure).

MFI 20 score variation between J0 and Month 3

- There were also **no statistically significant differences** in any secondary outcomes : fatigue according to Norris scale, affectivity, anxiety, depression and cognitive functions.