Session 3: MCGI: Presentation of the Initiative and the Study Protocol

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Introduction

- What we have heard so far:
  - Precision Medicine is here but routine implementation in oncologic practice has not been reached.
  - Genomic tests are rapidly developing, available and very powerful.
  - We can identify “use cases” for integrating genomic tests into patient care.
Introduction

- How do we remove barriers and advance precision medicine in the community?
  - Make genomic technology available for clinical use
  - Provide education on the technology
  - Create a network of practices and hospital to improve communication and promote collaborative research

= Maine Cancer Genomics Initiative
Introduction

- To increase the impact of the MCGI on our understanding of community genomic medicine, the initiative will be rolled out on a study protocol.

- The study protocol will allow us to
  - Measure the impact of the MCGI on oncology clinicians and cancer patients
  - Collect valuable clinical and genomic data and patient specimens for future research
Maine Cancer Genomics Initiative
- Partners
MCGI Study Protocol

Cohort 1: Oncology Clinicians

Cohort 2: Cancer Patients

Enrollment and Baseline Survey*

Annual Survey*

Report Survey*

JAX tests

Genomic Tumor Boards

PRO Surveys*

Clinical Data

Data Collection (REDCap Cloud/JAX)

Educational Modules

*developed in collaboration with MMCRI

Time (Study period)
MCGI Steering Committee

- **Mission:**
  - Oversight over study and deliverables of initiative.
  - Drives the iterative process of initiative and protocol refinement

- **Monitor study progress**
  - Is study meeting its recruitment goals?
  - Is current protocol feasible or do we need to make changes?

- **Monitor feasibility of MCGI implementation**
  - Time & resource requirements for test ordering and study participation
  - Timeliness of test reports being returned to the patient
  - Evaluate participation in Genomic Tumor Boards
  - Evaluate oncology clinician utilization of educational modules
MCGI Deliverables: JAX Genomic Tests

- Specific tests from the JAX Clinical Genomics Laboratory will be available to patients and clinicians enrolled on the MCGI study protocol (free of charge to the patient).

- These tests are CLIA-certified/CAP-accredited and can be used for clinical decision making (and can become part of the medical record).

- The exact tests and the appropriate patient populations will be defined by the study protocol.

- Within the study protocol, the test results are also used for educational purposes.
**MCGI Deliverables:**
**JAX ActionSeqPlus**

**FFPE Specimens:** One H&E stained slide and 5-10 adjacent unstained 5 um sections. ≥50% neoplastic content. We also accept tumor blocks.

<table>
<thead>
<tr>
<th>Metrics</th>
<th>ActionSeq</th>
<th>FusionSeq</th>
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</thead>
<tbody>
<tr>
<td>Genes covered</td>
<td>212</td>
<td>53</td>
</tr>
<tr>
<td>Mean target Coverage (MTC)</td>
<td>≥500X</td>
<td>Presence or absence of fusion</td>
</tr>
<tr>
<td>Limit of Detection</td>
<td>SNPs/InDels:8%; CNVs:≥6 copies (amplification), 0 copies (homozygous loss)</td>
<td>5% [minimum 5 reads for valid fusion]</td>
</tr>
</tbody>
</table>

**Turn around Time:** 10-14 days
JAX Liquid Biopsy Assay* – Plasma Monitor (cfDNA)

Panel of 14 genes, 84 hotspots

<table>
<thead>
<tr>
<th>AKT1</th>
<th>AR</th>
<th>BRAF</th>
<th>DDR2</th>
<th>EGFR</th>
<th>ERBB2</th>
<th>ERBB3</th>
<th>ESR1</th>
<th>FGFR2</th>
<th>KRAS</th>
<th>MAP2K1 (MEK1)</th>
<th>NRAS</th>
<th>PIK3CA</th>
<th>TP53</th>
<th>Total Hotspot regions</th>
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<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>8</td>
<td>7</td>
<td>13</td>
<td>14</td>
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<td>1</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>5</td>
<td>6</td>
<td>8</td>
<td>84</td>
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</table>

DNA input quantity: 10 ng

Estimated Mean Depth Coverage: 20,000x

Limit of detection: 0.05 - 1%

TAT: 7-10 days

*In validation currently
MCGI Deliverables: Educational program

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Module</th>
<th>Fact sheet/resource</th>
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<tbody>
<tr>
<td>1</td>
<td>MTB x3</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>MTB x3</td>
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</tr>
<tr>
<td>3</td>
<td>MTB x3</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MTB x3</td>
<td></td>
</tr>
</tbody>
</table>

- **Module:** Online or in-person education
- **Fact sheet/resource:** short education in response to community needs
- **MTB:** Molecular tumor boards – monthly, provides input into needed education/information resources
MCGI Deliverables: Educational modules—current status

- Module 1: “Exploring Somatic Cancer Panel Testing”
  - Ready to go for MCGI participants as soon as study is opened
- Module 2: “Interpreting a Test Report”
  - Will be ready to go in 3-4 months
- In general, modules will be accessible through a dedicated website at JAX.
- CME credit is available
- Prior to completing the module, clinicians will have to enroll on the study protocol.
MCGI Deliverables: Genomic Tumor Boards (1)

- Genomic Tumor Boards will discuss JAX assay results as they become available through the MCGI.

- Frequency depends on test volume (start with monthly, adjust as needed)

- Goal is to discuss cases prior to medical decision making based on test results.

- Multi-institutional participation through video- or teleconferencing (TBD)
  - De-identified patient data will be discussed
MCGI Deliverables: Genomic Tumor Boards (2)

- **Potential participants**
  - Oncology clinicians (enrolled on study protocol)
  - Pathologists
  - Genetic counselors
  - JAX internal and external subject matter experts
  - MCGI Medical Director and staff (discussion navigator, notes)

- **Format:**
  - Case vignette (including path),
  - Molecular results presentation,
  - Molecular results interpretation
  - Overall case discussion
  - Summary and Treatment recommendation
  - Follow up to previous cases
MCGI Study Design
Study Objectives

- Clinicians:
  - To evaluate oncology clinicians’ knowledge, attitudes, and clinical experiences regarding somatic genomic cancer tests

- Cancer patients:
  - To evaluate patients’ experiences with somatic genomic cancer tests through patient-reported outcome surveys (PRO’s).
  - To capture information related to JAX somatic genomic cancer tests

- These 3 objectives will enable us to report on the implementation of the MCGI.

Additional objective:

- To create a research data registry (containing PRO and clinical outcome data) and specimen repository of patient samples (blood, saliva)—optional and separate line on the consent.

Clinician cohort

- Licensed Physician practicing as an oncology clinician
  - Hematologist,
  - Medical oncologist,
  - Gynecologic oncologist,
  - Surgical oncologist
  - Radiation oncologist
- Nurse practitioner or physician assistant practicing under the supervision of an oncology physician
- Clinician enrolls by taking the baseline survey
- Enrolled clinicians can order a JAX test for a cancer patient on the MCGI study protocol.
Patient cohorts and associated assays

- Tests from the JAX Clinical Genomics test will be made available to clinicians for clinical use in patients to enable the achievement of the study objectives.
  - N= up to 1800 patients
- Specific tests will be available for defined sub-cohorts of patients
- First subcohort (up to 1200 patients)
  - All solid tumor patients (at first diagnosis and at relapse or progression)
- JAX Tests
  - ActionSeq Plus and JAX Plasma Monitor (cell-free DNA test)
- Additional tests for additional sub-cohorts will be developed over the study period.
- Pilot phase of 100 patients (or 6 months)
Patient sub-cohort A: JAX tests

Enrollment

Disease progression or relapse

New biopsy available

- ActionSeq Plus (tissue) most recent available tissue bx
- Plasma Monitor blood sample

No new biopsy available

- ActionSeq Plus (tissue) new tissue bx
- Plasma Monitor blood sample
Study procedures: Patient Cohort

- Tissue and/or blood sample for JAX assays
- PRO surveys: baseline, 3 months, 12 months
- If patient agrees to registry:
  - Clinical data collection at 3, 6, and 12 months
- If patient agree to repository:
  - Blood and saliva sample
Study Procedures: General Oncology Clinician Survey

- Assess knowledge, attitudes, and experiences of the oncology community in Maine regarding the use of cancer genomic testing in the routine care of cancer patients
  - Past experiences with cancer genomic testing
  - Perceptions of value, appropriate use of cancer genomic testing in clinical practice.
  - Perceptions of clinical utility, perceived barriers and facilitators of the use of cancer genomic testing
Study Procedures: General Oncology Clinician Survey

- Longitudinal: baseline and annual follow-up assessments
- Baseline survey completion is required for patient enrollment by the individual oncology clinician.
- Approximately 50 questions/20 minutes
Study Procedures: Point-of-care surveys and qualitative interviews

- Upon completion of genomic testing for individual patients
  - 2-3 questions requiring approximately 1 minute to complete
  - repeated for every patient who receives a genomic profiling test.

- Qualitative focus groups, individual interviews
  - Clinician perceptions, expectations, experiences with testing
  - Patient perceptions, expectations, experiences with testing
Regulatory Considerations

- JAX will utilize New England IRB (WIRB) as a central IRB for the study.

- Oncology Practices can participate in the MCGI study
  - By signing an external IRB agreement with WIRB
  - By completing appropriate research agreements with JAX

- Practices that don’t have the appropriate research infrastructure can enroll patients through the JAX MCGI Central Site.
Next steps and timeline

- Finalization of study protocol/consent followed by central IRB review
  - February 2017
- Continue evaluation of site-specific requirements for MCGI study protocol implementation
  - Site visits
  - Protocol review at sites
  - Research agreements
  - Start arranging this within next 2 weeks
- Site initiation visit
  - Baseline survey for clinicians
- First site, first patient
  - End of March 2017
Questions?