

European Association of NeuroOncology Magazine

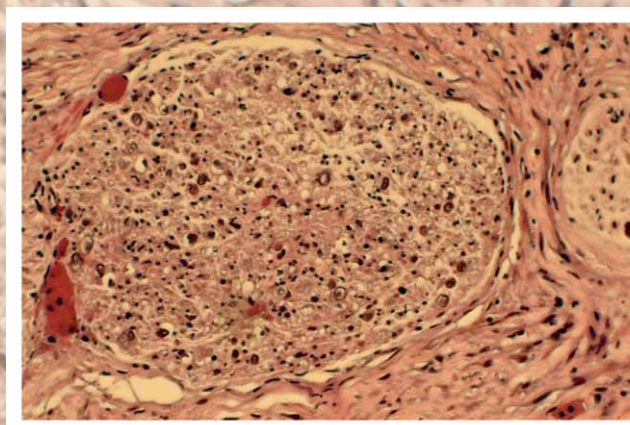
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Congress Report: Trends in Central Nervous System Malignancies

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This was the second of the so far very successful neuro-oncology meetings organised as a collaboration between EORTC and EANO. These meetings are deservedly popular as update meetings since delegates can expect to gain a thorough overview of new data and an insight into what is happening in the field in the space of 2 days of focused talks in neuro-oncology. The venue this year was **Bucharest**, perhaps not a city that is so familiar to many delegates, although the view of the immense palace constructed by Ceausescu during his years in power in Romania and within site of the conference venue certainly made it memorable.

It is very clear from the programme that the field of neuro-oncology is moving fast and that much of this progress is driven by basic science, particularly in the area of molecular pathology. It is amazing just how quickly new information has been taken up by the clinical community and **Prof Reifemberger's** talk on IDH1 was a reminder of the recent emergence of this extraordinary story in glioma. Although we still do not understand why mutations in the isocitrate pathway should be such powerful drivers of oncogenesis this talk introduced the idea of mutant proteins producing increased concentrations of moieties such as 2-hydroxyglutarate which may function as an 'onco-metabolite'. It is obvious that this will lead to much greater understanding of the biology of oncogenesis in CNS and IDH1 is already accepted as probably the most powerful biomarker for prognosis in astrocytic tumours and also an extremely useful diagnostic aid in identifying infiltrating tumour cells. A similarly arresting view of the power of molecular pathology in identifying tumour sub-groups was also given by **Prof Taylor**, reviewing recent data in medulloblastoma in which it is clear that tumours can be grouped into very distinct prognostic groups using gene expression data.

There has been huge interest in the field of angiogenesis in brain tumours in the last few years and it was extremely valuable to be able to hear updates on the clinical and regulatory status of anti-angiogenic agents along with some exciting new laboratory data. It is becoming clear that the success or not of these agents in the clinic may rely on a better understanding of the relationship between neo-angiogenesis and other tumour characteristics, such as invasion, and **Prof Bjerkvig** demonstrated that in pre-clinical models these may be quite distinct phenomena. He also drew our attention to the fact that phenotypic flexibility and adaptation to specific niches may be a marker for tumour stem cells which may allow them to either migrate through brain tissue or promote neoangiogenesis so that these processes may effectively become competing. While angiogenesis remains a fascinating target it is clear that other targets, particularly proteins involved in DNA repair, may also be effective in enhancing response of gliomas to treatment. **Prof Wen** overviewed several of these targets

which are the subject of ongoing research and early clinical studies including PARP, checkpoint signaling, and IDH1 targeting. It is clear that we need to be able to predict rational combinations of agents as well as to identify which pathways are relevant in glioma. In brain metastases there is an obvious need to identify whether molecular targeting agents that are active at the primary site are also effective in CNS disease.

We are all aware of the limitations of non-invasive imaging in assessing response to treatment in CNS and **Dr Bendszus** reviewed the approaches that are available and which may be most relevant in brain tumour monitoring. A major issue, which several research groups, including the EORTC, are addressing, is the need to standardize imaging parameters across study sites. There was a timely reminder of the limitations of conventional imaging applied to new agent studies, particularly those that alter blood brain barrier function as in for example review of the REGAL study of cediranib in relapsed gliomas, which failed to reach the primary end point and could have been limited by interpretation of MRI data.

Turning our attention away from glioma, **Prof Weller** gave an informative account of the state of the art in treatment of PCNSL. We were reminded that this has proven a remarkably difficult disease to treat which has not yet benefited from the advances that have been made in the treatment of lymphoma elsewhere. There are few large randomized studies in this area, but this will be remedied in the next few years with ongoing and proposed studies addressing the role of retuximab, intrathecal treatment and radiotherapy in patients with PCNSL in different age groups.

The improving outcome in treating glioma and the changing demographic of age at child birth has meant that most practitioners in neuro-oncology have had to face difficult questions involving young women who become pregnant with a diagnosis of brain tumour. Data on the risks of tumour progression during pregnancy are sparse, but **Dr Taillandier** presented some recently collated data which suggest that, at least in women who are referred for MRI during pregnancy, progression occurs in a significant proportion and may be a direct result of the physiological changes that are associated.

The final session of the conference included a session on the rather vexed question of appropriate treatment for elderly patients with gliomas. It is obviously a problem that we cannot define biological age with any certainty. It is more of a problem that recent studies have failed to reach consensus on appropriate management. These were reviewed and discussed by **Dr Malmstrom** and **Prof Stupp**. Although it seems clear that 6 weeks of radiotherapy is not usually an appropriate treatment for patients over 70, whether short-course radio-

therapy, temozolomide or the combination is the way forward is not yet clear, although this should be answered by the ongoing EORTC/RTOG study.

Brain metastases is another area in which treatment approaches have been slow to change. This may have been altered by the recent EORTC study data, confirming that WBRT improves progression in CNS but not overall survival in patients with oligometastases. These data and their implications were discussed by **Prof Soffietti** and considered in the context of modern radiotherapy approaches. It is clear that while radiotherapy can be used to deliver complex dose distributions to CNS, we do not yet have the knowledge that will allow us to recommend particular treatment approaches to improve local control and/or reduce toxicity, for example by hippocampal sparing. It should also be remembered that a significant proportion of patients with brain metastases have a very poor prognosis and **Prof Taphoorn** delivered a thought-provoking talk on end-of-life issues in brain tumour patients. This is an area where much research still needs to be done and one

which is still limited to some extent by differences in cultural attitudes towards end-of-life care.

It was appropriate that the meeting ended with a lively discussion on management issues in patient groups that provoke difficult questions. Overall, this meeting lived up to the expectation, the 403 attendees should have come away feeling that they have had a thorough update on the field with the opportunity to ask questions of experts from around the world.

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