Precision Personalized Therapy: Establish the Unique BTK Mutation Status of Leukemia and Non-Hodgkin's Lymphoma Patients

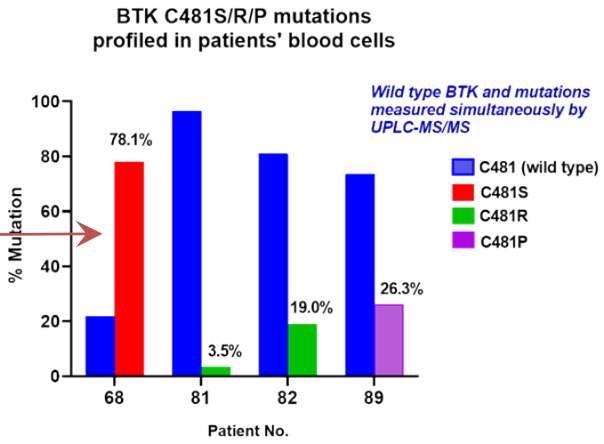
A drug's efficacy is influenced by its molecular target. Alterations of this target through genetic mutation, post-translational modification (PTM), or expression/activation level are among the ways cancer cells use to survive. BTK mutations affect the efficacy of small molecule kinase inhibitors by altering the contact points for binding or perturbing the conformational state of the target enzyme(1). Genetic differences can exist in patients at low (or non-detectable) levels within a cancer cell population before treatment and undergo positive selection during exposure to a clinically effective targeted agent(2). Genetic resistance is a major problem facing the clinical effectiveness of kinase inhibitors(2).

Absolutely quantitate BTK mutations in patients using advanced LC-MS/MS

Nextcea's clinical assays allow physicians and pharmaceutical sponsors to identify BTK mutations in patient blood cells. Signature peptides of wild-type and mutated BTK are simultaneously measured by LC-MS/MS. Our clinical assays provide a way to assess a patient's unique disease state and select an appropriate treatment option/regimen based on the presence/percentage of functional BTK genetic mutations.

Ibrutinib and other non-covalent inhibitors may not be effective in patients with high levels of mutations.

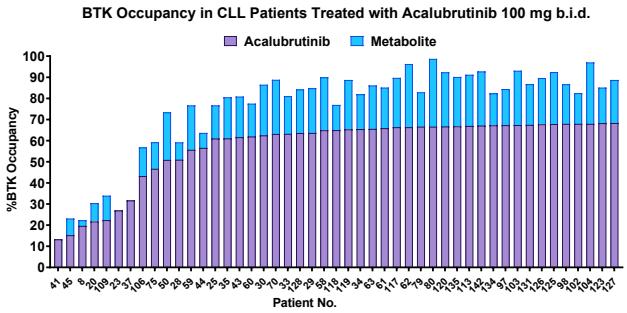
Physicians may consider non-covalent inhibitors or combination treatments tailored to individual refractory/relapsed patients.



Select the "right" treatment to enhance therapeutic efficacy

BTK mutations are an important molecular mechanism of underlying disease progression on therapy, with a high frequency in resistant patients

Physicians and pharmaceutical sponsors can correlate mutation status with the %BTK occupancy of an inhibitor to optimize treatment of resistant patients.



About Nextcea, Inc.

Nextcea, Inc. is a drug development service company dedicated to optimizing efficacy and minimizing toxicity in all phases of drug development. Nextcea integrates cross-species biomarker studies with traditional PK/PD and TK/TD. In-house platforms include HPLC/UPLC coupled to mass spectrometry LC-MS and LC-MS/MS (API-6500s and and TripleTOF 6600).

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2. Holohan C et al. Cancer drug resistance: an evolving paradigm. Nat Rev Cancer. 2013 Oct;13(10):714-26.