Enrollment Success, Factors, and Prediction Models in Cancer Trials (2008-2019)

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ABSTRACT

PURPOSE To investigate the enrollment success rate of cancer clinical trials conducted in 2008-2019 and various factors lowering the enrollment success rate.

METHODS This is a cross-sectional study with clinical trial information from the largest registration database ClinicalTrials.gov. Enrollment success rate was defined as actual enrollment greater or equal to 85% of the estimated enrollment goal. The association between trial characteristics and enrollment success was evaluated using the multivariable logistic regression.

RESULTS A total of 4,004 trials in breast, lung, and colorectal cancers were included. The overall enrollment success rate was 49.1%. Compared with 2008-2010 (51.5%) and 2011-2013 (52.1%), the enrollment success rate is lower in 2014-2016 (46.5%) and 2017-2019 (36.4%). Regression analyses found trial activation year, phase I, phase I/phase II, and phase II (*v* phase III), sponsor agency of government (*v* industry), not requiring healthy volunteers, and estimated enrollment of 50-100, 100-200, 200, and >500 (*v* 0-50) were associated with a lower enrollment success rate ($P < .05$). However, trials with placebo comparator, ≥5 locations (*v* 1 location), and a higher number of secondary end points (eg, ≥5 *v* 0) were associated with a higher enrollment success rate ($P < .05$). The AUC for prediction of the final logistic regression models for all trials and specific trial groups ranged from 0.69 to 0.76.

CONCLUSION This large-scale study supports a lower enrollment success rate over years in cancer clinical trials. Identified factors for enrollment success can be used to develop and improve recruitment strategies for future cancer trials.

ACCOMPANYING CONTENT

Appendix

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INTRODUCTION

Cancer is a leading cause of mortality and the main source for disease burden globally.[1] Innovations from clinical trials play a key role in the treatment of cancer. Through clinical trials, the innovations can be evaluated rigorously before possible approval and use in clinical practice, to cure the disease, prolong patient survival, and/or improve quality of life.[2] At the same time, eligible patients enrolled in the trials could have a chance to experience clinical benefits from the newest innovations before the regulatory approval for application in practice.

Despite the importance of cancer trials, ensuring success of patient enrollment is challenging. Studies showed nearly 35% of phase III cancer trials were closed because of insufficient enrollment.[3,4] Another study found that 18% of 4,269 phase I-III cancer trials were classified as slow enrolling, defined as less than two participants per year.[5] Accordingly, insufficient enrollment is a major barrier to progress in clinical trials, causing a waste of both time and money, and ultimately delaying promising treatments for patients. In fact, there are sufficient number of patients eligible for participation in clinical trials but only a few of them do so.[6]

Therefore, we conduct this large-scale, cross-sectional study investigating the prevalence of enrollment success rate and its factors among clinical trials for cancers. From this work, we expect that trialists including oncologists, researchers, policymakers, and stakeholders could take more attention to enrollment success in trials for cancers, especially considering identified factors for improving enrollment in future trials.

METHODS

Data Source and Setting

This cross-sectional study was conducted based on ClinicalTrials.gov, the largest clinical trial database currently run

CONTEXT

Key Objective

To investigate the prevalence of enrollment success rate, how its trend has been over time, and what factors associated with the enrollment success rate are in cancer clinical trials.

Knowledge Generated

The enrollment success rate was 49.1% in 2008-2019 with a decreasing tendency over time. A set of risk and preventive factors were found for the enrollment success rate on the basis of multivariable regression models with good prediction accuracy.

Relevance

The low and decreasing enrollment success rate should receive a close attention by oncologists, researchers, policymakers, and other stakeholders. Our analysis leads to a prediction model on enrollment success based on the trial-level information collected prior to trial activation; the variables that are strongly associated with the enrollment success rate and meanwhile are manipulable can be used by the trial investigators as actionable strategy to improve the enrollment success rate in cancer clinical trials.

by the US National Library of Medicine. ClinicalTrials.gov was established in 2000. The database experienced a major expansion after the Food and Drug Administration Amendment Act (FDAAA) was executed in 2007, which required all drug, biological, and device trials, besides phase I clinical trials, to be registered into the ClinicalTrials.gov database.[7] This publicly accessible web-based registry comprises a full-scale baseline characteristic of a clinical trial, including recruiting status, disease condition, phase of the study, eligibility criteria, location, etc, allowing us to conduct such a study as generalizable as possible.

Data Extraction and Trial Selection

To extract all needed trial information from the website, we separated the progress into two parts using R (Version 3.6.1). First, we used an R library (rclinicaltrials[8]) to download all possible information. During this process, however, the extracted data did not contain two main variables, the number of patients in estimated enrollment and the actual enrollment, for calculating enrollment success rate, the outcome of this study. Therefore, we conducted the second part of the extraction using web scraping methods in R to extract both variables.

Data extraction was completed on June 6, 2022, on the basis of the trial activation year of 2008-2019. The selection for the start year (2008) was in concordance with the FDAAA introduced in 2007, so that trials started after 2008 should have completer and more robust information as recorded in the registration website. The selection for the ending year (2019) was given that many trials started after 2019 are still ongoing, without enrollment completion; particularly, including those impacted by the COVID-19 pandemic.[9-12] Breast, lung, and colorectal cancers were selected according to their disease burden—all of them are of the top five cancer types with the highest mortality rate and disability-adjusted life-years among all cancer types in the globe.[1] Exclusion criteria were trials with completion date of 2020 and afterward; trials with no information in the Study Information dataframe, which contains key variables including trial activation date, number of patients in estimated enrollment, and actual enrollment; trials whose study type is not interventional; and trials with undefined enrollment names and unknown (marked as NA) phase status.

Outcome

Our outcome is enrollment success. It is a binary variable, defined as actual patient enrollment is ≥85% of the estimated patient enrollment goal of the trial (Appendix Table A1, online only). The rationale for using 85% as the cutoff value is that we could not conclude enrollment unsuccessful if the actual enrollment number were below the estimated number by a few participants. The cutoff of 85% gives the outcome definition with an acceptable margin to avoid the mentioned issue. According to the definition, we calculated the prevalence of enrollment success as the number of trials with enrollment success divided by the total number of included trials.

Exposure

To investigate the factor for enrollment success, the following trial characteristics were used as exposure: trial activation year, cancer type, number of conditions, phase, intervention type, number of interventions, type of intervention drug, lead sponsor agency, number of sponsors, eligibility of healthy volunteers, minimum age and maximum age, type of arms, number of arms, number of primary outcomes, number of secondary outcomes, number of countries, number of locations, and number of patients in estimated enrollment. In addition, recruitment status was extracted.

For the lead sponsor agency, the website has four categories: NIH, US Fed, industry, and other. We reclassified the categories by combining NIH and US Fed as government, and subdividing other into research institute and others by searching for keywords ("University," "Center," "Institute," "Group," "Hospital," and "Network") that could distinguish most of the research institutes from all the sponsors. For the type of intervention drug, we chose the top five most frequent types in the database.

Statistical Analysis

The association of trial characteristics with enrollment success (yes or no) was first evaluated via univariate analyses, using the chi-square test for categorical variables and the Kruskal-Wallis test for continuous variables. The association was further evaluated via the multivariable logistic regression model, adjusted for all the exposure variables mentioned above. The measure is the odds ratio: the point estimate and 95% CIs <1 indicate risk factors lowering the enrollment success rate. The above model was conducted for all included trials, trials by cancer type (breast cancer, lung cancer, and colorectal cancer) and by phase (phase I, phase II, phase III), as well as trials for drugs only. Last, the prediction accuracy for each model was measured by the area under the receiver operating curve (AUC).

RESULTS

From a total of 24,886 trials identified in the database for breast, lung, and colorectal cancers, 4,004 trials were included (Fig 1). Appendix Table A2 presents the details of trial characteristics. Among all trials, 37.2%, 32.6%, and 15.5%, respectively, were for breast, lung, and colorectal cancers only, the rest were the trials for multiple tumor types including any of the three cancers; 26%, 44.2%, and 13.7% were phase I, phase II, and phase III trials, respectively; 11.9%, 32.0%, 41.5%, and 14.6% were mainly sponsored by government, research institutes, industry, and others, respectively. Appendix Tables A3 and A4 present the characteristics by cancer type and by phase, respectively; Appendix Table A5 is for drug trials.

Prevalence of Enrollment Success Rate

The prevalence and the trend of enrollment success rate are shown in Figure 2. The overall enrollment success rate for all included trials was 49.1%. Compared with 2008-2010 (51.5%) and 2011-2013 (52.1%), enrollment success rate was lower in 2014-2016 (46.5%) and 2017-2019 (36.4%). The decreasing trend exists regardless of trials by cancer type and lead sponsor agency, as well as in phase I, phase II, biological, drug, and radiation trials, respectively. The enrollment success rate in phase III trials remained stable over time: 63.9% in 2008-2020, 64.1% in 2011-2013, 69.2% in 2013-2016, and 60.6% in 2017-2019. The rate in trials sponsored by government was low: 37.9% in all years, and 43.0%, 35.7%, 33.3%, and 21.7% in 2008-2010, 2011-2013, 2014-2016, and 2017-2019, respectively.

Factors for Enrollment Success Rate

Table 1 presents the multivariable logistic regression results on the associations between trial characteristics and enrollment success in all trials and trials for breast, lung, and colorectal cancers; Appendix Table A6 presents the results in phase I, phase II, phase III, and drug trials. For all trials, risk factors were trial activation year; phase I, phase I/phase II, phase II, and phase II/phase III trials, compared with phase III trials; radiation trials; trials with two interventions, compared with trials with 1 intervention; lead sponsor agencies of government and other, compared with industry; trials not requiring healthy volunteers; trials with patients recruited from an unknown number of countries, compared with one country; and estimated enrollment of 50-100, 100-200, 200-500, and >500 patients, compared with 0-50 patients. The risk factors of trial activation year, phase I, phase I/phase II, and phase II, sponsor agency of government, not requiring healthy volunteers, and estimated enrollment of 50-100, 100-200, 200, and >500 patients were still found in majorities of trials by cancer type and phase (I, II, III; Appendix Table A6) as well as drug trials (Table 1; Fig 3).

Preventive factors associated with a higher enrollment success rate in all trials were trials for colorectal cancer; trials for device; randomized trials, compared with non-randomized trials; trials with active comparator and placebo comparator arms; trials with ≥3 arms, compared with two arms; trials with two and ≥5 secondary end points, compared with 0 secondary end points; and trials with ≥5 locations, compared with one location (Table 1). The factors of trials with placebo comparator, ≥5 locations, and trials with ≥5 secondary end points were also found in majorities of trials by cancer type and phase (I, II, III; Appendix Table A6) as well as drug trials (Table 1; Fig 3).

Model Prediction

The prediction score, AUC, of the logistic regression model for all trials was 0.69. The AUC for breast, lung, colorectal, phase I, phase II, phase III, and drug trials was 0.71, 0.74, 0.74, 0.72, 0.69, 0.76, and 0.70, respectively.

DISCUSSION

This is a large-scale, cross-sectional study investigating the prevalence of enrollment success rate and its risk and preventive factors among clinical trials for breast, lung, and colorectal cancers—the ones accounting for the highest disease burden among all cancer types. Overall, the study estimated the enrollment success rate as <50% among all the included trials in 2008-2019; specifically, the trend presented was decreasing over time, with 36.39% in 2017-2019. Also, the study identified risk and preventive factors for enrollment success rate. Important risk factors included trial activation year, phase I, phase I/phase II, and phase II (*v* phase III), sponsor agency of government (*v* industry), not requiring healthy volunteers, and estimated enrollment of 50-100, 100-200, 200, and >500 (*v* 0-50); preventive factors

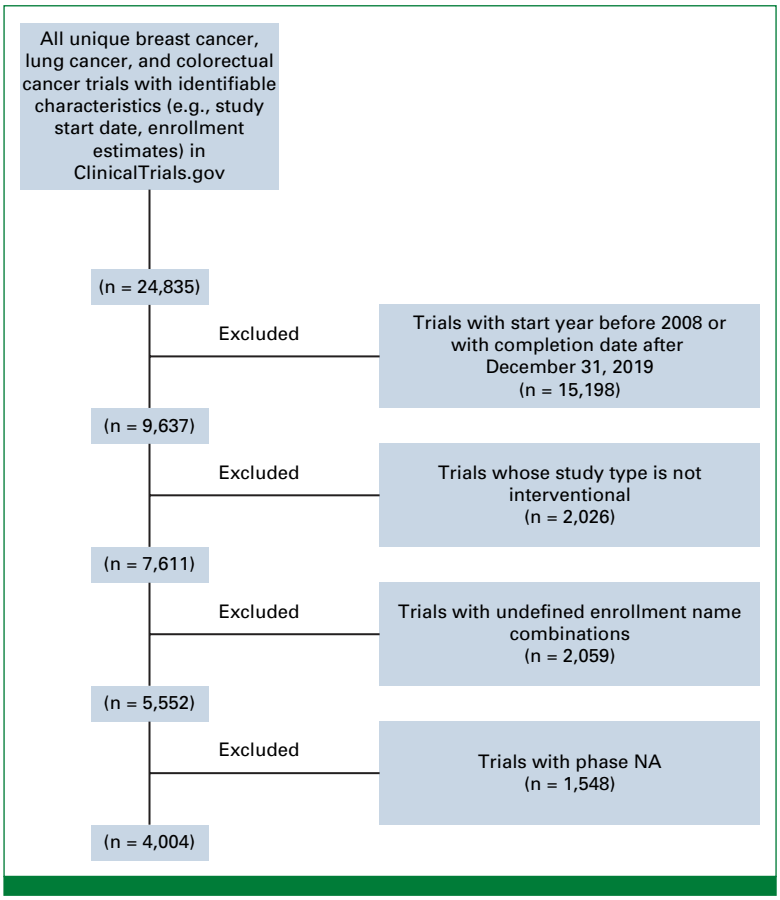

FIG 1. Flowchart of trial selection. NA, not applicable.

included placebo comparator, ≥5 locations (*v* one location), and a higher number of secondary end points (eg, ≥5 *v* 0). The final regression models for investigating the above associations present a decent prediction, with AUC in all trials and trials by characteristic ranging from 0.69 to 0.76.

Our study highlights the undesirable enrollment success rate in clinical trials for cancers, especially its decreasing tendency. Of note, these findings were based on the trials before the start of COVID-19 pandemic. Therefore, we hold the concern about enrollment success rate in the currently ongoing trials, especially given the published evidence supporting the difficulties in trial enrollment due to the COVID-19 pandemic.[9-12] Continuous investigations on enrollment success are needed whenever more robust data could be available for the trials started or completed during the COVID-19 years. Nevertheless, among the results for different trials, the enrollment success rate in phase III trials was high—ranging from 60.6% to 69.2% throughout the years of 2008-2019—which echoes the results in two previous studies on phase III trials in the same years of 1993-2002: 63% of enrollment success rate in 248 trials sponsored by the US National Cancer Institute,[4] and 66% in 238 trials of the US Clinical Trials Cooperative Groups.[3]

Regarding risk factors, specifically, the lower enrollment success rates in phase I and II trials should be of concern. This is given that the trials in both phases are the cornerstone of developing phase III trials from which, in general, the innovations could be considered for application in real-world practice. As such, enough patient enrollment ensures the rigor before being considered for and evaluated in phase III trials. Furthermore, we are surprised to see the difference in the enrollment success rate between lead sponsor agencies. Specifically, the rate in government-sponsored trials is very low, decreasing from 43.0% in 2008-2010 to 21.7% in 2017-2019. Such results should be scrutinized by the public, as the investment from government and the decision for such investment are made in collaboration with well-recognized scholars.

Last, the estimated enrollment of over 50 patients is a risk factor; as more patients are expected to be enrolled, there would be higher cost and difficulty in trial conduction. In addition, such results in the majority of these models suggest a higher number of estimated patients leads to a higher risk that the trial could not achieve the enrollment target number. In addition to the above risk factors, structural and clinical barriers have been well studied.[13,14] For example, a trial might not be available at the collaborating centers; patients may be ineligible for an available trial; and enrollment rates are different between academic and community settings.[13] Other common causes of enrollment failure are narrow eligibility criteria, overestimate of

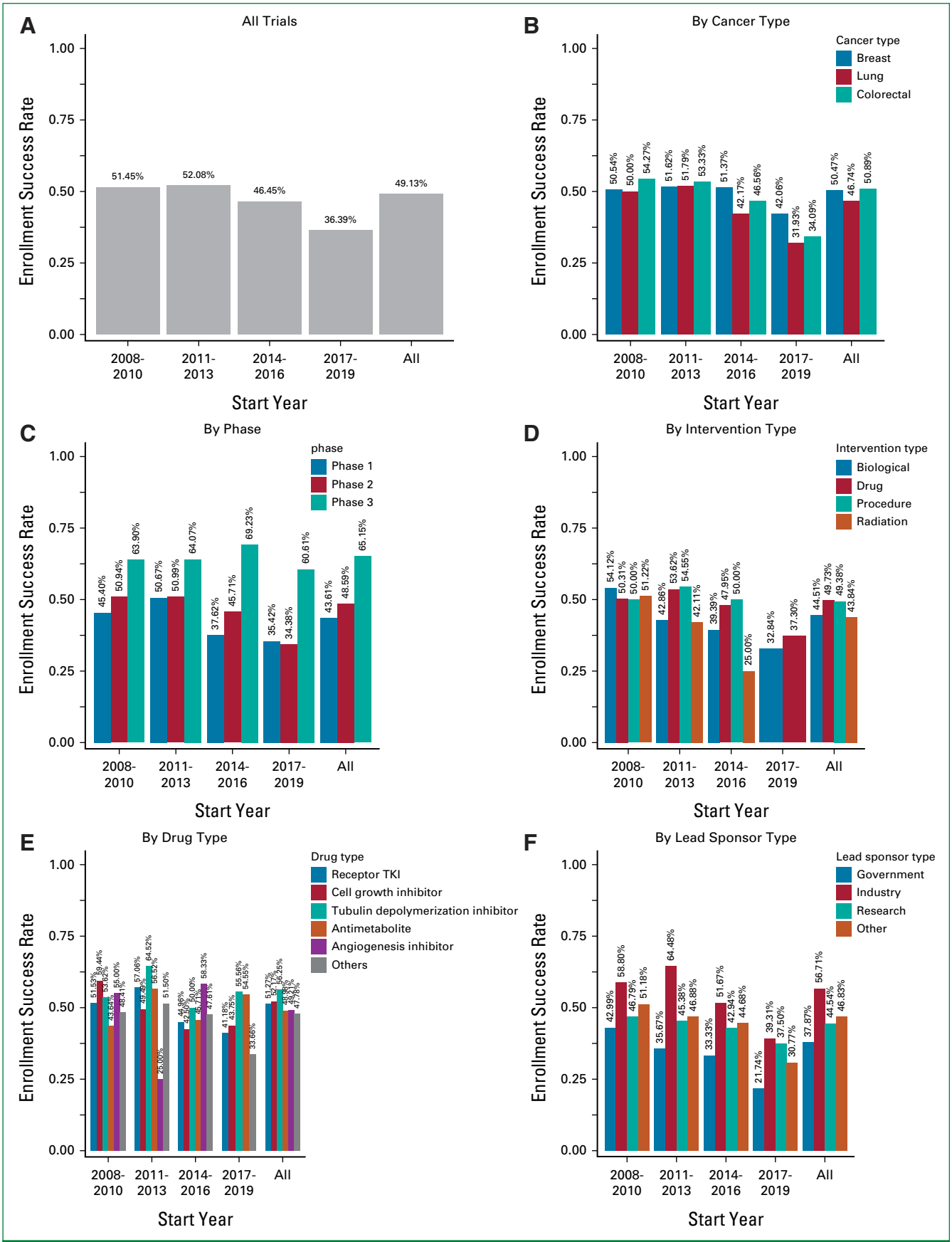

FIG 2. Enrollment success rate in clinical trials: (A) all trials, (B) by cancer type, (C) by phase, (D) by intervention type, (E) by drug type, and (F) by lead sponsor type. TKI, tyrosine kinase inhibitor.

TABLE 1. Factors for Enrollment Success Rate in All Included Clinical Trials and Trials by Cancer Type

Characteristic	All Trials, OR (95% CI)	Breast Cancer Trials, OR (95% CI)	Lung Cancer Trials, OR (95% CI)	Colorectal Cancer Trials, OR (95% CI)
Model prediction: AUC	0.69	0.71	0.74	0.74
Trial activation year	0.94 (0.91 to 0.96)[a]	0.95 (0.92 to 0.99)[a]	0.93 (0.88 to 0.97)[a]	0.88 (0.82 to 0.93)[a]
Cancer type				
Breast *v* no	1.19 (0.99 to 1.43)	NA	NA	NA
Lung *v* no	1.02 (0.85 to 1.22)	NA	NA	NA
Colorectal *v* no	1.26 (1.02 to 1.55)[a]	NA	NA	NA
No. of conditions				
1	1.00	1.00	1.00	1.00
2	0.82 (0.67 to 1.00)	1.07 (0.77 to 1.49)	0.83 (0.58 to 1.20)	0.59 (0.34 to 1.02)
3-4	0.79 (0.63 to 1.00)	0.90 (0.63 to 1.29)	0.67 (0.44 to 1.01)	1.43 (0.80 to 2.55)
≥5	1.04 (0.79 to 1.36)	1.12 (0.79 to 1.60)	1.67 (1.09 to 2.56)[a]	1.49 (0.87 to 2.57)
Phase				
I	0.37 (0.26 to 0.52)[a]	0.36 (0.21 to 0.61)[a]	0.36 (0.18 to 0.71)[a]	0.14 (0.06 to 0.35)[a]
I/II	0.34 (0.24 to 0.49)[a]	0.25 (0.14 to 0.45)[a]	0.38 (0.19 to 0.77)[a]	0.11 (0.04 to 0.29)[a]
II	0.41 (0.31 to 0.55)[a]	0.37 (0.23 to 0.58)[a]	0.40 (0.22 to 0.73)[a]	0.19 (0.09 to 0.43)[a]
II/III	0.47 (0.27 to 0.81)[a]	0.36 (0.15 to 0.86)[a]	0.55 (0.20 to 1.53)	0.29 (0.05 to 1.54)
III	1.00	1.00	1.00	1.00
IV	0.67 (0.44 to 1.04)	0.76 (0.38 to 1.52)	0.72 (0.27 to 1.98)	0.46 (0.14 to 1.51)
Intervention type				
Behavioral *v* no	0.95 (0.54 to 1.66)	0.59 (0.26 to 1.30)	1.93 (0.59 to 6.24)	2.95 (0.56 to 15.62)
Biological *v* no	0.86 (0.68 to 1.10)	0.79 (0.53 to 1.20)	0.85 (0.54 to 1.34)	0.71 (0.41 to 1.24)
Device *v* no	1.65 (1.04 to 2.62)[a]	2.84 (1.31 to 6.17)[a]	1.56 (0.63 to 3.90)	0.45 (0.13 to 1.54)
Diagnostic test *v* no	1.74 (0.37 to 8.15)	0.68 (0.06 to 7.16)	3.06 (0.34 to 27.59)	NA
Drug *v* no	0.85 (0.66 to 1.10)	0.86 (0.58 to 1.28)	0.93 (0.58 to 1.48)	0.80 (0.41 to 1.53)
Genetic *v* no	0.78 (0.29 to 2.12)	0.92 (0.21 to 3.98)	1.39 (0.17 to 11.28)	0.77 (0.07 to 8.65)
Procedure *v* no	1.15 (0.85 to 1.55)	1.24 (0.80 to 1.93)	1.36 (0.74 to 2.48)	0.39 (0.17 to 0.90)
Radiation *v* no	0.67 (0.49 to 0.92)[a]	0.84 (0.49 to 1.44)	0.67 (0.41 to 1.09)	1.16 (0.42 to 3.21)[a]
No. of interventions				
1	1.00	1.00	1.00	1.00
2	0.74 (0.61 to 0.89)[a]	0.75 (0.56 to 1.02)	0.71 (0.49 to 1.01)	0.65 (0.40 to 1.05)
≥3	0.81 (0.65 to 1.02)	0.82 (0.58 to 1.17)	0.72 (0.46 to 1.11)	0.67- (0.38 to 1.17)
Type of intervention drug				
Receptor TKI *v* no	1.08 (0.87 to 1.34)	1.05 (0.74 to 1.48)	1.39 (0.95 to 2.03)	1.43 (0.66 to 3.11)
Cell growth inhibitor *v* no	1.21 (0.93 to 1.57)	1.42 (0.85 to 2.39)	1.23 (0.80 to 1.91)	1.16 (0.58 to 2.32)
Tubulin depolymerization inhibitor *v* no	1.12 (0.88 to 1.43)	1.29 (0.89 to 1.86)	1.00 (0.66 to 1.51)	NA
Antimetabolite *v* no	0.92 (0.71 to 1.18)	1.04 (0.63 to 1.70)	1.05 (0.68 to 1.63)	0.95 (0.53 to 1.68)

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TABLE 1. Factors for Enrollment Success Rate in All Included Clinical Trials and Trials by Cancer Type (continued)

Characteristic	All Trials, OR (95% CI)	Breast Cancer Trials, OR (95% CI)	Lung Cancer Trials, OR (95% CI)	Colorectal Cancer Trials, OR (95% CI)
Angiogenesis inhibitor *v* no	1.34 (0.97 to 1.84)	1.25 (0.66 to 2.36)	2.06 (1.14 to 3.71)[a]	1.09 (0.61 to 1.95)
Lead sponsor agency				
Government	0.60 (0.45 to 0.78)[a]	0.74 (0.47 to 1.15)	0.36 (0.22 to 0.58)[a]	0.36 (0.18 to 0.73)[a]
Research institutes	0.82 (0.67 to 1.01)	0.81 (0.57 to 1.13)	0.66 (0.45 to 0.98)[a]	0.91 (0.55 to 1.52)
Industry	1.00	1.00	1.00	1.00
Others	0.78 (0.61 to 0.99)[a]	0.78 (0.54 to 1.14)	0.60 (0.37 to 0.96)[a]	0.71 (0.41 to 1.22)
No. of sponsors: >1 *v* 1	0.91 (0.79 to 1.06)	1.09 (0.86 to 1.39)	0.75 (0.57 to 0.99)[a]	1.04 (0.72 to 1.50)
Eligibility of healthy volunteers: No *v* yes	0.57 (0.36 to 0.91)[a]	0.53 (0.27 to 1.06)	0.99 (0.33 to 2.99)	0.16 (0.04 to 0.61)[a]
Eligibility of minimum age, years				
0-18	1.00	1.00	1.00	1.00
18-70	0.71 (0.43 to 1.16)	3.03 (0.24 to 37.84)	2.41 (0.40 to 14.40)	0.44 (0.13 to 1.50)
>70	0.81 (0.32 to 2.05)	1.04 (0.47 to 2.33)	0.79 (0.27 to 2.31)	0.31 (0.04 to 2.44)
Eligibility of maximum age, years: >70 *v* 0-70	0.79 (0.51 to 1.22)	1.33 (0.73 to 2.42)	0.51 (0.12 to 2.12)	0.76 (0.15 to 3.77)
Allocation				
Randomized	1.32 (1.01 to 1.73)[a]	1.42 (0.91 to 2.20)	1.42 (0.85 to 2.39)	1.19 (0.61 to 2.32)
Nonrandomized	1.00	1.00	1.00	1.00
Not provided	1.32 (0.95 to 1.83)	1.11 (0.65 to 1.89)	1.50 (0.79 to 2.84)	1.84 (0.89 to 3.81)
Type of arm				
Experimental *v* no	1.00 (0.74 to 1.35)	0.91 (0.57 to 1.44)	1.10 (0.59 to 2.07)	0.72 (0.34 to 1.50)
Active comparator *v* no	1.33 (1.05 to 1.69)[a]	1.13 (0.77 to 1.65)	1.55 (0.98 to 2.46)	1.71 (0.95 to 3.08)
Placebo comparator *v* no	1.55 (1.18 to 2.04)[a]	1.37 (0.88 to 2.13)	2.21 (1.27 to 3.84)[a]	1.07 (0.51 to 2.25)
No. of arms				
0	0.61 (0.33 to 1.12)	0.88 (0.32 to 2.43)	0.68 (0.20 to 2.29)	0.30 (0.07 to 1.22)
1	0.69 (0.48 to 1.01)	0.82 (0.45 to 1.53)	0.64 (0.32 to 1.30)	0.43 (0.18 to 1.00)
2	1.00	1.00	1.00	1.00
≥3	1.24 (1.00 to 1.54)[a]	1.48 (1.03 to 2.12)[a]	1.26 (0.85 to 1.86)	1.11 (0.64 to 1.93)
No. of primary end points				
1	1.00	1.00	1.00	1.00
>2	0.87 (0.71 to 1.07)	0.66 (0.48 to 0.90)[a]	1.21 (0.83 to 1.76)	1.25 (0.75 to 2.08)
≥3	1.21 (0.95 to 1.55)	1.41 (0.96 to 2.08)	1.11 (0.71 to 1.73)	0.88 (0.44 to 1.74)
No. of secondary end points				
0	1.00	1.00	1.00	1.00
1	1.27 (0.98 to 1.65)	1.16 (0.78 to 1.73)	0.95 (0.58 to 1.54)	2.16 (1.10 to 4.25)[a]
2	1.33 (1.01 to 1.75)[a]	1.40 (0.91 to 2.16)	0.78 (0.47 to 1.29)	1.49 (0.74 to 3.02)
3	1.29 (0.98 to 1.70)	1.32 (0.86 to 2.04)	0.96 (0.58 to 1.60)	0.94 (0.48 to 1.85)
4	1.20 (0.91 to 1.60)	1.22 (0.77 to 1.94)	0.83 (0.50 to 1.37)	1.36 (0.68 to 2.70)

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TABLE 1. Factors for Enrollment Success Rate in All Included Clinical Trials and Trials by Cancer Type (continued)

Characteristic	All Trials, OR (95% CI)	Breast Cancer Trials, OR (95% CI)	Lung Cancer Trials, OR (95% CI)	Colorectal Cancer Trials, OR (95% CI)
≥5	1.48 (1.16 to 1.88)[a]	1.65 (1.13 to 2.41)[a]	0.66 (0.42 to 1.04)	1.88 (1.06 to 3.34)[a]
No. of countries				
1	1.00	1.00	1.00	1.00
>1	1.07 (0.86 to 1.32)	0.81 (0.56 to 1.16)	1.37 (0.94 to 2.00)	0.93 (0.54 to 1.57)
Unknown	0.48 (0.34 to 0.68)[a]	0.35 (0.20 to 0.62)[a]	0.45 (0.24 to 0.84)[a]	0.55 (0.24 to 1.25)
No. of locations				
1	1.00	1.00	1.00	1.00
2-4	0.84 (0.68 to 1.03)	0.84 (0.60 to 1.16)	0.80 (0.54 to 1.19)	0.89 (0.54 to 1.49)
≥5	2.01 (1.65 to 2.46)[a]	2.48 (1.79 to 3.43)[a]	2.00 (1.37 to 2.91)[a]	1.99 (1.20 to 3.28)[a]
Estimated enrollment				
0-50	1.00	1.00	1.00	1.00
50-100	0.62 (0.51 to 0.75)[a]	0.65 (0.48 to 0.87)[a]	0.64 (0.45 to 0.90)[a]	0.46 (0.29 to 0.74)[a]
100-200	0.51 (0.40 to 0.65)[a]	0.50 (0.34 to 0.73)[a]	0.44 (0.28 to 0.69)[a]	0.44 (0.24 to 0.81)[a]
200-500	0.45 (0.33 to 0.61)[a]	0.50 (0.30 to 0.82)[a]	0.39 (0.22 to 0.69)[a]	0.18 (0.08 to 0.40)[a]
>500	0.19 (0.13 to 0.28)[a]	0.20 (0.10 to 0.40)[a]	0.17 (0.08 to 0.38)[a]	0.09 (0.03 to 0.26)[a]

NOTE. NA indicates not being included in analysis because of either the limited sample size or no eligible data.
Abbreviations: OR, Odds ratio; NA, not applicable; TKI, tyrosine kinase inhibitor.
[a]Statistical significance.

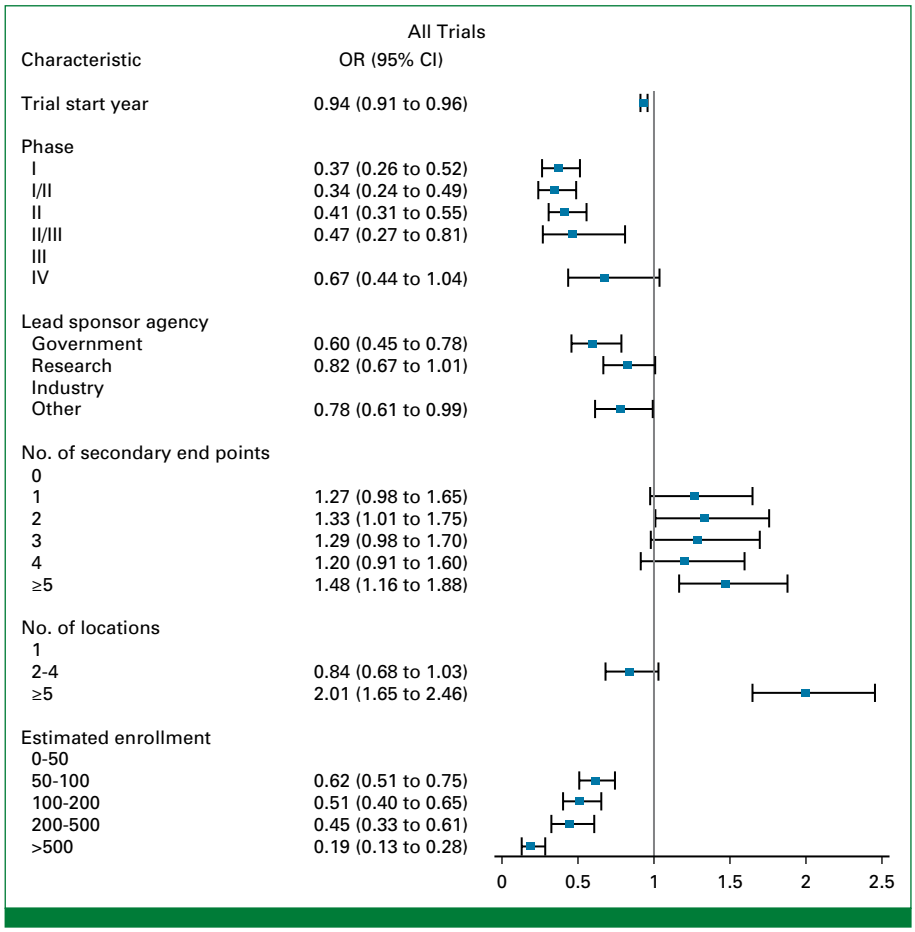

FIG 3. Forest plots for presenting selected factors for enrollment success rate. Direction of OR toward 0 from 1 indicates risk factor; on the contrary, direction from 1 to larger indicates preventive factor. OR, odds ratio.

targeted population, lack of willingness, training, and engagement among medical practitioners, recruiters, and patients, and insufficient funding.[15-18]

Correspondingly, here we discuss three feasible approaches to facilitate enrollment success in clinical trials. First, it is pragmatic to expand the number of collaborating centers for a trial. The expansion is supported by our study, showing that trials with five or more locations were twice as likely to achieve enrollment success than the trials with one location. Other approaches to improve enrollment are related to trial design: carefully expanding eligibility criteria[19] as well as lowering the sample size by using validated surrogate end point(s).[20-22] The former way has been debated for decades but is well supported by real-world evidence that many patients not eligible under the original trial could potentially benefit from the treatments.[23] At the same time, the expansion could improve trials' generalizability to a broader population, and help address the issues of disparities in access to and participation in clinical trials, in terms of race, sex, age, or other demographic and disease characteristics, as strongly supported by considerable studies.[17,24-34] Regarding the use of surrogate end points, its implementation is also helpful to reduce trial conduction time to save 11-19 months compared with trials using overall survival.[35] To safely and effectively implement the last two approaches as mentioned, we echo the need of strengthening the use of real-world studies and postmarket trials as guidance.[23,24,36-38]

This is one of the largest studies investigating enrollment success rates among clinical trials for breast, lung, and colorectal cancers. Relying on ClinicalTrials.gov, the study captured a large variety of clinical trial information for the cancers, applied the information to the prevalence and trend of enrollment success rate, evaluated its factors, and developed prediction models for enrollment success rate for the included trials. Regarding limitations, however, this study is strongly subjective to the robustness of data collection on ClinicalTrials.gov. Specifically, although ClinicalTrials.gov is the largest database for trial registration, our sample of trials cannot represent the whole of all trials registered and not registered in the globe, especially those conducted not in the United States. Also, the data quality and completeness depend on the trialists who submitted the trial data. Regarding the submission, there could be a time lag

between actual trial conduction and submission, which is why we failed to include ongoing trials and trials activated in the most recent years (after 2019) because of a large amount of missing data on trial information, especially the variables used for constructing the outcome variable (enrollment success rate). Otherwise, we would look at how the COVID-19 pandemic has affected enrollment success in cancer clinical trials, which deserves future investigations.

In addition, our analysis was also subject to the availability of data information developed on ClinicalTrials.gov. Rather than patient level or health system level, specifically, the analysis was based on the information at the trial level but the amount of analysis should provide informative implications as presented and discussed in the Result and Discussion sections. Last, the decreasing tendency found in our study could be accounted for by the more registrations of clinical trials in ClinicalTrials.gov, including those without successful enrollment. However, the decreasing trend is consistent with the findings from other studies in the high failure rate of oncology trials because of low enrollment rate.[15,17,39,40] In fact, there are increasing number of new therapies, especially with the development of immunotherapy,[41,42] to be evaluated, and persistent barriers to enrollment and trial completion.[13-18,39,40,43] As such, the low enrollment success rate found over the past decade should be paid attention to and be potentially improved by considering the factors as identified in this study.

In conclusion, this large-scale, cross-sectional study supports a lower enrollment success rate over years in cancer clinical trials, regardless of cancer types and lead sponsor agencies, and trials by many other characteristics. The findings could be of concern to the public, especially trialists including oncologists, researchers, policymakers, and other stakeholders. Our analysis leads to a model with good prediction on enrollment success on the basis of the trial-level information collected before trial activation. The identified risk factors for enrollment success can be used to develop and improve recruitment strategies for future cancer trials.

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Enrollment Success, Factors, and Prediction Models in Cancer Trials (2008-2019)

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APPENDIX

TABLE A1. Enrollment Name Combinations in ClinicalTrials.gov

Estimated Enrollment	Actual Enrollment
Original enrollment	Actual enrollment
Original enrollment	Enrollment
Original enrollment	Estimated enrollment
Original estimated enrollment	Actual enrollment
Original actual enrollment	Actual enrollment
Original estimated enrollment	Estimated enrollment
Original actual enrollment	Estimated enrollment

NOTE. Since the names of these two variables presented in ClinicalTrials.gov are not unified, we used the enrollment variable with an earlier post date for estimated enrollment, and the enrollment variable with a later post date for actual enrollment. The enrollment name combination of original actual enrollment—estimated enrollment seems an inaccurate input from some particular trials; because the number of this combination is small, we chose to retain this information.

TABLE A2. Characteristics of Included Trials

Characteristic	Enrollment Failure, No. (%)	Enrollment Success, No. (%)	*P*	Overall, No. (%)
Recruitment status			<.001	
Completed	900 (44.18)	1,698 (86.32)		2,598 (64.89)
Suspended	1 (0.05)	1 (0.05)		2 (0.05)
Terminated	796 (39.08)	91 (4.63)		887 (22.15)
Unknown status	30 (1.47)	35 (1.78)		65 (1.62)
Withdrawn	254 (12.47)	0 (0.00)		254 (6.34)
Active, not recruiting	56 (2.75)	142 (7.22)		198 (4.95)
Trial activation year			<.001	
Mean (SD)	2012 (3.00)	2012 (2.83)		2012 (2.93)
Min, max	2008, 2,019	2008, 2019		2008, 2019
Cancer type			.186	
Breast	737 (36.18)	751 (38.18)		1,488 (37.16)
Lung	695 (34.12)	610 (31.01)		1,305 (32.59)
Colorectal	304 (14.92)	315 (16.01)		619 (15.46)
Mix	301 (14.78)	291 (14.79)		592 (14.79)
No. of conditions			<.001	
1	1,304 (64.02)	1,390 (70.67)		2,694 (67.28)
2	297 (14.58)	242 (12.30)		539 (13.46)
3-4	231 (11.34)	171 (8.69)		402 (10.04)
≥5	205 (10.06)	164 (8.34)		369 (9.22)
Phase			<.001	
I	587 (28.82)	454 (23.08)		1,041 (26.00)
II/II	253 (12.42)	181 (9.20)		434 (10.84)
II	909 (44.62)	859 (43.67)		1,768 (44.16)
II/III	36 (1.77)	34 (1.73)		70 (1.75)
III	191 (9.38)	357 (18.15)		548 (13.69)
IV	61 (2.99)	82 (4.17)		143 (3.57)
Intervention type				
Behavioral			.813	
Yes	34 (1.67)	30 (1.53)		64 (1.60)
No	2,003 (98.33)	1,937 (98.47)		3,940 (98.40)
Biological			.037	
Yes	263 (12.91)	211 (10.73)		474 (11.84)
No	1,774 (87.09)	1,756 (89.27)		3,530 (88.16)
Device			.267	
Yes	42 (2.06)	52 (2.64)		94 (2.35)
No	1,995 (97.94)	1,915 (97.36)		3,910 (97.65)
Diagnostic test			>.999	
Yes	4 (0.20)	3 (0.15)		7 (0.17)
No	2,033 (99.80)	1,964 (99.85)		3,997 (99.83)
Drug			.608	
Yes	1,747 (85.76)	1,699 (86.38)		3,446 (86.06)
No	290 (14.24)	268 (13.62)		558 (13.94)
Genetic			.297	
Yes	13 (0.64)	7 (0.36)		20 (0.50)
No	2,024 (99.36)	1,960 (99.64)		3,984 (99.50)
Procedure			.608	
Yes	128 (6.28)	115 (5.85)		243 (6.07)
No	1,909 (93.72)	1,852 (94.15)		3,761 (93.93)

(continued on following page)

TABLE A2. Characteristics of Included Trials (continued)

Characteristic	Enrollment Failure, No. (%)	Enrollment Success, No. (%)	*P*	Overall, No. (%)
Radiation			<.001	
Yes	155 (7.61)	80 (4.07)		235 (5.87)
No	1,882 (92.39)	1,887 (95.93)		3,769 (94.13)
No. of interventions			.030	
1	676 (33.19)	599 (30.45)		1,275 (31.84)
2	670 (32.89)	624 (31.72)		1,294 (32.32)
≥3	691 (33.92)	744 (37.82)		1,435 (35.84)
Type of intervention drug				
Receptor TKI			.321	
Yes	233 (11.44)	246 (12.51)		479 (11.96)
No	1,804 (88.56)	1,721 (87.49)		3,525 (88.04)
Cell growth inhibitor			.161	
Yes	208 (10.21)	229 (11.64)		437 (10.91)
No	1,829 (89.79)	1,738 (88.36)		3,567 (89.09)
Tubulin depolymerization inhibitor			.005	
Yes	190 (9.33)	238 (12.10)		428 (10.69)
No	1,847 (90.67)	1,729 (87.90)		3,576 (89.31)
Antimetabolite			.966	
Yes	197 (9.67)	192 (9.76)		389 (9.72)
No	1,840 (90.33)	1,775 (90.24)		3,615 (90.28)
Angiogenesis inhibitor			.013	
Yes	93 (4.57)	126 (6.41)		219 (5.47)
No	1,944 (95.43)	1,841 (93.59)		3,785 (94.53)
Lead sponsor agency			<.001	
Government	297 (14.58)	181 (9.20)		478 (11.94)
Research institutes	711 (34.90)	571 (29.03)		1,282 (32.02)
Industry	719 (35.30)	942 (47.89)		1,661 (41.48)
Others	310 (15.22)	273 (13.88)		583 (14.56)
No. of sponsors			<.001	
1	1,193 (58.57)	1,279 (65.02)		2,472 (61.74)
>1	844 (41.43)	688 (34.98)		1,532 (38.26)
Eligibility of healthy volunteers			.071	
Accepts healthy volunteers	41 (2.01)	58 (2.95)		99 (2.47)
No	1,996 (97.99)	1,909 (97.05)		3,905 (97.53)
Eligibility of minimum age, years			.883	
0-18	38 (1.87)	38 (1.93)		76 (1.90)
18-70	1,986 (97.50)	1,914 (97.31)		3,900 (97.40)
>70	13 (0.64)	15 (0.76)		28 (0.70)
Eligibility of maximum age, years			.099	
0-70	46 (2.26)	62 (3.15)		108 (2.70)
>70	1,991 (97.74)	1,905 (96.85)		3,896 (97.30)
Allocation			<.001	
Randomized	703 (34.51)	943 (47.94)		1,646 (41.11)
Nonrandomized	370 (18.16)	310 (15.76)		680 (16.98)
Not provided	964 (47.32)	714 (36.30)		1,678 (41.91)
Arm: experimental			.367	
Yes	1,866 (91.61)	1,785 (90.75)		3,651 (91.18)
No	171 (8.39)	182 (9.25)		353 (8.82)

(continued on following page)

TABLE A2. Characteristics of Included Trials (continued)

Characteristic	Enrollment Failure, No. (%)	Enrollment Success, No. (%)	*P*	Overall, No. (%)
Arm: active comparator			<.001	
Yes	391 (19.19)	554 (28.16)		945 (23.60)
No	1,646 (80.81)	1,413 (71.84)		3,059 (76.40)
Arm: placebo comparator			<.001	
Yes	166 (8.15)	262 (13.32)		428 (10.69)
No	1,871 (91.85)	1,705 (86.68)		3,576 (89.31)
No. of arms			<.001	
0	55 (2.70)	34 (1.73)		89 (2.22)
1	1,013 (49.73)	753 (38.28)		1,766 (44.11)
2	683 (33.53)	828 (42.09)		1,511 (37.74)
≥3	286 (14.04)	352 (17.90)		638 (15.93)
No. of primary outcomes			.023	
1	1,533 (75.37)	1,502 (76.44)		3,035 (75.89)
2	327 (16.08)	264 (13.44)		591 (14.78)
≥3	174 (8.55)	199 (10.13)		373 (9.33)
Missing	3	2		5
No. of secondary outcomes			<.001	
0	276 (13.57)	185 (9.41)		461 (11.53)
1	332 (16.32)	294 (14.96)		626 (15.65)
2	255 (12.54)	220 (11.20)		475 (11.88)
3	262 (12.88)	239 (12.16)		501 (12.53)
4	257 (12.64)	221 (11.25)		478 (11.95)
≥5	652 (32.06)	806 (41.02)		1,458 (36.46)
Missing	3	2		5
No. of countries			<.001	
1	1,536 (75.41)	1,343 (68.28)		2,879 (71.90)
>1	343 (16.84)	566 (28.77)		909 (22.70)
Unknown	158 (7.76)	58 (2.95)		216 (5.39)
No. of locations			<.001	
1	1,025 (50.32)	706 (35.89)		1,731 (43.23)
2-4	373 (18.31)	241 (12.25)		614 (15.33)
≥5	639 (31.37)	1,020 (51.86)		1,659 (41.43)
Estimated enrollment			<.001	
0-50	874 (43.61)	747 (37.98)		1,621 (40.82)
50-100	308 (15.37)	354 (18.00)		662 (16.67)
100-200	159 (7.93)	260 (13.22)		419 (10.55)
200-500	537 (26.80)	464 (23.59)		1,001 (25.21)
>500	126 (6.29)	142 (7.22)		268 (6.75)
Missing	33	0		33

Abbreviation: TKI, tyrosine kinase inhibitor.

TABLE A3. Characteristics of Included Trials by Cancer Type

Characteristic	Breast Cancer, No. (%)	Lung Cancer, No. (%)	Colorectal Cancer, No. (%)	Mix, No. (%)	*P*	Overall, No. (%)
Enrollment status					.186	
Enrollment failure	737 (49.53)	695 (53.26)	304 (49.11)	301 (50.84)		2,037 (50.87)
Enrollment success	751 (50.47)	610 (46.74)	315 (50.89)	291 (49.16)		1,967 (49.13)
Overall status					<.001	
Completed	977 (65.66)	803 (61.53)	418 (67.53)	400 (67.57)		2,598 (64.89)
Suspended	0 (0.00)	1 (0.08)	0 (0.00)	1 (0.17)		2 (0.05)
Terminated	294 (19.76)	320 (24.52)	137 (22.13)	136 (22.97)		887 (22.15)
Unknown status	24 (1.61)	17 (1.30)	16 (2.58)	8 (1.35)		65 (1.62)
Withdrawn	91 (6.12)	98 (7.51)	39 (6.30)	26 (4.39)		254 (6.34)
Active, not recruiting	102 (6.85)	66 (5.06)	9 (1.45)	21 (3.55)		198 (4.95)
Trial activation year					.515	
Mean (SD)	2012 (2.87)	2012 (2.99)	2012 (2.81)	2013 (2.98)		2012 (2.93)
Min, max	2008, 2019	2008, 2019	2008, 2019	2008, 2019		2008, 2019
No. of conditions					<.001	
1	981 (65.93)	804 (61.61)	435 (70.27)	474 (80.07)		2,694 (67.28)
2	203 (13.64)	198 (15.17)	75 (12.12)	63 (10.64)		539 (13.46)
3-4	156 (10.48)	148 (11.34)	59 (9.53)	39 (6.59)		402 (10.04)
≥5	148 (9.95)	155 (11.88)	50 (8.08)	16 (2.70)		369 (9.22)
Phase					<.001	
I	350 (23.52)	362 (27.74)	127 (20.52)	202 (34.12)		1,041 (26.00)
I/II	136 (9.14)	160 (12.26)	73 (11.79)	65 (10.98)		434 (10.84)
II	689 (46.30)	576 (44.14)	310 (50.08)	193 (32.60)		1,768 (44.16)
II/III	27 (1.81)	23 (1.76)	9 (1.45)	11 (1.86)		70 (1.75)
III	224 (15.05)	155 (11.88)	80 (12.92)	89 (15.03)		548 (13.69)
IV	62 (4.17)	29 (2.22)	20 (3.23)	32 (5.41)		143 (3.57)
Intervention type						
Behavioral					.117	
Yes	33 (2.22)	15 (1.15)	8 (1.29)	8 (1.35)		64 (1.60)
No	1,455 (97.78)	1,290 (98.85)	611 (98.71)	584 (98.65)		3,940 (98.40)
Biological					.023	
Yes	151 (10.15)	166 (12.72)	90 (14.54)	67 (11.32)		474 (11.84)
No	1,337 (89.85)	1,139 (87.28)	529 (85.46)	525 (88.68)		3,530 (88.16)
Device					.532	
Yes	39 (2.62)	24 (1.84)	16 (2.58)	15 (2.53)		94 (2.35)
No	1,449 (97.38)	1,281 (98.16)	603 (97.42)	577 (97.47)		3,910 (97.65)
Diagnostic test					.324	
Yes	3 (0.20)	4 (0.31)	0 (0.00)	0 (0.00)		7 (0.17)
No	1,485 (99.80)	1,301 (99.69)	619 (100.00)	592 (100.00)		3,997 (99.83)
Drug					.532	
Yes	1,265 (85.01)	1,130 (86.59)	537 (86.75)	514 (86.82)		3,446 (86.06)
No	223 (14.99)	175 (13.41)	82 (13.25)	78 (13.18)		558 (13.94)
Genetic					.595	
Yes	8 (0.54)	5 (0.38)	5 (0.81)	2 (0.34)		20 (0.50)
No	1,480 (99.46)	1,300 (99.62)	614 (99.19)	590 (99.66)		3,984 (99.50)
Procedure					<.001	
Yes	117 (7.86)	62 (4.75)	45 (7.27)	19 (3.21)		243 (6.07)
No	1,371 (92.14)	1,243 (95.25)	574 (92.73)	573 (96.79)		3,761 (93.93)
Radiation					<.001	
Yes	72 (4.84)	121 (9.27)	24 (3.88)	18 (3.04)		235 (5.87)

(continued on following page)

TABLE A3. Characteristics of Included Trials by Cancer Type (continued)

Characteristic	Breast Cancer, No. (%)	Lung Cancer, No. (%)	Colorectal Cancer, No. (%)	Mix, No. (%)	*P*	Overall, No. (%)
No	1,416 (95.16)	1,184 (90.73)	595 (96.12)	574 (96.96)		3,769 (94.13)
No. of interventions					.002	
1	459 (30.85)	420 (32.18)	178 (28.76)	218 (36.82)		1,275 (31.84)
2	485 (32.59)	402 (30.80)	200 (32.31)	207 (34.97)		1,294 (32.32)
≥3	544 (36.56)	483 (37.01)	241 (38.93)	167 (28.21)		1,435 (35.84)
Type of intervention drug						
Receptor TKI					<.001	
Yes	208 (13.98)	173 (13.26)	34 (5.49)	64 (10.81)		479 (11.96)
No	1,280 (86.02)	1,132 (86.74)	585 (94.51)	528 (89.19)		3,525 (88.04)
Cell growth inhibitor					<.001	
Yes	77 (5.17)	238 (18.24)	66 (10.66)	56 (9.46)		437 (10.91)
No	1,411 (94.83)	1,067 (81.76)	553 (89.34)	536 (90.54)		3,567 (89.09)
Tubulin depolymerization inhibitor					<.001	
Yes	194 (13.04)	183 (14.02)	2 (0.32)	49 (8.28)		428 (10.69)
No	1,294 (86.96)	1,122 (85.98)	617 (99.68)	543 (91.72)		3,576 (89.31)
Antimetabolite					<.001	
Yes	83 (5.58)	155 (11.88)	97 (15.67)	54 (9.12)		389 (9.72)
No	1,405 (94.42)	1,150 (88.12)	522 (84.33)	538 (90.88)		3,615 (90.28)
Angiogenesis inhibitor					<.001	
Yes	54 (3.63)	73 (5.59)	79 (12.76)	13 (2.20)		219 (5.47)
No	1,434 (96.37)	1,232 (94.41)	540 (87.24)	579 (97.80)		3,785 (94.53)
Lead sponsor agency					<.001	
Government	193 (12.97)	171 (13.10)	74 (11.95)	40 (6.76)		478 (11.94)
Research institutes	548 (36.83)	376 (28.81)	201 (32.47)	157 (26.52)		1,282 (32.02)
Industry	499 (33.53)	602 (46.13)	225 (36.35)	335 (56.59)		1,661 (41.48)
Others	248 (16.67)	156 (11.95)	119 (19.22)	60 (10.14)		583 (14.56)
No. of sponsors					<.001	
1	886 (59.54)	812 (62.22)	354 (57.19)	420 (70.95)		2,472 (61.74)
>1	602 (40.46)	493 (37.78)	265 (42.81)	172 (29.05)		1,532 (38.26)
Eligibility of healthy volunteers					.011	
Accepts healthy volunteers	42 (2.82)	18 (1.38)	17 (2.75)	22 (3.72)		99 (2.47)
No	1,446 (97.18)	1,287 (98.62)	602 (97.25)	570 (96.28)		3,905 (97.53)
Eligibility of minimum age, years					.132	
0-18	29 (1.95)	19 (1.46)	12 (1.94)	16 (2.70)		76 (1.90)
18-70	1,455 (97.78)	1,274 (97.62)	601 (97.09)	570 (96.28)		3,900 (97.40)
>70	4 (0.27)	12 (0.92)	6 (0.97)	6 (1.01)		28 (0.70)
Eligibility of maximum age, years					<.001	
0-70	57 (3.83)	9 (0.69)	9 (1.45)	33 (5.57)		108 (2.70)
>70	1,431 (96.17)	1,296 (99.31)	610 (98.55)	559 (94.43)		3,896 (97.30)
Allocation					<.001	
Randomized	635 (42.67)	493 (37.78)	275 (44.43)	243 (41.05)		1,646 (41.11)
Nonrandomized	209 (14.05)	256 (19.62)	95 (15.35)	120 (20.27)		680 (16.98)
Not provided	644 (43.28)	556 (42.61)	249 (40.23)	229 (38.68)		1,678 (41.91)
Arm: experimental					.008	
Yes	1,349 (90.66)	1,213 (92.95)	547 (88.37)	542 (91.55)		3,651 (91.18)
No	139 (9.34)	92 (7.05)	72 (11.63)	50 (8.45)		353 (8.82)
Arm: active comparator					.140	
Yes	364 (24.46)	292 (22.38)	162 (26.17)	127 (21.45)		945 (23.60)
No	1,124 (75.54)	1,013 (77.62)	457 (73.83)	465 (78.55)		3,059 (76.40)

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TABLE A3. Characteristics of Included Trials by Cancer Type (continued)

Characteristic	Breast Cancer, No. (%)	Lung Cancer, No. (%)	Colorectal Cancer, No. (%)	Mix, No. (%)	*P*	Overall, No. (%)
Arm: placebo comparator					.077	
Yes	161 (10.82)	122 (9.35)	66 (10.66)	79 (13.34)		428 (10.69)
No	1,327 (89.18)	1,183 (90.65)	553 (89.34)	513 (86.66)		3,576 (89.31)
No. of arms					.099	
0	26 (1.75)	28 (2.15)	19 (3.07)	16 (2.70)		89 (2.22)
1	684 (45.97)	580 (44.44)	264 (42.65)	238 (40.20)		1,766 (44.11)
2	551 (37.03)	484 (37.09)	250 (40.39)	226 (38.18)		1,511 (37.74)
≥3	227 (15.26)	213 (16.32)	86 (13.89)	112 (18.92)		638 (15.93)
No. of primary outcomes					<.001	
1	1,123 (75.52)	974 (74.69)	499 (80.88)	439 (74.28)		3,035 (75.89)
2	228 (15.33)	201 (15.41)	85 (13.78)	77 (13.03)		591 (14.78)
≥3	136 (9.15)	129 (9.89)	33 (5.35)	75 (12.69)		373 (9.33)
Missing	1	1	2	1		5
No. of secondary outcomes					.071	
0	184 (12.37)	144 (11.04)	73 (11.83)	60 (10.15)		461 (11.53)
1	256 (17.22)	186 (14.26)	89 (14.42)	95 (16.07)		626 (15.65)
2	183 (12.31)	171 (13.11)	59 (9.56)	62 (10.49)		475 (11.88)
3	177 (11.90)	166 (12.73)	80 (12.97)	78 (13.20)		501 (12.53)
4	147 (9.89)	178 (13.65)	79 (12.80)	74 (12.52)		478 (11.95)
≥5	540 (36.31)	459 (35.20)	237 (38.41)	222 (37.56)		1,458 (36.46)
Missing	1	1	2	1		5
No. of countries					<.001	
1	1,131 (76.01)	892 (68.35)	466 (75.28)	390 (65.88)		2,879 (71.90)
>1	285 (19.15)	334 (25.59)	120 (19.39)	170 (28.72)		909 (22.70)
Unknown	72 (4.84)	79 (6.05)	33 (5.33)	32 (5.41)		216 (5.39)
No. of locations					.005	
1	685 (46.03)	532 (40.77)	284 (45.88)	230 (38.85)		1,731 (43.23)
2-4	223 (14.99)	189 (14.48)	97 (15.67)	105 (17.74)		614 (15.33)
≥5	580 (38.98)	584 (44.75)	238 (38.45)	257 (43.41)		1,659 (41.43)
Estimated enrollment					.821	
0-50	613 (41.39)	521 (40.29)	246 (40.00)	241 (41.41)		1,621 (40.82)
50-100	252 (17.02)	223 (17.25)	94 (15.28)	93 (15.98)		662 (16.67)
100-200	168 (11.34)	134 (10.36)	64 (10.41)	53 (9.11)		419 (10.55)
200-500	355 (23.97)	331 (25.60)	166 (26.99)	149 (25.60)		1,001 (25.21)
>500	93 (6.28)	84 (6.50)	45 (7.32)	46 (7.90)		268 (6.75)
Missing	7	12	4	10		33

Abbreviation: TKI, tyrosine kinase inhibitor.

TABLE A4. Characteristics of Included Trials by Phase

Characteristic	Phase I, No. (%)	Phase II, No. (%)	Phase III, No. (%)	*P*	Overall, No. (%)
Enrollment status				<.001	
Enrollment failure	587 (56.39)	909 (51.41)	191 (34.85)		1,687 (50.25)
Enrollment success	454 (43.61)	859 (48.59)	357 (65.15)		1,670 (49.75)
Overall status				<.001	
Completed	710 (68.20)	1,099 (62.16)	371 (67.70)		2,180 (64.94)
Suspended	0 (0.00)	2 (0.11)	0 (0.00)		2 (0.06)
Terminated	223 (21.42)	433 (24.49)	83 (15.15)		739 (22.01)
Unknown status	11 (1.06)	34 (1.92)	10 (1.82)		55 (1.64)
Withdrawn	60 (5.76)	123 (6.96)	19 (3.47)		202 (6.02)
Active, not recruiting	37 (3.55)	77 (4.36)	65 (11.86)		179 (5.33)
Trial activation year				<.001	
Mean (SD)	2012 (2.91)	2012 (2.88)	2012 (2.88)		2012 (2.90)
Min, max	2008, 2019	2008, 2019	2008, 2019		2008, 2019
Cancer type				<.001	
Lung	350 (33.62)	689 (38.97)	224 (40.88)		1,263 (37.62)
Breast	127 (12.20)	310 (17.53)	80 (14.60)		517 (15.40)
Colorectal	362 (34.77)	576 (32.58)	155 (28.28)		1,093 (32.56)
Missing	202 (19.40)	193 (10.92)	89 (16.24)		484 (14.42)
No. of conditions				<.001	
1	583 (56.00)	1,287 (72.79)	417 (76.09)		2,287 (68.13)
2	151 (14.51)	216 (12.22)	73 (13.32)		440 (13.11)
3-4	133 (12.78)	157 (8.88)	35 (6.39)		325 (9.68)
≥5	174 (16.71)	108 (6.11)	23 (4.20)		305 (9.09)
Intervention type					
Behavioral				.112	
Yes	10 (0.96)	32 (1.81)	12 (2.19)		54 (1.61)
No	1,031 (99.04)	1,736 (98.19)	536 (97.81)		3,303 (98.39)
Biological				<.001	
Yes	156 (14.99)	158 (8.94)	64 (11.68)		378 (11.26)
No	885 (85.01)	1,610 (91.06)	484 (88.32)		2,979 (88.74)
Device				.360	
Yes	26 (2.50)	31 (1.75)	13 (2.37)		70 (2.09)
No	1,015 (97.50)	1,737 (98.25)	535 (97.63)		3,287 (97.91)
Diagnostic test				.311	
Yes	4 (0.38)	2 (0.11)	1 (0.18)		7 (0.21)
No	1,037 (99.62)	1,766 (99.89)	547 (99.82)		3,350 (99.79)
Drug				<.001	
Yes	852 (81.84)	1,606 (90.84)	455 (83.03)		2,913 (86.77)
No	189 (18.16)	162 (9.16)	93 (16.97)		444 (13.23)
Genetic				.030	
Yes	9 (0.86)	6 (0.34)	0 (0.00)		15 (0.45)
No	1,032 (99.14)	1,762 (99.66)	548 (100.00)		3,342 (99.55)
Procedure				.154	
Yes	59 (5.67)	101 (5.71)	43 (7.85)		203 (6.05)
No	982 (94.33)	1,667 (94.29)	505 (92.15)		3,154 (93.95)
Radiation				.357	
Yes	68 (6.53)	106 (6.00)	26 (4.74)		200 (5.96)
No	973 (93.47)	1,662 (94.00)	522 (95.26)		3,157 (94.04)
No. of interventions				<.001	

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TABLE A4. Characteristics of Included Trials by Phase (continued)

Characteristic	Phase I, No. (%)	Phase II, No. (%)	Phase III, No. (%)	*P*	Overall, No. (%)
1	423 (40.63)	569 (32.18)	73 (13.32)		1,065 (31.72)
2	287 (27.57)	551 (31.17)	231 (42.15)		1,069 (31.84)
≥3	331 (31.80)	648 (36.65)	244 (44.53)		1,223 (36.43)
Type of intervention drug					
Receptor TKI				<.001	
Yes	80 (7.68)	237 (13.40)	83 (15.15)		400 (11.92)
No	961 (92.32)	1,531 (86.60)	465 (84.85)		2,957 (88.08)
Cell growth inhibitor				.008	
Yes	95 (9.13)	201 (11.37)	78 (14.23)		374 (11.14)
No	946 (90.87)	1,567 (88.63)	470 (85.77)		2,983 (88.86)
Tubulin depolymerization inhibitor				<.001	
Yes	72 (6.92)	195 (11.03)	103 (18.80)		370 (11.02)
No	969 (93.08)	1,573 (88.97)	445 (81.20)		2,987 (88.98)
Antimetabolite				<.001	
Yes	67 (6.44)	199 (11.26)	71 (12.96)		337 (10.04)
No	974 (93.56)	1,569 (88.74)	477 (87.04)		3,020 (89.96)
Angiogenesis inhibitor				<.001	
Yes	31 (2.98)	130 (7.35)	33 (6.02)		194 (5.78)
No	1,010 (97.02)	1,638 (92.65)	515 (93.98)		3,163 (94.22)
Lead sponsor agency				<.001	
Government	172 (16.52)	210 (11.88)	37 (6.75)		419 (12.48)
Research institutes	275 (26.42)	635 (35.92)	127 (23.18)		1,037 (30.89)
Industry	495 (47.55)	608 (34.39)	307 (56.02)		1,410 (42.00)
Others	99 (9.51)	315 (17.82)	77 (14.05)		491 (14.63)
No. of sponsors				<.001	
1	676 (64.94)	1,033 (58.43)	375 (68.43)		2,084 (62.08)
>1	365 (35.06)	735 (41.57)	173 (31.57)		1,273 (37.92)
Eligibility of healthy volunteers				<.001	
Accepts healthy volunteers	45 (4.32)	19 (1.07)	19 (3.47)		83 (2.47)
No	996 (95.68)	1,749 (98.93)	529 (96.53)		3,274 (97.53)
Eligibility of minimum age, years				.177	
0-18	17 (1.63)	28 (1.58)	9 (1.64)		54 (1.61)
18-70	1,022 (98.17)	1,722 (97.40)	535 (97.63)		3,279 (97.68)
>70	2 (0.19)	18 (1.02)	4 (0.73)		24 (0.71)
Eligibility of maximum age, years				<.001	
0-70	42 (4.03)	29 (1.64)	19 (3.47)		90 (2.68)
>70	999 (95.97)	1,739 (98.36)	529 (96.53)		3,267 (97.32)
Allocation				<.001	
Randomized	124 (11.91)	758 (42.87)	500 (91.24)		1,382 (41.17)
Nonrandomized	327 (31.41)	220 (12.44)	9 (1.64)		556 (16.56)
Not provided	590 (56.68)	790 (44.68)	39 (7.12)		1,419 (42.27)
Arm: experimental				.028	
Yes	975 (93.66)	1,609 (91.01)	497 (90.69)		3,081 (91.78)
No	66 (6.34)	159 (8.99)	51 (9.31)		276 (8.22)
Arm: active comparator				<.001	
Yes	53 (5.09)	426 (24.10)	306 (55.84)		785 (23.38)
No	988 (94.91)	1,342 (75.90)	242 (44.16)		2,572 (76.62)
Arm: placebo comparator				<.001	
Yes	28 (2.69)	195 (11.03)	140 (25.55)		363 (10.81)

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TABLE A4. Characteristics of Included Trials by Phase (continued)

Characteristic	Phase I, No. (%)	Phase II, No. (%)	Phase III, No. (%)	*P*	Overall, No. (%)
No	1,013 (97.31)	1,573 (88.97)	408 (74.45)		2,994 (89.19)
No. of arms				<.001	
0	26 (2.50)	41 (2.32)	3 (0.55)		70 (2.09)
1	635 (61.00)	834 (47.17)	34 (6.20)		1,503 (44.77)
2	185 (17.77)	667 (37.73)	443 (80.84)		1,295 (38.58)
≥3	195 (18.73)	226 (12.78)	68 (12.41)		489 (14.57)
No. of primary outcomes				<.001	
1	669 (64.27)	1,512 (85.67)	446 (81.39)		2,627 (78.32)
2	187 (17.96)	175 (9.92)	66 (12.04)		428 (12.76)
≥3	185 (17.77)	78 (4.42)	36 (6.57)		299 (8.91)
Missing	0	3	0		3
No. of secondary outcomes				<.001	
0	143 (13.74)	187 (10.59)	37 (6.75)		367 (10.94)
1	201 (19.31)	242 (13.71)	66 (12.04)		509 (15.18)
2	142 (13.64)	199 (11.27)	52 (9.49)		393 (11.72)
3	123 (11.82)	258 (14.62)	45 (8.21)		426 (12.70)
4	118 (11.34)	232 (13.14)	61 (11.13)		411 (12.25)
≥5	314 (30.16)	647 (36.66)	287 (52.37)		1,248 (37.21)
Missing	0	3	0		3
No. of countries				<.001	
1	801 (76.95)	1,309 (74.04)	273 (49.82)		2,383 (70.99)
>1	188 (18.06)	358 (20.25)	251 (45.80)		797 (23.74)
Unknown	52 (5.00)	101 (5.71)	24 (4.38)		177 (5.27)
No. of locations				<.001	
1	531 (51.01)	729 (41.23)	161 (29.38)		1,421 (42.33)
2-4	236 (22.67)	246 (13.91)	35 (6.39)		517 (15.40)
≥5	274 (26.32)	793 (44.85)	352 (64.23)		1,419 (42.27)
Estimated enrollment				<.001	
0-50	745 (72.12)	640 (36.38)	15 (2.78)		1,400 (42.03)
50-100	70 (6.78)	391 (22.23)	79 (14.66)		540 (16.21)
100-200	10 (0.97)	143 (8.13)	204 (37.85)		357 (10.72)
200-500	202 (19.55)	560 (31.84)	27 (5.01)		789 (23.69)
>500	6 (0.58)	25 (1.42)	214 (39.70)		245 (7.36)
Missing	8	9	9		26

Abbreviation: TKI, tyrosine kinase inhibitor.

TABLE A5. Characteristics of Drug Trials

Characteristic	Drug, No. (%)	Other Interventions, No. (%)	*P*	Overall, No. (%)
Enrollment status			.608	
Enrollment failure	1,747 (50.70)	290 (51.97)		2,037 (50.87)
Enrollment success	1,699 (49.30)	268 (48.03)		1,967 (49.13)
Overall status			.025	
Completed	2,214 (64.25)	384 (68.82)		2,598 (64.89)
Suspended	2 (0.06)	0 (0.00)		2 (0.05)
Terminated	771 (22.37)	116 (20.79)		887 (22.15)
Unknown status	52 (1.51)	13 (2.33)		65 (1.62)
Withdrawn	223 (6.47)	31 (5.56)		254 (6.34)
Active, not recruiting	184 (5.34)	14 (2.51)		198 (4.95)
Trial activation year			.591	
Mean (SD)	2012.09 (2.92)	2012.03 (2.98)		2012.08 (2.93)
Min, max	2008, 2,019	2008, 2019		2008, 2019
Cancer type			.333	
Lung	1,265 (36.71)	223 (39.96)		1,488 (37.16)
Breast	1,051 (30.50)	160 (28.67)		1,211 (30.24)
Colorectal	1,130 (32.79)	175 (31.36)		1,305 (32.59)
No. of conditions			.125	
1	2,341 (67.93)	353 (63.26)		2,694 (67.28)
2	456 (13.23)	83 (14.87)		539 (13.46)
3-4	343 (9.95)	59 (10.57)		402 (10.04)
≥5	306 (8.88)	63 (11.29)		369 (9.22)
Phase			<.001	
I	852 (24.72)	189 (33.87)		1,041 (26.00)
I/II	364 (10.56)	70 (12.54)		434 (10.84)
II	1,606 (46.60)	162 (29.03)		1,768 (44.16)
II/III	60 (1.74)	10 (1.79)		70 (1.75)
III	455 (13.20)	93 (16.67)		548 (13.69)
IV	109 (3.16)	34 (6.09)		143 (3.57)
No. of interventions			<.001	
1	967 (28.06)	308 (55.20)		1,275 (31.84)
2	1,121 (32.53)	173 (31.00)		1,294 (32.32)
≥3	1,358 (39.41)	77 (13.80)		1,435 (35.84)
Type of intervention drug				
Receptor TKI			<.001	
Yes	472 (13.70)	7 (1.25)		479 (11.96)
No	2,974 (86.30)	551 (98.75)		3,525 (88.04)
Cell growth inhibitor			<.001	
Yes	436 (12.65)	1 (0.18)		437 (10.91)
No	3,010 (87.35)	557 (99.82)		3,567 (89.09)
Tubulin depolymerization inhibitor			<.001	
Yes	427 (12.39)	1 (0.18)		428 (10.69)
No	3,019 (87.61)	557 (99.82)		3,576 (89.31)
Antimetabolite			<.001	
Yes	388 (11.26)	1 (0.18)		389 (9.72)
No	3,058 (88.74)	557 (99.82)		3,615 (90.28)
Angiogenesis inhibitor			<.001	
Yes	219 (6.36)	0 (0.00)		219 (5.47)
No	3,227 (93.64)	558 (100.00)		3,785 (94.53)

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TABLE A5. Characteristics of Drug Trials (continued)

Characteristic	Drug, No. (%)	Other Interventions, No. (%)	*P*	Overall, No. (%)
Lead sponsor agency			<.001	
Government	395 (11.46)	83 (14.87)		478 (11.94)
Research institutes	1,056 (30.64)	226 (40.50)		1,282 (32.02)
Industry	1,526 (44.28)	135 (24.19)		1,661 (41.48)
Others	469 (13.61)	114 (20.43)		583 (14.56)
No. of sponsors			.003	
1	2,160 (62.68)	312 (55.91)		2,472 (61.74)
>1	1,286 (37.32)	246 (44.09)		1,532 (38.26)
Eligibility of healthy volunteers			<.001	
Accepts healthy volunteers	66 (1.92)	33 (5.91)		99 (2.47)
No	3,380 (98.08)	525 (94.09)		3,905 (97.53)
Eligibility of minimum age, years			.001	
0-18	55 (1.60)	21 (3.76)		76 (1.90)
18-70	3,365 (97.65)	535 (95.88)		3,900 (97.40)
>70	26 (0.75)	2 (0.36)		28 (0.70)
Eligibility of maximum age, years			.036	
0-70	85 (2.47)	23 (4.12)		108 (2.70)
>70	3,361 (97.53)	535 (95.88)		3,896 (97.30)
Allocation			.586	
Randomized	1,417 (41.12)	229 (41.04)		1,646 (41.11)
Nonrandomized	593 (17.21)	87 (15.59)		680 (16.98)
Not provided	1,436 (41.67)	242 (43.37)		1,678 (41.91)
Arm: experimental			<.001	
Yes	3,166 (91.87)	485 (86.92)		3,651 (91.18)
No	280 (8.13)	73 (13.08)		353 (8.82)
Arm: active comparator			.002	
Yes	843 (24.46)	102 (18.28)		945 (23.60)
No	2,603 (75.54)	456 (81.72)		3,059 (76.40)
Arm: placebo comparator			.005	
Yes	388 (11.26)	40 (7.17)		428 (10.69)
No	3,058 (88.74)	518 (92.83)		3,576 (89.31)
No. of arms			.014	
0	67 (1.94)	22 (3.94)		89 (2.22)
1	1,522 (44.17)	244 (43.73)		1,766 (44.11)
2	1,296 (37.61)	215 (38.53)		1,511 (37.74)
≥3	561 (16.28)	77 (13.80)		638 (15.93)
No. of primary outcomes			.033	
1	2,587 (75.18)	448 (80.29)		3,035 (75.89)
2	523 (15.20)	68 (12.19)		591 (14.78)
≥3	331 (9.62)	42 (7.53)		373 (9.33)
Missing	5	0		5
No. of secondary outcomes			<.001	
0	364 (10.58)	97 (17.38)		461 (11.53)
1	484 (14.07)	142 (25.45)		626 (15.65)
2	394 (11.45)	81 (14.52)		475 (11.88)
3	442 (12.85)	59 (10.57)		501 (12.53)
4	432 (12.55)	46 (8.24)		478 (11.95)
≥5	1,325 (38.51)	133 (23.84)		1,458 (36.46)
Missing	5	0		5

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TABLE A5. Characteristics of Drug Trials (continued)

Characteristic	Drug, No. (%)	Other Interventions, No. (%)	*P*	Overall, No. (%)
No. of countries			<.001	
1	2,396 (69.53)	483 (86.56)		2,879 (71.90)
>1	858 (24.90)	51 (9.14)		909 (22.70)
Unknown	192 (5.57)	24 (4.30)		216 (5.39)
No. of locations			<.001	
1	1,369 (39.73)	362 (64.87)		1,731 (43.23)
2-4	534 (15.50)	80 (14.34)		614 (15.33)
≥5	1,543 (44.78)	116 (20.79)		1,659 (41.43)
Estimated enrollment			<.001	
0-50	1,336 (39.09)	285 (51.54)		1,621 (40.82)
50-100	594 (17.38)	68 (12.30)		662 (16.67)
100-200	355 (10.39)	64 (11.57)		419 (10.55)
200-500	900 (26.33)	101 (18.26)		1,001 (25.21)
>500	233 (6.82)	35 (6.33)		268 (6.75)
Missing	28	5		33

Abbreviation: TKI, tyrosine kinase inhibitor.

TABLE A6. Factors for Enrollment Success Rate in Phase I, Phase II, Phase III, and Drug Clinical Trials

Characteristic	Phase I Trials, OR (95% CI)	Phase II Trials, OR (95% CI)	Phase III Trials, OR (95% CI)	Drug Trials, OR (95% CI)
Model prediction: AUC	0.72	0.69	0.76	0.70
Trial activation year	0.89 (0.85 to 0.94)[a]	0.95 (0.91 to 0.99)[a]	0.92 (0.85 to 1.00)[a]	0.94 (0.92 to 0.97)[a]
Cancer type				
Breast *v* no	1.20 (0.86 to 1.68)	1.12 (0.81 to 1.54)	2.23 (1.21 to 4.10)[a]	1.24 (1.01 to 1.51)[a]
Lung *v* no	0.90 (0.64 to 1.27)	0.95 (0.69 to 1.31)	1.50 (0.79 to 2.84)	1.06 (0.87 to 1.30)
Colorectal *v* no	0.96 (0.64 to 1.43)	1.23 (0.86 to 1.76)	2.71 (1.27 to 5.78)[a]	1.29 (1.03 to 1.63)[a]
No. of conditions				
1	1.00	1.00	1.00	1.00
2	1.08 (0.72 to 1.63)	0.86 (0.63 to 1.17)	0.94 (0.49 to 1.80)	0.86 (0.69 to 1.07)
3-4	0.99 (0.64 to 1.53)	0.82 (0.56 to 1.19)	0.48 (0.21 to 1.11)	0.82 (0.64 to 1.06)
≥5	1.51 (0.94 to 2.44)	0.71 (0.44 to 1.14)	2.02 (0.58 to 7.07)	1.11 (0.82 to 1.49)
Phase				
I	NA	NA	NA	0.28 (0.19 to 0.41)[a]
I/II	NA	NA	NA	0.25 (0.17 to 0.38)[a]
II	NA	NA	NA	0.35 (0.25 to 0.49)[a]
II/III	NA	NA	NA	0.45 (0.24 to 0.82)[a]
III	NA	NA	NA	1.00
IV	NA	NA	NA	0.73 (0.44 to 1.20)
Intervention type				
Behavioral *v* no	1.03 (0.21 to 5.09)	1.05 (0.47 to 2.32)	1.08 (0.24 to 4.81)	NA
Biological *v* no	0.83 (0.49 to 1.41)	0.64 (0.43 to 0.96)[a]	1.03 (0.49 to 2.15)	NA
Device *v* no	2.04 (0.84 to 4.99)	1.39 (0.64 to 3.05)	1.36 (0.29 to 6.43)	NA
Diagnostic test *v* no	0.94 (0.09 to 10.23)	3.76 (0.22 to 64.13)	NA	NA
Drug *v* no	0.68 (0.41 to 1.14)	0.86 (0.57 to 1.31)	1.19 (0.55 to 2.58)	NA
Genetic *v* no	0.32 (0.04 to 2.83)	1.50 (0.25 to 8.89)	NA	NA
Procedure *v* no	1.34 (0.71 to 2.54)	1.42 (0.89 to 2.28)	1.19 (0.51 to 2.79)	NA
Radiation *v* no	0.86 (0.46 to 1.61)	0.59 (0.37 to 0.95)[a]	0.71 (0.25 to 1.98)	NA
No. of interventions				
1	1.00	1.00	1.00	1.00
2	0.98 (0.68 to 1.43)	0.84 (0.62 to 1.12)	0.70 (0.32 to 1.54)	0.81 (0.66 to 1.00)
≥3	0.80 (0.51 to 1.24)	0.90 (0.64 to 1.28)	0.84 (0.35 to 2.03)	0.88 (0.70 to 1.11)
Type of intervention drug				
Receptor TKI *v* no	1.04 (0.60 to 1.80)	1.28 (0.94 to 1.73)	0.75 (0.40 to 1.42)	1.04 (0.84 to 1.29)
Cell growth inhibitor *v* no	0.93 (0.50 to 1.70)	1.15 (0.79 to 1.68)	2.67 (1.14 to 6.26)[a]	1.17 (0.90 to 1.53)
Tubulin depolymerization inhibitor *v* no	1.07 (0.57 to 1.98)	1.01 (0.71 to 1.44)	1.37 (0.71 to 2.64)	1.08 (0.85 to 1.38)
Antimetabolite *v* no	1.03 (0.55 to 1.94)	0.93 (0.65 to 1.33)	0.75 (0.34 to 1.63)	0.89 (0.68 to 1.15)
Angiogenesis inhibitor *v* no	3.00 (1.28 to 7.03)[a]	1.22 (0.80 to 1.85)	1.04 (0.38 to 2.84)	1.29 (0.94 to 1.78)
Lead sponsor agency				
Government	0.51 (0.30 to 0.89)[a]	0.73 (0.48 to 1.10)	0.27 (0.09 to 0.79)[a]	0.58 (0.43 to 0.79)[a]
Research institutes	0.82 (0.53 to 1.27)	0.87 (0.63 to 1.19)	0.30 (0.14 to 0.64)[a]	0.77 (0.62 to 0.97)[a]
Industry	1.00	1.00	1.00	1.00
Others	0.61 (0.35 to 1.06)	0.95 (0.67 to 1.34)	0.34 (0.15 to 0.77)[a]	0.72 (0.55 to 0.93)[a]
No. of sponsors: >1 *v* 1	0.92 (0.67 to 1.26)	0.82 (0.65 to 1.02)	1.39 (0.84 to 2.30)	0.89 (0.76 to 1.05)
Eligibility of healthy volunteers: No *v* yes	0.35 (0.15 to 0.80)[a]	0.50 (0.18 to 1.37)	0.98 (0.27 to 3.58)	0.47 (0.27 to 0.84)[a]
Eligibility of minimum age, years				
0-18	1.00	1.00	1.00	1.00
18-70	0.62 (0.21-1.83)	0.77 (0.35 to 1.72)	1.34 (0.26 to 6.73)	0.86 (0.31 to 2.33)
>70	NA	1.01 (0.29 to 3.57)	9.18 (0.46 to 183.31)	0.86 (0.48 to 1.55)
Eligibility of maximum age, years: >70 *v* 0-70	0.64 (0.27 to 1.51)	1.31 (0.59 to 2.93)	0.96 (0.29 to 3.19)	0.74 (0.45 to 1.21)

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TABLE A6. Factors for Enrollment Success Rate in Phase I, Phase II, Phase III, and Drug Clinical Trials (continued)

Characteristic	Phase I Trials, OR (95% CI)	Phase II Trials, OR (95% CI)	Phase III Trials, OR (95% CI)	Drug Trials, OR (95% CI)
Allocation				
Randomized	1.43 (0.80 to 2.57)	1.12 (0.72 to 1.73)	0.53 (0.08 to 3.44)	1.31 (0.97 to 1.76)
Nonrandomized	1.00	1.00	1.00	1.00
Not provided	1.31 (0.76 to 2.25)	1.43 (0.86 to 2.37)	0.70 (0.07 to 6.94)	1.29 (0.90 to 1.85)
Type of arm				
Experimental *v* no	0.59 (0.27 to 1.25)	1.12 (0.71 to 1.78)	0.49 (0.21 to 1.13)	1.08 (0.77 to 1.51)
Active comparator *v* no	0.64 (0.29 to 1.43)	1.16 (0.81 to 1.65)	1.78 (0.97 to 3.27)	1.30 (1.00 to 1.69)
Placebo comparator *v* no	1.49 (0.56 to 3.99)	1.88 (1.25 to 2.83)[a]	1.42 (0.72 to 2.80)	1.58 (1.17 to 2.13)[a]
No. of arms				
0	0.20 (0.05 to 0.73)[a]	0.74 (0.29 to 1.87)	0.90 (0.05 to 17.00)	0.64 (0.31 to 1.31)
1	0.52 (0.27 to 0.99)[a]	0.77 (0.42 to 1.40)	0.73 (0.10 to 5.37)	0.76 (0.51 to 1.14)
2	1.00	1.00	1.00	1.00
≥3	1.24 (0.77 to 2.01)	1.45 (1.02 to 2.05)[a]	0.80 (0.41 to 1.57)	1.24 (0.98 to 1.57)
No. of primary end points				
1	1.00	1.00	1.00	1.00
>2	0.74 (0.50 to 1.08)	1.04 (0.73 to 1.48)	1.28 (0.64 to 2.54)	0.90 (0.72 to 1.12)
≥3	1.08 (0.73 to 1.60)	1.32 (0.80 to 2.17)	1.88 (0.72 to 4.87)	1.17 (0.90 to 1.52)
No. of secondary end points				
0	1.00	1.00	1.00	1.00
1	1.48 (0.90 to 2.43)	1.47 (0.97 to 2.23)	0.79 (0.30 to 2.10)	1.32 (0.98 to 1.78)
2	1.31 (0.77 to 2.23)	1.31 (0.84 to 2.03)	2.23 (0.79 to 6.32)	1.43 (1.05 to 1.95)[a]
3	1.23 (0.70 to 2.17)	1.63 (1.08 to 2.48)[a]	0.69 (0.24 to 1.99)	1.40 (1.03 to 1.90)[a]
4	1.21 (0.68 to 2.15)	1.21 (0.79 to 1.85)	1.72 (0.63 to 4.68)	1.26 (0.92 to 1.71)
≥5	1.48 (0.91 to 2.43)	1.72 (1.18 to 2.50)[a]	1.63 (0.70 to 3.76)	1.56 (1.19 to 2.03)[a]
No. of countries				
1	1.00	1.00	1.00	1.00
>1	1.17 (0.74 to 1.82)	0.98 (0.71 to 1.37)	1.43 (0.75 to 2.72)	1.05 (0.84 to 1.31)
Unknown	0.43 (0.20 to 0.93)[a]	0.51 (0.31 to 0.85)[a]	0.28 (0.09 to 0.83)[a]	0.41 (0.28 to 0.59)[a]
No. of locations				
1	1.00	1.00	1.00	1.00
2-4	0.78 (0.53 to 1.16)	0.87 (0.63 to 1.20)	0.53 (0.21 to 1.35)	0.86 (0.69 to 1.08)
≥5	2.27 (1.40 to 3.67)[a]	2.15 (1.62 to 2.87)[a]	0.83 (0.42 to 1.61)	2.17 (1.75 to 2.69)[a]
Estimated enrollment				
0-50	1.00	1.00	1.00	1.00
50-100	0.40 (0.26 to 0.59)[a]	0.90 (0.69 to 1.17)	1.57 (0.35 to 7.00)	0.64 (0.52 to 0.78)[a]
100-200	0.13 (0.06 to 0.25)[a]	0.86 (0.61 to 1.21)	2.94 (0.74 to 11.66)	0.55 (0.42 to 0.71)[a]
200-500	0.04 (0.00 to 0.35)[a]	0.65 (0.41 to 1.03)	1.21 (0.33 to 4.47)	0.44 (0.31 to 0.62)[a]
>500	0.81 (0.12 to 5.36)	0.18 (0.07 to 0.49)[a]	0.40 (0.11 to 1.52)	0.17 (0.11 to 0.26)[a]

NOTE. NA indicates not being included in analysis because of either the limited sample size or no eligible data.
Abbreviations: OR, Odds ratio; NA, not applicable; TKI, tyrosine kinase inhibitor.
[a]Statistical significance.