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# Ask the Expert Information Sheet

## Pseudo-Progression

### What is Pseudo-Progression Following Treatment for Glioblastoma Multiforme?

Glioblastoma Multiforme (GBM) is a rapidly dividing brain tumour. The current standard of care for newly diagnosed GBM is six weeks of radiotherapy with concurrent temozolomide (RT/TMZ) followed by maintenance monthly temozolomide for six months up to one year. The addition of temozolomide is a major advance in the treatment of GBM with improved patient overall survival as compared to radiation alone.

As RT/TMZ is now widely practiced and the standard of care for appropriately selected patients, we are learning more about the consequences of RT/TMZ. One phenomena, termed Pseudo-Progression (psPD), has become more apparent with the use of this more efficacious treatment approach as compared to radiation alone. Essentially psPD refers to post-treatment imaging changes in the tumour, where the tumour appears larger and/or brighter from greater contrast uptake as compared to the pre-treatment baseline CT or MRI image.

These changes may mislead the patient and the doctor in thinking the tumour is getting worse due to true progression when in fact these changes are transient. In true psPD, eventually the tumour stabilizes or even shrinks as opposed to further growth if true progression. It is important to also realize that the increase in tumour size may accompany a worsening in the patient's symptoms and these also either stabilize or resolve in the psPD situation.

Recent data reported by Sanghera, Perry, Sahgal et al. from the Sunnybrook Health Sciences Odette Cancer Centre reports that in the 26% percent of patients suspected of early true progression (defined as progression during radiation or within eight weeks of completing RT/TMZ), a psPD rate of 32% was determined (in press, Canadian Journal of Neuroscience).

Strict imaging criteria (RECIST) were used to ensure uniform analysis and a strength of the study. In terms of symptoms that accompanied imaging changes, 60% of patients also had clinical symptoms suggestive of true progression, however, in each case of psPD symptoms resolved with time. Patients with psPD were also found to have a better overall survival, and this has also been reported by other investigators.

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The rationale is that these patients may have favorable genetics to temozolomide response with O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation. Therefore, the enhanced response reflects the tumours biology to be more susceptible to treatment effect, and these patients live longer.

There are significant clinical impacts for patients with psPD with the RT/TMZ regimen. If a patient is thought to have true progression as opposed to psPD then several actions may be taken that would not be beneficial to the patient such as; the adjuvant schedule of TMZ may be discontinued; patients may be relegated to hospice with the notion that the disease is treatment resistant; or may be enrolled into clinical trials with an actual better prognosis as compared to patients with true progression and the resolution of the clinical and or radiological worsening falsely deemed secondary to further treatment versus the natural history of psPD.

Therefore, clinicians have to be aware of this phenomena and judge the patient's clinical status to either follow-up with MRI imaging at a shorter frequency to see if clinical and imaging changes resolve or stabilize, or initiate alternative therapeutic approaches assuming the patient to be truly progressing. It certainly is a difficult situation that we need to learn more about in order to treat patients effectively and appropriately.

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