Clinical Management of Hepatitis C Infection

LOI Applicant Town Hall
February 11, 2015
Agenda

Welcome

Overview

PFA Requirements

Administrative Requirements

Resources

Submitting Questions:
Submit questions via the chat function in Meeting Bridge.

Ask a question via phone (an operator will standby to take your questions).
Overview
Our Focus at PCORI

Comparative Clinical Effectiveness Research

- Patient-centered
- Answering questions that matter to patients and other clinical decision makers
- Comparisons of outcomes that matter to patients
- Attention to possible heterogeneity of treatment effects
Objective of this PFA:

Address *critical* clinical and healthcare delivery choices faced by hepatitis C patients, their caregivers, clinicians and/or delivery systems.

In this PFA we seek to fund:

- Pragmatic clinical trials
- Comparative observational studies

Available Funds and Duration:

- A total of $50 million (direct and indirect)
- Up to $20 million in total direct costs per project
- Projects should be completed within 5 years
What is a Pragmatic CER Trial?

- Answers a practical, real world comparative effectiveness research question
- Assesses whether two or more options differ in effectiveness when administered as they are in real life, and the project is conducted in a clinical setting that is as close as possible to a real world setting
- The methodological approach (including study design, outcome measures, and follow-up) is as simple as possible without sacrificing scientific rigor
Programmatic Requirements
Essential Characteristics of Studies

- Include patient populations representative of the underlying epidemiology of HCV
- Compare the effectiveness of two or more alternative approaches to management of HCV
- Have strong endorsement and participation by stakeholders
- Take place within typical clinical care and community settings
- Have a sufficiently large study population to enable precise estimates of effect sizes and to support evaluation of potential differences in intervention effectiveness in patient subgroups
- Describe, to the extent possible, what can be learned about the natural history of disease and heterogeneity of treatment effects
PCORI Four Priority Research Questions

1. How do new regimens of oral antiviral medications for the treatment of hepatitis C infection compare in long-term virologic response and adverse effects?

2. What are the comparative benefits and harms of treating patients with hepatitis C infection at the time of diagnosis versus waiting to treat only those patients who show early signs of progression of liver disease or other manifestations of hepatitis C infection?
   - What are the predictive factors of liver disease progression? How should they be combined to predict patients at low risk of progression?
Which HCV screening methods, confirmatory testing strategies, and clinical settings lead to the best rates of detection and linkage to treatment?

What is the comparative effectiveness of interventions to support the care of hard-to-treat patients with chronic hepatitis C infection (e.g., substance abusers, persons with complex medical regimens, the mentally ill), as measured by receipt of treatment, medication adherence, patient quality of life, and sustained viral response?
Head-to-Head Treatment Comparisons

How do new regimens of oral antiviral medications for the treatment of hepatitis C infection compare in long-term virologic response and adverse effects?

- Directly compare distinctly different drug regimens
- Study populations with important disparities, comorbidities or difficult social conditions

Outcomes of interest include:

- Viral response at 2 years or longer
- Drug side effects and systemic symptoms that may be due to HCV viremia
- Progression of liver disease – both short and long term
- Signs of recurrent HCV infection

Adaptive designs that could accommodate the emergence of new treatments during the course of the study are encouraged
Comparison of Immediate and Delayed Treatment

- What are the comparative benefits and harms of treating patients with hepatitis C infection at the time of diagnosis versus waiting to treat only those patients who show early signs of progression of liver disease or other manifestations of hepatitis C infection?

- What are the predictive factors of liver disease progression? How should they be combined to predict patients at low risk of progression?

- Outcomes of interest include:
  - Development of liver fibrosis/cirrhosis and its sequelae
  - Viral response at 2 years or longer
  - Other patient-relevant outcomes, including symptoms

- An observational study might complement a randomized trial to achieve sufficient power to detect small differences in outcomes.
Screening and Diagnosis Tests

Which HCV screening methods, confirmatory testing strategies, and clinical settings lead to the best rates of detection and linkage to treatment?
- Justify the choice of screening strategies
- Address the availability of the clinical tests

Responsive applications should directly compare strategies for linking HCV screening to HCV diagnosis, appropriate follow-up care, and ultimately treatment.

Studies should target populations at high risk of active infection, as defined by the CDC, and/or pregnant women and hard-to-reach populations.

Outcomes of interest include:
- Attendance at an ongoing source of care for HCV
- Starting treatment (if available to the patient)
- Measures of treatment outcome
Care Delivery

What is the comparative effectiveness of interventions to support the care of hard-to-treat patients with chronic hepatitis C infection (e.g., substance abusers, persons with complex medical regimens, the mentally ill), as measured by receipt of treatment, medication adherence, patient quality of life, and sustained viral response?

Applicants should directly compare alternative models for providing support of care for HCV populations deemed hard to treat due to their risk for nonadherence and reinfection

- PCORI is not interested proposals to study the efficacy of a new model, nor of comparisons of a model of care to “usual care”

Outcomes of interest include:

- Measure of viral eradication
- Adherence to antiviral regimens
- Changes in clinical measures of comorbidities
- Avoidance of reinfection over 1 year
Responsive Applications

Investigators must propose projects that address at least one of the four priority research questions

- Other investigator initiated projects will not be considered responsive to this PFA

Given the significant treatment costs associated with many of the newly available therapies, investigators must address the support from payers, health plans, industry sponsors, or others in covering the study drugs and non-study protocol-related clinical costs and services rendered in the care processes.
Research Activities Not Supported in the Clinical Management of Hepatitis C Infection PFA

- Studies of decision aids
- Efficacy trials
- Evidence syntheses
- Cost-effectiveness analyses
- Research that aims to compare the overall costs of care between two or more alternatives and use the results to determine the preferred alternative
PCORI Methodology Standards

- 47 standards in 11 groups
- The Methodology Standards do not address all issues related to study designs and methods
- Note that PCORI is not using a specific set of methodological standards for “pragmatic studies.”
  - Consider design tradeoffs (e.g., blinding vs not blinding)
  - Refer to other respected sources for additional guidance.
  - View report and standards here:
    http://www.pcori.org/research-we-support/research-methodology-standards/
“Gap analysis and systematic reviews should be used to support the need for a proposed study. If a systematic review is not available, a systematic review should be performed using accepted standards in the field (see standard SR-1), or a strong rationale should be presented for proceeding without a systematic review. In the case where a systematic review is not possible, the methods used to review the literature should be explained and justified.”

Justification for the Design Elements of a Large Pragmatic Study

- Suggest reviewing pragmatic–explanatory continuum indicator summary (PRECIS) tool
- Consider tradeoffs
  - Eligibility criteria
  - Flexibility of intervention
  - Range and types of outcomes
  - Follow up intensity
  - Adherence
  - Etc.

Patient-Centeredness vs. Patient Engagement

Patient-centeredness is about whether the project aims to answer questions or examine outcomes that matter to patients/caregivers.

Patient engagement is about having patients/caregivers as partners in research, as opposed to merely being recruited as study participants.
Several approaches to engagement can succeed. PCORI provides many engagement resources for applicants:

- PCORI’s “The Patient and Family Engagement Rubric”
- Sample Engagement Plans
- Engagement in Research website page
- PCORI’s Methodology Standards PC-1 to PC-4
Administrative Requirements
Budget and Period Limitations

Funds & Budget
- Total Direct costs up to $20 million over the life of the project
- Indirect costs: up to 40%
- Institutional base salary up to $200,000
- Indirect costs are capped on subcontracts / sub awards
- The limit for Scientific Travel is $10,000 over the duration of the project. There is no cap on Programmatic Travel

Period of Performance
- Maximum of 5 years
- Requests to extend are not permitted during any stage
- Do not anticipate receiving a cost OR no-cost time extension
Costs of Interventions

PCORI will not cover costs for clinical care alternatives that are being compared in the project.

PCORI will consider covering costs for ancillary tasks necessary in the implementation or monitoring of a clinical intervention or strategy as part of the research program.

Examples include costs for obtaining consent, collecting data, or monitoring that would not normally be performed in routine care.

Support for the study by the involved healthcare delivery systems must be documented.
Guidelines for Intervention Cost/Coverage

- Costs for study interventions must be covered by delivery system, payer, manufacturer or developer of the intervention.
- The willingness of one or more of the stakeholder groups to cover treatment costs, even when one of the proposed intervention arms is not currently covered by insurance, will be taken as strong endorsement of the study by the health system or payer and of the likelihood that they will implement or use the study‘s findings if definitive.
- In exceptional cases, PCORI may consider coverage of the co-payment or coinsurance costs of participating patients when that is necessary to preserve blinding in a study or to assure access to the study for vulnerable populations.
- Contact PCORI with cost questions.
Eligibility to Submit a Letter of Intent

- Any private sector (non-profit or for-profit) research organization
- Any public sector research organization (university or college hospital or healthcare system, laboratory or manufacturer, unit of local, state, or federal government)
- Non-domestic components of organizations based in the US and foreign organizations may apply, as long as there is demonstrable benefit to the US healthcare system and US efforts in the area of patient-centered research can be clearly shown.
- Individuals are not permitted to apply.
Competitive LOI Process

New screening LOI process for Spring 2015 cycle:

- PCORI Online Pre-screen Questionnaire.
- All applicants are required to complete this form prior to proceeding to the LOI.
- The purpose of the pre-screen questionnaire is to help ensure projects meet minimum PCORI criteria.
This is a competitive LOI process:

- An LOI is required and must be submitted prior to the deadline. To submit an LOI, download the “Letter of Intent Template” in the Applicant Resources and complete the required fields in the PCORI Online System.
- The LOI is due on March 6, 2015 by 5:00 p.m. (ET).
- Only those LOIs deemed most responsive (programmatically and administratively) to this PFA will be invited to submit a full application.
- Applicants will be notified by March 23, 2015 whether or not to submit a full application.
Letter of Intent (LOI)

- Download the **Letter of Intent Template specifically for the Clinical Management of Hepatitis C Infection announcement** from the Funding Center to begin your LOI.
- LOIs cannot be more than 5 pages. All references should be included as in – text citations. LOIs that exceed five pages will not be reviewed.
- You must answer all questions, including the question on brief justification for the cost (“Will not exceed $20 million” is not a sufficient answer!).
- Do not upload additional documents as part of your LOI.
- Letters of endorsements or support are not accepted at this stage.
- You must upload your LOI as a PDF in PCORI Online.
- You must follow the naming conventions stated on the guidelines.
Formatting:

- Include the Principal Investigator’s (PI’s) full name on every page in the top left corner of the page header.
- Use at least half-inch margins and single spacing.
- Use size 11 Times New Roman for the main body of the text. Figures and captions may have smaller type.
- Each page must be numbered consecutively for each PDF upload.
- Keep the numbering of the LOI questions within the LOI template.
Using the PCORI Online System

- An applicant can save information by clicking the ‘Save and Review’ button on the save and review page.
- A PI can add an Administrative Official. The PI and the AO cannot be the same individual.
- Begin the LOI as soon as possible.
- Log into the PCORI system early to address additional LOI questions.
- Please only use Chrome or Safari browsers to access the system.
Resources
Resources

Refer to the Clinical Management of Hepatitis C Infection page in our Funding Center (http://www.pcori.org/announcement/hepatitis-c) for the following resources:

- PFA and Application Guidelines
- PCORI Online User Manuals
- Sample Engagement Plans
- Hepatitis-C FAQs: http://www.pcori.org/content/hepatitis-c-applicant-faqs
- PCORI Online: https://pcori.fluxx.io/
- Methodology Standards: http://www.pcori.org/research-we-support/research-methodology-standards/
## Submission and Key Dates

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<thead>
<tr>
<th>What</th>
<th>When</th>
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<tr>
<td>LOI-Applicant Town Hall</td>
<td>February 11, 2015 at 11:00am ET</td>
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<tr>
<td>LOI due in PCORI Online</td>
<td>March 6, 2015 by 5:00pm ET</td>
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<tr>
<td>Applicants notified as to whether they have been selected to submit a full application</td>
<td>March 23, 2015 by 5:00pm ET</td>
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<tr>
<td>Applicant Town Hall (if invited)</td>
<td>April 8, 2015 at 12:00 noon ET</td>
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<tr>
<td>Application Deadline (by invitation only)</td>
<td>May 5, 2015 by 5:00pm ET</td>
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<td>Merit Review Dates</td>
<td>August 6-7, 2015</td>
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<td>Awards Announced</td>
<td>September 2015</td>
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<td>Earliest Start Date</td>
<td>November 2015</td>
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Questions and Answers

Submit questions via the chat function in Meeting Bridge

Ask a question via phone (press 7)

Contact Us:
- Call 202-627-1884 (programmatic inquires)
- E-mail us at sciencequestions@pcori.org
- Call 202-627-1885 (administrative and technical inquires)
- E-mail us at pfa@pcori.org