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Tumor-Specific Success Probabilities and Factors Associated With Phase III Trials in Oncology Drug Development

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ABSTRACT

Despite advances in novel therapeutic modalities, such as molecularly targeted agents and immunotherapies, the probability of success in Phase III oncology trials remains low. This study quantitatively characterized success probabilities of Phase III trials in oncology drug development and evaluated the factors associated with trial success. Phase III interventional oncology drug trials registered at ClinicalTrials.gov between 2007 and 2023 with publicly available primary endpoint results were included. Trial success was defined as the achievement of at least one primary endpoint, and tumor-specific success probabilities were calculated. Multivariable logistic regression analyses were conducted to assess the association between trial success and key trial characteristics. We analyzed 824 trials (358 successful and 466 unsuccessful). Overall success probabilities were comparable between solid tumors and hematologic malignancies, although substantial heterogeneity was observed across solid tumors, with particularly low success probabilities for central nervous system tumors and pancreatic cancer. Multivariable analyses showed that biomarker-based patient selection, more recently initiated trials, line of therapy, and the number of primary endpoints were associated with trial success. Trials evaluating molecularly targeted therapies and those with short-term evaluable endpoints showed higher success probabilities, whereas trials evaluating chemotherapy or assessing overall or event-free survival endpoints showed lower success probabilities. Phase III trial success in oncology is associated with tumor-specific characteristics and development-stage factors, including biomarker-based patient selection and trial design. These results provide quantitative evidence to inform decision-making and trial design in oncology drug development.

1 | Introduction

Recent advances in therapeutic modalities, including molecularly targeted therapies, immune checkpoint inhibitors, and antibody–drug conjugates (ADCs), have caused substantial progress in oncology drug development. These modalities, based on tumor biology, are expected to improve therapeutic efficacy in selected patient populations [1–4]. Despite these scientific advances, oncology remains a therapeutic area with a low probability of clinical trial success across drug development [5–8]. The low probability of success is usually attributed to tumor heterogeneity and clinical complexity; however, it may also reflect trial design decisions, such as dose selection, patient selection, and choice of primary endpoints, based on data from Phase I and II studies, translating into outcomes in late-stage development. Because Phase III trials are conducted under conditions

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Study Highlights

- What is the current knowledge on the topic?
  - Phase III oncology trials have a relatively low probability of success, and trial failure has been attributed to biological complexity, tumor heterogeneity, and challenges in late-stage clinical development. However, relatively few studies have quantitatively characterized tumor-specific success probabilities and comprehensively evaluated trial design-related factors across oncological indications.
- What question did this study address?
  - This study examined tumor-specific success probabilities and quantitatively evaluated the factors associated with Phase III trial success in oncology drug development using publicly available trial data and multivariable logistic regression analysis.
- What does this study add to our knowledge?
  - This study demonstrates substantial heterogeneity in Phase III trial success probabilities across tumor types and identifies key developmental stage factors associated with trial success, including biomarker-based patient selection, therapeutic modality, line of therapy, and primary endpoint selection.
- How might this change clinical pharmacology or translational science?
  - These findings provide quantitative evidence to inform decision-making and trial design in late-stage oncology drug development, supporting more rational and efficient development strategies for precision oncology.

in which these design elements are fixed, trial success or failure indicates the appropriateness of trial design decisions made during late-stage development. These design elements, fixed at Phase III, make trial success or failure a reflection of late-stage design decisions.

Phase III trials with these characteristics have increased development risk owing to multiple factors, including increasing trial complexity, rapid changes in standards of care driven by therapeutic innovation, biomarker-based patient stratification, and prolonged follow-up to demonstrate survival benefit [9, 10]. Among these factors, the choice of primary endpoint significantly influences Phase III trial design and the associated risk. In oncology, overall survival (OS) remains a key regulatory endpoint [11–14]; however, surrogate endpoints such as response rate and progression-free survival (PFS) are widely used in practice, and the selection of these endpoints reportedly influences trial risk and the probability of success [15–17].

The outcome (success or failure) of Phase III trials has implications beyond scientific and clinical significance, affecting patients, regulatory authorities, and pharmaceutical companies involved in drug development. Phase III trials require substantial resources, and failure may delay patient access to effective therapies, causing significant financial losses for sponsors. Therefore, identifying the factors associated with Phase III trial success is critical for evaluating the efficiency of oncology drug development. Moreover, cancer is not a single disease, but a heterogeneous group of diseases characterized by differences in tumor biology, molecular targets, and clinically relevant endpoints across tumor types and molecular subgroups. Consequently, overall average success probabilities in oncology may obscure meaningful differences in development risk across tumor types. The quantitative characterization of tumor-specific success probabilities during late-stage development may provide valuable information for indication selection and trial design.

Although previous studies have examined clinical trial success probabilities or associated factors, many have focused on a few tumor types, and the data analyzed have been limited to trials conducted until the end of 2017. Furthermore, few studies have simultaneously and quantitatively evaluated tumor-specific success probabilities and factors associated with Phase III trial success across oncological indications [7, 18, 19]. Therefore, in this study, we analyzed Phase III trials registered between 2007 and 2023 to estimate tumor-specific success probabilities and comprehensively evaluate the factors associated with trial success using multivariable logistic regression analysis. Through this approach, we aim to identify the factors associated with Phase III trial success and provide quantitative evidence for trial design and decision-making in late-stage oncology drug development.

2 | Materials and Methods

2.1 | Study Overview

Phase III trials represent the most resource-intensive stage of clinical development and are crucial for decision-making. In this study, the analyses were restricted to Phase III trials to quantitatively evaluate the associations between trial success and design-related factors during late-stage development.

2.2 | Data Collection

Phase III interventional trials of oncology drug therapies registered at ClinicalTrials.gov between January 1, 2007, and December 31, 2023, with publicly available primary endpoint results, were identified. Trials were excluded if the primary endpoint evaluated safety only, compared different dosing regimens, were extension studies, or evaluated cancer vaccines. When the achievement status of the primary endpoints was not reported at ClinicalTrials.gov, information was supplemented using peer-reviewed publications and other publicly available sources related to the investigational drug, such as conference abstracts. Trial success or failure was adjudicated based on whether the primary endpoint(s) were reported as met according to the predefined statistical criteria of each study, as described in these sources. Trials for which the primary endpoint outcomes could not be confirmed from these sources were excluded from the analysis. Through these classification and adjudication procedures, we minimized potential misclassification of trial success.

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2.3 | Definition of Trial Success

Trials were classified as "successful" if at least one primary endpoint was achieved. Trials in which no primary endpoints were achieved were classified as "unsuccessful." In this study, trial success was not considered equivalent to regulatory approval or clinical benefit but was used to indicate achievement status in late-stage clinical trials.

2.4 | Study Variables

The tumor-specific success probabilities of Phase III trials were calculated and summarized according to tumor classification (solid tumors or hematologic malignancies). To evaluate factors associated with trial success, the following variables were examined:

- Presence or absence of biomarker-based patient selection
- Trial size (dichotomized by the median number of enrolled patients, $n = 481$)
- Tumor classification (solid tumors or hematologic malignancies)
- Trial initiation period (2012 or later vs. earlier)
- Number of primary endpoints (single vs. multiple)

Therapeutic modalities were categorized as chemotherapy, molecularly targeted therapy, immunotherapy, ADCs, and endocrine therapy, with the remaining modalities classified as Other. The line of therapy was categorized as neoadjuvant/adjuvant or advanced/metastatic for solid tumors, and as first-line or relapsed/refractory for hematologic malignancies.

Primary endpoints were classified as OS, PFS, time to progression (TTP), event-free survival (EFS), disease-free survival (DFS), relapse-free survival (RFS), response rate, or Other. The Other category included non-standard endpoints, such as pharmacokinetics, pharmacodynamics, hormone levels, bone metastasis-free survival, and quality of life.

2.5 | Statistical Analysis

Trial success (successful vs. unsuccessful) was used as the dependent variable, and multivariable logistic regression analysis was performed to evaluate the factors associated with trial success. An overall model was constructed, with biomarker-based patient selection, trial size, tumor classification, trial initiation period, and number of primary endpoints as independent variables. In contrast, separate univariable logistic regression analyses without adjustment for other covariates were constructed for the treatment modality, line of therapy, and primary endpoint type.

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for all analyses, and a two-sided p value < 0.05 was considered statistically significant. As a sensitivity analysis, multivariable logistic regression was repeated in trials with a single primary endpoint using the same covariates as in the main analysis, except for primary endpoint multiplicity. All analyses were performed using the R software. These analyses were conducted for exploratory and descriptive purposes to primarily characterize the overall trends in the associations between trial success and the evaluated factors. Accordingly, causal relationships cannot be directly inferred from the results of this study.

2.6 | Ethical Considerations

This study was conducted using publicly available, de-identified information from databases, such as ClinicalTrials.gov. No new interventions or collection of personal data were performed. Therefore, this study did not involve animals or human participants, and approval by the Institutional Review Board and informed consent were not required.

3 | Results

Phase III oncology drug trials ($n = 1202$) registered at ClinicalTrials.gov between 2007 and 2023 were identified. Of these, 378 trials were excluded because the primary endpoint evaluated safety only, the trials compared dosing regimens, were extension studies, evaluated vaccines for cancer prevention, or did not have publicly available primary endpoint results. Ultimately, 824 trials were included in the analysis, comprising 653 trials on solid tumors and 171 trials on hematologic malignancies (Figure 1).

The overall success probability of Phase III trials was 43.4% (358 out of 824 trials). The probability of success was 42.6% (278 out of 653 trials) for solid tumors and 46.8% (80 out of 171 trials) for hematologic malignancies. Tumor-specific success probabilities are summarized in Table 1. To ensure the interpretability of the estimated success probabilities, the results are presented primarily for tumor types with ≥ 10 trials for solid tumors and hematologic malignancies. Among solid tumors, the highest success probabilities were observed in melanoma (58.1%, 18 out of 31 trials), followed by renal cell carcinoma (57.9%, 11 out of

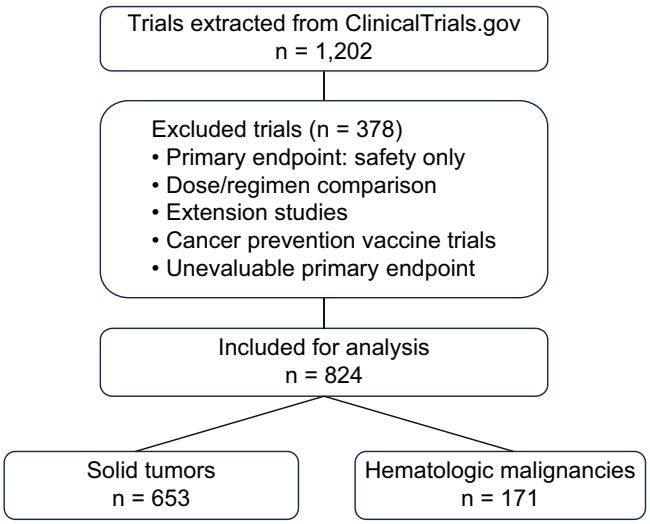

FIGURE 1 | Study selection flow for Phase III oncology drug trials.

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TABLE 1 | Success rates of Phase III trials by cancer category.

Category	Total	Success	Failure	Success rate (95% CI)
Summary				
All	824	358	466	43.4% (40.0–46.9)
Solid	653	278	375	42.6% (38.7–46.5)
Hematologic malignancies	171	80	91	46.8% (39.1–54.6)
Solid tumors				
Non-small-cell lung cancer	127	59	68	46.5% (37.6–55.5)
Breast	127	59	68	46.5% (37.6–55.5)
Prostate	54	25	29	46.3% (32.6–60.4)
Colorectal	46	20	26	43.5% (28.9–58.9)
Melanoma	31	18	13	58.1% (39.1–75.5)
Ovarian	29	12	17	41.4% (23.5–61.1)
Head and neck	28	5	23	17.9% (6.1–36.9)
Gastric	28	9	19	32.1% (15.9–52.4)
Urothelial	22	5	17	22.7% (7.8–45.4)
Hepatocellular carcinoma	21	9	12	42.9% (21.8–66.0)
Pancreatic	19	3	16	15.8% (3.4–39.6)
Renal cell carcinoma	19	11	8	57.9% (33.5–79.7)
Central nervous system tumors	14	2	12	14.3% (1.8–42.8)
Small-cell lung cancer	13	3	10	23.1% (5.0–53.8)
Sarcoma	12	4	8	33.3% (9.9–65.1)
Cervical	10	3	7	30.0% (6.7–65.2)
Esophageal	8	6	2	75.0% (34.9–96.8)
Neuroendocrine	8	6	2	75.0% (34.9–96.8)
Gastrointestinal stromal tumor	8	4	4	50.0% (15.7–84.3)
Nasopharyngeal	6	3	3	50.0% (11.8–88.2)
Mesothelioma	6	1	5	16.7% (0.4–64.1)
Thyroid	5	3	2	60.0% (14.7–94.7)
Biliary	4	1	3	25.0% (0.6–80.6)
Endometrial	3	1	2	33.3% (0.8–90.6)
Neuroblastoma	2	2	0	100.0% (15.8–100.0)
Germ cell	2	1	1	50.0% (1.3–98.7)
Carcinoma of unknown primary	1	0	1	0.0% (0.0–97.5)
Hematologic malignancies				
Lymphoid neoplasms				
Lymphoid neoplasms (total)	87	37	50	42.5% (32.0–53.6)
Non-Hodgkin lymphoma	54	18	36	33.3% (21.2–47.5)
Chronic lymphocytic leukemia	23	14	9	60.9% (38.5–80.3)
Acute lymphoblastic leukemia	6	3	3	50.0% (11.8–88.2)

(Continues)

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TABLE 1 | (Continued)

Category	Total	Success	Failure	Success rate (95% CI)
Hodgkin lymphoma	4	2	2	50.0% (6.8–93.2)
Myeloid neoplasms				
Myeloid neoplasms (total)	43	17	26	39.5% (25.0–55.6)
Acute myeloid leukemia	25	7	18	28.0% (12.1–49.4)
Chronic myelomonocytic leukemia	9	5	4	55.6% (21.2–86.3)
Myelodysplastic syndromes	5	3	2	60.0% (14.7–94.7)
Myeloproliferative neoplasms	4	2	2	50.0% (6.8–93.2)
Plasma cell neoplasms				
Plasma cell neoplasms (total)	41	24	17	58.5% (42.1–73.7)
Multiple myeloma	41	24	17	58.5% (42.1–73.7)

Note: Success rates are presented as percentages with 95% confidence intervals.
Abbreviation: CI, confidence interval.

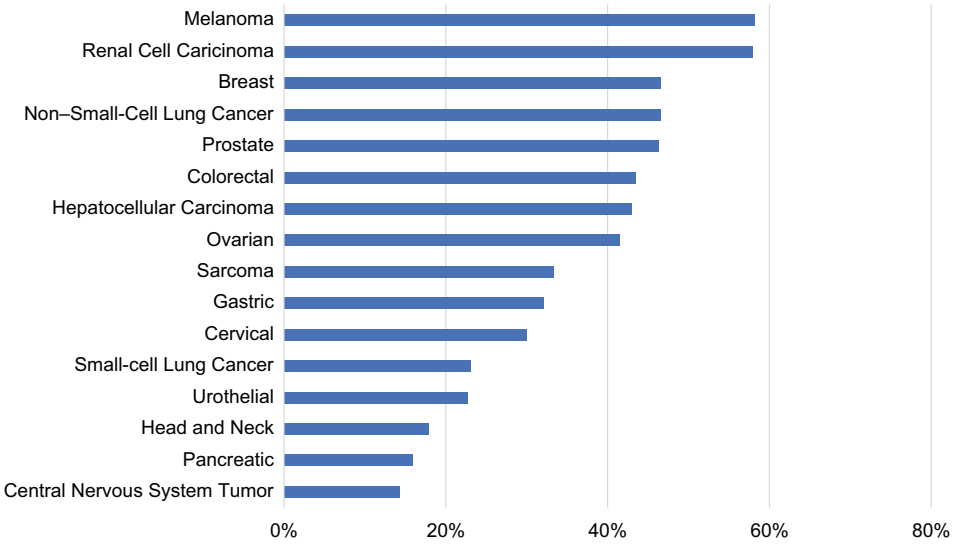

FIGURE 2 | Phase III success rates in solid tumors (tumor types with ≥ 10).

19 trials) and breast cancer (46.5%, 59 out of 127 trials). In contrast, the lowest success probabilities were observed in central nervous system tumors (14.3%, 2 out of 14 trials), followed by pancreatic cancer (15.8%, 3 out of 19 trials) and head and neck cancer (17.9%, 5 out of 28 trials) (Figure 2). The probability of success for hematologic malignancies was 60.9% (14 out of 23 trials) for chronic lymphocytic leukemia, 58.5% (24 out of 41 trials) for multiple myeloma, 33.3% (18 out of 54 trials) for non-Hodgkin lymphoma, and 28.0% (7 out of 25 trials) for acute myeloid leukemia (Figure 3).

Multivariable logistic regression analysis was performed to evaluate the associations between trial success and characteristics (overall model). The distributions of tumor type, biomarker-based patient selection, trial size, trial initiation period, and number of primary endpoints are presented in Table 2, and the results of the analysis are summarized in Table 3. Multivariable analysis revealed that biomarker-based patient selection was associated with trial success (OR 1.75, 95% CI 1.22–2.51; $p = 0.002$), as were trials initiated in or after 2012 (OR 1.36, 95% CI 1.02–1.82; $p = 0.035$) and trials with multiple primary endpoints (OR 1.68, 95% CI 1.09–2.60; $p = 0.019$). In contrast, trial size (large vs. small) and tumor type (hematologic vs. solid) were not significantly associated with trial success. For the overall model, the McFadden R^2 and Nagelkerke R^2 were 0.021 and 0.038, respectively.

In univariable logistic regression analyses stratified by therapeutic modality, chemotherapy was negatively associated with trial success (OR 0.48, 95% CI 0.34–0.70; $p = 0.0001$), whereas molecularly targeted therapies were positively associated with trial success (OR 1.43, 95% CI 1.08–1.88; $p = 0.012$). Immunotherapy, endocrine therapy, antibody–drug conjugates, and other therapeutic modalities were not significantly associated with trial success.

In analyses stratified by line of therapy, trials conducted in the advanced or metastatic setting were associated with higher success probabilities than those in neoadjuvant or adjuvant

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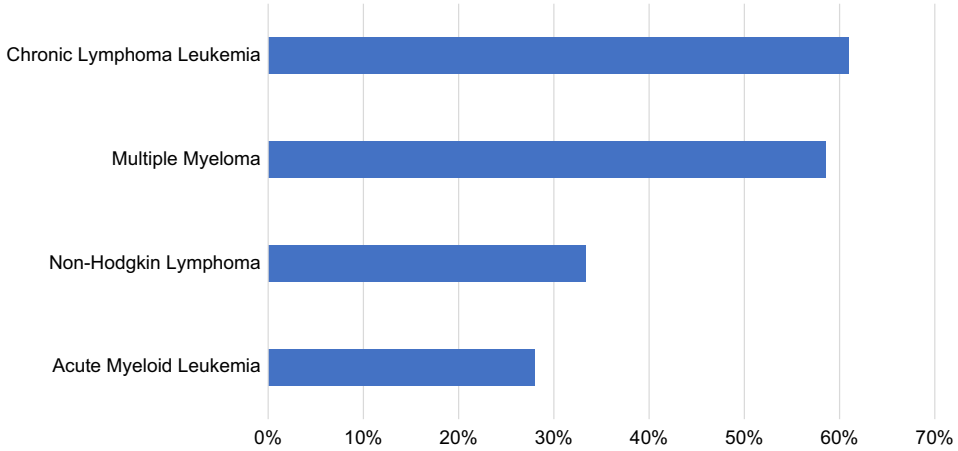

FIGURE 3 | Phase III success rates in hematologic malignancies (tumor types with ≥10).

settings for solid tumors (OR 1.57, 95% CI 1.02–2.43; $p=0.042$). In hematologic malignancies, trials conducted in the relapsed or refractory setting were associated with higher success probabilities than those in first-line settings (OR 1.97, 95% CI 1.07–3.63; $p=0.0287$).

In analyses stratified by primary endpoint, trials assessing OS (OR 0.52, 95% CI 0.39–0.70; $p<0.0001$) or EFS/DFS/RFS (OR 0.47, 95% CI 0.30–0.74; $p=0.001$) as the primary endpoint were negatively associated with trial success. In contrast, trials assessing PFS or TTP (OR 1.89, 95% CI 1.43–2.49; $p<0.0001$), response-based endpoints (OR 2.23, 95% CI 1.46–3.41; $p=0.0002$), or other endpoints (OR 3.68, 95% CI 1.53–8.84; $p=0.0037$) were positively associated with trial success.

4 | Discussion

In this study, we comprehensively analyzed Phase III trials of oncology drug therapies registered at ClinicalTrials.gov and characterized trial success probabilities and associated factors. Recent cross-therapeutic analyses have indicated that oncology remains a high-risk field for clinical development. In the present analysis, the overall success probability of Phase III trials in oncology was approximately 40%, confirming that the success rates in oncology remain lower than those observed in other therapeutic areas [7]. Previous studies have reported lower success probabilities for solid tumors than for hematologic malignancies [18, 20]. However, in this study, success probabilities were comparable between the two groups. The proportion of trials initiated in or after 2012 involving the use of novel therapeutic modalities, such as molecularly targeted therapies, immunotherapies, and antibody–drug conjugates, was 81% (254 out of 313 trials) for solid tumors and 85% (78 out of 92 trials) for hematologic malignancies, whereas the corresponding proportions before 2012 were lower (59% and 54%, respectively). In addition, the proportion of trials incorporating biomarker-based patient selection increased after 2012 for solid tumors (from 13% to 27%) and hematologic malignancies (from 2.5% to 12%). The narrowing difference in success probabilities between solid tumors and hematologic malignancies observed in this study may reflect advances in therapeutic modalities and the increased use of biomarker-based patient selection, particularly for solid tumors.

Among solid tumors, substantial heterogeneity in success probabilities was observed across tumor types, with particularly low success probabilities for central nervous system tumors and pancreatic cancers. These findings may be explained by tumor-specific biological challenges such as limited drug penetration across the blood–brain barrier and a lack of actionable therapeutic targets. In contrast, the higher success probabilities observed in melanoma and renal cell carcinoma possibly reflect recent advances in immunotherapy and molecularly targeted therapies over the past decade, such as immune checkpoint inhibitors and BRAF/MEK inhibitors combinations in melanoma, as well as immune checkpoint inhibitor-based combinations with tyrosine kinase inhibitors in renal cell carcinoma [21–23]. Among hematologic malignancies, relatively high success probabilities were observed in chronic lymphocytic leukemia and multiple myeloma, whereas lower success probabilities were observed in non-Hodgkin lymphoma and acute myeloid leukemia. Compared with solid tumors, hematologic malignancies had limited overall variability in success probabilities across tumor types.

Multivariable analyses revealed that biomarker-based patient selection was significantly associated with trial success, consistent with the ongoing evolution of precision oncology. These findings are consistent with previous reports suggesting that molecularly selected patient populations can improve the likelihood of success in Phase III trials [18, 24, 25]. Biomarker-driven development strategies may contribute to improved clinical trial success probabilities; however, they may also limit the market size by restricting the eligible patient population. For example, biomarkers, such as PD-L1 expression, HER2-low status, and HRD scores, have been discussed as enrichment factors rather than absolute response predictors, allowing for the observation of treatment effects beyond biomarker-defined subgroups [26]. Efficacy in biomarker-negative populations complicates commercial decisions on indication scope and development strategy [27–29]. Therefore, the present study characterizes development strategies from the perspective of success probability, providing an objective view of the factors associated with trial success rather than prescribing specific development strategies.

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TABLE 2 | Characteristics of included trials ($n = 824$).

Category	Variable	Overall, *n*
Tumor type	Solid tumors	653
	Hematologic malignancies	171
Biomarker incorporation	Present	160
	Absent	664
Trial size[a]	Large (≥481)	418
	Small (<481)	406
Initiation period	Before 2012	419
	2012 or later	405
Primary multiplicity	Single primary endpoint	726
	Multiple primary endpoints	98
Treatment modality[b]	Chemotherapy	164
	Molecular targeted drug	396
	Immunotherapy	155
	Endocrine therapy	41
	Antibody–drug conjugate (ADC)	24
	Other	44
Treatment line (solid tumors)	Neo/adjuvant	107
	Advanced or metastatic	546
Treatment line (hematologic malignancies)	First-line	88
	Relapsed/refractory	83
Primary endpoint[c,d]	OS	324
	PFS/TTP	367
	EFS/DFS/RFS	103
	Response-based endpoint	102
	Other	26

Abbreviations: DFS, disease-free survival; EFS, event-free survival; OS, overall survival; PFS, progression-free survival; RFS, relapse-free survival; TTP, time to progression.
[a]Trial size was dichotomized using the median number of enrolled patients (481).
[b]Other treatment modalities included therapies that could not be classified into the predefined categories.
[c]Some trials included more than one primary endpoint; therefore, the number of primary endpoints is not the sum of the total number of trials.
[d]Other primary endpoints included pharmacokinetics (PK), pharmacodynamics (PD), hormone levels, bone metastasis-free survival (BMFS), quality-of-life (QOL), and other non-standard or insufficiently specified endpoints.

The higher success probabilities observed in trials initiated after 2012 may reflect advances in immunotherapies, including the approval of ipilimumab in 2011 as the first immune checkpoint inhibitor and the broader adoption of biomarker-driven development strategies. In the main analysis, trials with multiple primary endpoints were associated with success. However, in a sensitivity analysis limited to trials with a single primary endpoint, the presence or absence of biomarkers and time of trial initiation were significantly associated with trial success, similar to the primary analysis results. These results suggest that the number of primary endpoints is not a general determinant of trial success.

Analyses stratified by therapeutic modality showed that chemotherapy was negatively associated with trial success, whereas molecularly targeted therapies were positively associated. Molecularly targeted therapies, acting on specific molecular abnormalities, may achieve clearer treatment effects when evaluated in selected patient populations. In contrast, chemotherapy exerts non-specific cytotoxic effects on tumor and normal cells and has been a standard treatment modality across diverse tumor types, making it challenging for Phase III trials to demonstrate incremental benefits beyond the existing standards of care. These results suggest that advances in therapeutic modalities and selective treatment strategies are associated with higher trial success probabilities. Regarding the line of therapy, trials conducted in later lines of treatment were more likely to succeed, potentially because limited therapeutic options in comparator arms facilitated the detection of treatment effects and the achievement of primary endpoints.

Analyses stratified by the primary endpoint type indicated lower success probabilities for trials involving the use of OS or EFS/DFS/RFS, whereas trials involving PFS/TTP or response-based endpoints showed higher success probabilities. The OS and EFS/DFS/RFS reflect long-term outcomes and usually require prolonged follow-up, making them more susceptible to confounding factors. In contrast, endpoints such as PFS and response can be assessed over shorter time frames, which may increase the likelihood of trial success. These findings highlight the significant influence of the primary endpoint selection on Phase III trial outcomes. However, surrogate endpoints such as PFS and response do not necessarily translate into improvements in long-term outcomes [30]. Therefore, when selecting primary endpoints for Phase III trials, it is essential to consider the likelihood of trial success and clinical relevance, given disease prognosis and the follow-up duration.

Collectively, the present results indicate that Phase III trial success in oncology is influenced by drug efficacy and strategic decision-making during development. The tumor-specific differences in success probabilities observed in this study suggest that development risk can vary significantly across tumor types, even for the same therapeutic modality, underscoring the relevance of tumor-specific considerations in development planning. Trial design factors, including biomarker-based patient selection, line of therapy, and primary endpoint selection, should be carefully considered from the early developmental stages, as they may directly affect the likelihood of success in Phase III trials. The quantitative characterization of success probabilities and the associated factors provided in this study may serve as a valuable reference for prioritizing development strategies and allocating limited resources in future oncology drug development programs.

This study has some limitations. Restricting analysis to trials registered at ClinicalTrials.gov may introduce a reporting bias, excluding unregistered trials and trials with unreported results. In addition, reliance on information available at ClinicalTrials.gov limited the adjustment for detailed trial design

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TABLE 3 | Factors associated with trial success in Phase III oncology trials.

Category	Variable	Main analysis OR (95% CI)	*p*	Sensitive analysis OR (95% CI)	*p*	Consistency
Over model	Biomarker (present vs. absent)	1.75 (1.22–2.51)**	0.00244	1.66 (1.13–2.42)**	0.00895	Yes
	Trial size (large vs. small)	1.15 (0.86–1.54)	0.34601	1.07 (0.79–1.46)	0.65387	Yes
	Tumor type (hematologic vs. solid)	1.33 (0.93–1.90)	0.11343	1.27 (0.87–1.84)	0.21920	Yes
	Initiation period (after 2012 vs. before 2012)	1.36 (1.02–1.82)*	0.03485	1.45 (1.10–2.04)*	0.01015	Yes
	Primary Multiplicity (Multiple vs. Single)	1.68 (1.09–2.60)*	0.01863	—	—	—
Treatment modality	Chemotherapy	0.48 (0.34–0.70)***	0.0001	—	—	—
	Molecular targeted drug	1.43 (1.08–1.88)*	0.0117	—	—	—
	Immunotherapy	1.16 (0.82–1.65)	0.402	—	—	—
	Endocrine therapy	1.25 (0.67–2.35)	0.48	—	—	—
	Antibody–drug conjugate (ADC)	1.31 (0.58–2.96)	0.512	—	—	—
	Other	0.66 (0.35–1.25)	0.201	—	—	—
Treatment line	Solid: Advanced/Metastatic vs. Neo/Adjuvant	1.57 (1.02–2.43)*	0.042	—	—	—
	Hematologic: Relapsed/ Refractory vs. First line	1.97 (1.07–3.63)*	0.0287	—	—	—
Primary endpoint	OS	0.52 (0.39–0.70)***	<0.0001	—	—	—
	PFS/TTP	1.89 (1.43–2.49)***	<0.0001	—	—	—
	EFS/DFS/RFS	0.47 (0.30–0.74)**	0.001	—	—	—
	Response	2.23 (1.46–3.41)***	0.0002	—	—	—
	Other	3.68 (1.53–8.84)**	0.0037	—	—	—

Note: Sensitivity analysis was restricted to trials with a single primary endpoint ($n = 726$), and primary endpoint multiplicity was not included as a covariate. Consistency was defined as concordance in statistical significance between the main and sensitivity analysis. Odds ratios and 95% confidence intervals were estimated using logistic regression analysis. The overall model included biomarker status, trial size (dichotomized at a median enrollment of 481 participants), tumor type, and initiation period. The treatment modality, treatment line, and each of the five primary endpoints (OS, PFS/TTP, EFS/DFS/RFS, Response, and Other) were analyzed separately for subgroup analyses. Statistical significance is indicated as * ($p < 0.05$), ** ($p < 0.01$), and *** ($p < 0.001$). A two-sided p value < 0.05 was considered statistically significant. Abbreviations: CI, confidence interval; OR, odds ratio.

features and potential confounding factors, resulting in the possibility of residual confounding. This study focused exclusively on Phase III trials and did not evaluate early-stage development or selection bias. Furthermore, trial success was defined solely based on the achievement of primary endpoints, without fully capturing the magnitude or clinical relevance of the treatment effects or directly reflecting regulatory approval or patient access in clinical practice. Consequently, trial success, as defined in this study, may not necessarily correspond to therapeutic adoption. Additionally, substantial heterogeneity across trials, including differences in study design, patient populations, and endpoint definitions, may not be fully captured in the available data. Despite these limitations, this study provides a comprehensive and multifaceted evaluation of Phase III trial success probabilities and associated factors in oncology.

This study comprehensively analyzed Phase III trials of oncology drug therapies, characterizing trial success probabilities and associated factors. Among solid tumors, clear differences in success probabilities were observed across tumor types, with particularly low success probabilities in central nervous system tumors and pancreatic cancers. Trial success was associated with biomarker-based patient selection, a contemporary development environment, and differences in trial design. Higher success probabilities were observed in trials of molecularly targeted therapies, later-line therapies, and those with short-term primary endpoints. These findings provide quantitative evidence to inform decision-making and trial design in late-stage oncology drug development for precision oncology.

Author Contributions

K.Y. wrote the manuscript; K.Y. and H.M. designed the research; K.Y., A.I., and H.M. performed the research; K.Y. analyzed the data.

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The authors have nothing to report.

Conflicts of Interest

K.Y. is an employee of Genmab K.K. H.M. has received advisory fees from Takeda Pharmaceutical Co. Ltd., Sawai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Mochida Pharmaceutical Co. Ltd., Tsumura & Co., Tensegrity Pharma, Seagen Inc., CMIC Holdings Co. Ltd., IQVIA Inc., MI Force Inc., One Capital Inc., and Vista Health. In addition, he owns stock acquisition rights in Tensegrity Pharma. All other authors declare no conflicts of interest.

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