Ibrutinib-A double-edge sword in cancer and autoimmune disorders.

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Abstract

Targeted therapies have appeared as new treatment options for several disease types, including cancer and autoimmune disorders. Of several targets, tyrosine kinases (TKs) are among the most promising. Overexpression of TKs provides a target for novel therapeutic agents, including small molecule inhibitors of tyrosine kinases (TKI). Ibrutinib (PCI-32765) is a TKI of Bruton's tyrosine kinase (Btk), a key kinase of the B-cell receptor signaling pathway that plays a significant role in the proliferation, differentiation and survival of B cells. In addition to inhibitory effects, recent studies have shown that ibrutinib has multiple immunomodulatory effects. It binds covalently to IL-2 inducible tyrosine kinase (Itk) in T lymphocytes and suppresses the survival of T-helper (Th) 2 cells. This changes the balance of Th1/Th2 cells toward Th1 subset, which are the main immune cells targeting tumor cells. The dual activity of ibrutinib has paid a great attention and several studies are evaluating the anti-tumor and immunomodulatory effects in cancer, autoimmune disorders and infectious diseases. In this article we review the inhibitory and immunomodulatory effects of ibrutinib in B-cell malignancies, autoimmune diseases and infections, as well as the communication between the Ror1 receptor tyrosine kinase and BCR and effects of ibrutinib on this crosstalk.

KEYWORDS:

Bruton’s tyrosine kinase; Ror1; ibrutinib; small-molecule Inhibitors; targeted cancer therapy; tyrosine kinases