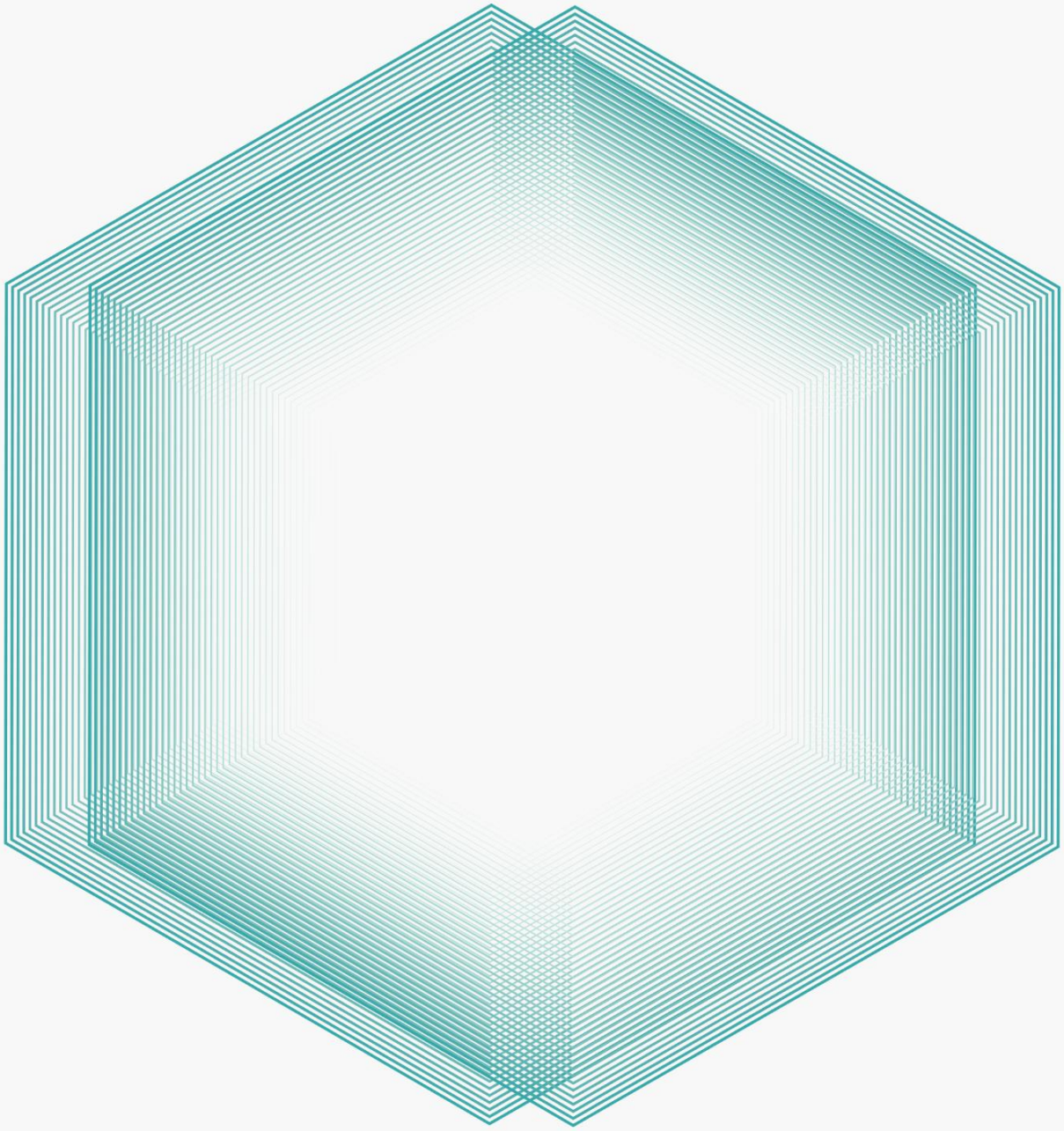
June 2022

Annual Report on the Current Status of **Clinical Trials for New Drug Registration in China**

2021



Center for Drug Evaluation
National Medical Products Administration

The Annual Report on Clinical Trials for New Drug Registration in China (2021) is Released by the Center for Drug Evaluation, NMPA

Release date: June 7, 2022

To better understand the progress of clinical trials for new drug registrations in China; to use informatization technology to improve the ability of intelligent supervision of drugs; to promptly disclose information about the progress of clinical trials to the public; and to provide a reference for new drug research and development (R&D), resource allocation, and drug review and approval, the Center for Drug Evaluation has conducted a comprehensive summary and analysis of clinical drug trials in China in 2021 based on data from the Drug Clinical Trial Registration and Information Disclosure Platform for its *Annual Report on Clinical Trials for New Drug Registration in China (2021)*.

The annual report mainly summarizes and analyzes the overall trend changes, main characteristics and outstanding problems based on clinical trials registered in 2021. It is compiled from the perspective of drug types, variety and target characteristics, indications, types of sponsors, registration classifications, trial classifications, trial phases, trials in special populations, leading institutions for clinical trials and duration from initiation to completion. Moreover, it summarizes and analyzes trends in recent years by comparing clinical trial registration data from the past three years.

Attachment: Annual Report on Clinical Trials for New Drug Registration in China (2021)

Center for Drug Evaluation, National Medical Products Administration

June 7, 2022

Abstract

Objectives

To better understand the current status of clinical trials for new drug registrations in China, to disclose clinical trial progress information to the public, and to provide a reference for new drug research and development (R&D), resource allocation, drug review and approval, the Center for Drug Evaluation of the National Medical Products Administration (hereinafter referred to as "CDE") has produced a comprehensive summary and analysis of clinical trials in China in 2021 according to data from the Drug Clinical Trial Registration and Information Disclosure Platform, and analyzed the change trend characteristics in the past three years to gradually improve the ability of supervision of drugs by using informatization technology.

Methods

The annual report mainly summarizes and analyzes the overall trend changes, main characteristics and outstanding problems of clinical trials based on the information of drug clinical trials registered in 2021, from the perspective of the type of drugs, varieties and target characteristics, indications, type of sponsors, registration classification, trial classification, trial phases, trials in special population, leading institution of clinical trials and duration from initiation to completion. It also summarizes and analyzes trends in recent years by comparing the clinical trial registration data in the past three years and complies with the *Annual Report on Clinical Trials for New Drug Registration in China (2021)*.

Key Findings

1. Number of Clinical Trials for New Drug Registration

The total number of clinical trials on the Drug Clinical Trial Registration and Information Disclosure Platform in 2021 exceeded 3,000 for the first time. It increased by 29.1% compared with the total registered number in 2020, in which the number of new drug clinical trials (exploratory and confirmatory clinical trials registered with an acceptance number) was 2,033, with an increase of 38.0% compared with the registered number in 2020.

2. Types of Drugs and Target Characteristics

According to the classification of chemical drugs, biological products and traditional Chinese medicines (TCMs) from the data analysis of the past three years, the percentages of new drug clinical trials of chemical drugs and biological products were relatively high, with an annual average of 54.6% and 40.4% respectively. The targets were relatively concentrated in the past three years, among which PD-1 and PD-L1 were particularly prominent. The indications were mainly concentrated in the anti-tumor field. From the analysis of trial phases, the percentage of phase Ⅲ clinical trials of PD-1 and PD-L1 targets was also higher than that of other targets.

3. Trial Classification and Sponsors

Drug clinical trials were classified into new drug clinical trials and bioequivalence trials (BE trials). In 2021, new drug clinical trials accounted for 60.5%, and BE trials accounted for 39.5%. From the data analysis of the past three years, the percentage of new drug clinical trials has increased year by year, while the percentage of BE trials has decreased year by year, from 47.3% in 2019 to 39.5% in 2021. Domestic sponsors still accounted for the majority, about 80% each year in the past three years.

4. Target Indications and Clinical Trial Phases

The target indications of clinical trials of chemical drugs and biological products were mainly concentrated in the anti-tumor and preventive vaccine fields. Affected by the COVID-19 epidemic, the number of clinical trials for novel coronavirus inactivated vaccines (n=20) in 2021 ranked first in preventive vaccine trials. In the past three years, TCMs were concentrated in four indications, i.e., respiratory, digestive, cardiovascular and psychoneurological indications.

The trend in the percentage of clinical trial phases in the past three years has remained the same, with phase I clinical trials accounting for the highest percentage. The overall percentage of phase I clinical trials in 2021 was 42.9%. Relatively few clinical trials were conducted in specific populations in the past three years, and clinical trials carried out only in the elderly and pediatric populations did not exceed 0.2% and 3% of the overall percentage of trials over the years, respectively. Rare disease drugs were mainly for the treatment of nervous system diseases and blood system diseases, and the number of clinical trials and indications showed a year-on-year growth trend.

5. Geographical Distribution of Clinical Trials

The leading and participating clinical trial institutions were still mainly in Beijing, Shanghai, Jiangsu Province and Guangdong Province.

6. Implementing Efficiency of Clinical Trials

An analysis of the clinical trials of new drugs registered for the first time showed that in 2021, more than half of the trials (51.4%) initiated subject recruitment within six months of approval, and the percentage of chemical drug and biological product trials were 51.2% and 58.1%, respectively, significantly higher than that of TCM trials. Nearly 90% (89.1%) of TCM trials initiated subject recruitment more than one year of approval. The analysis of the location of clinical trial institutions suggested that in provinces, autonomous regions and municipalities directly under the Central Government with more leading clinical trial institutions, it took longer to initiate clinical trials. But in provinces, autonomous regions and municipalities directly under the Central Government with fewer leading clinical trial institutions, it took less time to initiate clinical trials.

An analysis of the recruitment of subjects after the approval of clinical trials in the past three years showed that the average initiation time decreased from 6.4 months in 2019 to 3.8 months in 2021, and the percentage of clinical trials that initiated subject recruitment within six months of approval increased year by year, reaching 85.7% in 2021.

Conclusion

The total number of clinical trials on the Drug Clinical Trial Registration and Information Disclosure Platform in 2021 reached 3,358, exceeding 3,000 for the first time. The percentage of new drug clinical trials increased year by year, and phase I clinical trials have accounted for the highest percentage over the years, most of which were domestic trials initiated by domestic sponsors. The percentage of BE trials has shown a gradual downward trend in the past three years.

Clinical trials of chemical drugs and biological products were still mainly for tumor indications. The drug targets were relatively concentrated, especially PD-1 and PD-L1, and the number of phase Ⅲ clinical trials was relatively large. Affected by the COVID-19 epidemic in 2021, inactivated novel coronavirus vaccines underwent the largest number of clinical trials among all preventive vaccine biological products. TCMs underwent the smallest number of clinical trials, mainly concentrated in four indications, i.e., respiratory, digestive, cardiovascular and psychoneurological indications.

The percentage of clinical trials carried out in the elderly and pediatric populations (except for preventive vaccines) was still relatively low, and the clinical trials of rare disease drugs still involved a small number of diseases. In the 2021 registration information, the percentage of clinical trials with subject recruitment initiated within six months increased significantly (51.4%).

To sum up, the number of new drug clinical trials in China has been constantly growing, and most of them were new drug clinical trials initiated and implemented by domestic sponsors. With the continuous increase in the number of phase Ⅲ new drug clinical trials, the number of new drug marketing applications in China is expected to increase as well and the process will be accelerated to meet the new drug treatment needs of Chinese patients, including treatments for the pediatric population and treatments for rare diseases.

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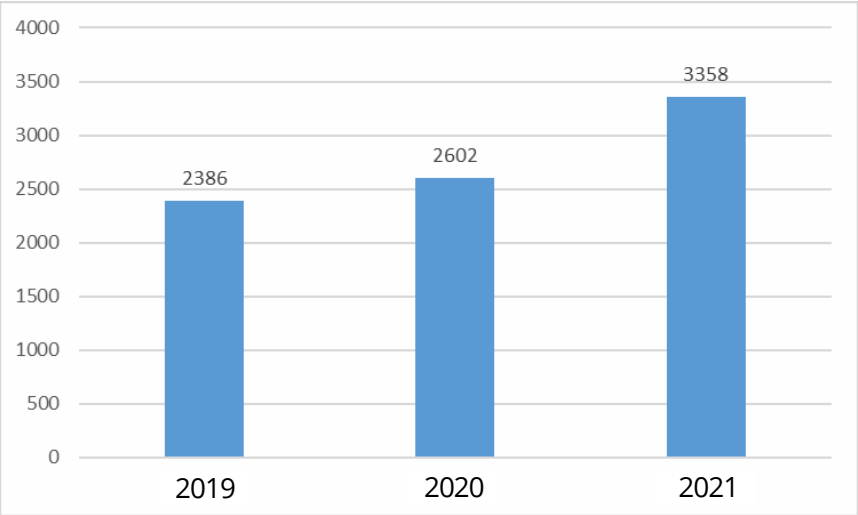
Chapter I Overview of Drug Clinical Trial Registration

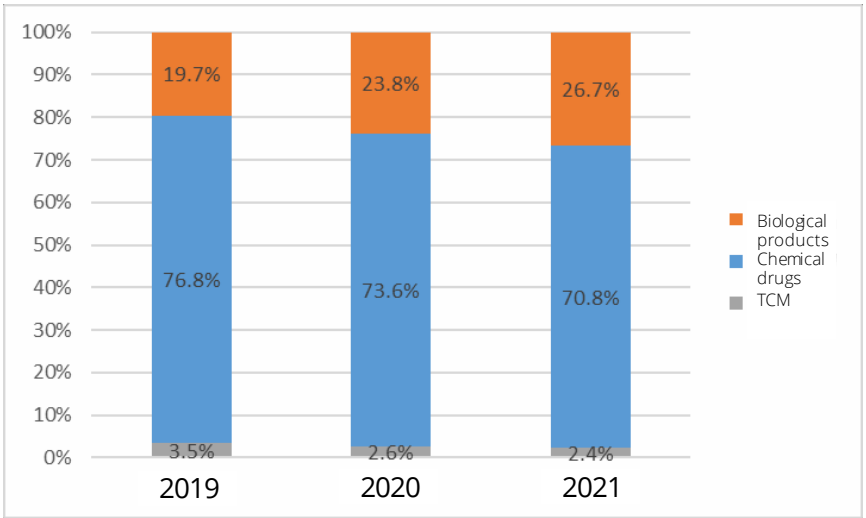
A total of 3,358 drug clinical trials were registered in China in 2021, exceeding 3,000 for the first time. The total number of clinical trials registered in 2020 and 2021 showed an increase of 9.1% and 29.1% over the previous year, respectively.



Changes in the total number of clinical trial registrations in 2019-2021 (based on CTR)

2021

According to the classification of chemical drugs, biological products and TCMs, in 2021, China's drug clinical trials were dominated by chemical drugs, accounting for 70.8%, followed by biological products, accounting for 26.7%, and then TCMs, accounting for only 2.4%. A comparison of the data in the past three years showed that the percentages of clinical trials of various drugs were similar, but the percentage of biological products was increasing year by year, while the percentages of chemical drugs and TCMs were decreasing year by year.

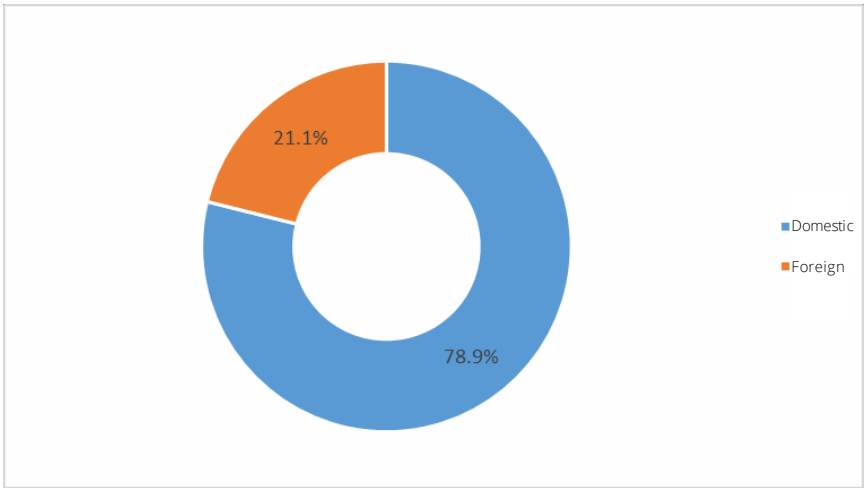


Changes in the overall percentages of various drugs (2019-2021)

Chapter Ⅱ Analysis of Basic Clinical Trial Characteristics

Ⅰ. Type of Sponsors

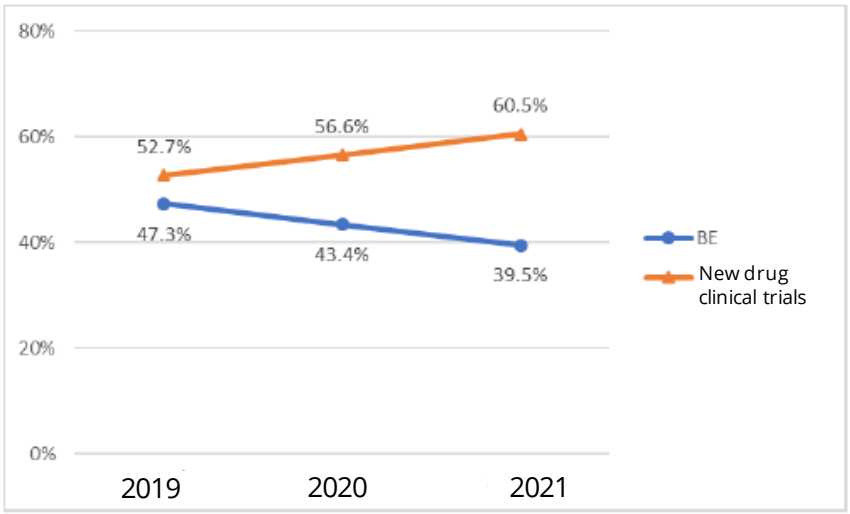
The types of sponsors were analyzed in accordance with the type of acceptance number, i.e., those with the initial letter J were counted as foreign sponsors, while the others were domestic sponsors. Clinical trials registered in 2021 were still mainly initiated by domestic enterprises, accounting for 78.9% (1,678 trials). In the past three years, there has been little change in the percentage of sponsor types, with foreign enterprises accounting for less than 30%, and only 19.1% in 2019, which was the lowest.



Distribution of types of clinical trial sponsors in 2021

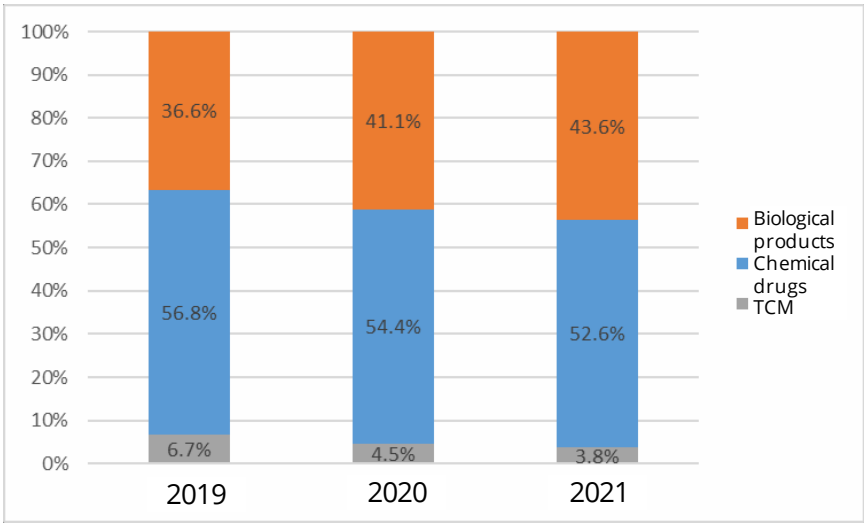
Ⅱ. Types of Clinical Trials

According to the new drug clinical trial statistics (registered by acceptance number) and bioequivalence trials (BE trials, mainly registered by filing number), in 2021, 2,033 new drug clinical trials (60.5%) and 1,325 BE trials (39.5%, including 94 BE trials registered by acceptance number) were registered. A comparison of the data in the past three years showed that the percentage of new drug clinical trials was increasing year by year, while the percentage of BE trials was decreasing year by year.



Changes in the percentage of new drug clinical trials for different types of drugs (2019-2021)

A comparison of the new drug clinical trial registration data over the past three years showed that the percentages of various drugs remained the same, with chemical drugs registered most (with an annual average percentage of 54.6%), followed by biological products (with an annual average percentage of 40.4%) and TCMs. Among the new drug clinical trials registered by acceptance number in 2021, 1,069 (52.6%), 886 (43.6%) and 78 (3.8%) were registered for chemical drugs, biological products and TCMs, respectively. The number of biological product trials increased significantly. In 2020 and 2021, the number of registrations increased by 31.5% and 46.4% over the previous year, and the number of registrations in 2019 and 2020 was 460 and 605 respectively.



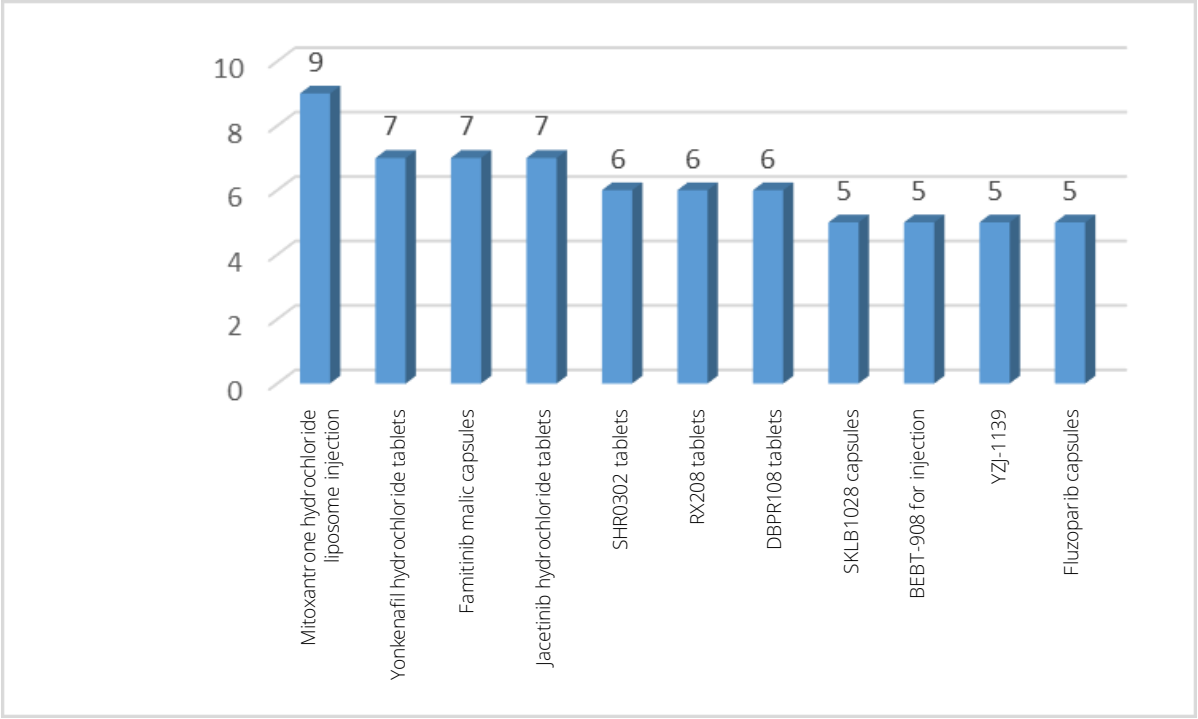
Changes in the percentage of new drug clinical trials for different types of drugs (2019-2021)

Ⅲ. Drug Types and Targets Involved

1. Types of New Drugs in Clinical Trials

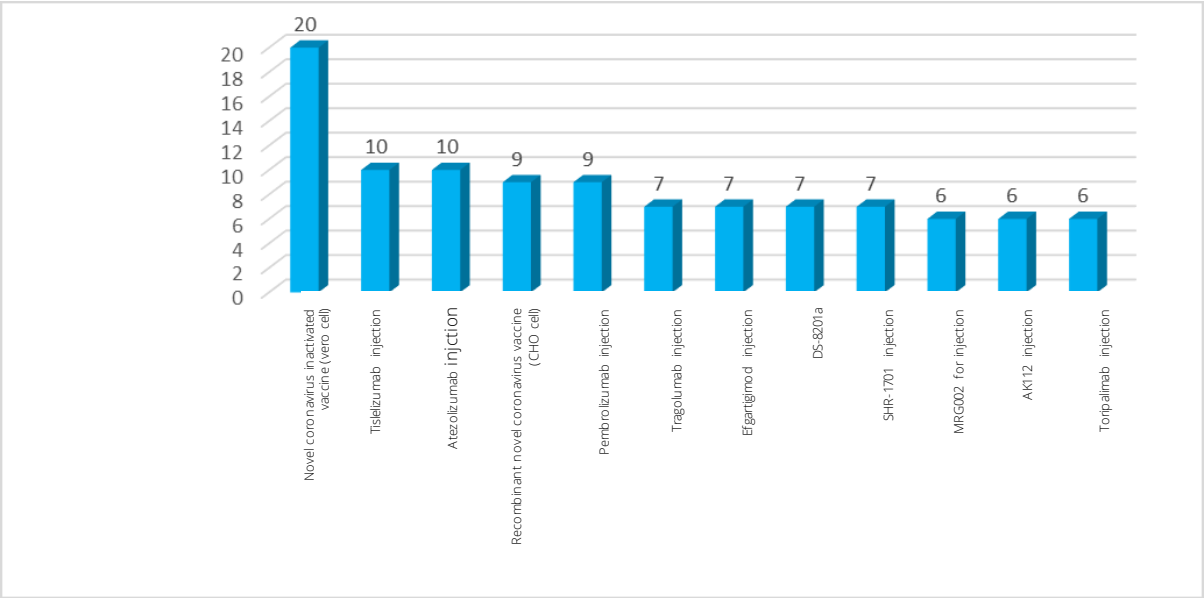
TCMs: Only one clinical trial was performed for nearly 90% of all TCMs. Varieties that underwent two clinical trials included Qishen Yiqi Dropping Pills, Suzi Afu Tablets, Baofukang Suppositories and Artificial Bear Bile Powder. Among them, Suzi Afu Tablets involved one suspended trial, which would be reinitiated after the protocol was updated. The overall trend of the data was basically the same, and only one trial was carried out in the same year for nearly 90% of the varieties.

Chemical drugs: In 2021, a total of 68 trials were registered for the top 10 varieties of chemical drugs. Mitoxantrone hydrochloride liposome injection underwent the largest number of clinical trials (n=9). As of 2020, the top 10 varieties all included anti-tumor drugs mitoxantrone hydrochloride liposome injection, famitinib malic capsules, jacetinib hydrochloride tablets and fluzoparib capsules. The difference was that the top 10 varieties included four non-anti-tumor drugs, namely yonkenafil hydrochloride tablets, SHR0302 tablets, DBPR108 tablets and YZJ-1139. As can be seen from an analysis of the data, more than 50% of the top 10 varieties were anti-tumor drugs, and fluzoparib capsules remained one of the top 10 varieties over the past three years.



Top 10 varieties of chemical drugs in terms of number of clinical trials in 2021

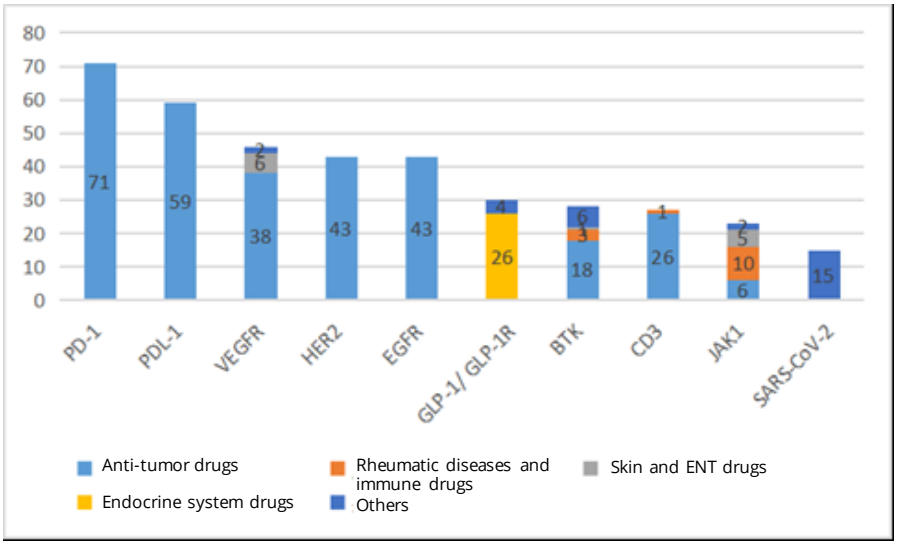
Biological products: In 2021, a total of 104 clinical trials were registered for the top 10 varieties of biological products, mainly therapeutic biological products, involving a total of 75 trials (72.1%) for 10 varieties. Preventive biological products involved 29 trials (27.9%) for two varieties, all of which were novel coronavirus vaccines. Novel coronavirus inactivated vaccines (vero cell) underwent the largest number of clinical trials (n=20), followed by tislelizumab injection and atezolizumab injection (n=10 for each), both of which were among the top 10 varieties in 2020. A comparison of the data in the past three years showed that the top 10 varieties were all dominated by therapeutic biological products, which accounted for the highest percentage of 88.7% (94 vs. 106) in 2019. Pembrolizumab injection remained one of the top 10 varieties in the past three years.



Top 10 varieties of biological products in terms of number of clinical trials in 2021

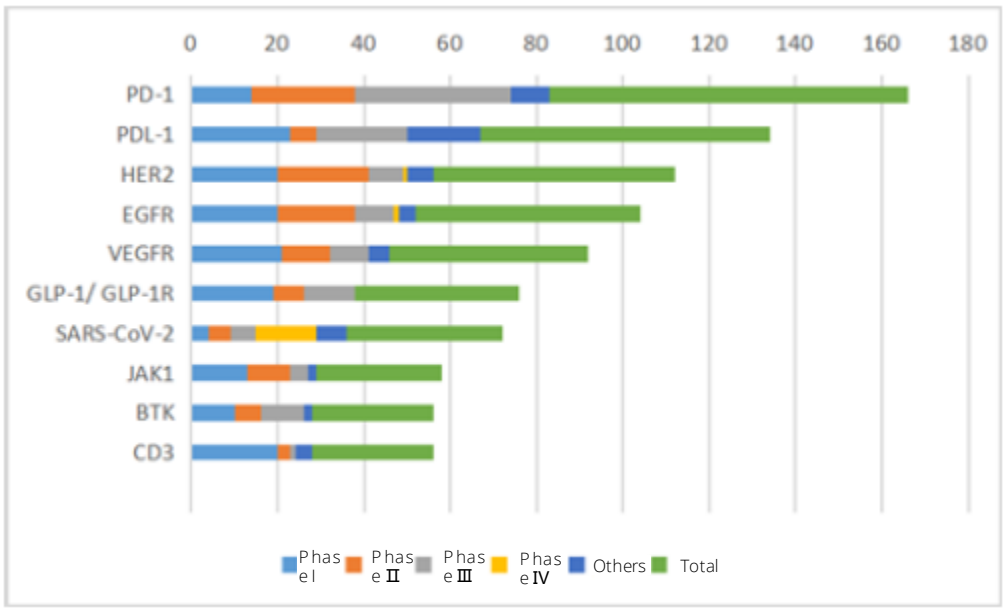
2. Targets of Varieties in New Drug Clinical Trials

The top 10 targets of drug varieties with registered clinical trials in 2021 were PD-1, PD-L1, VEGFR, HER2, etc. The number of varieties involved was up to 71, 59, 46, and 43, respectively (not repeatedly counted by "acceptance number" field), of which more than 90% of the drug indications of five targets (PD-1, PD-L1, HER2, EGFR and CD3) were concentrated in the anti-tumor field, and the drug indications of four targets (PD-1, PD-L1, HER2 and EGFR) were all concentrated in the anti-tumor field.



Top 10 targets of drug varieties and indications field distribution in 2021

The top 10 targets with the greatest number of clinical trials in 2021 were PD-1, PD-L1, HER2, EGFR, etc. The number of varieties involved reached 84, 68, 57 and 53 respectively. Among them, PD-1 and PD-L1 targets underwent 36 and 21 phase Ⅲ clinical trials, respectively. In addition, the percentages of phase I clinical trials in drug clinical trials of four targets (VEGFR, GLP-1/GLP-1R, JAK1 and CD3) exceeded 40%, and the percentage of phase Ⅱ clinical trials in each target was between 8% and 37%.

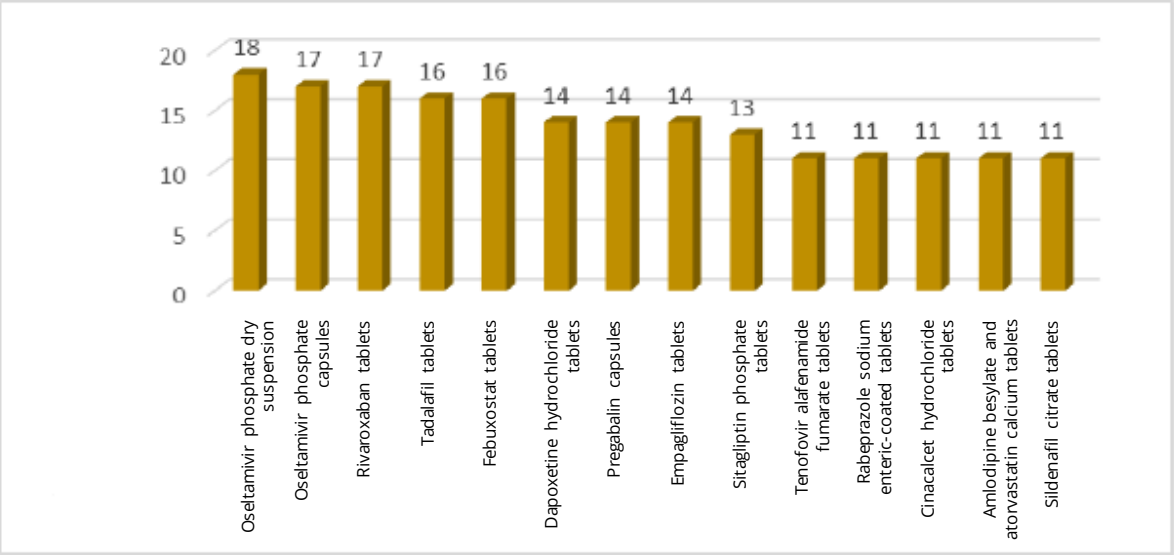


Top 10 targets and trial phases in terms of the number of clinical trials in 2021

A comparison of the data in the past three years showed that either by the number of drug varieties or the number of clinical trial registrations, drug targets were still relatively concentrated, among which PD-1 and PD-L1 were particularly prominent, and the indications were mainly concentrated in the anti-tumor field. From the analysis of trial phases, the percentages of PD-1 and PD-L1 targets in phase Ⅲ clinical trials were also higher than other targets. Other targets were still mainly in phase I clinical trials.

3. Drugs Involved in Bioequivalence Trials

The top 10 varieties involved in BE trials (including registrations by acceptance number) in 2021 are as follows. Oseltamivir phosphate dry suspension registered the largest number of trials (n=18), as shown below.



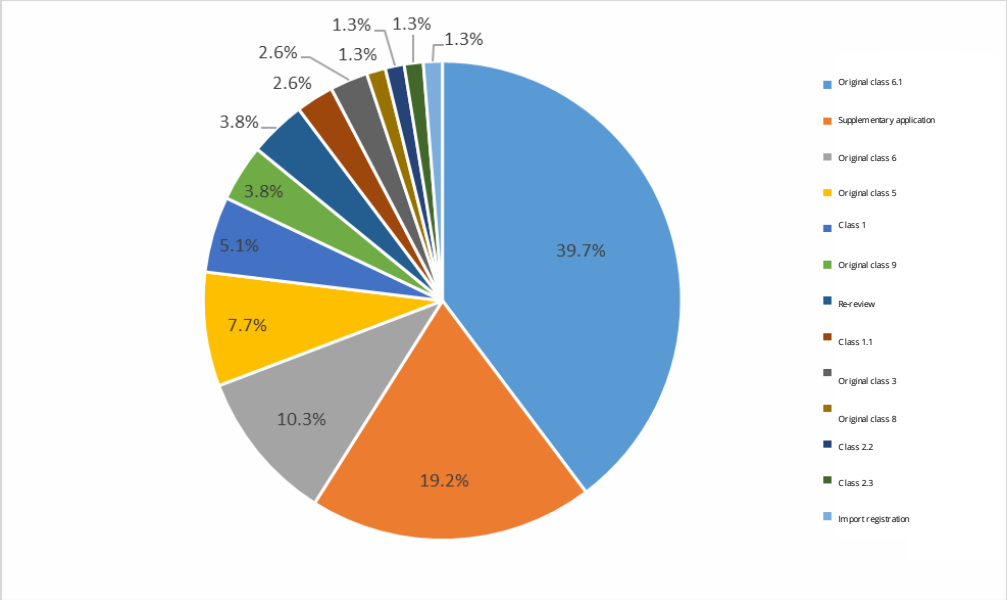
Top 10 varieties in terms of number of BE trials in 2021

Compared with 2020, four varieties remained in the top 10 varieties, namely oseltamivir phosphate capsules, rivaroxaban tablets, tadalafil tablets and tenofovir fumarate tablets. From the data analysis of the past three years, rivaroxaban tablets were one of the top three varieties over the years.

IV.Drug Types and Registration Classifications

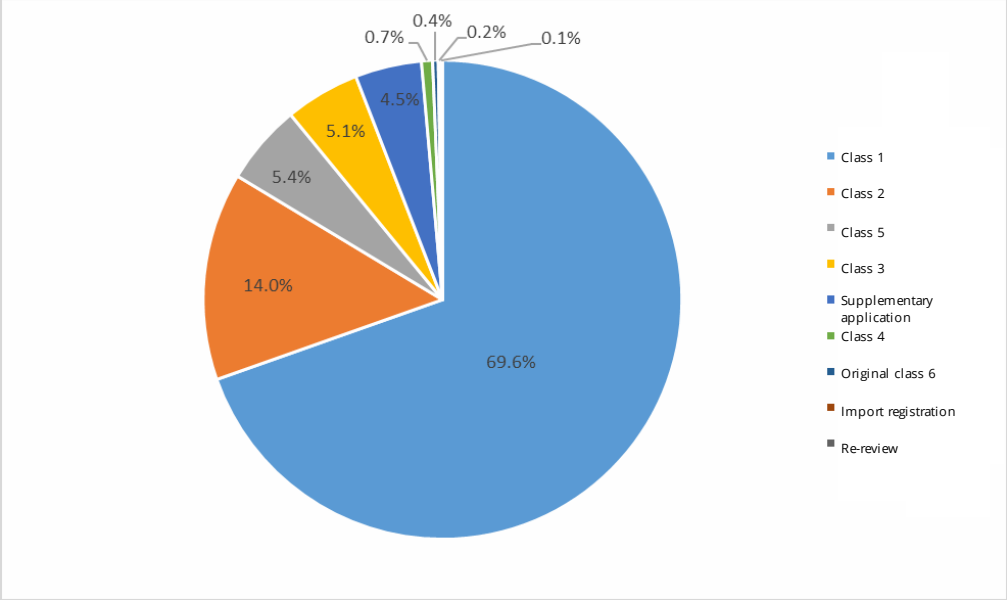
TCMs: 78 clinical trials were registered in 2021, mainly in the original registration classification class 6 (including class 6 and class 6.1), which accounted for 50.0%, followed by supplementary applications.

A comparison of the data in the past three years showed that in 2019, the original registration classification class 6 (including class 6 and class 6.1) accounted for the highest percentage, reaching 63.1%; in 2020, the registration classification class 1 (including the original registration classification) was dominant, accounting for 62.5%.



Registration classification of TCMs in 2021

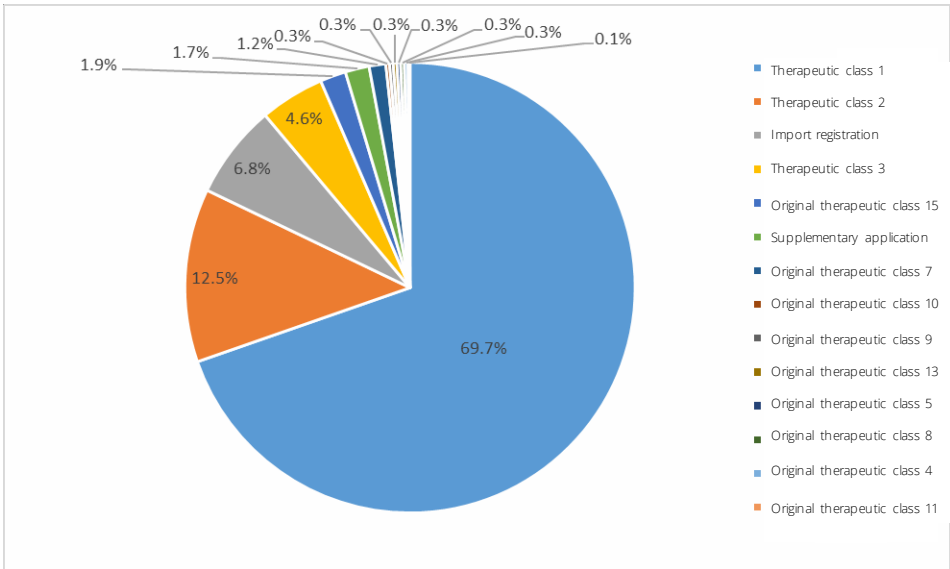
Chemical drugs: For new drug clinical trials registered by acceptance number, the drugs in registration class 1 (including the original registration classification) accounted for the largest percentage in the past three years, and the percentage peaked at 71.2% in 2020, and was 69.6% and 54.2% in 2021 and 2019, respectively.



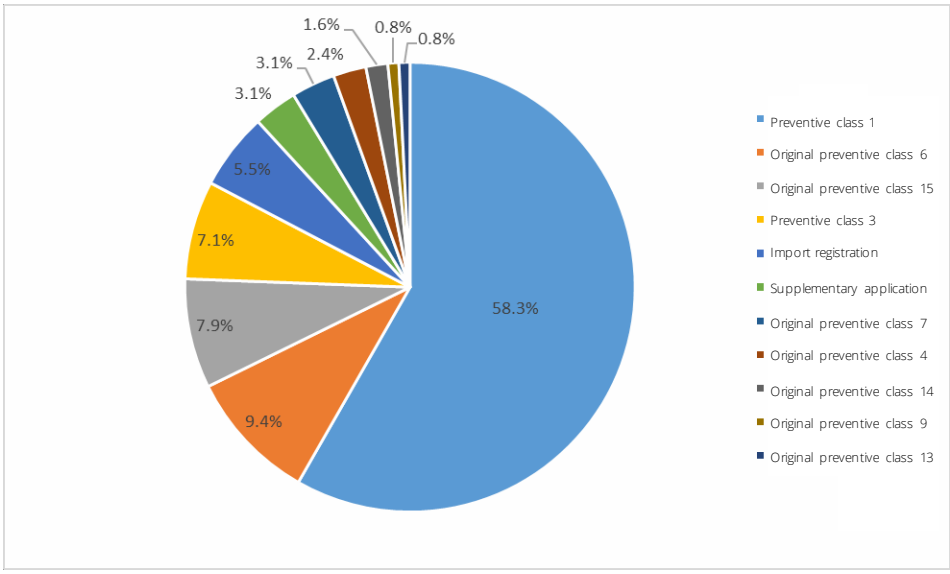
Registration classification of chemical drugs in 2021

Biological products: In 2021, therapeutic biological products were mainly class 1 and class 2 (including the original registration classification), accounting for 69.7% and 12.5%, respectively; preventive biological products were mainly class 1 and class 6, accounting for 58.3% and 9.4%, respectively.

As can be seen from the comparison of the data over the past three years, the percentage of class 1 therapeutic biological products showed year-on-year growth of 48.7% and 65.4% in 2019 and 2020, respectively. The percentage of class 1 preventive biological products also showed a year-on-year growth trend, jumping from 31.3% in 2019 to 46% in 2020.



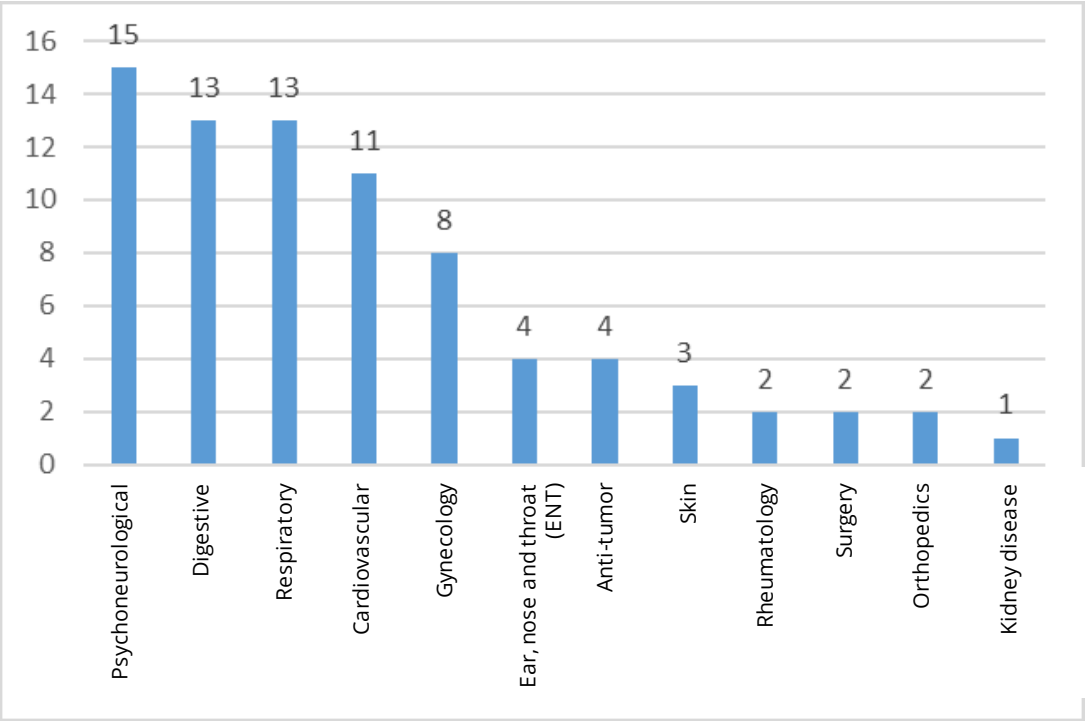
Registration classification of therapeutic biological products in 2021



Registration classification of preventive biological products in 2021

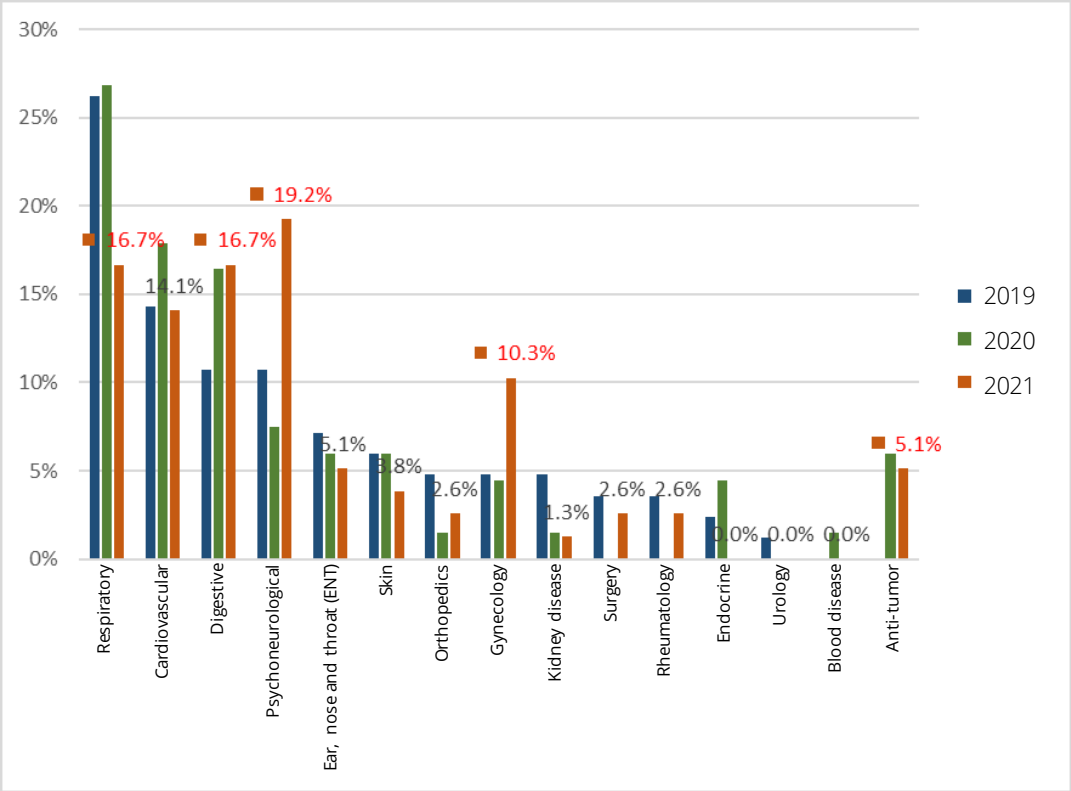
V. Target Indications

TCMs: New drug clinical trials for TCMs mainly focused on five indications, i.e., psychoneurological, digestive, respiratory, cardiovascular and gynecology indications, accounting for approximately 76.9% of the overall clinical trials of TCMs. Among them, psychoneurological indications accounted for the highest percentage of 19.2%; digestive and respiratory indications accounted for the same percentage of 16.7%.



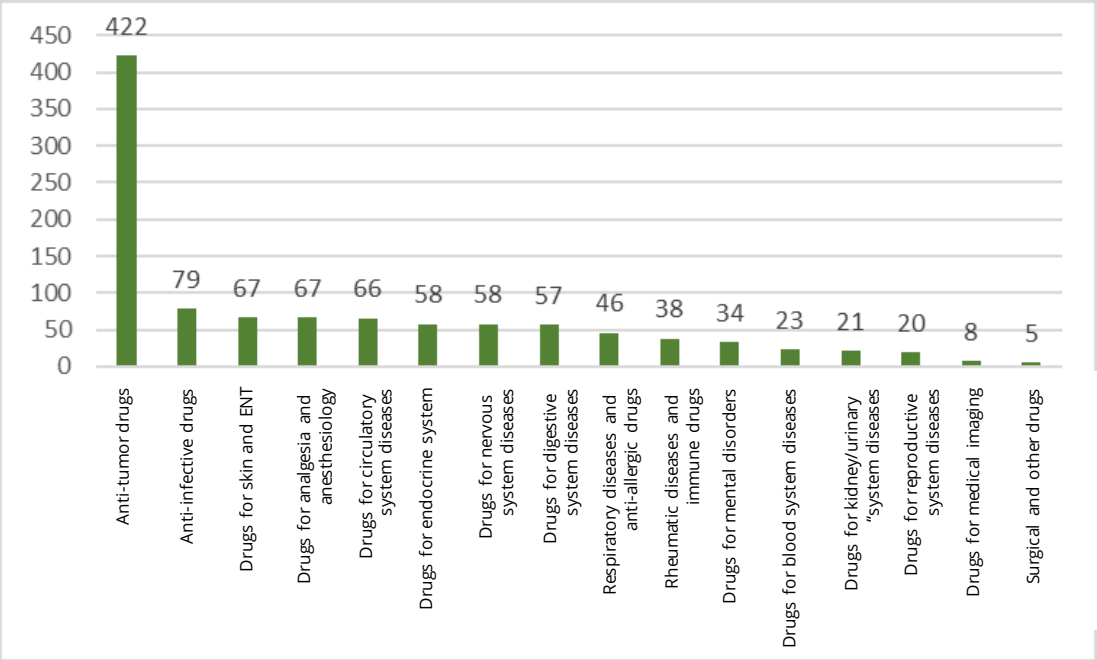
Registration classification of therapeutic biological products in 2021

A comparison of the data in the past three years showed that clinical trials were mainly concentrated in four indications, i.e., respiratory, digestive, cardiovascular and psychoneurological indications, whose overall percentages over the years all exceeded 60% (61.9%, 68.6% and 66.7% from 2019 to 2021, respectively), but the percentage of trials in respiratory indications in 2021 dropped significantly compared to 2019 and 2020, from 26.2% in 2019 to 16.7% in 2021. The percentages of trials in digestive and psychoneurological indications increased significantly compared to 2019. In addition, the percentages of trials in gynecology and anti-tumor indications increased significantly compared to 2019.



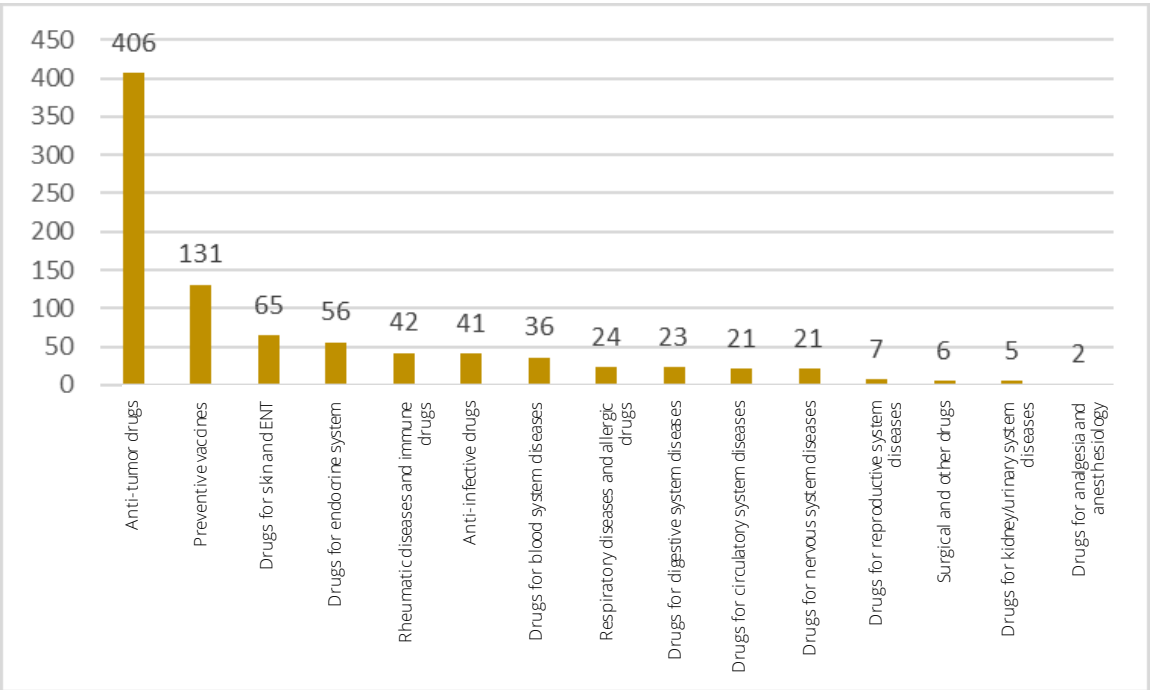
Changes in indication distribution of TCM clinical trials (2019-2021)

Chemical drugs: In 2021, chemical drug indications were mainly concentrated in anti-tumor drugs, accounting for 39.5% of all clinical trials of chemical drugs, followed by anti-infective drugs (7.4%), drugs for skin and ENT (6.3%), drugs for analgesia and anesthesiology (6.3%), drugs for circulatory system diseases (6.2%), and drugs for endocrine system (5.4%).



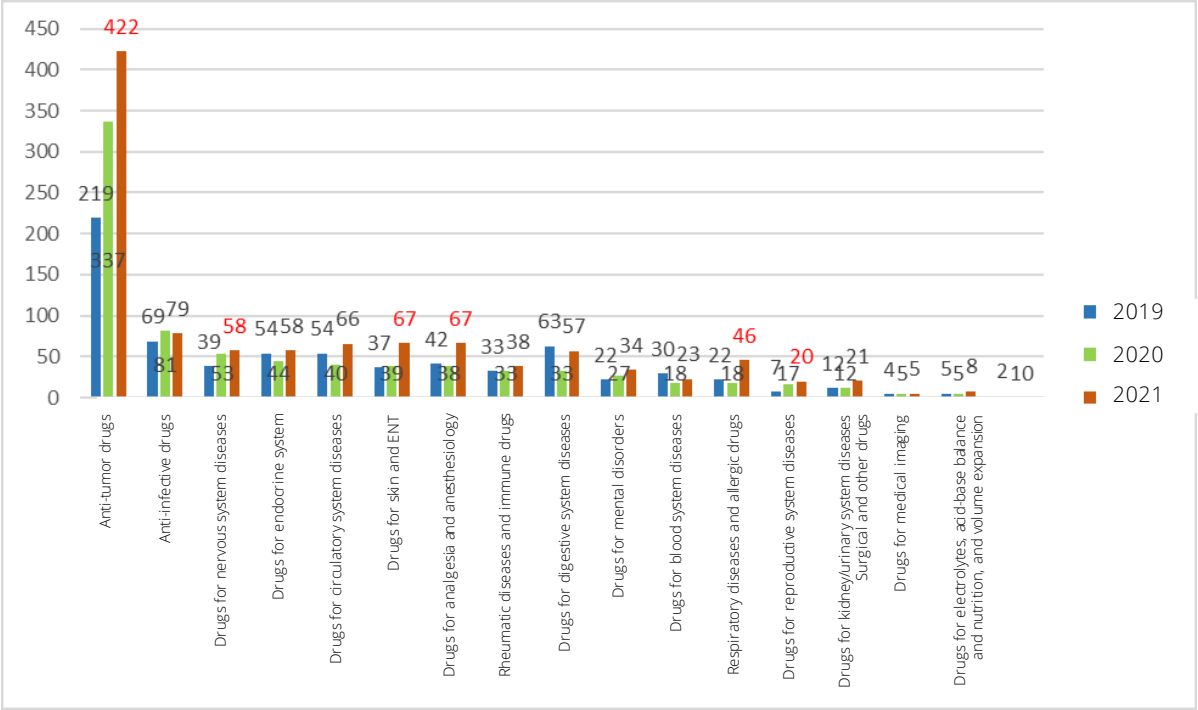
Indication distribution of clinical trials of chemical drugs in 2021

Biological products: In 2021, biological product indications were also mainly anti-tumor drugs, accounting for 45.8% of the overall clinical trials of biological products, followed by preventive vaccines (14.8%), drugs for skin and ENT (7.3%), drugs for endocrine system (6.3%) and rheumatic diseases and immune drugs (4.7%).



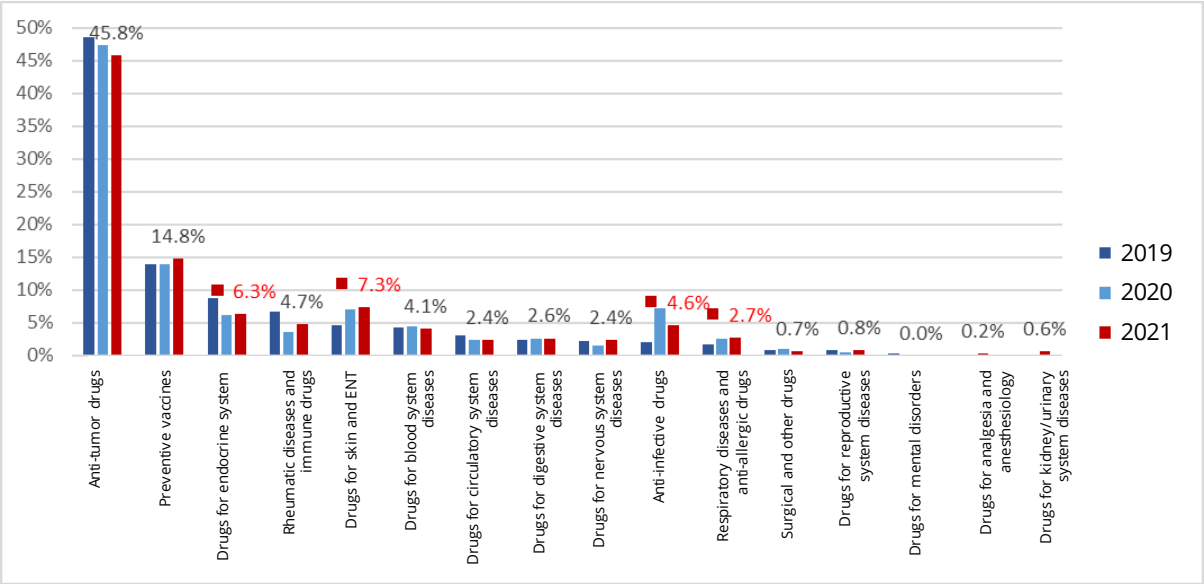
Indication distribution of clinical trials of biological products in 2021

The data in the past three years were all dominated by anti-tumor drugs, which accounted for 30.1%-42.1%, and the number of clinical trials showed a significantly increasing yearly trend. There were twice as many anti-tumor clinical trials in 2021 as in 2019 (422 vs. 219). Anti-infective drugs ranked second among all indications over the years, accounting for 7.4%-10.1%. Drugs for circulatory system diseases and drugs for endocrine drugs ranked among the top five among all indications over the years. In addition, the number of clinical trials of drugs for skin and ENT, drugs for analgesia and anesthesiology, and respiratory diseases and allergic drugs also grew significantly in 2021, about 1.7-2.5 times more than the previous year. Clinical trials of drugs for nervous system and reproductive system diseases grew significantly in 2020 and 2021, 1.3-1.4 and 2.4-2.8 times 2019 figures, respectively.



Changes in indication distribution of clinical trials of chemical drugs (2019-2021)

A comparison of the data in the past three years showed that anti-tumor drugs and preventive vaccines both ranked top in the top two over the years. Percentages were basically consistent (45.8-48.5% and 13.9-14.8%, respectively). Drugs for skin and ENT and endocrine system drugs ranked among the top five. The percentage of clinical trials of drugs for skin and ENT showed a year-on-year growth trend, growing from 4.6% in 2019 to 7.3% in 2021, while the percentage of clinical trials of drugs for endocrine system showed a downward trend, dropping from 8.7% in 2019 to 6.3% in 2021. In addition, the percentage of clinical trials of respiratory diseases and anti-allergic drugs showed year-on-year growth, from 1.7% in 2019 to 2.7% in 2021. Clinical trials of anti-infective drugs, however, dropped from 7.3% in 2020 to 4.6% in 2021.

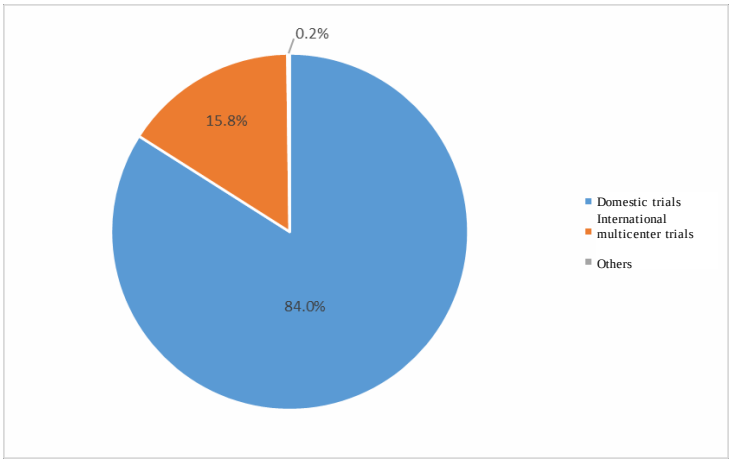


Changes in indication distribution of clinical trials of biological products (2019-2021)

Ⅵ. Domestic and Foreign Distribution of Clinical Trials

Overall, new drug clinical trials were still dominated by domestic clinical trials. Domestic drug clinical trials in 2021 accounted for 89.8% (n=3,014), and international multi-center trials accounted for 9.7% (n=325). Single-center clinical trials that did not recruit subjects in China or were only conducted abroad were counted under the classification of "others" and accounted for 0.6% (n=19). Among the new drug clinical trials registered by acceptance number in 2021, international multi-center trials of new drugs accounted for a relatively high percentage, reaching 15.8% (n=321), and domestic trials accounted for 84.0% (n=1,708).

A comparison of the data in the past three years showed that the drug clinical trials were generally dominated by domestic clinical trials. The percentage of international multi-center trials showed a year-on-year growth trend. The number of registrations in 2020 and 2021 increased by 21.6% and 54.3% compared with the previous year, respectively (n=171 and n=208 in 2019 and 2020, respectively).

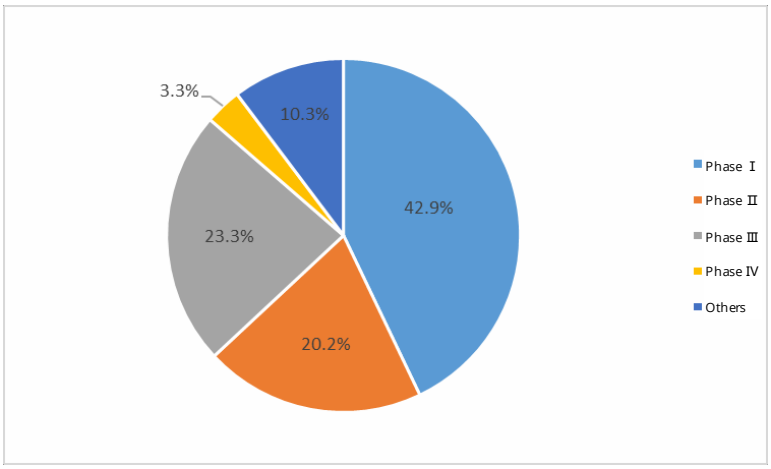


Distribution of new drug clinical trials in 2021

Ⅶ. Clinical Trial Phases

Among the new drug clinical trials registered by acceptance number in 2021, phase Ⅰ accounted for 42.9% (n=872), and phase Ⅲ and phase Ⅱ accounted for 23.3% (n=474) and 20.2% (n=410), respectively. There were 68 phase Ⅳ clinical trials (mainly clinical trials explicitly required in the marketing approval). Trials that could not be completely divided into phases Ⅰ-Ⅳ should be counted as "others", such as phase Ⅰ/Ⅱ.

The percentage of clinical trials in each phase has remained the same in the past three years. The percentage of phase Ⅰ clinical trials was the highest, followed by phase Ⅲ and phase Ⅱ and then phase Ⅳ.



Percentage of different phases of new drug clinical trials in 2021

Ⅷ. Sample Size Distribution of Clinical Trials

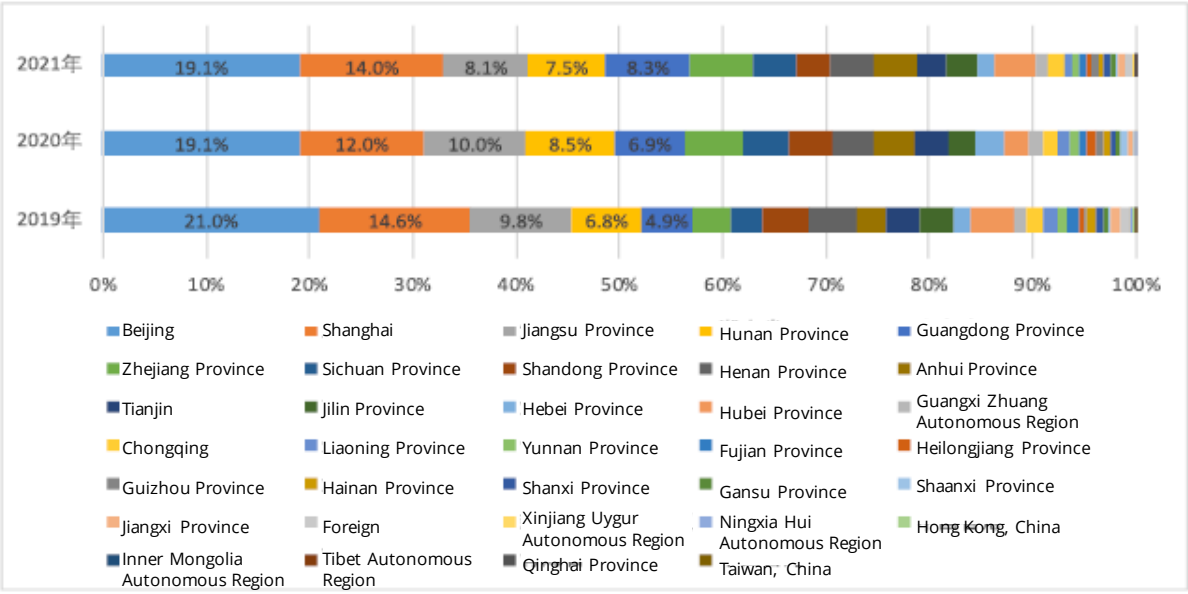
Among the new drug clinical trials registered by acceptance number in 2021, a total of 1,929 trials had domestic target enrollments registered, with the average target enrollments of 943.5. According to the drug types and trial phases, the sample size distribution is as follows:

Drug Type	Average Target Enrollment				
	Phase Ⅰ	Phase Ⅱ	Phase Ⅲ	Phase Ⅳ	**Others**
Chemical drugs	51.6	102.0	285.7	817.5	**156.1**
Biological products	76.3	161.2	639.1	37290.8	**487.4**
TCMs	**62.0**	**174.3**	**413.8**	**2200.0**	**280.0**

Ⅸ. Leading Clinical Trial Institutions

Among the drug clinical trials registered in 2021, clinical trial institutions in Beijing participated as the leading institutions (if an institution participated in multiple trials as a leading institution at the same time, it was counted separately) most frequently (753 times), accounting for about 19.1% of the total. This was consistent with 2020.

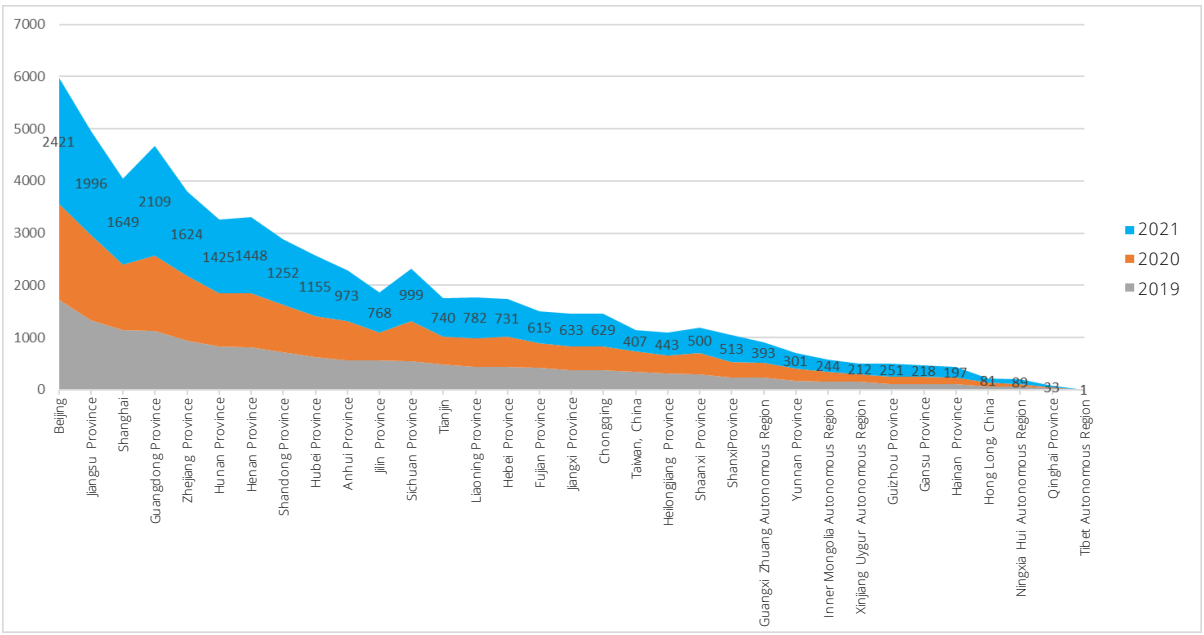
According to all the clinical trials registered in the past three years, the five provinces, autonomous regions and municipalities under the Central Government (including Hong Kong, Macao and Taiwan) with clinical institutions that participated in clinical trials most frequently as leading institutions over the years have always been Beijing, Shanghai, Guangdong Province, Jiangsu Province and Hunan Province, accounting for 57.0%, 56.4% and 56.9% of the total number of clinical trial registrations from 2019 to 2021. Among them, Beijing and Shanghai both ranked as the top two, accounting for 35.6%, 31.1% and 33.1% of clinical trial registrations from 2019 to 2021, respectively.



Changes in the percentage of leading clinical trial institutions in different provinces, autonomous regions and municipalities under the Central Government (2019-2021)

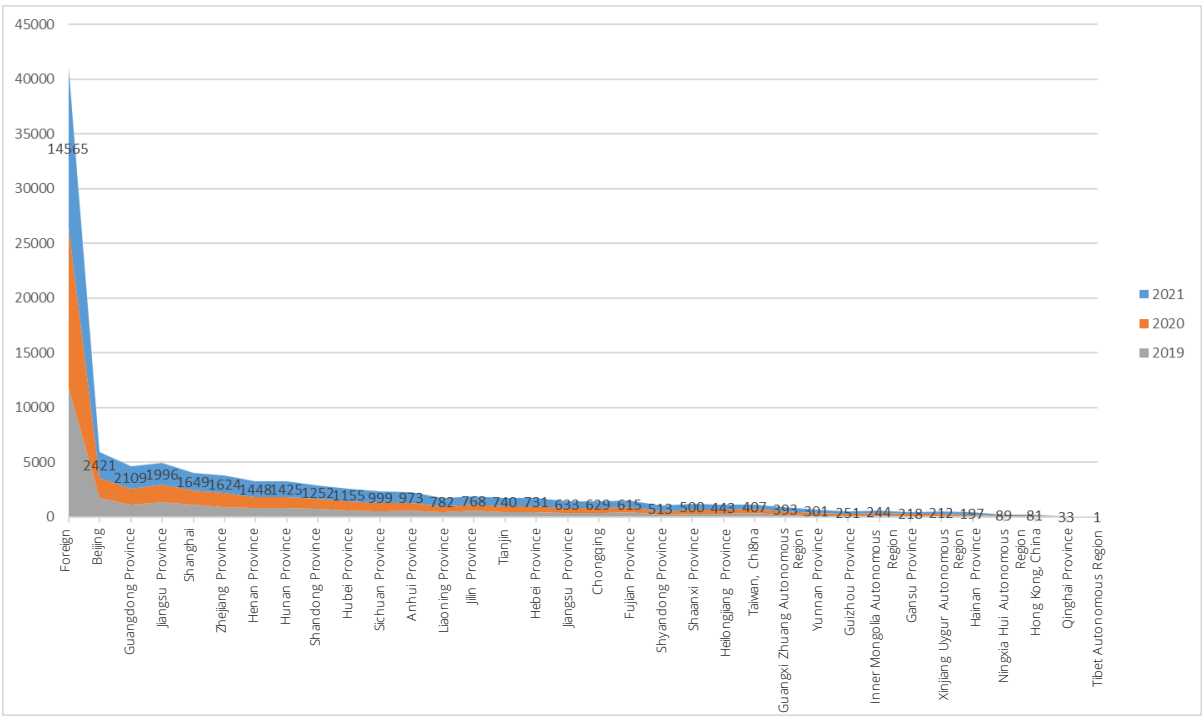
X. Participating Clinical Trial Institutions

Clinical trial institutions participated in trials 40,397 times in China and abroad in all drug clinical trials registered in 2021 (if a clinical trial institution participated in multiple clinical trials at the same time, it was counted separately) and 25,832 times in China (including Hong Kong, Macau, and Taiwan). Five provinces, autonomous regions and municipalities under the Central Government with clinical institutions that participated in clinical trials more than 1,500 times in 2021 included Beijing, Guangdong Province, Jiangsu Province, Shanghai, and Zhejiang Province, significantly higher than 2020. The institutions in Beijing and Guangdong Province participated more than 2,000 times.

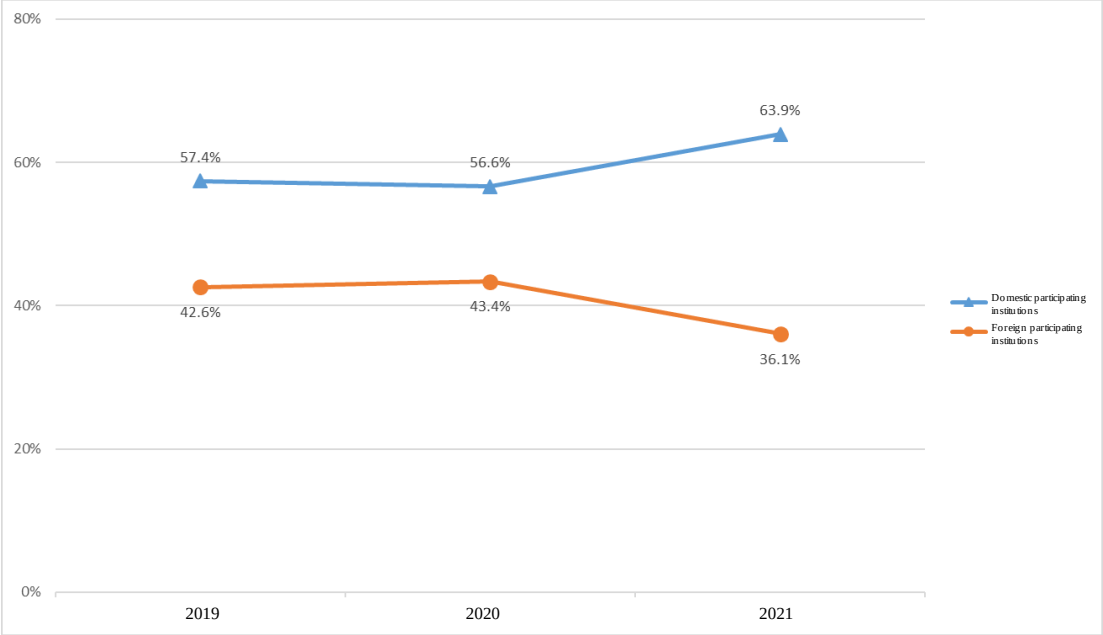


Frequency of participation in clinical trials by provinces, autonomous regions and municipalities under the Central Government in China (2019-2021)

A comparison of the data in the past three years showed that the percentages of times of participation in domestic clinical trials for foreign institutions in 2019 and 2020 basically remained the same at 42.6% and 43.4%, respectively, and the percentage in 2021 dropped to 36.1%.



Frequency of participation in clinical trials for participating institutions at home and abroad (2019-2021)



Changes in the percentage of participating institutions at home and abroad (2019-2021)

Chapter Ⅲ Other Characteristics of Clinical Trials

I. Drug Clinical Trials in Special Populations

1. Drug Clinical Trials in Geriatric Populations

There were 1,515 trials involving geriatric subjects in drug clinical trials in 2021, accounting for 74.5% (1,515 vs. 2,033) of the new drug clinical trials registered by acceptance number. Three trials were carried out only in the geriatric population, accounting for 0.1%. The specific information is as follows.

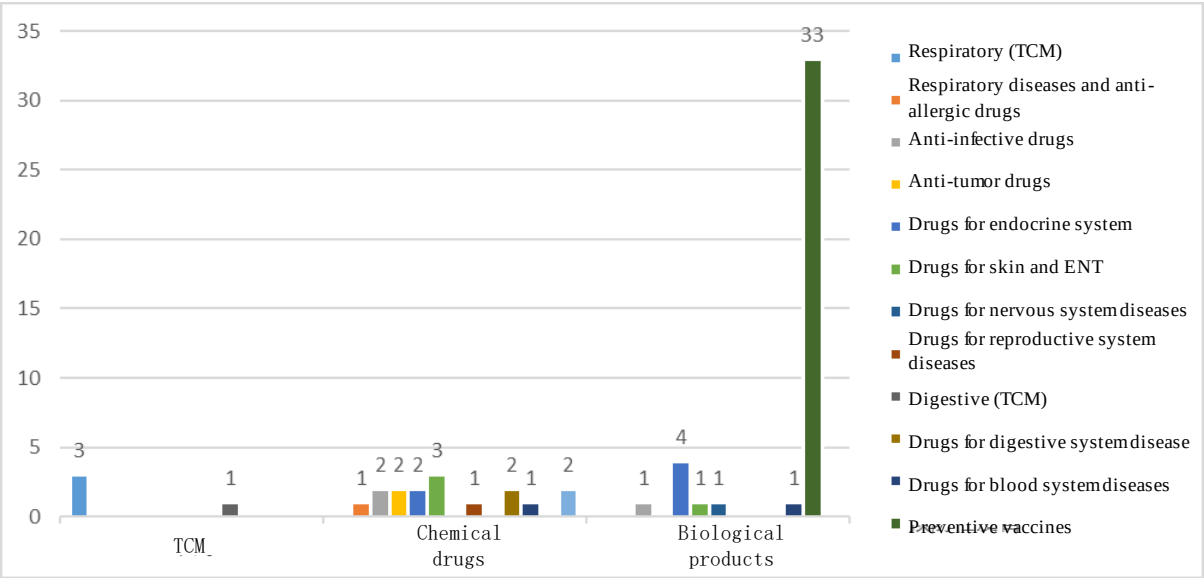
Drug Type	Trial Phase	Indication			Total
		Insufficient secretion of endogenous growth hormone in adults	Parkinson's disease	Mild to moderate Alzheimer's disease	
Chemical drugs	Phase Ⅰ	-	1	-	**1**
Biological products	Phase Ⅱ	1	-	-	**1**
TCMs	**Phase Ⅱ**	**-**	**-**	**1**	**1**

A comparison of the data in the past three years showed that the number and percentage of trials in the geriatric population maintained a consistent trend. Trials involving geriatric subjects accounted for about 70% over the years. Trials conducted only in the geriatric population accounted for no more than 0.2% of clinical trials over the years. No geriatric subjects entered phase Ⅲ clinical trials.

2. Drug Clinical Trials in Pediatric Populations

There were 168 trials involving pediatric subjects in 2021, which accounted for 8.3% (168 vs. 2,033) of the new drug clinical trials registered by acceptance number. According to an analysis by drug types, 110 trials were registered for biological products, the largest amount, followed by chemical drugs and TCMs; according to the analysis by indications, chemical drugs were mainly anti-tumor drugs and drugs for skin and ENT. Biological products were mainly preventive vaccines and blood system disease drugs. TCMs were mainly respiratory drugs.

A total of 61 new drug clinical trials were registered only for the pediatric population, accounting for 3.0% (61 vs. 2,033) of all new trials. 41 trials for biological products were registered, the largest amount, followed by 16 chemical drug trials and four TCM trials. According to the analysis by indications, biological products were mainly preventive vaccines, accounting for 80.5% of overall biological products. Chemical drugs were mainly for skin and ENT indications. TCMs were mainly for respiratory indications.

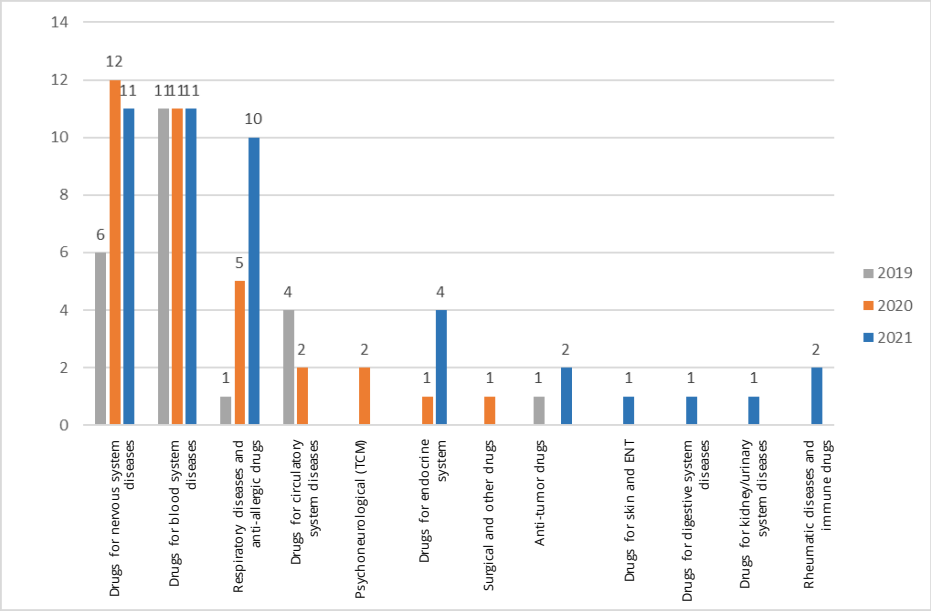


Number and indication distribution of clinical trials conducted only in the pediatric population in 2021

A comparison of the data in the past three years showed that the percentage of new drug clinical trials conducted only in the pediatric population did not exceed 3%. Biological product trials were conducted most for preventive vaccines. TCMs were mainly for respiratory indications. The distribution of chemical drug indications was relatively scattered, with no obvious trend characteristics.

3. Clinical Trials of Rare Disease Drugs

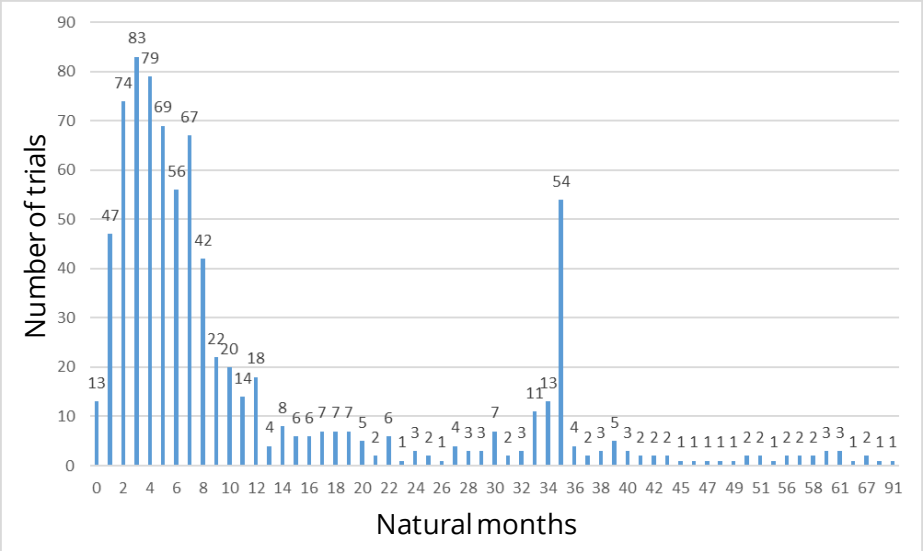
Using the Chinese term "rare diseases" as keywords, clinical trials of rare disease drugs in the past three years were analyzed. The drugs for the treatment of rare diseases were mainly chemical drugs and biological products. The number of clinical trials showed year-on-year growth. The total number of clinical trials in 2021 was nearly twice that of 2019 (43 vs. 23). Trials were mainly for nervous system diseases and blood system diseases in the past three years. Compared with 2019, the indication fields in 2020 and 2021 gradually expanded.



Changes in indication distribution of clinical trials of rare disease drugs (2019-2021)

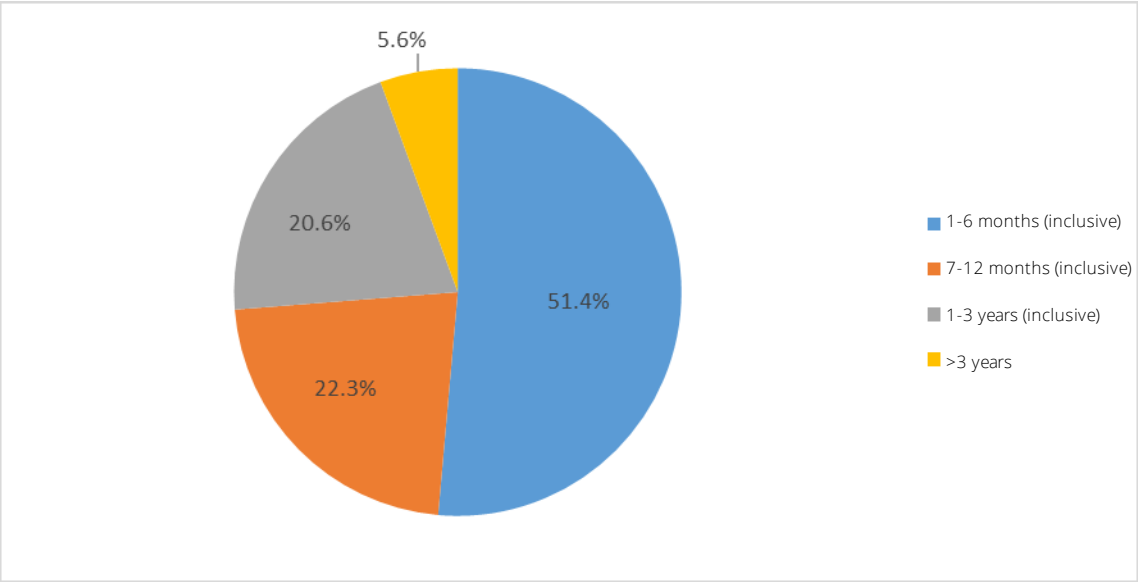
Ⅱ. Clinical Trial Startup Times

There were 819 trials registered in 2021 with the first valid subject's Informed Consent Form (ICF) date and no relevant registration number information (i.e., excluding trials approved before 2021 but newly added in 2021) in China. The elapsed time for clinical trial initiation (calculated by the ICF date and the clinical trial approval date) ranged from three days to 91 months, with an average of 12.2 months.

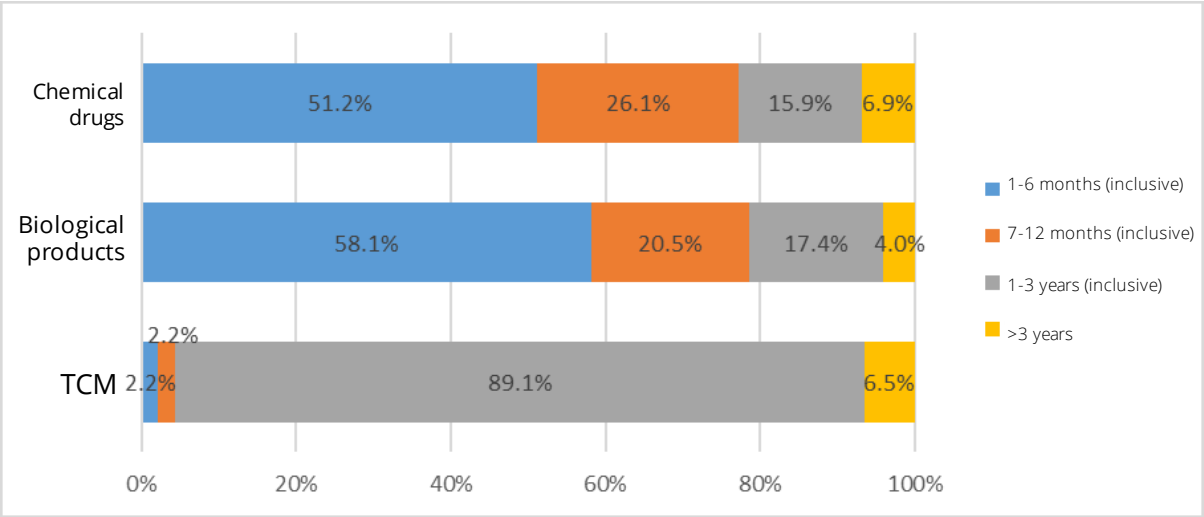


Distribution of startup times for new drug clinical trials in 2021

Overall, more than half of the trials (51.4%) were able to initiate subject recruitment within six months of approval. In terms of drug types, the percentages of chemical drug and biological product trials that initiated subject recruitment within six months (51.2% and 58.1%, respectively) were significantly higher than that of TCM trials, while nearly 90% (89.1%) of TCM trials initiated subject recruitment more than one year after approval.

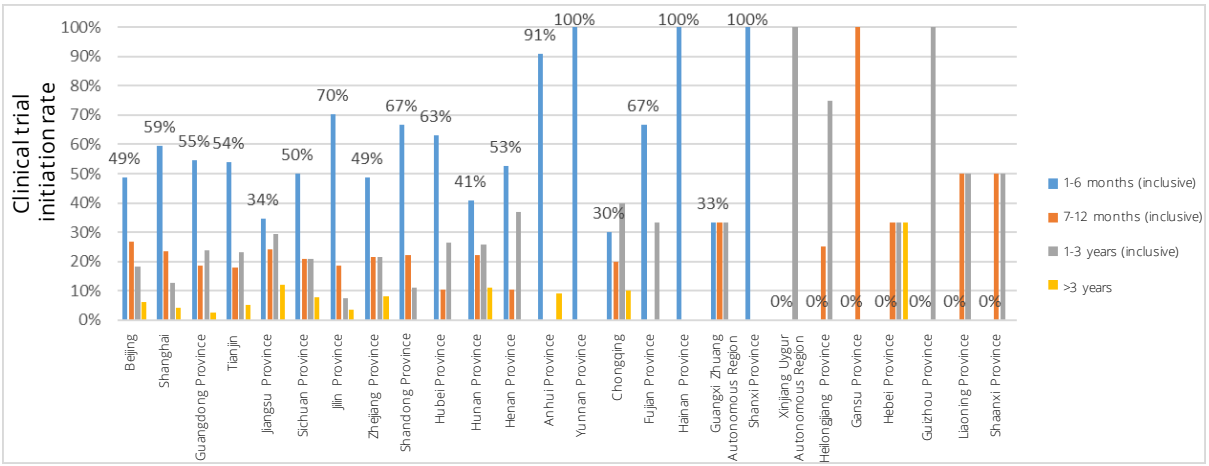


Percentage of overall startup time of new drug clinical trials in 2021



Percentage of overall startup time of new drug clinical trials for different drug types in 2021

Further analysis based on the location of clinical trial institutions suggested that in provinces, autonomous regions and municipalities directly under the Central Government with more leading clinical trial institutions, it took longer to initiate clinical trials. For example, in the top five provinces, autonomous regions and municipalities directly under the Central Government, trials that initiated subject recruitment within six months of approval accounted for no more than 60%, while in Anhui, Jilin, Shandong and other provinces, it took shorter to initiate clinical trials. 100% of trials in Yunnan, Hainan and Shanxi Provinces were able to initiate subject recruitment within six months after approval.

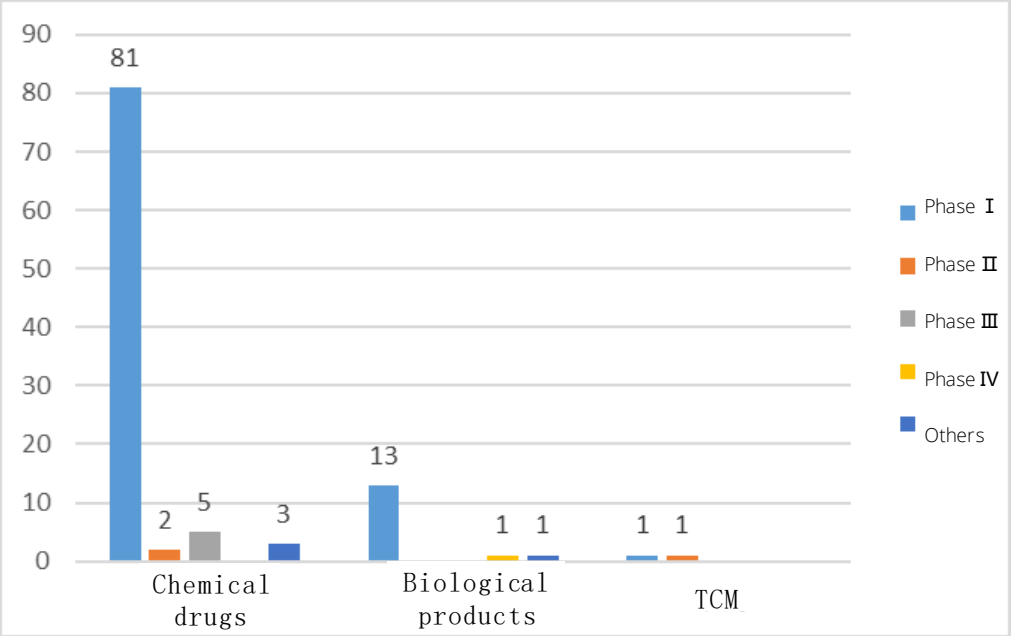


New drug clinical trial initiation rate by provinces, autonomous regions and municipalities directly under the Central Government in 2021

Analyzing only the recruitment of subjects initiated after the trial approval (if there were multiple relevant acceptance numbers in the current year, the earliest approval date would be calculated), there were 378 trials in 2021 with startup times ranging from three days to 11 months, with an average of 3.8 months. 85.7% of them initiated subject recruitment within six months of approval. There were 390 trials in 2020 with startup times ranging from zero days to 14 months, with an average of 4.7 months. 75.6% of them initiated subject recruitment within 6 months after approval. There were 152 trials in 2019 with startup times ranging from 26 days to 25 months, with an average of 6.4 months. 64.5% of them initiated subject recruitment within six months after approval.

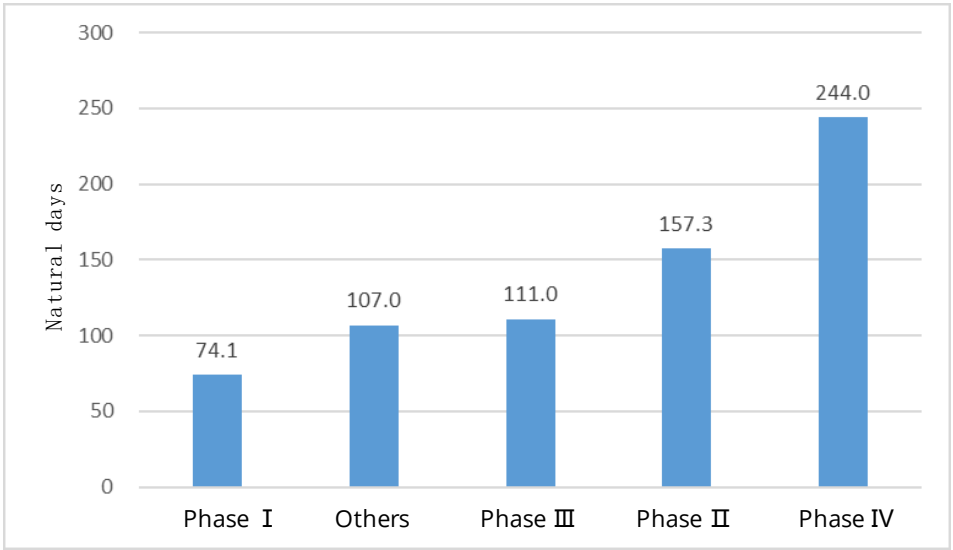
Ⅲ. Completion of Clinical Trials

Among the 2,033 new drug clinical trials registered by acceptance number in 2021, 108 were completed in the same year (the trial status was "completed", and the first ICF date and trial completion date were both in 2021), which were all domestic, mainly phase I clinical trials (n=95, 87.9%). The number of chemical drug trials completed was the largest (n=91, 83.0%), including five phase Ⅲ clinical trials. 15 biological product trials were completed, including one phase Ⅳ clinical trial.



Completion and trial phases of new drug clinical trials in 2021

Trial completion times ranged from 13 to 244 days (natural days), with an average of 80.9 days. The average completion time of phase I clinical trials was the shortest at 74.1 days, and the average completion time of phase Ⅳ clinical trials was the longest at 244 days.



Completion times of new drug clinical trials by phase in 2021

In 2021, six trials were voluntarily suspended (one for chemical drugs, four for biological products, one for TCMs), and 18 trials were voluntarily terminated (14 for chemical drugs and four for biological products). The reasons for the suspension and termination are as follows:

Type of Drugs	Voluntary Suspension	Voluntary Termination	Reasons (Number of Clinical Trials)
TCMs	1	-	**Revision of clinical trial protocol after communication.**
Chemical drugs	1	14	**1) Limited clinical benefits (1);** **2) Safety issues (2);** **3) Protocol design issues (1);** **4) Adjustment of R&D strategy (10);** **5) Suspension after communication (1).**
Biological products	4	4	**1) Suspension due to inability to meet the enrollment target (1);** **2) Suspension due to safety reasons (2);** **3) Suspension due to adjustment of R&D strategy (1);** **4) Termination due to adjustment of R&D strategy (1);** **5) Termination due to limited clinical benefits (2);** **6) Termination of domestic enrollment after global enrollment ended (1).**
Total	**6**	**18**	

Phase I clinical trials of chemical drugs were dominant, accounting for 69.6%, 61.2% and 75.0% respectively from 2019 to 2021. Phase I clinical trials took a relatively shorter time for completion, ranging from 74.1 to 95.7 days. The total number of trials suspended and terminated in 2021 was significantly higher than in 2019 and 2020. 50% of the reasons for suspension and termination were adjustment of R&D strategy (12 vs. 24); by trial phases, the highest percentage of trials were voluntarily terminated in phase I at 37.5% (9 vs. 24); in addition, 12.5% (3 vs. 24) trials were voluntarily terminated in phase Ⅲ, including 1 trial whose interim analysis failed to obtain positive results.

Chapter Ⅳ New Drug Clinical Trial Trends in Past Three Years

Ⅰ. New Drug Clinical Trials Increased Significantly, But Lacked Diversity

The total annual registration on the Drug Clinical Trial Registration and Information Disclosure Platform exceeded 3,000 for the first time in 2021. This is the highest annual registration since the platform was launched, with an overall increase of nearly 30% compared with 2020. The percentage of new drug clinical trials has also increased, showing a year-on-year growth trend and exceeding 60% in 2021. The research and development of new drugs was still dominated by early clinical trials, with phase I clinical trials accounting for the highest percentage, exceeding 40% over the years.

From 2019 to 2021, the clinical trials of chemical drugs and biological products were mainly for anti-tumor drugs, accounting for more than 30% and 40% over the years. In 2021, the number of chemical drug trials of anti-tumor drugs was 5.3 times that of anti-infective drugs (422 vs. 79); the number of biological product trials of anti-tumor drugs was 3.1 times that of preventive vaccine trials (406 vs. 131). The targets were relatively concentrated, among which PD-1 and PD-L1 were particularly prominent, and the percentage of their phase Ⅲ clinical trials was higher than that of other targets.

Ⅱ. A Small Number of TCM Clinical Trials, With Implementation to Be Improved

From 2019 to 2021, the percentage of TCM clinical trials was low, less than 4%. The clinical indications of TCM varieties were also relatively concentrated. The data in the past three years showed that they were concentrated in four indications: respiratory, digestion, cardiovascular and psychoneurological indications. The total amount exceeded 60% of all TCM clinical trials from 2019 to 2021. The implementation of clinical trials still needed to be improved after approval. The registration data in 2021 showed that nearly 90% of the clinical trials initiated subject recruitment more than one year after approval, and it took a long time for clinical trials to initiate subject recruitment.

Ⅲ. More Attention Should Be Paid to Clinical Drugs in Special Populations

In 2021, only three clinical trials were conducted in the geriatric population, one each for TCM, chemical drugs and biological products, accounting for only 0.1%. Clinical trials conducted only in the pediatric population accounted for 2.9% and were mainly for preventive vaccines among biological products. The number of trials in other indication fields was only one to five. A comparison and analysis of the data from the past three years showed that there was no significant change in the overall trend between 2019 and 2021.

According to the 121 diseases included in the *Catalog of First Batch of Rare Diseases*, clinical trials and indications for rare diseases showed a year-on-year growth trend, but there were still few clinical trials for the disease included in the Catalog. In the current rare disease clinical trials, the neurological diseases were mainly multiple sclerosis and neuromyelitis optica spectrum disorders, the blood system diseases were mainly hemophilia, and the respiratory system diseases were mainly idiopathic pulmonary fibrosis.

Ⅲ. More Attention Should Be Paid to Clinical Drugs in Special Populations

Clinical trial institutions in Beijing participating as leading institutions accounted for about 1/5 of the total, which was consistent with 2020. Data from 2019 to 2021 showed that the top five provinces, autonomous regions and municipalities directly under the Central Government with the largest number of leading clinical trial institutions were always Beijing, Shanghai, Guangdong Province, Jiangsu Province and Hunan Province, accounting for more than half of the total over the past years. In provinces, autonomous regions and municipalities directly under the Central Government with more leading clinical trial institutions, it took longer to initiate clinical trials. In provinces, autonomous regions and municipalities directly under the Central Government with fewer leading clinical trial institutions, trials started much quicker.

Appendix: Instructions for Compilation

1. This report is statistically described and analyzed with the clinical trial registration (CTR) number by searching the clinical trial registration information first published from January 1, 2021 to December 31, 2021 in the Drug Clinical Trial Registration and Information Disclosure Platform database (hereinafter referred to as the "registration platform"), as well as by referring to the public database retrieval information in the industry. As there may be cases such as applicants deleting duplicated registration information, the number of clinical trials published in the report is slightly different from the real-time data published on the Center for Drug Evaluation's website.

2. This report mainly focuses on the summary analysis of the registration information of new drug clinical trials (exploratory and confirmatory clinical trials registered by acceptance number). The registration information of bioequivalence trials (including the consistency evaluation of quality and efficacy of generic drugs) is only a general analysis and description.

3. In this report, the clinical trial registration information is classified and analyzed mainly by drug classification (TCMs [including natural drugs], chemical drugs and biological products), registration classification (including the original registration classification information), indications, drug targets, clinical trial phases and trial progress. The Center for Drug Evaluation's annual drug review report is referenced to maintain consistency in the classification of indications.

4. The pediatric population is defined as subjects aged ≤ 14, and the geriatric population is defined as subjects aged ≥ 65.

5. For rare diseases, refer to the *Catalog of First Batch of Rare Diseases* jointly formulated and released by five departments including the National Health Commission on May 11, 2018.

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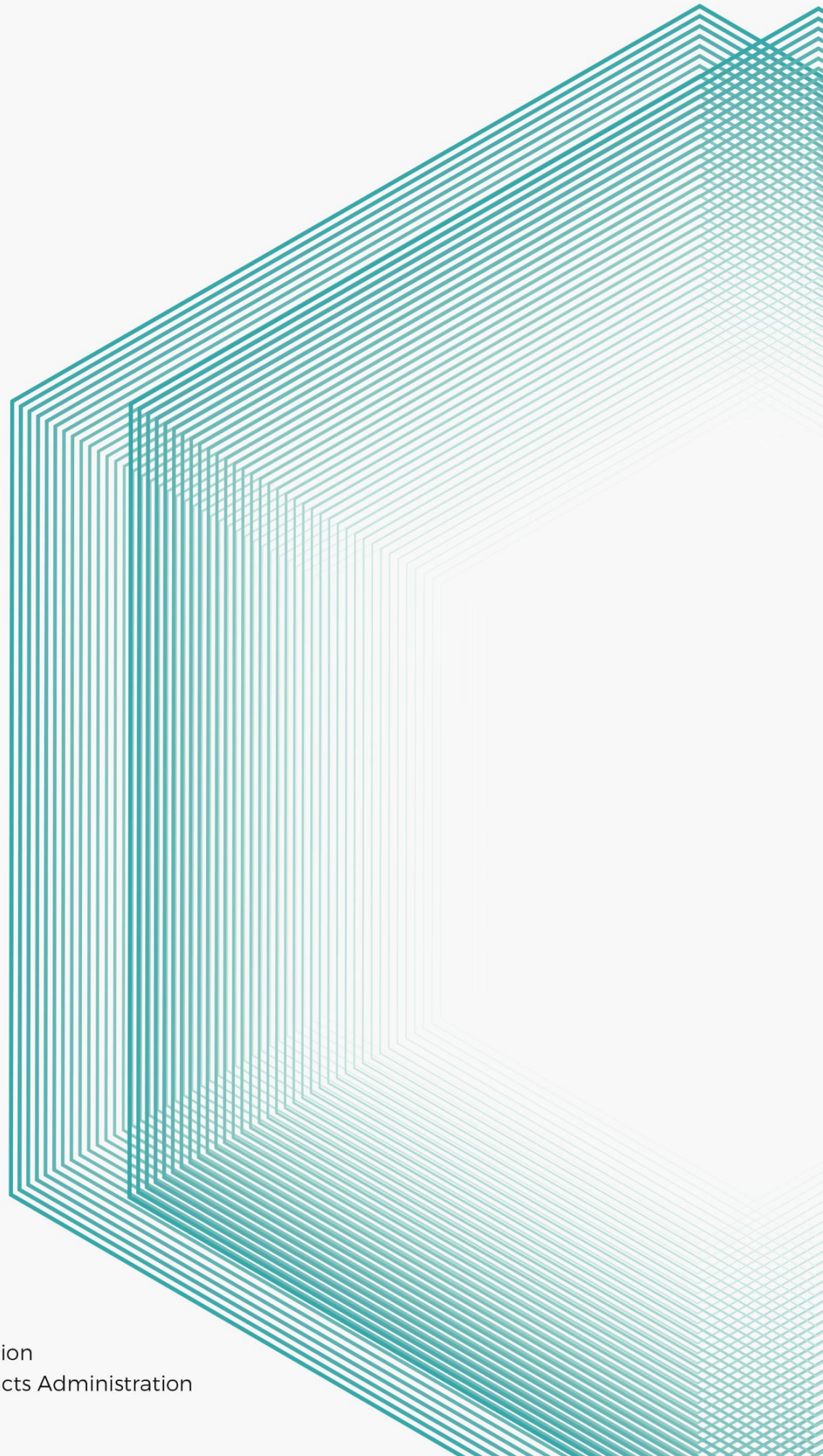

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National Medical Products Administration