

# Nearly half of oncology drugs approved since 1998 are precision therapies

October 18 2023

---



Credit: CC0 Public Domain

Of the 198 new oncology drugs approved by the U.S. Food and Drug Administration (FDA) between 1998 and 2022, approximately 43% were precision oncology therapies, the use of which is guided by

biomarker testing.

A study authored by Debyani Chakravarty, Ph.D. from Memorial Sloan Kettering Cancer Center (MSK) and Sarah P. Suehnholz, Ph.D., senior scientist, OncoKB at MSK has been published in [Cancer Discovery](#).

"For this study, we mark the beginning of the field of precision [oncology](#) as 1998 with the approval of trastuzumab (Herceptin), one of the first molecularly targeted therapies indicated for HER2-positive breast cancer. Since then, the field has exponentially grown with the discovery of novel biomarkers and corresponding [drug approvals](#), thanks in part to a progressive decrease in the cost of genomic sequencing and improvements in sequencing technology," said Chakravarty.

"To our knowledge, there has not been a systematic assessment of how much this field has grown and the extent to which its expansion has benefitted patients with cancer."

To quantify the expansion and impact of precision oncology, Chakravarty and colleagues reviewed the oncology drugs approved by the FDA from 1998 to 2022.

"We defined a precision oncology therapy as a [drug](#) that is most effective in a molecularly defined subset of patients and for which pretreatment molecular profiling is required for optimal patient selection," said first author Sarah P. Suehnholz.

In the second part of the study, the researchers used two versions of OncoKB, deployed in 2017 and 2022, to assess the clinical actionability of the genetic alterations detected by the MSK-IMPACT sequencing assay in a set of 47,271 solid tumor samples. For example, the authors determined whether a certain mutation in a patient's tumor that was considered predictive of response to an investigational drug in 2017 was

then recognized as a biomarker predictive of response to an FDA-approved drug in 2022.

The genomic data used in this study are publicly available through [AACR Project GENIE](#), a registry of real-world clinico-genomic data assembled through data sharing between international cancer centers.

Among the 198 new oncology drugs approved by the FDA, 82.8% were classified as molecularly targeted therapies—drugs for which the mechanism of action is known but that do not require biomarker testing for patient selection.

Approximately 43% (86 out of 198) were classified as precision oncology drugs. These include [kinase inhibitors](#), [monoclonal antibodies](#), [small molecule inhibitors](#), antibody-drug conjugates, and immune checkpoint inhibitors, among others, all of which require genomic biomarker screening for patient selection.

The analysis showed a slow expansion in the rate of FDA approvals of precision oncology therapies from 1998 to 2017 and a rapid increase from 2017 to 2022.

"The highest number was registered in 2020, with 12 FDA approvals, and the number appears to drop in 2021 and 2022, suggesting that we may have reached the peak of single biomarker-based precision oncology therapies," said Chakravarty.

"This finding also emphasizes the need for innovative combination approaches that can address multiple genomic alterations, as well as targeted therapies effective in patients whose tumors are driven by alterations in common tumor suppressor genes or transcription factors."

To assess the innovation in the field, the researchers further classified

precision oncology therapies into four categories based on the novelty of their mechanism of action. They found that 42% of these drugs worked through a similar mechanism of action as a previously approved therapy or targeted resistance to an existing drug.

"The majority of these therapies target only seven biomarkers, highlighting the narrow scope of precision oncology drug development during this period," added Chakravarty. "Several targets have remained undruggable since 1998. We are now making inroads with some, for example, targeting specific mutant forms of KRAS, but we need to continue to expand the number of actionable genetic alterations."

Results from the second part of the study showed that the fraction of patient samples carrying genomic alterations that make them eligible for treatment with standard-of-care precision oncology therapies or for enrollment in a clinical trial with promising clinical data nearly doubled (from 18.1% to 35.9%) from 2017 to 2022.

In parallel, there was an almost 50% decrease (from 44.2% to 22.8%) in the fraction of samples with oncogenic alterations that are currently non-actionable.

"Despite the dramatic growth of the field, the clinical impact of precision oncology is still debated. By thoroughly and systematically mapping out the landscape of precision oncology, our study revealed that these therapies are a mainstay of current oncology care," said Chakravarty.

"Unfortunately, these drugs can be extremely expensive, and insurance coverage often dictates whether a patient will receive them. Our findings support that coverage of precision oncology therapies is essential and should not be available to only a select few."

Another aspect highlighted by this study is the importance of universal genetic testing that can help develop treatments targeting rare genomic alterations regardless of the site of tumor origin, added Chakravarty.

According to the authors, one limitation of their analysis is that it does not have information on whether patients actually received the precision therapy for which they were found to be eligible.

"Eligible patients may not receive a precision oncology drug for several reasons related to their disease or to our current health care landscape," said Chakravarty. "It is also important to note that not all patients treated with a genomic-matched [therapy](#) will benefit equally."

As for further limitations, the study did not acquire information on germline mutations that determine eligibility for certain targeted therapies, and the patient population studied was not diverse.

In addition, the analysis was based on U.S. FDA drug approvals, and different countries may have different regulatory status and approaches to precision oncology, the authors explained.

**More information:** Sarah P. Suehnholz et al, Quantifying the Expanding Landscape of Clinical Actionability for Patients with Cancer, *Cancer Discovery* (2023). [DOI: 10.1158/2159-8290.CD-23-0467](https://doi.org/10.1158/2159-8290.CD-23-0467)

Provided by American Association for Cancer Research

Citation: Nearly half of oncology drugs approved since 1998 are precision therapies (2023, October 18) retrieved 28 April 2024 from <https://medicalxpress.com/news/2023-10-oncology-drugs-precision-therapies.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.