罕见疾病药物临床研发技术指导原则

State Drug Administration

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1. Background

Rare diseases refer to a group of diseases with extremely low incidence/prevalence. Incidence/patients

Low disease incidence is an important feature of rare diseases. Due to China's large population base, rare disease patients

The absolute number of victims is not small, and their impact on society, economy, medical care and other aspects cannot be ignored.

The impact is one of the important public health issues.

Due to the extremely low incidence/prevalence of rare diseases and the complexity of their conditions, the current understanding of rare diseases is relatively low.

Limited resources make the development of drugs for rare diseases far more difficult than those for common multiple diseases.

Patients with rare diseases have far unmet treatment needs.

Due to the small number of patients with rare diseases, it is difficult to conduct clinical trials, so rare diseases

The clinical research and development of disease drugs should not only follow the research and development rules of general drugs, but also closely

Combined with the characteristics of the disease and on the basis of ensuring rigorous science, a more flexible design is adopted.

Make full use of limited patient data to obtain scientific evidence that satisfies the assessment of benefits and risks,

Support regulatory decisions.

This guideline will combine the characteristics of rare diseases to propose clinical research and development of rare disease drugs.

It is recommended to provide reference for clinical trials of rare disease pharmaceutical science. This guiding principle is based on

To be applicable to chemicals and therapeutic biologics, other types of new drugs or treatments

Research and development can refer to the ideas and scientific principles provided in this guideline.

This guideline only represents the current views and understanding of the drug regulatory authorities. With the medical department

In accordance with the development of science and clinical trials, the relevant content in this guideline will be continuously improved and updated.

When applying this guidance to design and conduct studies, please also refer to the quality management of drug clinical trials.

International harmonization of good clinical practice (GCP) and technical requirements for pharmaceuticals for human use

International Council for Harmonization of Technical

Requirements for Pharmaceuticals for Human Use (ICH) and other domestic

Published relevant guidelines.

2. Special considerations for drug development for rare diseases

1. Obtain clinical data on rare diseases

Rare diseases not only have extremely low incidence/prevalence, but also have many types of diseases and complex phenotypes.

The clinical manifestations are diverse, and the patient population can range from newborns to elderly patients. In addition, clinical diagnosis and treatment

There is limited knowledge about it, and the basic data accumulated so far is significantly less than that of common common diseases.

This brings great challenges to the trial design and effectiveness evaluation of clinical development of new drugs. to improve rarity

The efficiency of drug research and development for diseases is primarily to encourage research on the pathogenic mechanisms of rare diseases to provide

Clinical research and development provides important basis and research and development direction.

For rare diseases whose pathogenic mechanisms are unclear or poorly understood, applicants are encouraged to

At the beginning of drug research and development, clinical research and natural history research of the disease are first conducted on the indications to be developed.

Research to understand the incidence/prevalence of the disease, diagnostic methods and their accuracy, disease symptoms/

Characteristics, main disease groups, and treatment status, etc., and relatively sufficient clinical data of the disease have been obtained.

The clinical data of the disease can be used to carry out follow-up clinical trials based on the ideas of rare disease drug development.

Provide a rational basis for research and development; it can also provide a basis for the definition of indication groups, key research design, clinical

Provide valuable information such as endpoint selection for clinical trials; it may also serve as an important part of subsequent clinical research

Required external comparison data.

Rare disease clinical data can be obtained through (including but not limited to) the following channels:

ý Research on the natural history of diseases. Consider conducting well-designed, disease-specific

Cross-sectional studies of the natural history of the disease, case-control studies or prospective cohort studies, etc.

ýRelevant natural history research literature reports published at home and abroad. Consideration may be given to relevant

A comprehensive analysis of the literature was conducted as a support for the natural history of the target indication and the clinical characteristics of the disease.

sustainable data, but attention needs to be paid to whether there is heterogeneity between different countries or regions (such as pathogenic

differences in genes, incidence/prevalence, severity, clinical medical practices, etc.), are

Can it reflect the characteristics of the sick population in my country?

ÿ Patient registration platform. Clinical data on rare diseases can be collected through patient registration platforms

according to.

ÿ Survey of clinical staff. Targeted medical staff can be targeted at target indications

Research work.

ÿ Patient survey. Encourage patient interviews at the beginning of development and throughout the development process

Incorporate the opinions of patients/guardians into the process to fully understand the patients' clinical treatment needs, experiences and

Treatment status and integrated into the formulation of R&D strategies.

Due to the complexity of rare diseases, it is sometimes difficult for a single study to fully reflect rare diseases.

clinical characteristics, therefore encouraging the acquisition of clinical data on rare diseases through multiple channels and encouraging

Encourage exchanges and cooperation among R&D units and promote data sharing.

2. Pay attention to the application of biomarkers

Biomarkers usually refer to things that can be measured and evaluated objectively and reflect physiological or pathological processes.

and indicators of biological effects of exposure or therapeutic intervention. Rare disease patients

The group is small and it is difficult to carry out large-scale clinical trials. Even if clinical trials are carried out, they can only

Limited effectiveness and safety information is available. Because the clinical symptoms of most rare diseases are complex

Diverse, some rare diseases require a longer period of drug intervention to produce clinically identifiable

differences, therefore, in order to improve the identification of therapeutic effects resulting from drug interventions during development or

sensitivity to patient safety risks, encourage the use of as many biomarkers as possible, as limited

An important complement to clinical safety and efficacy data. For example, safety biomarkers can be used

drugs to identify patients with higher potential drug safety risks during drug treatment; or use pharmacodynamics

Biomarkers to assist in determining a reasonable dosing regimen for experimental drugs, or to develop biomarkers that can be used clinically

Surrogate endpoints for trials, etc.

On the other hand, diagnostic biomarkers can also be used to improve the diagnosis of rare diseases.

rate, and if necessary, companion diagnostics need to be developed based on relevant biomarkers. About rare disease companions

For diagnostic development, please refer to relevant technical guidelines [1].

3. Actively apply quantitative pharmacology tools

Based on the characteristics of limited subjects for rare diseases and a wide age range of patients, we encourage research and development

Quantitative pharmacology tools are fully applied in the process to improve research and development efficiency. For example, establishing group medicine

The pharmacokinetic-pharmacodynamic model helps to scientifically and efficiently determine the effectiveness of experimental drugs in rare diseases.

Recommended doses in; useful for extrapolating data from adult subjects to pediatric patients of different ages

Recommended dosage; helps determine recommended dosage for special populations, etc.

4. Encourage the establishment of patient registration systems

Rare diseases have fewer patients per disease, and clinical data are usually scattered, so collection and acquisition are difficult.

Difficulties in representing clinical data for rare diseases encourage the establishment of standardized patients

Registration system. Through the patient registration system, it helps to obtain relatively complete and accurate high-quality

Clinical data lays a good foundation for statistics and analysis, and also adds value to real-world research.

Possible indications related to rare diseases.

3. Clinical R&D Plan

According to the mechanism of action of rare disease drugs, they can be divided into two situations: (1) only suitable for

Used for target rare diseases; (2) Applicable to both rare diseases and non-rare diseases.

For investigational drugs that are only suitable for rare diseases, general drug development regulations are usually required.

laws, conduct early exploratory research, complete proof of concept, and determine recommended doses, target populations,

Once preliminary effectiveness data are obtained, critical studies will be conducted on this basis to support the launch of the drug.

In some cases, it is sometimes difficult to conduct independent studies due to the limited number of subjects with rare diseases.

proof-of-concept studies, it is therefore encouraged to conduct key studies in stages, enrolling small groups in the first stage

sample size subjects, as a proof of concept and to build on the results of this phase for subsequent trials

The phases will be adjusted, and eventually the recommended dose of treatment will be received in the first phase and subsequent research phases.

The overall effectiveness of the treatment in patients is used as the key efficacy data to support marketing.

For drugs that are suitable for a variety of diseases, including rare and non-rare diseases,

Basket trial design can be adopted in the early stage to include people with multiple diseases and fully learn from and utilize

Clinical data obtained in non-rare diseases to guide the determination of prescribing the drug in rare diseases

development, guidance price for the development of indications for rare diseases based on clinical data obtained in other diseases

value, consider directly conducting proof-of-concept clinical trials in rare disease indications, or directly

directly enter the pivotal clinical trial; when directly entering the pivotal clinical trial, please refer to the aforementioned adaptation.

sexual design ideas.

Drugs for a variety of diseases, including rare and non-rare diseases, are also available

To select the first choice to develop rare diseases, please refer to the situation "(1) only applies to target rare diseases"

Develop in case of “disease”.

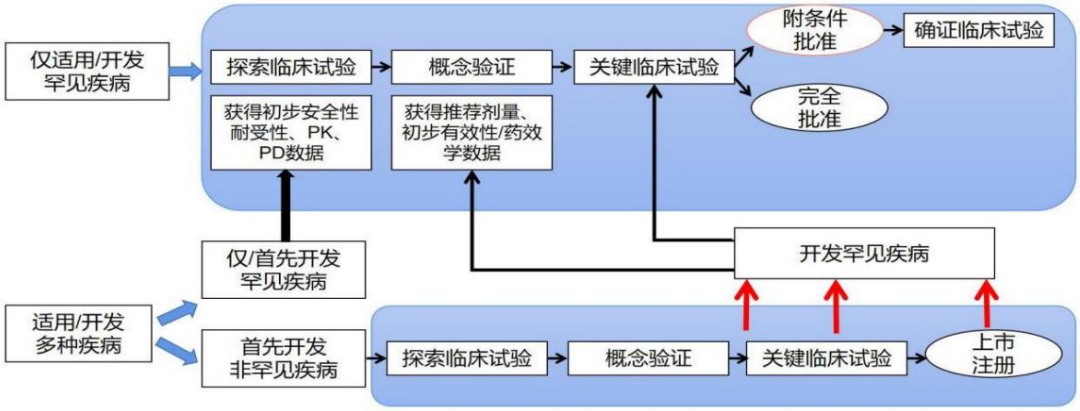

Figure **1** Example of clinical development plan for rare disease drugs

Rare diseases are complex, have many types of diseases, and are difficult to develop drugs. It is recommended that rare diseases be carried out in

When working on disease drug research and development, the research and development plan should be fully considered. Applicants are encouraged to pursue research and development

During the process, we actively communicated with regulatory agencies on drug research and development plans.

4. Clinical trial design

According to the mechanism of action of the drug, rare disease treatment drugs can generally be divided into alternative treatments and

Non-replacement treatment. Replacement therapy refers to diseases caused by lack of endogenous substances in the human body.

A treatment method that uses exogenous substances to supplement; because replacement therapy supplements the body's

Lack of endogenous substances, therefore usually alternative therapeutic drugs with clear mechanisms of action, pharmaceutical agents

Amounts also tend to correlate with physiological levels of endogenous substances. Non-alternative treatments refer to treatments other than alternative treatments

Other interventional treatments, non-replacement treatment drugs are by interfering with the development of the disease

One or more processes in the disease, or through the intervention of bypass pathways that are not directly causative, achieve

Therapeutics to treat disease/relieve symptoms. Compared with alternative treatments, non-replacement treatments are

The mechanism of use is usually more complex, and the exploration of drug therapeutic dosage is also relatively complex.

At different stages of development of drugs for rare diseases, the incidence of rare diseases must be fully considered/

The prevalence rate is extremely low. At the same time, combined with the mechanism of action of the drugs developed, clinical design can be rationally

test.

(1) Exploratory research stage

1. Consideration of the research population

(1) Healthy subjects

Usually healthy subjects are more homogeneous and have fewer interfering factors. They are early exploratory studies (the first ideal population for human clinical trials). Especially for rare diseases with limited patient populations, Obtain pharmacokinetics (PK) and pharmacodynamics in healthy subjects Pharmacodynamics (PD), preliminary PK-PD relationship and preliminary safety information Information is very important. The drug's mechanism of action is not expected to affect healthy subjects within the proposed dose range. cause serious harm to persons, and non-clinical research can support the development of clinical trials in healthy people. Under this condition, first-in-human clinical trials can be conducted in healthy adult subjects.

(2)Patient

For drugs that are not suitable for clinical trials in healthy subjects, they can be used in patients with rare diseases. If research needs to be conducted in pediatric patients, in principle, it should be selected first Adult patients, after achieving tolerability/safety, pharmacokinetics, pharmacodynamics (if available can), and then gradually transition to adolescents and young adults in accordance with the general principles of pediatric drug research and development [2] child.

For some drugs that are not only used to treat rare diseases, that is, they can also be used as drugs for other diseases. For drugs that can potentially treat rare diseases, it is recommended that first human clinical trials be conducted in non-rare disease populations. test. Encourage the use of a basket design in early studies to include drugs based on their mechanism of action A variety of potential indication groups including target rare disease groups, collected in different diseases The safety and pharmacokinetic data in the drug will provide a basis for later research and development.

For the very few healthy adult subjects who cannot be selected, the disease population is only children and no adults

In special circumstances where patients can choose, caution should also be taken on the premise of fully assessing safety risks.

are considering conducting first-in-human trials in pediatric patients.

2. Selection of starting dose

The determination of the starting dose of the drug should follow the relevant guidelines and technical requirements of pharmacology and toxicology

[3]ÿ

Alternative therapeutic drugs for rare diseases due to lack of endogenous substances in the human body

The physiological level of the disease is usually clear, so non-clinical research and clinical studies that take full advantage of the disease are encouraged.

Clinical research data are used to establish the relationship between the dosage of the drug for replacement therapy and the level of the substituted substance,

Before complying with the starting dose requirements of pharmacology and toxicology-related technical guidelines and being safe and controllable

Under this circumstance, try to choose a level as close to the target therapeutic dose as the starting dose to maximize the

Reduce futile exposure in rare disease subjects and increase the efficiency of dose-finding studies.

3. Determination of recommended dosage

Typically, recommended doses are based on the drug's PK, PD, safety and initial

Based on the comprehensive judgment of step effectiveness data. In rare disease drug development, focus on science is recommended

Use of Tools. For example, model-informed drug development

development, MIDD) [4], conduct population pharmacokinetics research and establish pharmacokinetics

Science-pharmacodynamic models, etc., to realize the transformation from healthy people to patients, or from adult patients to pediatric patients,

or extrapolation of doses from patients with other diseases to patients with the target rare disease.

For alternative treatments with clear mechanisms of action, it is also possible to fully understand the PK-PD relationship.

Research to clarify the drug dose-exposure-effect relationship to determine the recommended dose.

4. Medication for special groups of people

Typically, drug development is developed for adult indications first and then

Development in pediatric patients; in the case of rare diseases, development by age group

It is more difficult, and some rare diseases mainly start in childhood and then progress to adulthood.

Pediatric patients are an important treatment group and the group with the strongest clinical needs; on the other hand,

Usually drugs will be developed to a certain stage, and some even start liver/kidney research after the drug is on the market.

Research on special populations such as functional insufficiency is at a critical stage due to the lack of research data on special populations.

These special populations are often excluded from research. However, for rare diseases, because the disease itself

often have an impact on patients' liver and kidney functions. Therefore, if the above characteristics are used in clinical trials,

If special groups are excluded, it will be more difficult to enroll patients, and the research results will not be representative.

The law guides scientific and reasonable clinical use of drugs to meet the needs of patients.

Therefore, in the early stages of rare disease drug development, it is recommended to conduct timely research on special populations

The study of drug use will facilitate the inclusion of as many as possible in subsequent key clinical trials.

A broader, more representative population of rare disease patients. When different groups of people (such as the elderly, children, etc.)

(children, those with liver/kidney damage), even if the usage and dosage of different groups of people are different.

At the same time, inclusion in key clinical trials can also be considered to improve research and development efficiency.

5. Preliminary effectiveness inspection

Obtaining preliminary efficacy data of drugs is the basis for conducting critical clinical trials. For rare

For diseases, preliminary effectiveness data are generally required.

Effectiveness evaluation indicators can use clinical endpoints or surrogates closely related to clinical endpoints.

Endpoint, for cases where the mechanism of drug action is clear (such as enzyme replacement therapy), PD can also be used

Indicators serve as alternative indicators to examine effectiveness. Also encourage the development and application of PD indicators

(such as target occupancy rate, target cell clearance rate, etc.) as support for effectiveness data.

For situations where the drug can be used to treat other non-rare diseases at the same time, such as

The mechanism of action is the same in the treatment of rare diseases and non-rare diseases, and it can also be considered to treat other non-rare diseases.

Examine the effectiveness of drugs in rare diseases and complete proof of concept of drugs.

(2) Key research stage

1. Experimental design selection

1.1 Parallel controlled study over the same period

Parallel controlled studies at the same time are the gold standard for confirming the efficacy of drugs, so parallel controlled studies

is the preferred experimental design. Depending on the control drug, it can be divided into placebo control and positive

Medication comparison.

(1) Placebo control

When using a placebo control, a superiority design and preliminary exploratory study of the drug are required.

and disease natural history data, which can be used as statistical hypotheses to predict the difference in efficacy of the test group compared to placebo

in accordance with.

In placebo-controlled studies, attention should be paid to the proportion of subjects between groups. Use a balanced design (each

The number of cases in the comparison group is the same), the statistical power is the highest, and it is more conducive to the evaluation of safety. if early

Phase 1 clinical trials have shown that the experimental drug is significantly better than placebo. In order to make more patients accept

to potentially superior treatments, a higher allocation ratio of the trial drug (e.g., a 2:1 allocation

Proportion).

Randomized withdrawal trials may also be considered when long-term placebo treatment is unacceptable. exist

In a randomized withdrawal trial, patients who receive the experimental drug and achieve the desired effect are randomly assigned to

are eligible to continue receiving trial drug treatment or placebo treatment. Any differences between the two groups

The results will demonstrate the therapeutic effects of the experimental drugs.

(2) Positive drug control

For target indications where drugs have been approved and marketed in China and are accessible, you can choose

Positive control drug. Active control studies can usually adopt a superiority design or a non-inferiority design.

When superiority design is adopted, early exploratory studies of drugs and positive drugs are used to adapt to the target.

The therapeutic effect in the disease will provide the basis for the estimated therapeutic effect difference between the experimental group and the control drug when making statistical assumptions.

according to. The ratio of subjects between groups is usually 1:1. If preliminary data indicate that the trial drug is effective,

When the potential is significantly better than that of the positive control drug, a ratio of 2:1 can also be used.

When using a non-inferiority design, relevant guidelines must be consulted [5]. Need to pay attention to the non-inferiority boundary

Value setting issues, the non-inferiority margin can be appropriately relaxed when appropriate and necessary. suggestion

Communicate with regulatory authorities before conducting clinical trials to clarify the non-inferiority margin.

1.2 Non-contemporaneous external controlled studies

For rare diseases where it is difficult to carry out simultaneous parallel controlled studies, external controls may be considered

For research methods, external controls can be parallel or historical external controls. This kind of design

The main problem is the inability to eliminate systematic differences between nonconcurrent treatment groups. When using historical numbers

When used as a comparison, a single-arm design is usually used. In principle, the following conditions must be met at the same time:

ÿ There is no effective treatment in clinical practice; or compared with existing treatments, early data show that

Indicates that the experimental drug has outstanding efficacy;

ÿThe disease process is clear, predictable, and can be measured and verified objectively (for example, when the disease

The disease itself has the possibility of spontaneous remission and is not suitable for a single-arm trial design);

ÿThe disease severity is high and the prognosis is poor;

ÿHigher quality external control data. External control data are preferred to come from the past

RCT study results, and optionally real-world data, external to real-world studies

Controlled data, natural history studies of diseases, patient registration studies, literature reports, etc. Need to pay attention to the history

Whether the historical data can represent the current clinical practice in my country; pay attention to the quality of the data.

Data derived from natural history studies may be used to

External control group for treatment. The use of external controls requires careful planning and evaluation, including the following

consider:

i) The external control group needs to match the drug treatment group in all aspects, including disease severity

Severity, duration of disease, previous treatments, and disease may affect outcome and outcome

Other aspects of the time of occurrence can facilitate objective comparison and evaluation of treatment effects.

ii) Selection bias can be reduced by using good designs (e.g. entry/exclusion criteria, vs.

The research protocol was almost parallel to the statistical analysis plan). Data selection bias is caused by using external pairs

The main problem with timing of exposure is that there is no randomization and that unidentified baseline differences may affect

The ending. Key considerations may include:

- Patient disease characteristics may not have been assessed or may be based on historical methods

Patients underwent different assessments, which would result in a lack of comparability (e.g., disease definition, diagnosis

(interruption technology and safety monitoring methods have changed).

- Standard treatments may have changed.

- Data collection intervals and quality may lack consistency and are not comparable.

- Also if the outcome assessment used in the external control group is not well defined or unreliable

can make applying external control groups challenging.

In addition to meeting the above conditions ÿ-ÿ, when the incidence/prevalence of the target indication is extremely low,

There are very few patients who can be recruited who meet the inclusion criteria, and there are no conditions for conducting controlled studies.

A single-arm experimental design may be considered.

Single-arm trials typically support only conditional approval of a drug. Usually after listing, randomization is required

Controlled trials serve as confirmatory studies. For extremely rare diseases where controlled studies cannot be carried out,

Another independent single-arm study, a real-world study, may also be considered as a confirmatory clinical trial.

test.

In some special cases, for example, the mechanism of drug action is very clear, the mechanism of drug action

Full approval may also be supported when effectiveness has been established in other indications.

Single-arm trials have a lower level of evidence than randomized controlled trials, and there are certain inconsistencies in the trial results.

Certainty, therefore when planning to support marketing of a drug with a single-arm study, it is recommended that the applicant

The applicability of the trial and post-marketing requirements must be communicated with regulatory agencies in advance.

1.3 Self-control

Self-control is a special type of historical comparison design. Its historical data comes from reference

The patients themselves who are subjects of interventional clinical trials with investigational drugs. Need to ensure patient history/baseline

Accuracy of data. When using a self-control design, the preferred recommendation is to first conduct a prospective

Observational study, using the results of the observational study as the patient's baseline data, and subsequent testing of the drug

Interventional study results are compared with patient baseline data to confirm the efficacy of the experimental drug.

1.4 Real World Research

In addition to serving as external control data for single-arm trials, real-world studies can also be used to

Support the expansion of rare disease indications for already marketed drugs. You can refer to relevant guiding principles to carry out real-life

World Studies[6-8].

In addition to the above clinical trial designs, applicants are encouraged to try other more flexible designs in R&D

Experimental design, such as adaptive design, basket design, platform experimental design, etc.; encouraged

Applicants engage in active communication with regulators, for example when planning to use adaptive seamless trial equipment

planning, especially when the number of patients in the study is limited, should be discussed with the regulatory agency before the trial is initiated

On comprehensive statistical analysis planning, including key features of experimental design and pre-planned analyses.

2. Selection of trial endpoints

Clinical endpoints remain the preferred primary efficacy indicators in pivotal studies to support drug launch.

The main efficacy indicators should be selected according to the characteristics of the disease and the main purpose of clinical research, and should be consistent with the clinical

Clinical benefits are highly relevant and should also be objective, sensitive, easy to quantify, and repeatable.

Features. Fully understand the onset characteristics, clinical manifestations, and development process of the target indication population

etc., determining the therapeutic target of a drug based on its mechanism of action can help to identify meaningful, more

Sensitive clinical endpoints.

Encourage exploration and development related to clinical endpoints during the research and development process, and have a strong understanding of clinical endpoints.

Surrogate endpoints of predictive value, through sensitive surrogate endpoints, to simplify clinical trials and improve

The purpose of high R&D efficiency.

Patient-reported outcomes (***patient reported outcome*** ÿ ***PRO*** ÿ

PROs are one of the forms of clinical outcomes that are increasingly used in drug registration clinical studies.

The more widely used it is, the more attention it receives. In rare disease drug development, encourage the application of

PRO, to reflect the improvement of the quality of life and experience of patients with rare diseases and their clinical value.

value, and use its PRO as important supporting data for the primary endpoint; encourage the development of PRO

scale; you can also consider developing a PRO as the primary endpoint and communicate with regulatory agencies to develop the PRO

Feasibility as primary endpoint to support regulatory decisions [9].

3. Research population

The trial population of the pivotal study includes representative patients based on the results of earlier studies.

In early research, if the usage of patients of different age groups, special groups, etc. can be clarified as early as possible,

volume, it would be beneficial to include a broader and more diverse patient population in a pivotal study.

body to reduce the difficulty of recruiting subjects.

4. Sample size of key clinical trials

In principle, the sample size of a pivotal study design for a rare disease drug needs to be based on statistical

The relevant principles are determined based on the statistical assumptions for the primary endpoint.

Because patients with rare diseases vary widely in clinical manifestations and physiological status,

Inclusion of a wider range of patients in pivotal studies may lead to further variability in the study population.

increase, so choosing a sensitive primary endpoint and adopting a more flexible trial design will result in

Helps reduce sample size.

5. Security Assessment Requirements

For the treatment of rare diseases with chronic disease characteristics and requiring long-term treatment, in principle, the

Comply with the requirements of ICH E1. The number of patients with rare diseases is small, and safety data can include both

He has data from non-rare disease populations. For targets that are expected to only be used in rare disease treatments,

Drugs with clear goals and clear mechanisms of action (such as alternative therapies), based on patient benefits and risks

assessment, which may reduce exposure requirements, and applicants are advised to conduct this with the regulatory agency in advance

communicate.

Because the data accumulated in clinical trials for rare diseases are generally very limited, the above

Post-marketing safety data collection is very important, a pharmacovigilance system should be established, and a pharmacovigilance system should be established before marketing.

Combining product and disease characteristics, improve post-market risk analysis and management plan (Risk

Management Plan, RMP) [10], and strictly implement and continuously improve the RMP after listing.

6. Communication

There are many types of rare diseases, covering a wide range of treatment areas, with differences in disease manifestations and progression.

large, and at the same time faced with limited understanding of the natural history of the disease, relevant clinical development experience and

There is a lack of precedents to refer to, the number of patients is limited, and clinical trial subjects often involve children.

and various complex situations, it is difficult to cover all the difficulties encountered in drug development for rare diseases through one guiding principle.

various issues. Regulators encourage applicants to discuss drug development for rare diseases

timely submit applications for communication and exchange on key technical issues, and discuss the challenges encountered during development

On possible solutions to jointly improve the efficiency and success of rare disease clinical trial development

Rate. Communications include both new molecular entities to treat rare diseases and already marketed products

Expand indications related to rare diseases. Contents that may be covered by communication include but are not limited to:

- Flexible and efficient clinical trial design
- Use of innovative clinical endpoints/surrogate endpoints
- Reasonable safety patient data set
- Extrapolation of clinical trial data (including extrapolation to the Chinese patient population based on overseas data)
- Leverage real-world data
- Collection of post-market data
- Post-IPO risk management plan

It is recommended that applicants also strengthen supervision and supervision during the design and implementation of clinical trials.

Institutional communication.

7. Summary

The incidence/prevalence of rare diseases is extremely low, the condition is complex, and diagnosis is difficult; rare diseases

Limited patient numbers make it difficult to conduct clinical trials, factors that lead to rare diseases

Clinical research and development of drugs faces many difficulties. However, drug development for rare diseases should still be based on science

This guideline allows for “streamlining” research designs through sophisticated scientific methods, but cannot reduce

“Simplifying” the R&D process at the expense of scientific standards. Rare disease drug development should not only follow a

In addition to the rules of research and development of general drugs, we should closely combine the characteristics of rare diseases and explore more scientific methods.

and sophisticated research methods to improve R&D efficiency.

There are many types of rare diseases, so it is difficult for this guideline to cover all rare diseases.

Requirements for drug development. This guideline aims to propose generally applicable guidelines for rare disease research and development.

Technical support. For issues that are not covered, applicants are encouraged to actively communicate with regulatory agencies

Communication.

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