Seizure prophylaxis in gliomas (SPRING): a phase III randomised controlled trial comparing prophylactic Levetiracetam versus no prophylactic anti-epileptic drug in glioma surgery

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Objectives

There is no consensus regarding the need for prophylactic anti-epileptic drug (AED) in seizure-naive newly-diagnosed glioma patients. Data regarding prophylactic AED use are scant and inconclusive - most evidence comes from older, small studies that enrolled patients with brain metastases and benign tumours in addition to gliomas. A definitive randomised clinical trial is needed to determine whether the policy of prophylactic AED therapy reduces the risk of first seizures in this patient population

Design

Multi-centre RCT.

Subjects

Inclusion criteria: (i) seizure-naive, (ii) suspected supratentorial glioma suitable for surgery (biopsy/resection), (iii) age ≥16 years-old; (iv) Karnofsky performance status of > 60.

Methods

Patients are randomised 1:1. Levetiracetam will be given at 500mg bd for 2 weeks, increased to 750mg bd thereafter for 1 year. Non-blinded study. No placebo control. Primary Outcome: one year risk of first seizure. Secondary outcomes: time to first seizure, time to first tonic-clonic seizure, mood, personality, fatigue, memory, quality of life, progression free survival, overall survival and incremental cost per QALY. Estimate of 1 year seizure rate in patients with suspected glioma after surgery is 20%. Based on a reduction in seizure rate to 10% in the treatment arm, a total of 806 patients will be recruited

Results

Grant awarded by NIHR HTA . Feasibility questionnaire demonstrated prophylactic AED rarely used in UK and neurosurgeons are willing to randomise. 15 UK centres have expressed interest in participating.

Conclusions

SPRING will establish class I evidence for the use of seizure prophylaxis in glioma surgery. The trial will open to recruitment in January 2019.