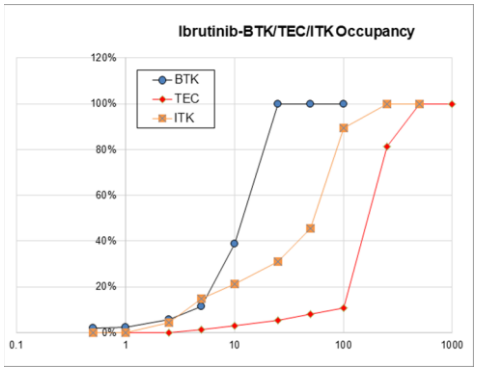
Minimize the Off-Target Effects of BTK Inhibitors in Leukemia and Non-Hodgkin's Lymphoma Patients

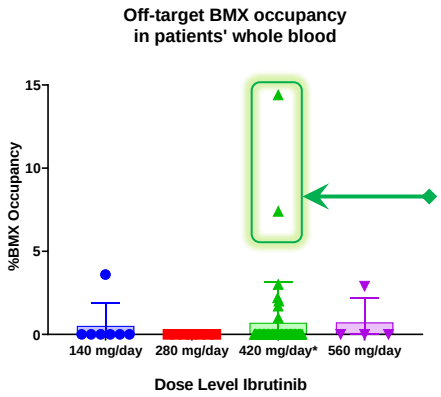
Although small molecule kinase inhibitors have demonstrated meaningful benefits in clinical trials, much to learn exists about their side-effects over time[1,2]. The Bruton's protein-tyrosine kinase (BTK) inhibitor ibrutinib, for example, produced marked efficacy in chronic lymphocytic leukemia (CLL) clinical trials. It is approved by the US FDA as a treatment for CLL patients in any line of therapy[2]. However, it is not selective for BTK and associated with well-recognized toxicities – atrial fibrillation, infection, pneumonitis, bleeding, and arthralgia. Managing toxicities to keep patients on the drug long enough to achieve a response is critical to ibrutinib benefit, and at present, little is known about the potential durability of response after ibrutinib discontinuation for adverse events[2].

Quantitate drug off-target effects and design more selective inhibitors using advanced LC-MS/MS

Kinase inhibitors can be active against multiple kinases and have diverse selectivity profiles. Nextcea's clinical assays enable pharmaceutical sponsors to design potent inhibitors with desired selectivity profiles. Sponsors and physicians can optimize dosing/regimen conditions using quantitative methods for the on- and off-target engagement of kinase inhibitors.



Define dosing level & frequency to reduce safety risks in pateints



Precision personalized therapeutics allows physicians to assess the off-target effects of BTK inhibitors in individual patients.

Patients on standard ibrutinib therapy (420 mg/day) with increased risk of off-target effects (ex. BMX occupancy associated with bleeding). Reduction in dose may be warranted.

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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1. Gross S et al. Targeting cancer with kinase inhibitors. The Journal of Clinical Investigation 2015 125(5):1780-1789.
2. Brown JR. How I treat patients with ibrutinib. Blood 25 January 2018, 131(4):379-386.