In the past two decades there has been a tremendous increase in the understanding of the molecular basis of human malignancies. In a variety of neoplasms, specific molecular markers became part of disease classifications and are now routinely used to define specific entities. Molecular analyses discriminate prognostic groups, guide differential treatment strategies and identify targets for molecular defined cancer therapy. A battery of new drugs has been developed to specifically inhibit oncogenic pathways. For an increasing number of solid and haematological malignancies, the availability of molecular targeted drugs has fundamentally changed treatment algorithms. However, the diagnostic, prognostic and therapeutic impact of selected molecular markers is still limited in many cases. After all, the success of a molecular targeted therapy is clearly determined by the significance of the targeted structure for the biology of cancer and the ability of the malignant cell to evade specific inhibition.