OVERVIEW

On January 7th, 2020, NMPA published a new guideline on "Real-World Evidence that defines Real-World Data (RWD) and Real-World Evidence (RWE) terms and clarifies their use during drugs’ research and development and registration in China.

Before the adoption of the RWE concept, it was necessary to conduct Randomized and Controlled Trials (RCTs) in China to demonstrate the efficacy and safety of new drugs in Chinese population. It’s true that data collected from Randomized Controlled Trials (RCTs) provides reliable evidence of efficacy of new drugs and helps minimize the impact of factors that potentially can affect the causal interference.

Unfortunately, data collected during RCTs doesn’t represent the whole target population of the new drug and doesn’t reflect how the drug is going to be used in real clinical setting. These limitations bring some challenges when extrapolating the RCT conclusions to real world clinical practice. To overcome these RCT limitations, Real-Word Data (RWD) and Real-Word Evidence (RWE) were created.

DEFINITIONS

Real-Word Data (RWD) are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources, outside the traditional clinical trials. RWD can come from a number of sources, for example:

- Electronic health records (EHRs)
- Claims and billing activities
- Product and disease registries
- Patient-generated data including in home-use settings
- Data gathered from other sources that can inform on health status, such as mobile devices

Real-Word Evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD. RWE can be generated by different study designs or analyses, including but not limited to, randomized trials, including large simple trials, pragmatic trials, and observational studies (prospective and/or retrospective).
# WHAT ARE THE ADVANTAGES AND LIMITATION OF RWE?

## Advantages of RWE

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>
| 1. | ✓ Less time and cost consumption compared with RCT  
   | ✓ Possible to shorten the duration of clinical research  
   | ✓ No period needed for patient recruitment/enrollment |
| 2. | Provides direction when designing RCT |
| 3. | Makes it possible to do research that cannot be done with RCT for safety reasons |
| 4. | Detects less frequent side effects |
| 5. | Allows rapid and easy access to lot of information and retrieved data |
| 6. | Helps Prteod ict model for high-risk group selection |
| 7. | Sets a foundation for Artificial Intelligence |

## Limitation RWE

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>For correct analysis, a massive amount of data should be collected</td>
</tr>
<tr>
<td>2.</td>
<td>Much time needed for Data Quality Management</td>
</tr>
<tr>
<td>3.</td>
<td>Experienced experts needed for the analysis of the massive amount of data</td>
</tr>
<tr>
<td>4.</td>
<td>Lack of privacy and confidentiality for lost data</td>
</tr>
</tbody>
</table>
| 5. | ✓ Standardized research protocol needs to be established before starting research  
   | ✓ High possibility of bias  
   | ✓ Possible to interpret with bias or incorrectly based on research results |
WHAT IS THE DIFFERENCE BETWEEN RCT AND RWE?

<table>
<thead>
<tr>
<th>Variables</th>
<th>RCTs</th>
<th>RWE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purpose</td>
<td>Efficacy</td>
<td>Effectiveness</td>
</tr>
<tr>
<td>Setting</td>
<td>Experimental setting</td>
<td>Real-world setting</td>
</tr>
<tr>
<td>Follow up</td>
<td>Designed</td>
<td>In actual practice</td>
</tr>
<tr>
<td>Treatment</td>
<td>Fixed pattern</td>
<td>Variable pattern</td>
</tr>
<tr>
<td>Study group</td>
<td>Homogenous</td>
<td>Heterogeneous</td>
</tr>
<tr>
<td>Attending physician</td>
<td>Investigator</td>
<td>Many practitioners</td>
</tr>
<tr>
<td>Comparator</td>
<td>Placebo/selective alternative interventions</td>
<td>Many alternative interventions</td>
</tr>
<tr>
<td>Patient monitoring</td>
<td>Continuous, per protocol</td>
<td>Changeable</td>
</tr>
</tbody>
</table>

HOW RWE WILL BE USED BY NMPA?

Real-World Evidence RWE will be used by NMPA to support its decision during the review of new drugs application, or changes to the efficacy and safety profile of approved drugs. NMPA will be using RWE to support strategies for new drugs’ research and development.

In summary, RWE will be used in the following situation:

1. To Support New Drugs' Registration in China

To demonstrate the safety and efficacy of a new drug, Randomized Clinical Trials (RCT) need to be conducted. Realistically, the collected data doesn't represent the real word utilization of the new drug and the whole population. Therefore, using high quality data as RWE will complement the safety and efficacy information collected by RCT and will help NMPA to take decision about the approval of the new drug.
2. To Support Decision about Changes to Approved Drugs in China

In general, to be able to change the indication of a marketed drug, new clinical studies (RCT) need to be performed to demonstrate the efficacy and safety of the drug in the new indication. Unfortunately, in many cases conducting a new RCT is not feasible economically or because of the small size of the target patient population that is seen with orphan drugs for rare diseases. In these cases, using well designed RWE can add a lot of value for getting the new indications approved quickly.

3. To Support Post-Marketing Studies in China

Usually, new drugs that have been approved based on RCT evidence, have limited safety information, and the extrapolation of their safety profile requires either post-marketing studies or strict post-marketing surveillance. In these situations, RWE helps design the post-marketing studies and shorten them.

WHAT ARE THE REQUIREMENTS FOR RWE?

- The research environment and data collection are close to the real-world, such as more representative target population, the diversification of intervention accord with clinical practice, and natural choices of intervention.
- Suitable control.
- More comprehensive evaluation of results.
- Effective bias control, such as the use of randomization, the unification of measurement and evaluation method.
- Appropriate statistical analysis, such as correct use of casual inference methods, reasonable transparency and reproducibility of evidence.
- Reasonable explanation of search.
- All the parties concerned reach a consensus.
- Reasonable transparency and reproducibility of evidence.
WHAT ARE GRP RECOMMENDATIONS?

Before starting the collection of RWE that will be supporting a new drug registration in China, applicants should have a consultation meeting with NMPA to discuss and clarify with them the purpose, the scope, data collection and analysis process of RWE, to ensure that they will accept it as part of new drug application in China.

After compiling RWE, applicants should have a per-consultation meeting with NMPA to discuss the collected data and confirm how to incorporate the contents RWE in the New Drug Application.

It’s important to note that all research designs, hypothesis and specific definitions related to the generation of RWE shall be stated clearly in the research protocol beforehand, otherwise it won’t be accepted by NMPA.

References

  https://doi.org/10.3346/jkms.2018.33.e213 eISSN 1598-6357·pISSN 1011-8934
ABOUT GLOBAL REGULATORY PARTNERS, INC

Global Regulatory Partners Inc, (GRP) provides regulatory affairs, clinical, quality and safety services to medical devices and pharmaceutical companies globally. As a qualified and licensed legal representative with offices in USA, China, Japan, Brazil, Mexico and Argentina, the company can represent life science companies in those countries and help them register their products in compliance with local regulations and in record time.

For additional information, please contact us at info@globalregulatorypartners.com

Corporate Office

Address: 400 Fifth Avenue, Suite #115, Waltham, MA 02451
Email: info@globalregulatorypartners.com
Website: www.globalregulatorypartners.com
Telephone: 781.672.4200

Brazil
Rafael Marino Street, NETO 600
Karaiba Garden
UBERLANDIA – 38411-186
Minas Gerais (MG)
Telephone: (+55) 34-3235-1971

Japan
Ark Mori Building, Suite 50, 12/F
1-12-32 Akasaka Minato-K
Tokyo, 107-6012
Telephone: (+81)-3-4360-9287

Mexico
Lake Alberto 442 – 5th floor
Tower A – Office 509
Col. Anahuac 1st Section
Delegation Miguel Hidalgo, C.P. 11320
Telephone: (+52) 55 7312 4169

China
21st Centry Tower, Suite 6030, 6/F
210 Centry Avenue, Pudong District
Shanghai, 200120
Telephone: (+86) 021-517-27278