Summary of Panel Discussion in HBD East 2019 Think Tank Meeting

HBD For Children

The regulatory uses of pediatric registry data were discussed. While registry data have supported some marketing approvals in the US, the use of streamlined data elements would facilitate adoption and use of registries. Registries may also have special value for post-market surveillance and studies where the focus is often on unexpected uses or events which are less likely to be seen pre-market. Collaboration with experienced academic groups may help refine the optimal use of registries. Funding is also important, and it has at times comes from industry, medical societies, or government groups. Working with academic groups and using their registries can be helped by resolving issues such as who will pay for each aspect of the project, who will write the protocol, and the opportunity costs of using registries vs committing resources to other projects. Small companies often have a more limited understanding of how to work with registries, which may be helped by having a multi-stakeholder consortium similar to what exists in the US for Early Feasibility Studies. For industry, profit margin is a very important consideration for pediatric device development, and further US-Japanese harmonization could make these projects more profitable. For Japanese companies entering the US market, costs are very important, including cost associated with potentially required changes to manufacturing or other operations, familiarizing the company with the US regulatory system and market, and identifying new distribution networks. Venture capital money can be helpful, but the Japanese industry does not have a well-developed track record in this area. Further collaboration can help resolve these issues.

Real-World Evidence

When using RWE for regulatory purposes from the Japanese regulatory perspective, it is generally easier to use prospective data for marketing approval, while the FDA perspective is that retrospective may be appropriate if the data collection mechanism incorporated the appropriate parameters or elements from the beginning. Other uses of retrospective RWE are identification of a particular patient population to inform a prospective trial. Confidence in the analysis of retrospective data value can be higher if the statistical plan is established prior to looking at data. When considering the role RWE in Japan, the Japanese academic perspective is that they are encouraged by FDA's acceptance of RWE but think collaboration among stakeholders in Japan will also be important. There are examples of "RWE-like" experiences with new technology in Japan that can be built on. RWE should not just be looked at as replacement for traditional data, but offer an additional way to collect unique types of information. In order to maximize the quality of RWE, it should only include information that would be considered as part of standard of care, which typically would not include endpoints requiring adjudication unless these would normally be captured and used to guide treatment of the patient. RWE also isn't just about data, but also about having an infrastructure that allows reliable collection of real-world information. The costs associated with RWE projects can be misleading since there may involve high startup cost to generate the infrastructure, but future re-uses of the same mechanism will be cheaper. It is also important to consider whether the cost is different for establishing infrastructure versus pulling data

later. PMDA has used registry or literature to support approvals before, and that the "registry consultation" pathway exists and should be used to establish the exact purposes of registry data. In thinking about future directions for RWE, we should be realistic about the current limitations of contemporary RWE sources so that we can improve what is collected in the future. It would also be helpful to identify global RWE-related collaborations. Industry would like to hear more examples of how RWE has been used, to better inform their decision-making. One particularly good area for RWE may be surgical devices, for areas where traditional studies have typically been small or difficult to control or blind.

Early Patient Access

It is important to consider current and potential future ways to create synergies with existing US and Japanese regulatory approaches intended to facilitate timely access to promising medical devices. Given the prevalence of Early Feasibility Studies (EFS) in the US, it may be valuable to consider whether EFS data from one country can be applicable in the other, or whether EFS data from the US and Japan can be pooled to strengthen the conclusions that can be drawn. In this case, it will be important to consider the impact of differences in factors like clinical practice and experience, especially given the small size of these studies. For post-market schemes, involvement from academia is important. Some companies may feel that working with both regulators may ultimately slow down the approval timeline in either country. While there may be the fear that one regulator will inform the other about their concerns with a given product, typically these communications result in reduced rather than increased concerns and have overcome barriers to approval. Increased outreach and transparency regarding HBD activities may be helpful in this regard. Since the US and Japan represent very large markets, receiving these approvals is a significant achievement for companies, and if other regulatory jurisdictions were to acknowledge these approvals as a sufficient basis for marketing in their own jurisdiction, this would further encourage early-stage evaluation and marketing in the US and Japan and reinvestment of profits into research and development of new products. This is especially true given the uncertainty with implementation of the EU Medical Device Regulation and differences across each European market, and some countries in Asia already give some preference to devices that have Japanese approval.