REGOMA trial

- Genome-wide CRISPR-Cas9 screens identify BCL family members as modulators of response to regorafenib in experimental glioma
- Regorafenib and glioblastoma: a literature review of preclinical studies, molecular mechanisms and clinical effectiveness
- Exploring Regorafenib Responsiveness and Uncovering Molecular Mechanisms in Recurrent Glioblastoma Tumors through Longitudinal In Vitro Sampling
- Clinical activity of regorafenib in elderly patients with recurrent glioblastoma
- Characterization of Glioblastoma Cells Response to Regorafenib
- Regorafenib beyond the Second Line in Relapsed Glioblastoma: A Case Report and Literature Review
- Efficacy and tolerability of regorafenib in pretreated patients with progressive CNS grade 3 or 4 gliomas
- Phosphorylated Acetyl-CoA Carboxylase Is Associated with Clinical Benefit with Regorafenib in Relapsed Glioblastoma: REGOMA Trial Biomarker Analysis

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Clinical options for GBM patients remained unaltered for almost two decades until the encouraging results obtained by the phase II REGOMA trial allowed the introduction of the multikinase inhibitor regorafenib as a preferred regimen in relapsed GBM treatment by the National Comprehensive Cancer Network (NCCN) 2020 Guideline. Regorafenib, a sorafenib derivative, targets kinases associated with angiogenesis (VEGFR 1-3), as well as oncogenesis (c-KIT, RET, FGFR) and stromal kinases (FGFR, PDGFR-b). It was already approved for metastatic colorectal cancers and hepatocellular carcinomas [1)].

The phase 2 REGOMA trial suggested an encouraging overall survival benefit in glioblastoma patients at first relapse treated with the multikinase inhibitor regorafenib [2)]

Despite multimodal treatment with surgery and radiochemotherapy, the prognosis of glioblastoma remains poor, and practically all glioblastomas relapse. To date, no standard treatment exists for recurrent glioblastoma patients and traditional therapies have showed limited efficacy. Regorafenib is an oral multi-targeted tyrosine kinase inhibitor showing encouraging benefits in recurrent Glioblastoma patients enrolled in the REGOMA trial. We performed a large study to investigate clinical outcomes and the safety of regorafenib in a real-life population of recurrent glioblastoma patients. Patients receiving regorafenib outside clinical trials at the Veneto Institute of Oncology were retrospectively reviewed. The major inclusion criteria were: histologically confirmed diagnosis of glioblastoma, prior first line therapy according to “Stupp protocol”, Eastern Cooperative Oncology Group (ECOG) performance status score ≤1. According to the original schedule, patients received regorafenib 160 mg once daily for the first 3 weeks of each 4-week cycle. The primary endpoints of the study were overall survival and safety. A total of 54 consecutive patients were enrolled. The median age was 56, MGMT methylated status was found in 28 out of 53 available patients (52.8%), IDH mutation in 5 (9.3%) and 22 patients were receiving steroids at baseline. The median overall survival was 10.2 months (95% CI, 6.4-13.9), the OS-12 was 43%. Age, MGMT methylation status and steroid use at baseline were not statistically significant on a multivariate analysis for OS. Patients reporting a disease control as best response to regorafenib demonstrated a significant longer survival

(24.8 months vs. 6.2 months for patients with progressive disease, p = 0.0001). Grade 3 drug-related adverse events occurred in 10 patients (18%); 1 patient (2%) reported a grade 4 adverse event (rash maculo-papular). No death was considered to be drug-related. This study reported the first large “real-life” experience of regorafenib in recurrent glioblastoma. Overall, our results are close to the ones reported in the previous phase 2 study, despite the fact that we had a longer survival. We showed the encouraging activity and tolerability of this treatment in recurrent glioblastoma patients when used as a second-line treatment [3)].

Regorafenib did not negatively affect HRQoL in patients with recurrent glioblastoma. These data combined with the survival benefit shown in the REGOMA trial support the use of regorafenib as a treatment option for these patients [4)].

REGOMA trial showed an encouraging overall survival benefit of regorafenib in glioblastoma recurrence. This drug might be a new potential treatment for these patients and should be investigated in an adequately powered phase 3 study [5)]

AMPK pathway activation is associated with clinical benefit from treatment with regorafenib in relapsed Glioblastoma [6)].

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