A Randomized, Pragmatic, Adaptive trial of Metformin for Glucose Intolerance or Increased Body Mass Index in Prostate Cancer Patients

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PI – PEET project #1
Translational Science Barriers to address via this project

Significant barriers to clinical trial participation
• Present before pandemic and more acute during pandemic

Clinical trials imbedded in the EMR have the potential to address
• Takes significant coordination between research and EMR/hospital IT/regulatory

Patient barriers
• Easier to learn about trial opportunities via patient portal
• Research integrated into existing care team and treatment

Provider barriers
• Research occurs in context of existing care encounters
• Order sets in the EMR in the context of the encounter
Goals of this effort

- Complete feasibility study and use experience to inform future efforts
- Establish practical roadmap for future studies
  - Understand institutional resources needed
  - Identify key services needed for success
- Coordinate with the dissemination and evaluation core
  - Establish pathway for future efforts
  - Gather feedback from providers & patients
Background and Rationale

- Metformin is used widely in the treatment of type 2 diabetes.
  - It has off-label indications for use in the prevention of diabetes and in hyper-insulinar obesity.
- Multiple retrospective investigations have also shown a clinical benefit in men with prostate cancer who are incidentally treated with metformin.
- This pragmatic study will test the feasibility of enrolling patients who have glucose intolerance and/or who have increased BMI (BMI ≥ 25 kg/m²) to a randomized study of metformin plus lifestyle modification information versus lifestyle modification information only.
- For purposes of the scope of this project and the study’s feasibility, this will be implemented in a group of prostate cancer patients, who may have additional benefits from metformin.
Primary Objective:
To assess the feasibility of a randomized, pragmatic, adaptive, interventional trial in a multi-center hospital system.

Primary Endpoint:
Study Enrollment: 200 patients signing consent to enroll in the metformin/lifestyle study (consent #2 or #3) in My Health Connection.

Set to be adaptive with ability to increase participant number after initial 200 enrollees.
Rationale for Selection for Element E (first PEET Project)

<table>
<thead>
<tr>
<th>We have institutional strengths in this area</th>
<th>Novel clinical trial design</th>
<th>Chance to disseminate</th>
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<tbody>
<tr>
<td>• Health system EMR integration</td>
<td>• Less impact on providers and patients</td>
<td>• Plan to use this project as a model</td>
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<td>• Past e-consent efforts (biobank)</td>
<td>• Imbedded in EMR</td>
<td>• Assess patient engagement</td>
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<tr>
<td>• Health Data Compass</td>
<td>• Less data transcription</td>
<td>• Assess provider experience</td>
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<tr>
<td>• Institutional engagement</td>
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The Operations

- EPIC identifies patients based on eligibility criteria
- Electronic consent via patient portal to patient before appt. with provider
- Provider notified of consented patient (through EPIC)
- Randomization to arm of study
- Providers confirm consent and start intervention at time of next visit (pended orders)
- EPIC sends reminders to prescribing provider on needed SOC labs and monitoring per protocol
- Data extraction occurs for key endpoints via HDC (PSA, glucose, BMI, wt, BP) over time. No ECRF’s
Study Schema

Consent #1
Join the consortium

Consent #2 and #3
Pragmatic Metformin study specific arms (metformin or lifestyle information)
<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
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<tbody>
<tr>
<td>Cecilia Low-Wang, MD</td>
<td>Endocrinology faculty/study management (CPC)</td>
</tr>
<tr>
<td>Marc Bonaca, MD</td>
<td>Cardiology faculty/study management (CPC)</td>
</tr>
<tr>
<td>Tom Campbell, MD</td>
<td>Chief Clinical Research Officer, UCHealth/Associate Dean School of Medicine</td>
</tr>
<tr>
<td>Alison Lakin, RN, LLB, LLM, PhD</td>
<td>Associate Vice Chancellor for regulatory compliance</td>
</tr>
<tr>
<td>John Heldens</td>
<td>Director of the COMIRB</td>
</tr>
<tr>
<td>Anne Martin</td>
<td>Cancer Center - IIT study start up support</td>
</tr>
<tr>
<td>Tiffany Cull</td>
<td>Cancer Center – Regulatory support</td>
</tr>
<tr>
<td>Dexiang Gao</td>
<td>Cancer Center biostatistics</td>
</tr>
<tr>
<td>Andrew Nicklawsky</td>
<td>Cancer Center Biostatistics</td>
</tr>
</tbody>
</table>
Investigator Roster for the Metformin Pragmatic PCA trial

- **Metro – Tom Flaig Site PI**
  - Medical Oncology
    - Elaine Lam
    - Elizabeth Kessler
    - Eryn Callihan
    - Scott Kono (CCMC)
    - Timothy Waxweiler (CCMC)
    - Haider Yusufi (CCMC)
    - Megan Spradlin
    - Dwight Macero
    - Laura Graham
    - Christopher Geiger
  - Urology
    - Paul Maroni
    - Simon Kim
    - Janet Kukreja
    - John Dodge
  - Radiation Oncology
    - Brian Kavanagh
    - Tyler Robin
    - Sam Nath
    - Shelley Beckley
    - Molly Olm-Shipman (HRH)

- **Northern Colorado – Steve Schuster Site PI**
  - Medical Oncology
    - James Moore
    - Anne Kanard
    - Douglass Kemme
    - Ross McFarland
  - Radiation Oncology
    - Joshua Petit
    - Arthur Liu
    - Gwen Lisella

- **Southern Colorado – Robert Hoyer Site PI**
  - Medical Oncology
    - Geetika Srivastava
  - Radiation Oncology
    - Jeff Olson
Study update - March 2024

Enrollment to the consortium via consent #1 is robust: 1,111

• 23 have signed consent #2 or #3

Have been able to pilot a number of PEET functionalities:

• EMR-based participant identification
• Electronic consent within the EMR with integrated study video
• Real time provider EMR advisory for enrollment during routine visit
• EMR-based study information distribution to participants
• EMR-based Dashboard develop for participant tracking
• Collection of safety data (adverse events of interest, hospitalizations, etc.)
Future study plans

Work within the PEET program and CCTSI Dissemination and Implementation Core on participant transition to Consent #2 and #3

• Had previous patient advisory group at the study planning phase

Work with IT team do develop a CONSORT participant flow to better understand participant who do advance to consent #2 and #3

Add physical, clinic-based recruitment posters in select clinic with QR code/information for consent #1

Supplemental submission planning

• Participant and provider survey on experience with the process
Question for the EAC

• Any additional advice on how to best integrate this project within the PEET program and inform the second/future demonstration projects?

• Is this study serving an appropriate role to pilot a path for future PEET studies?

• Additional recommendations related to the operations of the study?