For many years, the diagnosis and classification of gliomas have been based on histology. Although studies including large populations of patients demonstrated the prognostic value of histologic phenotype, variability in outcomes within histologic groups limited the utility of this system. Nonetheless, histology was the only proven and widely accessible tool available at the time, thus it was used for clinical trial entry criteria, and therefore determined the recommended treatment options. Research to identify molecular changes that underlie glioma progression has led to the discovery of molecular features that have greater diagnostic and prognostic value than histology. Analyses of these molecular markers across populations from randomized clinical trials have shown that some of these markers are also predictive of response to specific types of treatment, which has prompted significant changes to the recommended treatment options for grade III (anaplastic) gliomas.