INTRODUCTION: To assess the effects of bevacizumab (BEV) in recurrent GBMs, a three-arm randomized phase II study was initiated (the BELOB trial) comparing BEV monotherapy, CCNU monotherapy and BEV + CCNU combination therapy. Primary endpoint was 9 months OS and was 38% [25,51], 43% [29,57] and 59% [43,72] in the BEV, lomustine and combination arms respectively. The BELOB trial results therefore provide evidence for clinical efficacy of BEV, at least in a recurrent GBM setting and when given in combination with lomustine. However, not all patients in this trial appeared to benefit equally from the combination treatment. In this study, we therefore aimed to identify patients that benefit from BEV.

METHODS: RNA expression profiling was performed using DASL (Illumina, n = 118) and RNA sequencing (n = 78) of samples. RESULTS: The DASL and RNA-seq platform both show a high concordance between technical and biological replicates and with expression profiling on snap frozen tissue samples. Sample assignment to one of seven ‘intrinsic glioma subtypes’ (IGS; molecular subtypes of glioma based on similarities in gene-expression profiles [PMID: 19920198]) was also highly similar between the different platforms. Analysis of BELOB samples shows that most are assigned to poor prognostic subtypes (IGS-18 "EGFR-amplified, classical" n = 73 and IGS-23 "mesenchymal" n = 28). Nine patients were assigned to prognostically more favourable subtypes (IGS-9 and IGS-17), but these do not explain the more favourable outcome in the BEV + CCNU arm. Patients with tumors assigned to IGS-18 show benefit from combined treatment with bevacizumab + CCNU. In contrast, tumors assigned to IGS-23 may have worse performance in this arm, though patient numbers are small. CONCLUSIONS: DASL and RNA-seq perform well on RNA isolated from FFPE tissues stored (up to 20 years) in paraffin. Specific molecular subtypes of recurrent GBM show benefit from BEV + CCNU treatment.