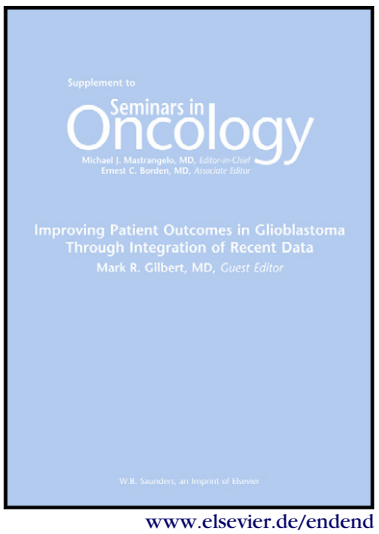

The PI3K Pathway: Clinical Inhibition in CLL

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The PI3K Pathway: Clinical Inhibition in CLL

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Abstract

Constitutive or mutational activation of the phosphatidylinositol 3 kinase, or PI3K, has been implicated in many cancers, including CLL. The delta isoform of the p110 catalytic subunit of PI3K has its primary physiologic function in B cells and appears to be the predominant mediator of most PI3K signals in CLL cells. Idelalisib is a first-in-class inhibitor of the PI3K delta isoform which shows near complete inhibition of AKT phosphorylation in CLL cells in vitro and in vivo. Idelalisib shows the classic pattern of response to BCR inhibition in CLL, with rapid nodal response and transient increase in lymphocytosis. The phase 1 study established the recommended dose as 150 mg twice per day. Subsequent registration trials have