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Ready, Set, Go: China To Use Patient-Reported Outcomes In Clinical Studies

Hot On Heels Of FDA Draft Guidance

by Brian Yang

As a part of real-world evidence, patient-reported outcomes can serve to evaluate a drug's efficacy against primary or secondary endpoints and also reflect safety and quality of life, notes a just-released draft regulation from China's Center for Drug Evaluation.

Patient diaries, smartphone snapshots, videos and data from wearable monitors are all expected to play an increasingly important role in the evaluation of clinical study results, say China's drug regulators.

These so-called patient-reported outcomes, or PROs, will have a potentially wider use beyond a patient's perception of a drug's efficacy, extending also to safety profile and actual practical daily benefits, new draft guidance from the country's Center for Drug Evaluation (CDE) states. "The patient-reported outcomes selected should reflect the patient's perception of the drug's efficacy but not limited to effectiveness, they can also reflect safety or quality of life," noted the 3 September document.

The CDE draft guidance comes hot on the heels of the US Food and Drug Administration's own draft guidelines in June, which outlined recommendations for systematic assessment of a core set of PROs in registrational studies, using fit-for-purpose tools and includes examples of acceptable instruments. (Also see "*Cancer Trials: Patient-Reported Outcomes Should Measure Five Core Concepts, US FDA Says*" - Pink Sheet, 9 Jun, 2021.)

In explaining its own approach, the CDE noted that "the changes in the proper selection of the PRO help to better reflect patients' outcomes in the study experience that highlight a patient-centric drug development approach."

To that end, two categories of PROs are proposed. One would be a traditional record of patient experience in written form, the other being recorded via technology such as smartphones, tablets, video cameras, computers and wearable medical devices. “Patients are allowed to record responses using keystrokes on mobile phones, with data stored directly into a centralized database," the CDE draft stated.

These "ePROs" could also be recorded via patients’ own wearable medical devices, sometimes known as a BYOD (Bring Your Own Device) approach. “Patients can access the device’s website or software, select answers based on their own circumstances and be recorded,” noted the regulator.

Another key aspect under the planned Chinese regulation is that PROs could serve as primary or secondary endpoints in clinical studies. To that end, though, patients would need to be aware of the following considerations:

1. PROs need to be well-founded and consistent with the purpose of the study;

2. greater risk of subjective evaluation bias;

3. study length should be sufficient to detect clinically significant changes in PROs;

4. potential for human error;

5. PROs would need to have clinical significance.

Data Reliability, Security

In general, ensuring the quality and reliability of individually generated and collected data is a large issue for PROs.

Personal data protection considerations are also increasingly critical to overall privacy and data security amid China’s recently enacted Personal Data Protection Law; the draft noted a need to safeguard all data generated from patients, especially via ePROs.

“The ePRO system can be docked with the electronic medical records or electronic data acquisition system, to form a complete data flow at the individual level,” the draft guideline observes. “A time recording function can effectively prevent and identify back-filling or other behaviors affecting data reliability.”

In the case of remote gathering of data, the regulators stressed a need for real-time monitoring and correction. “A remote monitoring function helps researchers and data managers to carry out

real-time online data management and remote data monitoring, question the data in doubt and make timely visits to the subjects," the draft states.

Multiple Implications

While still in the early stages, the PRO concept is gaining traction in China, where the number of clinical trials is exploding but patient resources for controlled trials are also becoming scarce.

In certain crowded areas of drug development, especially oncology, study sponsors are already elbowing each other to enroll qualified patients. China is now the second-largest destination for studies for cancer and cell and gene therapies after the US. With a large number of ongoing trials and new biotech startups emerging daily, the need for patients is acute and wider adoption of PROs is likely to ease the congestion.

PROs may also reduce the burden for study subjects and clinical study professionals to have face-to-face data collection and evaluation, enabling further relief against the backdrop of the ongoing global pandemic. (Also see "*Cancer Drug Developers Cry Foul As Costs Soar In China*" - Scrip, 23 Jun, 2021.)
However, some observers see the PRO system as requiring rigorous monitoring and supervision to ensure the quality and usability of such data, while missing data is another major concern.

Meanwhile, others say the application of PROs is likely to accelerate studies for rare diseases treatments in particular. These have a much smaller population and can thus require a lengthy period to enroll sufficient qualified patients, and new tools may help.

When planning to use PROs as part of a clinical study, the draft guideline recommends communicating with regulatory authorities during the pilot design phase. Public comments on the draft (click *here* for this in Chinese language) are being gathered until 3 October. Any comments may also be sent to zhaojun@cde.org.cn.