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Pulmonary complications of Bcr-Abl tyrosine kinase inhibitors

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Bcr-Abl tyrosine kinase inhibitors have been associated with certain pulmonary complications, including exudative pleural effusions, chylothorax, interstitial lung disease and pulmonary arterial hypertension https://bit.ly/3cG6QnG

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ABSTRACT Tyrosine kinase inhibitors (TKIs) targeting the Bcr-Abl oncoprotein revolutionised the treatment of chronic myelogenous leukaemia. Following the success of imatinib, second- and third-generation molecules were developed. Different profiles of kinase inhibition and off-target effects vary between TKIs, which leads to a broad spectrum of potential toxicities.

Pulmonary complications are most frequently observed with dasatinib but all other Bcr-Abl TKIs have been implicated. Pleural effusions are the most frequent pulmonary complication of TKIs, usually associated with dasatinib and bosutinib. Pulmonary arterial hypertension is an uncommon but serious complication of dasatinib, which is often reversible upon discontinuation. Bosutinib and ponatinib have also been associated with pulmonary arterial hypertension, while imatinib has not. Rarely, interstitial lung disease has been associated with TKIs, predominantly with imatinib.

Mechanistically, dasatinib affects maintenance of normal pulmonary endothelial integrity by generating mitochondrial oxidative stress, inducing endothelial apoptosis and impairing vascular permeability in a dose-dependent manner. The mechanisms underlying other TKI-related complications are largely unknown. Awareness and early diagnosis of the pulmonary complications of Bcr-Abl TKIs is essential given their seriousness, potential reversibility, and impact on future treatment options for the underlying chronic myelogenous leukaemia.