e23125 Publication Only

Pivotal studies of pharmacotherapies approved by the United States Food and Drug Administration for the treatment of cancer: A systematic review.

Ronald Chow, Georgia C Richards, Camilla Zimmermann, Carl Heneghan; Centre for Evidence-Based Medicine, University of Oxford, Oxford, United Kingdom; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

Background: The development of pharmacotherapies for cancer treatment has increased significantly. However, an assessment of approvals by the US Food and Drug Administration (FDA) and sample sizes for pivotal studies leading to approval has not yet been conducted. Our aim was to determine the number of pharmacotherapies approved by the FDA for people with cancer and assess the characteristics of studies, including sample size. **Methods:** We developed a web scraper to collect approved pharmacotherapies for cancer treatments from the FDA website until December 31, 2024. Pharmacotherapies with different routes of administration (i.e., intravenous or a previously approved oral formulation of the same pharmacotherapy) and combinations of previously approved pharmacotherapies were excluded. For each pharmacotherapy, we noted: the pivotal study as per the product monograph; the proposed sample size from the study protocol; and the final sample size of the completed study. We recorded the type of pharmacotherapy (chemotherapy, hormonal therapy, immunotherapy, or targeted therapy) and study design (phase 1, 2, or 3). Regression analyses and data discretisation were conducted to identify trends in sample size. Type I error was set at 0.05. Quality assessment was conducted. OSF Registration DOI: 10.17605/OSF.IO/KVA23. **Results:** We identified 255 pharmacotherapies: 49.0% were targeted therapies, 23.9% chemotherapies, and 18.4% immunotherapies. A larger proportion of recent novel pharmacotherapies were targeted therapies, compared to previous decades (59.7% in 2020 to 2024 vs 12.0% in 1990 to 1999). The mean and median sample size were 386 (SD 361) and 290 (IQR 427). Three-quarters (75.3%) of studies were at low risk of bias. Table 1 shows that sample sizes were larger in studies since 1990, but no difference from 1990 onwards. Stratified analysis by study design reports phase 2 studies between 1970 and 1979 had smaller median sample sizes than those since 1990; there was no difference among phase 3 studies. For 165 studies reporting proposed sample sizes, these were lower from 2020 to 2024 than from 2010 to 2019. **Conclusions:** There was a substantial increase in sample size in the 1990s, likely driven by new policies and legislation. There has since been no significant increase, likely due to increasing proportion of novel pharmacotherapies being targeted therapies, employing biomarker-defined subpopulations and modern trial designs such as basket and umbrella studies that require smaller proposed samples. Research Sponsor: None.

Year	Median	IQR	Q1, Q3	Mean	SD
1950-1959 (n = 6)	61	86	21, 107	66.3	52.6
1960-1969 (n = 9)	40	37	33, 70	54.4	36.8
1970-1979 (n = 9)	48	29	46, 75	104.9	157.6
1980-1989 (n = 8)	169	421	74, 495	290.6	318.2
1990-1999 (n = 25)	407	561	222, 764	510.5	398.9
2000-2009 (n = 39)	329	344	153, 497	398.4	343.3
2010-2019 (n = 92)	350	460	190, 650	461.5	403.1
2020-2024 (n = 67)	290	386	126, 512	350.9	292.6