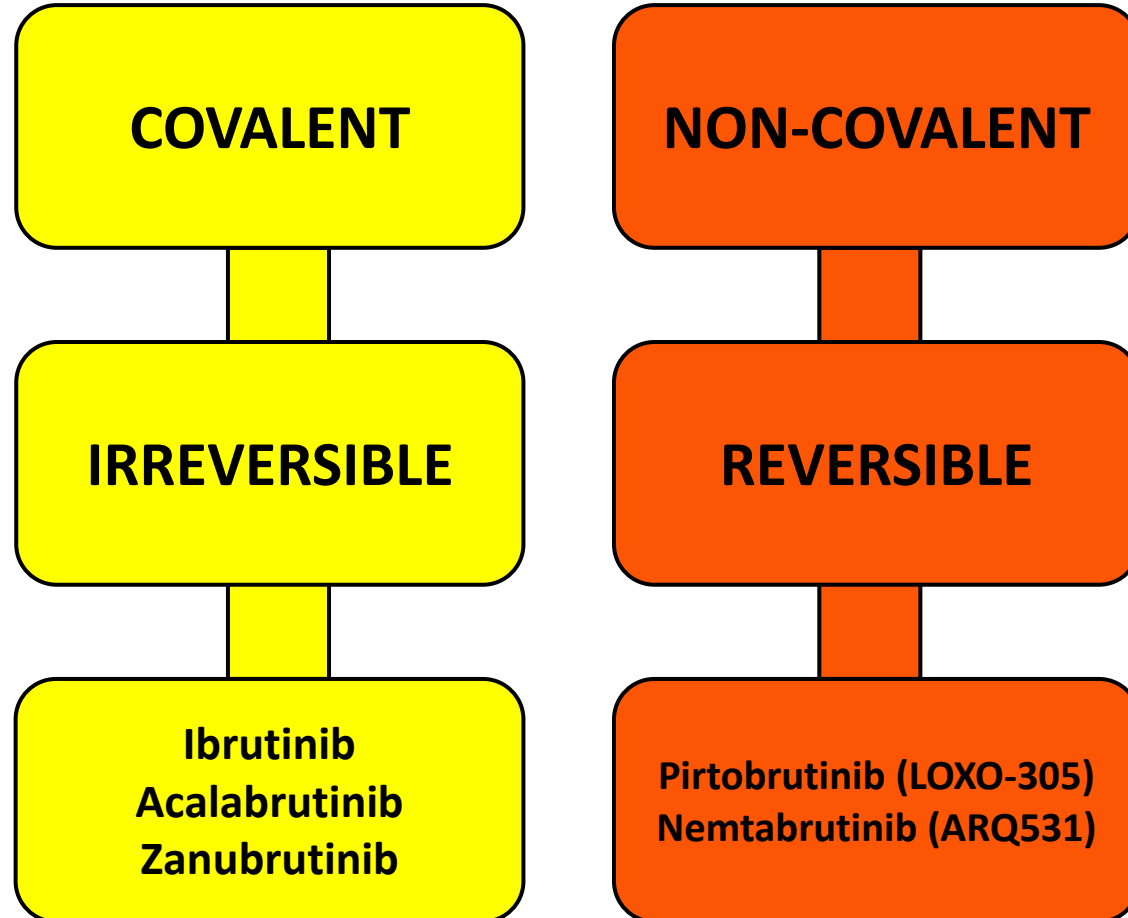
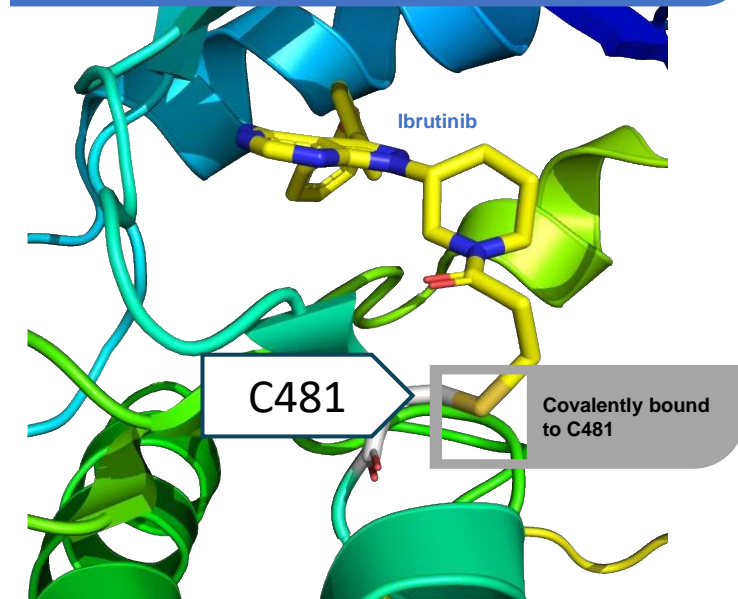


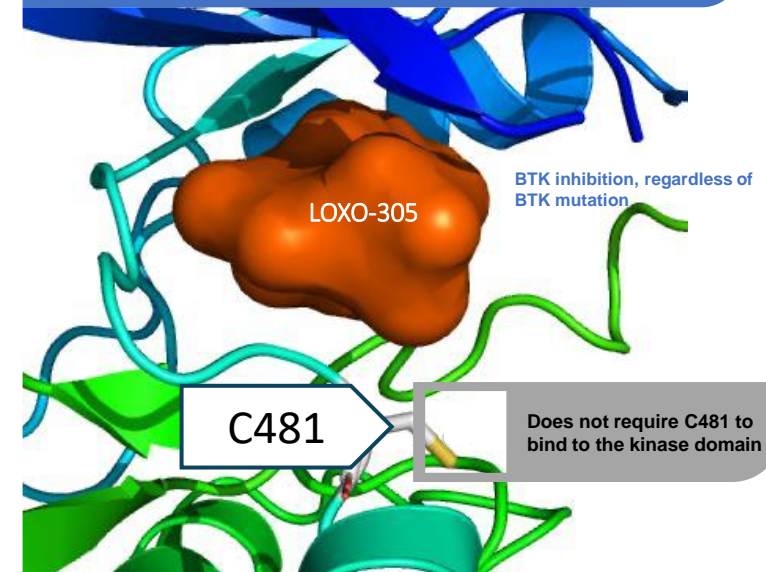
Classes of BTK Inhibitors



Covalent BTK inhibitors (ibrutinib, acalabrutinib, zanubrutinib) require WT BTK for activity



LOXO-305 is a non-covalent BTK inhibitor that is potent against both WT and C481-mutant BTK



R/R CLL

abs25-7227 Toby Eyre

Pirtobrutinib outcomes in second-line (2L) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) after first-line (1L) cBTKi therapy: A pooled analysis from the BRUIN LOXO-BTK- 18001 and BRUIN CLL-321 studies

1L cBTKi therapy and no prior exposure to a BCL2i
37 eligible patients
48% had del(17p).
median TTNT 32.5 months.

abs25-15839 Kanishka Uttam Chandani

Impact of prior venetoclax use on mortality in CLL patients treated with pirtobrutinib: A propensity-matched cohort study

TriNetX Global Collaborative Network

200 pts in V+P and 172 pts in P

Pirtobrutinib in venetoclax-exposed pts associated with higher odds of mortality at 1 year,
Anemia, neutropenia, TLS, sepsis, and neutropenic fever
higher in the venetoclax exposed (not statistical significant)

abs25-2584 Alexey Danilov

The efficacy and safety of pirtobrutinib in patients with CLL/SLL: A phase 2 dose optimization trial in progress

Multicenter, global study

249 previously treated patients with CLL/SLL

Three different dose groups

Stratified by del(17p) status and number of prior lines

1L CLL

LBA-3 Wojciech Jurczak

Pirtobrutinib vs bendamustine plus rituximab (BR) in patients with CLL/SLL: First results from a randomized phase III study examining a non-covalent BTK inhibitor in untreated patients

Improved IRC-assessed PFS versus BR

One of the largest treatment effects for a single-agent BTKi

Low rates of discontinuation and atrial fibrillation/flutter.

OS: trend favoring pirtobrutinib (despite 52.9% of BR pts crossing over)

abs25-2587 Jennifer Woyach

Pirtobrutinib vs ibrutinib in treatment-naïve and relapsed/refractory CLL/SLL: Results from the first randomized phase III study comparing a non-covalent and covalent BTK inhibitor

Favorable overall response rate (ORR) and a positive PFS trend with pirtobrutinib compared to the cBTKi ibrutinib in a subset of pts with treatment-naïve CLL.

abs25-12906 Nitin Jain

Time-limited pirtobrutinib, venetoclax, and obinutuzumab combination in first-line chronic lymphocytic leukemia

Very high rate of BM and blood U-MRD6 remission after 6-months and 12-months of combined treatment