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**CONGRESS NWZ
POSITION PAPER STUDY GROUP BRAIN TUMOURS BELGIUM**

1. My Profile:

- Born on 20.07.1953 in Cologne, Germany.
- Belgian nationality.
- Teacher of mathematics.
- Headmaster of a boarding school.
- High grade brain tumour (anaplastic astrocytoma/glioblastoma) in 1997.
- Treatment: surgery, radiotherapy and antihormone therapy.
- Founder of “Werkgroep Hersentumoren vzw” – Study Group Brain Tumours Belgium – in 2005.

2. Facts about high grade brain tumours (BT):

- 10 years ago the 2-year survival was below 2 %.
- BT are becoming the most frequent cancer with children under 14.
- Medical treatment is essential to have a chance of survival, but long term survivors all suffer from chronic sequels: acquired brain deficits, non-congenital brain deficits. This implies support and follow up.
- Screening and prevention are not possible at this time.
- Surgery has reached a high degree of perfection, limiting the damage to the brain, and thus guaranteeing a higher quality of life after treatment.
- This progress has **not** substantially contributed to raise the life expectancy.
- The introduction of temozolomide, administrated together with radiotherapy, has led to a 2-year survival of 27 % **in a selected group**. Patients with a methylated MGMT-gen respond better than others.
- Overall 2-year survival is still below 10 %.
- The effectiveness of temozolomide is rapidly decreasing. It may be regarded as a palliative drug.
- There is a great need for **diversity** of treatments. One single agent will not solve the problem.
- Organizing phase 3 randomized trials for patients with high grade brain tumours may have **unethical** aspects if placebo are used. Treating 50 % of the sample with placebo means that they do not have a chance of survival. Moreover the result for the control-arm is already known: these patients will all die, data about mortality of high grade brain tumours without supportive treatment are known.

- High grade brain tumours are a “rare cancer”, with less than 50 new cases/100.000 inhabitants/year. Pharmaceutical companies have a near monopoly in the development and application for registration of new drugs. It is an evidence that companies have a greater interest in developing medical products for larger groups.
- There are 120 types of CNS-tumours.
- Note that low grade intracranial tumours may not be labeled as benign brain tumours. It is also a “space consuming process”, and therefore they may cause the same symptoms as high grade brain tumours, including death. It just takes more time.
- Even the EMEA regulations in matters of “orphan drugs” not really has altered the current practice.
- The actual situation has created a great inequality between. Some countries have a fund designed for those cases, for instance “Heilversuch” in Germany.
- There may be an inequality for patients within one country between people who can afford the treatment, and others who cannot.
- The actual situation has also led to a decrease of the number of trials of 30 % within the European Union during the last 2 years (2007/2008).

3. **How to cope with this situation ?**

- Europe should make use of the sheer size of its population and its intellectual capabilities to reorganize the development and registration of medical products for the treatment of rare diseases.
- Create a network of European centers of excellence for brain tumour treatment, possibly in cooperation with other networks worldwide. These centers could receive a certificate of the EANO (European Association for Neuro-Oncology), in analogy with the ESMO for integrated palliative care.
- Organize a systematic exchange and availability of data.
- Replace the “phase 3 randomized trials” imposed by the European Directive 2001/20/EC about clinical trials by another model, less expensive and more dynamic. A good example is the methodology used by the “Al Musella Foundation”, New York, www.virtualtrials.com.
- The use of a new drug should be discussed in a multidisciplinary committee or in an ethical committee. Coordination could be done by the EANO.
- The multidisciplinary and ethical committees should not only consist of MD, but also of psychologists, and other professionals involved. We have made consistent proposals about treatment and support of brain tumour patients in our proposal of an advisory European guideline.
- Registration of a new drug could be granted depending on the effect, rather than on a pathology. For instance: bevacizumab is an angiogenesis inhibitor which was registered for the treatment of colon cancer because it blocks vascular endothelial growth factor A (VEGF-A). Evidence has shown that it might be effective for high grade brain tumours. Why insist on a totally new procedure. Another good example is tamoxifen, which blocks EGFR, and interferes with protein kinase A.
- Translational research and the creation of “tissue banks” should be promoted.
- Grant the possibility for application for registration also to the scientific world, and not only to the commercial companies. This may be a win/win situation for both stakeholders, and, in the end, for patients too. The scientific world

would have a greater impact, the pharmaceutical industry would have lower costs, and a bigger market, without having to comply with all the regulations as they exist at this moment.

- Organize consultation between all stakeholders, including patient groups.
- The European Commission should assume its responsibility for establishing a framework and funding the research.