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Decision-Making Analysis of next generation sequencing in glioblastoma in Switzerland

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Glioblastoma is the most frequent and most malignant primary brain tumour with an annual incidence of 3.2/100'000 1,2. The combination of histopathological features (nuclear atypia, mitosis, neoangiogenesis and/or necrosis) and molecular aberrations (IDH 1/2 status, TERT-promotor mutations) leads to the integrated diagnosis of the common IDH-wildtype glioblastoma. Additionally, the gain of chromosome 7 and loss of chromosome 10 as well as EGFR-overexpression and other mutations (EGFRvIII variant) are genetic hallmarks of glioblastomas leading to the diagnosis of diffuse gliomas with molecular features of glioblastoma, when histological criteria are missing 3.Glioblastoma is common in the elderly but quite rare in young adults with an annual incidence of 0.41 and 1.23/100000 in 20-34 and 35-44 year-old patients, respectively. In the typically elderly glioblastoma patients (65-74 years) the incidence is 20 to 10-fold higher (13.09/100000) 2. Younger glioblastoma patients sometimes harbour an unusual genotype (i.e. IDH-aberrations) 2,4. IDH-mutant glioblastoma account for 10% of all glioblastoma with a median age of manifestation of 45 years 5. These glioblastoma arise from lower grade gliomas through malignant progression and have a far better prognosis as their IDH-wildtype counterparts 6. However, overall survival of glioblastoma patients is grim and most recent clinical phase III studies failed to improve the prognosis using various therapeutic strategies7. "Actionable" mutations in the BRAF gene and NTRK gene fusions are mostly found in younger glioblastoma patients or in glioblastoma subtypes such as epitheloid glioblastoma 5,7. However, at which age to search for actionable mutations remains undefined. Furthermore, there is no consensus which genetic aberrations should be screened for (i.e. glioblastoma panel) and which technique is best suited to detect these aberrations (mutations, fusions) remains to be defined. Of note, actionable gene mutations in glioblastoma a rare. In a recent study of 48 glioblastomas, genetic aberrations were found in only 30 of 212 genes (14%) investigated 8. Beside mutations in the TP53, IDH1, EGFR and PTEN genes, EGFR and CDK4 amplifications as well as CDKN2A deletions were the most frequent copy number alterations. CDK4/6 and PI3K inhibitors were used in this cohort to target the detected aberrations in this small cohort of glioblastoma patients.
When considering these criteria, individual decision makers may use a wide variety of decision making criteria 9 and these often differ among clinical

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experts or hospitals 10-15.
We will perform a decision-making analysis of decision criteria regarding the application of next generation sequencing in glioblastoma among Swiss neuro-oncology centres on. This project will be performed among the members of the SWISS neuro-oncology society (SWISS-NOS). The group is motivated to collaborate, setting up new clinical

project partner	SwissNOS; Swiss society of neuro-oncology
type of project	clinical studies
status	automatically closed
start of project	2021
end of project	2021
responsible person	PD Dr. Thomas Hundsberger