Integration of Clinical Outcome Assessments (COA) in Drug Approval Process to Foster Patient-Centric Clinical Trials:

CO194

A Review of 3 Regulatory Guidelines for Drug Development in APAC

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Background

The purpose of medical interventions is to better patients' lives, necessitating an understanding of their experiences, needs, and priorities.

Clinical outcome assessment (COA) evaluates a patient's feelings and functional status through subjective assessment. It includes domains like symptoms, routine functions, health status, quality of life, and satisfaction. COA-based clinical endpoints include patient-reported outcomes, clinician-reported outcomes, observer-reported outcomes, and performance outcomes.

COA-based clinical endpoints can serve as primary or secondary endpoints of clinical benefits, focusing on patients' personal feelings, performance, or survival. For instance, in hereditary angioedema trials, the VAS can be used as the primary endpoint, while in myelofibrosis trials, imaging findings and symptom improvement can be secondary endpoints. COA can also assess safety and risk tolerability.

In this context, Clinical Outcome Assessments (COAs) serve a crucial role within clinical trials. However, standards for COAs differ across countries, as reflected in their distinct drug approval guidelines. This study compares the incorporation of COAs in the guidelines of China, Japan, and India.

Methods

We utilized a conceptual thematic analysis of the guidelines: China's patient-centered clinical trial design issued by the National Medical Products Administration (NMPA), Japan's Pharmaceutical and Medical Devices Agency (PMDA) guidelines, and India's drug approval guidelines.

Our focus was on the content comparison of these guidelines concerning the application, evaluation, and articulation of COA standards aiding regulatory decisions.

Results

NMPA- China

- NMPA- China provided guidelines on designing, implementing, and benefit-risk assessment of patient-centered clinical trials. These guidelines recommended using Patient Experience Date (PED) based COA endpoints in assessing clinical efficacy, benefit, patient experience on risks, and risk management of the whole drug lifecycle (Figure 1).

Guidelines for patient-centered clinical trials issued by NMPA-China emphasized the advantages for patients' functional status, emotional and physical health, and chance of survival. It was advised that clinical trials collect Patient Experience Data (PED) utilizing the clinical outcome assessment (COA)-based efficacy evaluation method. It was advised that the use of COA-based endpoints be contingent upon elements such as the purpose of the trial, the target indication, the drug's mechanism of action, and the clinical orientation.

Figure 1- Summary of COA component of NMPA guidelines

Guidelines on	NMPA key recommendations
Designing	• Positioning of COA based end points in efficacy evaluation • Selection of fit for purpose COA based on the intended assessment contents and application scenarios • Propose appropriate threshold for COA based on PED data to reflect clinically significant change
Implementing	• Collection of PED using appropriate COA tool • Use of digital technology in collecting storing and utilizing PED data
Benefit- risk assessment	• Treatment background analysis to identify the burden of the disease, the natural history of the disease, risks, and benefits of existing treatment, and unmet clinical needs • To evaluate the COA endpoint's relevance, importance • To evaluate the benefits, safety, and tolerability of a drug • Assess the severity of safety events, also to understand the risks patients are informed of, and the burden on patients due to risk management measures

NMPA-China emphasized that implementing PED involves accurate and truthful collection, using COA to support efficacy or safety evaluation in specific trials. And recommended that Digital health technology (DHTs) can be used to collect PED, but careful selection, validation, and usability studies are essential.

NMPA-China mentioned that the extent of clinical benefits and potential risks should be considered, and the benefit-to-risk ratio should be weighed to determine effective risk management measures.

JCOG- Japan

The Japan Clinical Oncology Group (JCOG) has reorganized its research committee to address the lack of consensus on standardized methods for assessing patient-reported outcomes and health-related quality of life in cancer clinical trials.

The Quality-of-Life Assessment Policy, created in 2006, was reorganized to address the lack of consensus on standardized methods for analyzing and interpreting results. This move aimed to improve patient experiences during and after cancer treatment.

India

India lacks country-specific guidelines on COA endpoint assessment of efficacy, patients' experience of disease burden, and benefit-risk assessment.

Summary

The analysis unveiled a more detailed elaboration of COA content in China's guidelines compared to Japan's and India's. Integral COA aspects such as measure selection, patient involvement in study design, and assessment of respondent burden are distinctly outlined in Chinese guidelines. China also emphasizes COA-based endpoint considerations in its regulations. In contrast, Japan and India lack similarly detailed, nation-specific data, leaning heavily on US and EU regulatory guidelines instead. Despite COA modules being considered during clinical trial protocol approval in both countries, explicit mention of COAs in their guidelines is lacking.

Conclusions

- China exemplifies substantial progress in establishing patient-centric clinical trial design with COA integration. However, comparable advancements are yet to be seen in other APAC regions like Japan and India. Future efforts should concentrate on APAC collaboration to implement COA guidelines, factoring in participants' literacy, technological capabilities, and cultural, and personal needs. This would foster a more tailored, patient-centric approach in clinical trials across these culturally diverse nations.

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