25 Years of TKIs: A Timeline of Transformation

iCMLf 25 years of TKIs

The development of TKIs for CML revolutionised cancer treatment, offering a targeted therapy model for other malignancies. Each generation of TKIs improved upon the last, addressing resistance, intolerance, and specific mutations. Continued innovation, including the new allosteric inhibitors, ensures further advancements in managing CML.

Pre-TKI Era

"The identification of BCR::ABL1 and its ability to cause leukemia was a key moment to understanding this disease. It was a moment of hope as I realised we had the potential to change the trajectory of the disease."
– Professor Brian Druker

1959

Philadelphia Chromosome

The discovery of the Philadelphia (Ph) chromosome in CML patients was the first chromosomal abnormality linked to cancer.

1973

BCR::ABL Fusion Gene

Identification of the BCR::ABL1 fusion gene, resulting from the Ph+ translocation (t(9;22)(q34;q11)).

1985

BCR::ABL Oncoprotien

Discovery that the BCR::ABL1 fusion protein has constitutive tyrosine kinase activity, driving uncontrolled cell growth.

First-Generation TKI

1990

Targeting BCR::ABL1

Collaboration between academia and Novartis began on a drug discovery program to target BCR::ABL

1992

STI571

STI571 (imatinib) is shown to specifically target and kill CML cells.

"The approval of imatinib was more than a milestone; it was a lifeline for patients around the world."
– Professor Jorge Cortes

1998

Phase I trials

Phase I trials showed unprecedented response rates for a cancer treatment, with minimal toxicity.

2000

Phase II & III trials

Phase II and III trials demonstrated dramatic improvements in major molecular response and complete cytogenetic response rates in chronic-phase CML patients.

2001

Imatinib

FDA approved imatinib for the treatment of CML.

"These innovations reminded us that progress never stops - we must keep pushing the boundaries and be relentless in our efforts to improve the outlook of people living with CML."
– Professor Neil Shah

2004
TFR
The first TFR pilot study showed 50% of CML patients off imatinib maintained undetectable BCR::ABL1 levels for over 2 years.

Treatment Free Remission becomes a reality

Second Generation TKI

2006
Dasatinib
FDA approved dasatinib for patients with imatinib-resistant or intolerant CML.

2007
Nilotinib
FDA approved nilotinib for patients with imatinib-resistant or intolerant CML.

"Asciminib offers new hope for patients, proving that biomedical innovation can overcome even the toughest challenges in CML treatment."
- Professor Oliver Hantschel

2012
Bosutinib
FDA approved bosutinib for CML patients with resistance or intolerance to prior therapy.

Third-Generation TKI

2012
Ponatinib
Ponatinib was specifically designed to inhibit T315I, a mutation that confers resistance to all prior TKIs.

Fourth-Generation TKI

2021
Asciminib
Asciminib is the first allosteric TKI targeting the ABL myristoyl pocket (STAMP inhibitor), offering a novel mechanism of action.

Today

2025
New TKIs and formulations are in development

Twenty-five years ago, TKIs revolutionised CML care, turning a five-year survival prognosis into a normal lifespan. Today, we honour this remarkable legacy and remain steadfast in our journey toward a cure.