Guidelines for cases submitted for EXaCT-1 Clinical Genomics testing:
NYS approved CLIA-certified Laboratory

Introduction: The Clinical Genomics Laboratory now offers EXaCT-1 testing for metastatic and treatment resistant patients. The test examines the genomic mutations of all genes (about 22,000 genes in human being) in each patient’s cancer cells. The high cost of genomics testing coupled with the relatively low reimbursement from third party payers requires a set of guidelines to govern test utilization.

Purpose: The purpose of this document is to: 1) establish the clinical scenarios in which targeted panels or large cancer panels are considered relevant diagnostics for WCM-NYP oncology patients; and 2) define clinical scenarios in which immediate genomics testing is appropriate.

Utilization guidelines:

Criteria for immediate testing in the inpatient setting:
1. An immediate inpatient treatment decision will be made using genomic data. Examples of such scenarios include:
   a. Tumor with high mutation burden will make the patient eligible for immunotherapy
   b. Case Management Identified Patient
2. Patient’s genomic profile will impact the selection of therapeutic agents at the patient’s first follow-up visit as an outpatient.
3. The tumor will be “untestable” after initiation of treatment (e.g., AML) and tumor cells cannot be stored or archived.

Appropriate clinical setting for repeat targeted genomic testing or possibly Exact-1 testing:
1. Patients in whom a targeted therapy or other therapy has ceased to work suggesting clonal evolution.
2. Patients changes in clinical status suggestive of disease progression, including transformation of low grade lymphoma to high grade lymphoma.

Clinical setting where Exact-1 testing is beneficial but experimental:
1. Patients potentially recruitable to clinical trials per WCM Clinical team.
2. Advanced cancers with negative panel testing and no clear treatment options are eligible for WCM-NYP Joint Initiative Genomic lab testing.
3. Pediatric cancers covered by existing protocols.

When is genomic testing not advised/not possible:
1. No genomic testing currently offered in the laboratory is appropriate for the monitoring of minimal residual disease (MRD).
2. There are certain cancer types considered inappropriate for genomic testing including in-situ lesions, low grade papillary lesions of bladder and basal cell carcinoma (see Table 2).
3. Patients with low performance status such that they are not candidates for further therapy regardless of molecular findings.
4. Patients with high cure rate with standard therapies (e.g., ER/PR positive low-stage breast cancer, clinically localized prostate cancer).
5. Patients in whom a known driver mutation has been previously identified by earlier testing, and there has been no interval change that warrants a repeat test.
What are the indications for EXaCT-1:

1. Cancer Patients with late stage, recurrent advanced malignancy, including both solid tumor and hematopoietic neoplasm for which there is no conventional therapy and for which no actionable target identified by 50 gene or OnCORSQq.
2. Malignant Pediatric neoplasms.
3. Self-paid referral patients’ elective for Whole Exome Sequencing.
4. Any exceptions must be vetted and approved by Medical Director.

Table 1: Types of malignant neoplasms that will be considered genomics testing

<table>
<thead>
<tr>
<th>Neoplasms considered for genomics testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung carcinoma (adenoc, large cell neuroendocrine, squamous, small cell)</td>
</tr>
<tr>
<td>Brain tumor Grade III and IV (glioblastoma, anaplastic astrocytoma / oligodendroglia)</td>
</tr>
<tr>
<td>Breast carcinoma</td>
</tr>
<tr>
<td>Pancreas carcinoma</td>
</tr>
<tr>
<td>Hepatocellular carcinoma, cholangiocarcinoma</td>
</tr>
<tr>
<td>Melanoma</td>
</tr>
<tr>
<td>Ovarian carcinoma (endometrial, serous, mucinous, clear cell)</td>
</tr>
<tr>
<td>Ovarian sex cord stromal tumors</td>
</tr>
<tr>
<td>Uterine adenocarcinoma, serous carcinoma, or carcinosarcoma</td>
</tr>
<tr>
<td>Cervical cancer</td>
</tr>
<tr>
<td>Gestational Trophoblastic Disease</td>
</tr>
<tr>
<td>Salivary gland carcinoma, high grade</td>
</tr>
<tr>
<td>Renal cell carcinoma (e.g. sarcomatoid)</td>
</tr>
<tr>
<td>High grade urothelial carcinoma</td>
</tr>
<tr>
<td>Testicular tumors, non-seminomatous</td>
</tr>
<tr>
<td>Carcinoma of GI tract (colorectal, gastric and esophagus)</td>
</tr>
<tr>
<td>Thymic carcinoma, high grade</td>
</tr>
<tr>
<td>High grade sarcoma (e.g. osteosarcoma, dedifferentiated liposarcoma, MPNST, angiosarcoma, undifferentiated sarcoma)</td>
</tr>
<tr>
<td>Pediatric cancer (e.g. neuroblastoma, rhabdoid tumor)</td>
</tr>
<tr>
<td>Hematologic neoplasm (e.g. therapy resistant lymphoma)</td>
</tr>
<tr>
<td>Other advanced/high grade malignant tumors not mentioned above</td>
</tr>
</tbody>
</table>

Table 2: Examples of malignant neoplasms that will NOT typically be considered for genomics testing

<table>
<thead>
<tr>
<th>Neoplasms NOT considered for genomics testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive (in-situ) carcinoma of any type</td>
</tr>
<tr>
<td>Carcinoid tumor, low grade neuroendocrine tumor</td>
</tr>
<tr>
<td>Meningioma, low grade astrocytoma</td>
</tr>
<tr>
<td>Non-melanocytic skin cancer (e.g. basal cell carcinoma, squamous cell carcinoma)</td>
</tr>
<tr>
<td>Vulvar and vaginal cancer</td>
</tr>
<tr>
<td>Ovarian germ cell tumors</td>
</tr>
<tr>
<td>Uterine Leiomyosarcoma</td>
</tr>
<tr>
<td>Classical renal cell carcinoma (clear cell, chromophobe, papillary)</td>
</tr>
<tr>
<td>Typical squamous cell carcinoma of larynx / pharynx</td>
</tr>
<tr>
<td>Typical seminoma</td>
</tr>
<tr>
<td>Thymoma</td>
</tr>
<tr>
<td>Low grade sarcoma (e.g. well-differentiated liposarcoma)</td>
</tr>
</tbody>
</table>