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Honorable Robert M. Califf, M.D.
Administrator
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Dear Administrator Califf:

Thank you for the opportunity to comment on the importance of patient preference information (PPI). We applaud the Food and Drug Administration (FDA) for this effort to engage all stakeholders, including patients, to help clarify the main considerations needed to design and demonstrate a fit-for-purpose PPI study, key information for inclusion in premarket PPI, and generalized examples of PPI studies that help support regulatory decisions.

Having formerly served as the Interim Executive Director of the Patient-Centered Research Foundation, now known as PCORnet, as well as a former member of the Board of the Innovation and Value Initiative (IVI), I am eager to see continued innovative research methods to measure outcomes that matter to patients and the science of patient preferences. When I founded Global Liver Institute, it was clear to me that patient perspectives were lacking in research and policy discussions, particularly related to the differences among patients that are under-represented in the data. We appreciate that the FDA is prioritizing efforts to address such challenges.

At Global Liver Institute, we are committed to improving the lives of individuals and families impacted by liver disease through innovative awareness and promotion efforts, encouraging collaboration, and scaling optimal approaches to help eradicate liver diseases and liver cancers. It is critically important that patients living with liver disease and liver cancer maintain reliable access to groundbreaking treatments, medical technology, and services that have been shown to decrease the burden of their disease and improve the likelihood of favorable outcomes.

We are pleased to provide the following comments to the FDA related to the questions posed in the agency's request for early feedback regarding revisions to its final guidance on PPI.

What are important factors that the sponsor should consider when designing a patient

preference study to ensure that it will address the question that it is meant to address?

It is imperative for any PPI study to include diverse perspectives representing all the subpopulations that may be impacted. Liver cancer patients experience health disparities across racial, ethnic, gender, and education groups, all of whom have unique preferences related to the outcomes they want to achieve through treatment.[1] Advancing innovation, and therefore access to clinically proven therapies and medical technology, is critical to our collective efforts of fostering health equity and improving outcomes for patients living with liver cancer. Innovation should be driven by patient preferences, delivering important patient-centered values for improved quality of life. Those preferences may differ among subpopulations and should not be viewed in a one-size-fits-all manner. Amplifying the patient voice provides a greater opportunity for collaborative decision making in choosing among the many therapeutic and medical technology options for treatment of complex liver tumors.

What are some methods for eliciting patient preference information (PPI), and when might it be appropriate for sponsors to use them?

We appreciate the ongoing work of the Medical Device Innovation Consortium (MDIC) to engage stakeholders, including patients, to identify approaches for utilizing PPI to inform clinical trial design.[2] Their resulting patient-centered framework was developed to help researchers interested in conducting rigorous patient preference studies for medical device design, development, evaluation, and regulatory submissions.[3] Among their recommendations, we would emphasize the need for early buy-in from patient stakeholders to ensure that a PPI study is conducted in a manner that genuinely reflects the patient voice to inform clinical trial endpoints. Researchers should be accountable for partnering with patient organizations to inform the study design and ensure recruitment from impacted populations, with an emphasis on achieving diverse participation. We believe these goals can be realized without creating undue burdens or expenses for study sponsors and academic researchers.

Additionally, the Innovation and Value Initiative recently completed a project funded by the Patient-Centered Outcomes Research Institute (PCORI) on “Designing Equitable Measures and Methods for Patient Priorities in Healthcare Value Assessment” that emphasized shared leadership with engaged patients and patient organizations, as well as compensation for patient engagement that may provide useful insights for FDA.[4] Their recent work related to preferences for treatments for major depressive disorder demonstrates that the methods exist to identify the trade-offs important to patients and the potential for meaningfully incorporating the patient experience in preference measures.[5]

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1 American Association for Cancer Research (AACR). (2021, October 18). Reflecting on the Racial Disparities in Liver Cancer. AACR Blog. Retrieved from https://www.aacr.org/blog/2021/10/18/reflecting-on-the-racial-disparities-in-liver-cancer/.

2 Kim, J., et al. (2022). Development and Application of the Engaged Research Partnerships Evaluation Rubric for Patient-Centered Outcomes Research. Journal of General Internal Medicine, 37(5), 1213-1219. doi:10.1007/s43441-022-00450-9.

3 Medical Device Innovation Consortium (MDIC). (n.d.). Using Patient Preference Information in the Design of Clinical Trials Framework. Retrieved from https://mdic.org/resource/using-patient-preference-information-in-the-design-of-clinical-trials-framework/.

4 The Value Initiative. (2022). 2021 Methods Summit Report. Retrieved from https://thevalueinitiative.org/wp-content/uploads/2022/03/2021-Methods-Summit-Report_FINAL.pdf.

5 Vreman, R. A., et al. (2022). Budgeting for Patient and Public Engagement Activities in Health Research: A Conceptual Framework and Practical Guidance. PharmacoEconomics, 40(10), 1275-1287. doi:10.1007/s40271-022-00596-6.

What are important considerations for the selection of attributes and attribute levels when designing a PPI study?

The goal should be to align on an approach to evaluate and weight measurable factors that matter most to patients. The endpoints identified in patient preference studies supplement other clinical trial endpoints and can be useful to prioritize relevant outcomes. As an example, for patients with liver cancer, the delivery of therapeutics into liver tumors using innovative drug delivery technologies, across therapeutic classes, decreases toxicity by lowering off-target deposition, making treatment less toxic and potentially more effective. PPI could better identify how placing greater weight on selection of appropriate medical technology, as understood from patient preferences, may reduce toxicity, improve quality of life, and better align treatment decisions with patient goals. Using language from the statute creating the PCORI, the selection of attributes and attribute levels should be informed by "patient needs, outcomes and preferences."[6]

What information is important to provide to the FDA about the patient preference protocol, study conduct, and PPI results to inform a medical device regulatory decision?
For devices impacting the treatment of liver disease and liver cancer, we would advise a patient preference protocol that is developed with engagement from organizations such as Global Liver Institute that have a breadth of knowledge about liver disease and liver cancer. These groups can reach and recruit participation from diverse patient populations. Early engagement is essential,[7] and resources should be made available to engaged patient organizations to ensure their engagement is meaningful versus "token" engagement. Study sponsors should demonstrate how they engaged patient partners and how their input was incorporated into the study design, and could be incentivized to do so with certain incentives such as expedited review of their applications. As with any other engaged partner, whether clinicians or researchers, the engaged patient partner organizations advising on study design and recruitment should be compensated. PCORI provides useful tools for patient engagement,[8] compensation,[9] and budgeting for engagement activities[10] that are useful tools for FDA's consideration related to best practices and protocols for conducting a PPI study.

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6 United States Code (U.S.C.). (n.d.). 42 USC §1320e(d)(1)(A).
7 Kim, J., et al. (2022). Development and Application of the Engaged Research Partnerships Evaluation Rubric for Patient-Centered Outcomes Research. Journal of General Internal Medicine, 37(5), 1213-1219. doi:10.1007/s43441-022-00450-9.
8 Patient-Centered Outcomes Research Institute (PCORI). (n.d.). Engagement Rubric. Retrieved from https://www.pcori.org/sites/default/files/Engagement-Rubric.pdf.
9 Patient-Centered Outcomes Research Institute (PCORI). (n.d.). Compensation Framework for Engaged Research Partners. Retrieved from https://www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf.
10 Patient-Centered Outcomes Research Institute (PCORI). (n.d.). Budgeting for Engagement Activities. Retrieved from https://www.pcori.org/sites/default/files/PCORI-Budgeting-for-Engagement-Activities.pdf.

What are some examples of PPI studies that could help support medical device regulatory decisions?

We strongly recommend that FDA look to the ongoing work of PCORI, IVI and MDIC both in terms of methods and for guidance on PPI information studies that could be useful to support the FDA's medical device regulatory decisions.

In closing, Global Liver Institute applauds FDA's outreach for input on this important issue. We look forward to continuing to play a role in the development of revised guidance on PPI to ensure that the patient voice is genuinely reflected in the attributes identified and incorporated into clinical trials.
Sincerely,

Sincerely,

Donna R. Cryer, JD
President & CEO
Global Liver Institute

About Global Liver Institute

Global Liver Institute (GLI) was built to solve the problems that matter to liver patients, equipping advocates to improve the lives of individuals and families impacted by liver disease. GLI promotes innovation, encourages collaboration, and supports the scaling of optimal approaches to help eradicate liver diseases. GLI believes liver health must take its place on the global public health agenda commensurate with the prevalence and impact of liver illness. GLI is the only patient-created, patient-driven nonprofit organization tackling liver health and all liver disease holistically, operating globally. Follow GLI on Facebook, Instagram, LinkedIn, and YouTube.