# Glioblastoma

## Regorafenib compared with lomustine in patients with relapsed glioblastoma (REGOMA): a multicentre, open-label, randomised, controlled, phase 2 trial.

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### Background:

Glioblastoma is a highly vascularised tumour and there are few treatment options after disease recurrence. Regorafenib is an oral multikinase inhibitor of angiogenic, stromal, and oncogenic receptor tyrosine kinases. We aimed to assess the efficacy and safety of regorafenib in the treatment of recurrent glioblastoma.

### Methods:

REGOMA is a randomised, multicentre, open-label phase 2 trial done in ten centres in Italy. Eligible patients (aged ≥18 years) with histologically confirmed glioblastoma, Eastern Cooperative Oncology Group performance status 0 or 1, and documented disease progression after surgery followed by radiotherapy and temozolomide chemoradiotherapy were randomly assigned (1:1) by a web-based system, stratified by centre and surgery at recurrence (yes vs no), to receive regorafenib 160 mg once daily for the first three weeks of each four-week cycle or lomustine 110 mg/m2 once every six weeks until disease progression, death, unacceptable toxicity, or consent withdrawal. The primary endpoint was overall survival in the intention-to-treat population. This trial is registered with ClinicalTrials.gov, NCT02926222, and is currently in follow-up.

### Findings:

Between 27 November 2015 and 23 February 2017, 124 patients were screened and 119 eligible patients were randomly assigned to receive regorafenib (n=59) or lomustine (n=60). Median follow-up was 15.4 months (IQR 13.8-18.1). At the analysis cut-off date, 99 (83%) of 119 patients had died: 42 (71%) of 59 in the regorafenib group and 57 (95%) of 60 in the lomustine group. Overall survival was significantly improved in the regorafenib group compared with the lomustine group, with a median overall survival of 7.4 months (95% CI 5.8-12.0) in the regorafenib group and 5.6 months (4.7-7.3) in the lomustine group (hazard ratio 0.50, 95% CI 0.33-0.75; log-rank p=0·0009). Grade 3-4 treatment-related adverse events occurred in 33 (56%) of 59 patients treated with regorafenib and 24 (40%) of 60 with lomustine. The most frequent grade 3 or 4 adverse events related to regorafenib were hand-foot skin reaction, increased lipase, and blood bilirubin increased (in six [10%] of 59 patients each). In the lomustine group, the most common grade 3 or 4 adverse events were decreased platelet count (eight [13%] of 60 patients), decreased lymphocyte count (eight [13%]), and neutropenia (seven [12%]). No death was considered by the investigators to be drug related.

### Interpretation:

REGOMA showed an encouraging overall survival benefit of regorafenib in recurrent glioblastoma. This drug might be a new potential treatment for these patients and should be investigated in an adequately powered phase 3 study.

### Comment in

Drug development for glioma: are we repeating the same mistakes? [Lancet Oncol. 2019]