deciphEHR™
connecting the dots in oncology

SUPPORTING SUSPECT PATIENT RECOGNITION FOR FURTHER BIOMARKER TESTING

HER2+ Cancer Program Implementation Guide

deciphEHR™ provides educational resources to help health systems, hospitals, and specialty practices leverage their electronic health record (EHR) systems. Data from the EHR system may help triage suspect patients for further clinician evaluation.

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- HER2+ cancer is characterized by the overexpression of the HER2 protein, a tyrosine kinase receptor growth-promoting protein expressed on the surface of various tissue cells.[1,2]
- Various HER2+ cancers may be associated with a more aggressive tumor, poor prognosis, and shorter survival upon diagnosis.[1-4]
- With a rise in treatments for HER2+ in many solid tumors, integrating routine actionable HER2 screening across tumor types may be pivotal in improving patient outcomes.[5,6]
- The objective of this guide is to help healthcare providers (HCPs) increase routine HER2 biomarker testing in the appropriate patient populations. Specifically, the program will make use of relevant patient history data, disease codes, and test codes to develop suspect patient lists, order sets, and best practice alerts (BPAs).

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HER2=Human epidermal growth factor receptor 2.

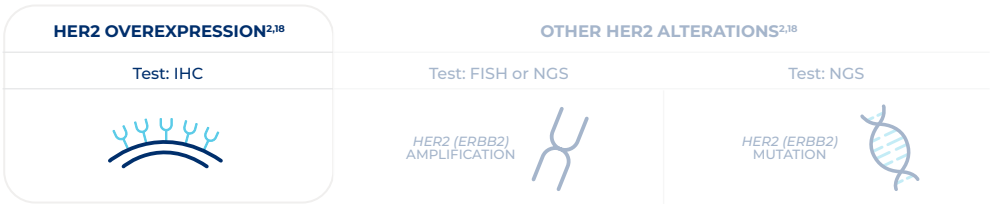
Clinical Criteria for HER2+ Cancer

1

While HER2 is a clinically significant biomarker that can have prognostic implications,[1-4] there are few unique signs or symptoms for many types of HER2+ cancers. Clinical guidelines, including NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), recommend testing for HER2 by IHC in multiple solid tumor types.[7-15] Now that HER2 is actionable across multiple solid tumors, widely assessing HER2 status across these tumor types may help to inform clinical decisions and improve patient outcomes.[5,6]

How to Test for HER2+ Cancer

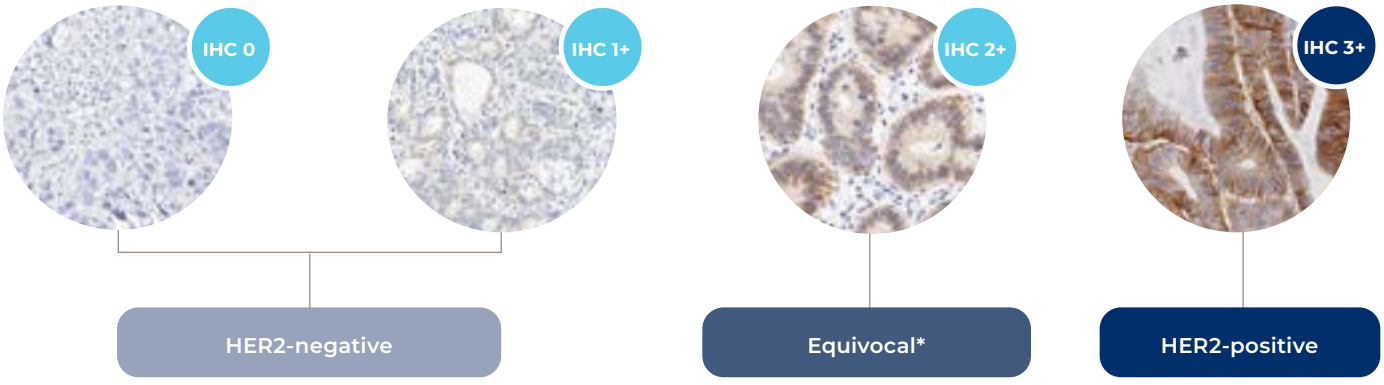
Choosing which HER2 biomarker test to run should be informed by (1) which biomarker is being assessed: overexpression, amplification, or mutation and (2) which test results have actionable, therapeutic options in each tumor type. Actionable HER2 protein overexpression (IHC 3+) may occur in any solid tumor type, regardless of HER2 (ERBB2) gene amplification or mutation status. HER2 overexpression, HER2 (ERBB2) amplification and HER2 (ERBB2) mutation are distinct biomarkers, and the testing methods for identifying these biomarkers are distinct.[5,17]



Note: IHC testing is the standard for detecting HER2 protein overexpression. FISH and NGS cannot measure HER2 protein overexpression and cannot be substituted for an IHC test.

Immunohistochemistry (IHC)

IHC uses antibodies to assess changes in the amount or expression of specific proteins in tissue samples.[6] **HER2 IHC testing is included in many NCCN Guidelines®, to assess for HER2 protein overexpression, which is a clinically relevant biomarker across tumor type.**[7-15] The ASCO/CAP HER2 Testing Guidelines can provide recommendations on how to interpret and classify HER2 expression status based on solid-tumor type. For additional guidance on tumor-specific HER2 testing, consult your local pathologist. **An IHC score of 3+ is considered HER2+ cancer across tumor types**.[2]



Stain images provided by Discovery Life Sciences
Example of guidelines for gastric cancer.

All IHC tests will require a tissue biopsy, but archival tissue or fine needle aspirations can be used for HER2 IHC testing.[6]

IHC=Immunohistochemistry, FISH=Fluorescence in situ hybridization, NGS=Next-generation sequencing, ERBB2=erb-b2 receptor tyrosine kinase 2.
*Further FISH testing recommended for some tumor types.
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When to Test for HER2[19,20]

For patients currently on treatment, even prior to disease progression

- **Refer to all pathology reports**
  - » Look back at the previous pathology report to determine whether HER2 IHC testing was already performed and if those results were positive
  - » Note: Only IHC can detect HER2 overexpression and is actionable across tumor types

- **Request HER2 IHC testing if not already performed**
  - » Work with your multidisciplinary team to reassess archival tissue for HER2 biomarkers
  - » HER2 IHC testing may be conducted with limited tissue from core needle biopsies or cytology
  - » Consider re-biopsying new tumor tissue when archival tissue is unavailable or inadequate for the HER2 IHC biomarker testing

For newly diagnosed metastatic patients

- **Request HER2 testing**
  - » Ask your pathologist to order or perform HER2 IHC biomarker testing based on the actionable therapeutic options available
  - » Incorporate HER2 IHC biomarker testing into the upfront comprehensive biomarker analysis to avoid delayed results
  - » HER2 IHC biomarker testing may be reflexed for all patients with a metastatic solid tumor

Note: NCCN Guidelines recommend HER2 testing in metastatic patients in a variety of solid tumor types.[7-16*] Determining implementation is at the discretion of the institution.

The College of American Pathologists (CAP) Cancer Protocols provide guidelines for collecting the essential data elements for complete reporting of malignant tumors and optimal patient care. These protocols incorporate the latest standards directly within their anatomic pathology laboratory information system (AP-LIS) workflow to help pathologists and laboratories keep abreast of the advances and updates in cancer reporting. Most AP-LIS vendors offer a CAP eCP synoptic module that can enhance the efficiency of pathology reporting and facilitate incorporation of vital diagnostic information into the EHR. HER2 IHC is part of the CAP Biomarkers Reporting Templates for Breast, Gastric, Colorectal, Gynecological, and Lung specimens. For other tumor types, the General IHC Quantitative Biomarkers Template is available.[21-28]

*See the NCCN Guidelines for detailed recommendations.

2

A Guide to Generating Suspect HER2+ Cancer Patient Lists

Utilizing the data in your EHR to generate suspect patient lists may encourage HCPs to implement the appropriate HER2 biomarker test rapidly and efficiently.[29,30]

Suggested Clinical Criteria for Suspect HER2+ Cancer Patient Lists

In an EHR system, a suspect patient list, also referred to as a patient list report, is a list of patients meeting certain clinical criteria. Generating a suspect patient list requires the same clinical criteria used to generate clinical suspicion for HER2 IHC biomarker testing. In addition to creating a list of cancer patients for further biomarker testing, a suspect patient list can also be used to flag patient charts with a best practice alert to recommend biomarker testing (potentially leveraging order sets) or clinical referral. Please see the charts below for guidance.

For Patients Currently on Treatment, Even Prior to Disease Progression

PATIENTS WITH SOLID TUMOR CANCER DIAGNOSIS

ASSESS PREVIOUS BIOMARKER TESTING

Cancer diagnosis ICD-10 and SNOMED codes can exist in the EHR and be leveraged to identify patients who should be considered for HER2 biomarker testing. The following tumors have National Comprehensive Cancer Network® (NCCN®) recommendations for HER2 testing[7-15]:

- Biliary tract
- Bladder
- Cervical
- Colon
- NSCLC
- Ovarian
- Pancreatic
- Uterine
- Vaginal

PATIENTS WITH NO HISTORY OF APPROPRIATE HER2 IHC BIOMARKER TESTING

SUSPECT PATIENT LIST

ASSESS IF THERE IS ARCHIVAL TISSUE FOR TESTING

Biomarker test results can exist in the EHR as LOINC codes and can be leveraged to identify patients that have not had the appropriate HER2 test. Note: Only IHC testing can assess HER2 overexpression.

RUN APPROPRIATE HER2 IHC BIOMARKER TEST ON ARCHIVAL TISSUE OR RE-BIOPSY

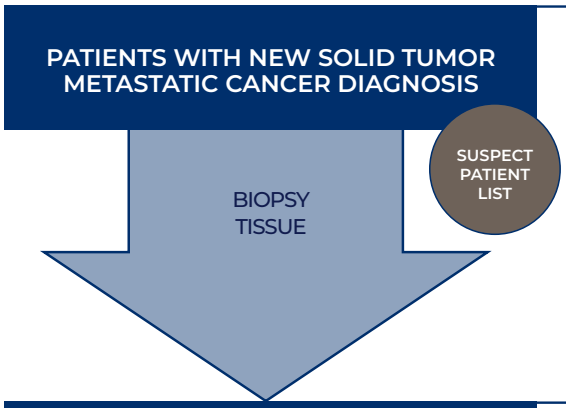
HER2 IHC TESTING

Due to the potential need for invasive re-biopsy and/or the cost to test archival tissue, it may be suggested to prioritize testing in metastatic patients. **Determining implementation is at the discretion of the institution.**

PATIENTS MEETING DIAGNOSTIC CRITERIA FOR HER2+ CANCER

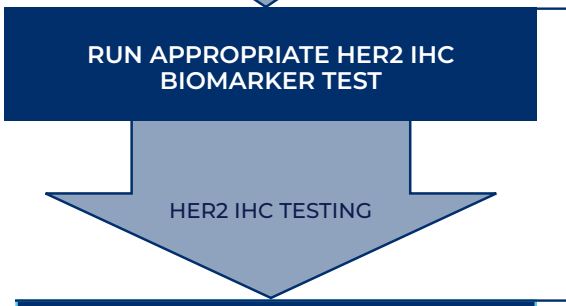
HER2+ test results can exist in the EHR as LOINC codes. Positive results may be considered as exclusionary criteria for the suspect patient list to decrease continued flagging of patients who have already been triaged and assessed.

For Newly Diagnosed Metastatic Patients*



Cancer diagnosis ICD-10 and SNOMED codes can exist in the EHR and be leveraged to identify patients who should be considered for HER2 biomarker testing. The following tumors have NCCN recommendations for HER2 testing[7-15]:

- Biliary tract
- Bladder
- Cervical
- Colon
- NSCLC
- Ovarian
- Pancreatic
- Uterine
- Vaginal



Note: Only IHC testing can assess HER2 overexpression.

HER2+ test results can exist in the EHR as LOINC codes. Positive results may be considered as exclusionary criteria for the suspect patient list to decrease continued flagging of patients who have already been triaged and assessed.

*HER2 biomarker testing can be assessed in any disease stage, and NCCN Guidelines® vary on which stage HER2 testing is recommended (all NCCN Guidelines® do include metastatic cancer). Determining implementation is at the discretion of the institution.

IMPORTANT NOTE: While EHR systems may assist providers in generating suspect patient lists, it is the sole responsibility of the HCP to make a diagnosis based on in-person patient evaluation. It is important to indicate that the final suspect list of patients will be sent to the HCP(s) for review. Including criteria for a suspect patient list helps explain to the HCP why the patient is on the report.

HCP=Healthcare provider.

For IT Department: High-Level Technical Considerations for Generating Suspect Patient Lists

To leverage EHR codes effectively to build a suspect patient list, you should engage with your healthcare organization's IT department to manage and configure suspect patient lists. See below for an example process and considerations for establishing a suspect patient list in Epic EHR.*

When configuring a suspect patient list, consider addressing the following questions:

- What will the suspect patient list be named?
- Who will own the suspect patient list? (e.g., HCP super user or practice)
- Who will receive the suspect patient list?
- What criteria will be used to determine which patients appear on the suspect patient list based on comorbidities, laboratory results, and signs and symptoms?
- What information will be included on the patient list report? (see clinical criteria above)

Additional considerations for creating an effective suspect patient list:

- The suspect patient list should exclude patients that are deceased or have been ruled out as HER2+ cancer patients
- Suspect patient lists will be impacted by the data stored in your EHR; for example, any testing that has been conducted and recorded by an outside facility may not be recorded in the EHR, which may lead to a patient being erroneously excluded from the suspect patient list
- Identify and engage with users that have the security privileges and/or technical expertise to configure and monitor suspect patient lists in your EHR
- Consider consulting with epidemiologists to optimize suspect patient list criteria, if available to your institution

NOTE: The above processes and considerations may not be applicable to all EHR systems. Please consult with your IT department for specific processes and considerations.

Alternatively, your IT department can create patient lists by creating SQL queries allowing near real-time information extraction that can more rapidly account for any changes to suspect patient list criteria. This method may be more efficient and can allow for machine learning and rapid patient list requirement updates, but will only be applicable if all EHR data is mapped to an existing data warehouse.

*In Epic EHR, a suspect patient list is referred to as a patient list report (a report that identifies all patients meeting certain clinical criteria).

SQL=structured query language.

3

Tumor-Agnostic Biomarker Order Sets

Order sets are a clinical decision support tool in EHR systems consisting of groups of related, evidence-based orders for a particular disease state that physicians can order instantly within their EHR system.[31]

HER2 is one of multiple tumor-agnostic biomarkers that could be considered for a pan-tumor order set. Order sets are available for use and customization in most EHR systems. A tumor-agnostic order set may allow for efficient and simultaneous ordering of necessary biomarkers to drive precision medicine and optimize patient care. Listed below is an example order set that could be considered for implementation. **This list is not exhaustive and should be modified to meet the clinical needs of your healthcare organization and providers.**

Tumor agnostic, actionable biomarker order sets and their qualifiers may include[32]:

- HER2 overexpression (IHC)
- NTRK gene fusion (NGS)
- MSI-H (NGS)
- dMMR (IHC)
- TMB-H ≥10 mut/Mb (NGS)
- BRAF V600E mutation (NGS)
- RET gene fusion (NGS)

When bringing an order set build request to your IT department or EHR support person, consider including the following information:

- The name of the order set (for example, Tumor-Agnostic Biomarkers)
- A list of common and medically appropriate labs, diagnostic orders, and clinical tests to include in the order set
- Any subheadings of the order set and more specific tests
- Clinicians who will have access to the order set; for example, Community Oncologists & Pathologists, Gynecologic Oncologists, Gastrointestinal Oncologists, Genitourinary Oncologist, Thoracic Oncologists
- Who will be responsible for adding or removing tests based on clinical need

The use of order sets has been found to promote adherence to evidence-based guidelines, enhance workflow with intuitive instructions, reduce potential for medical errors, and ultimately, improve patient outcomes. However, if standard order sets are not carefully designed, reviewed, and maintained to reflect best practices and ensure clear communication, they may actually contribute to errors.[32]

For full Institute for Safe Medication Practices (ISMP) guidelines, see here.

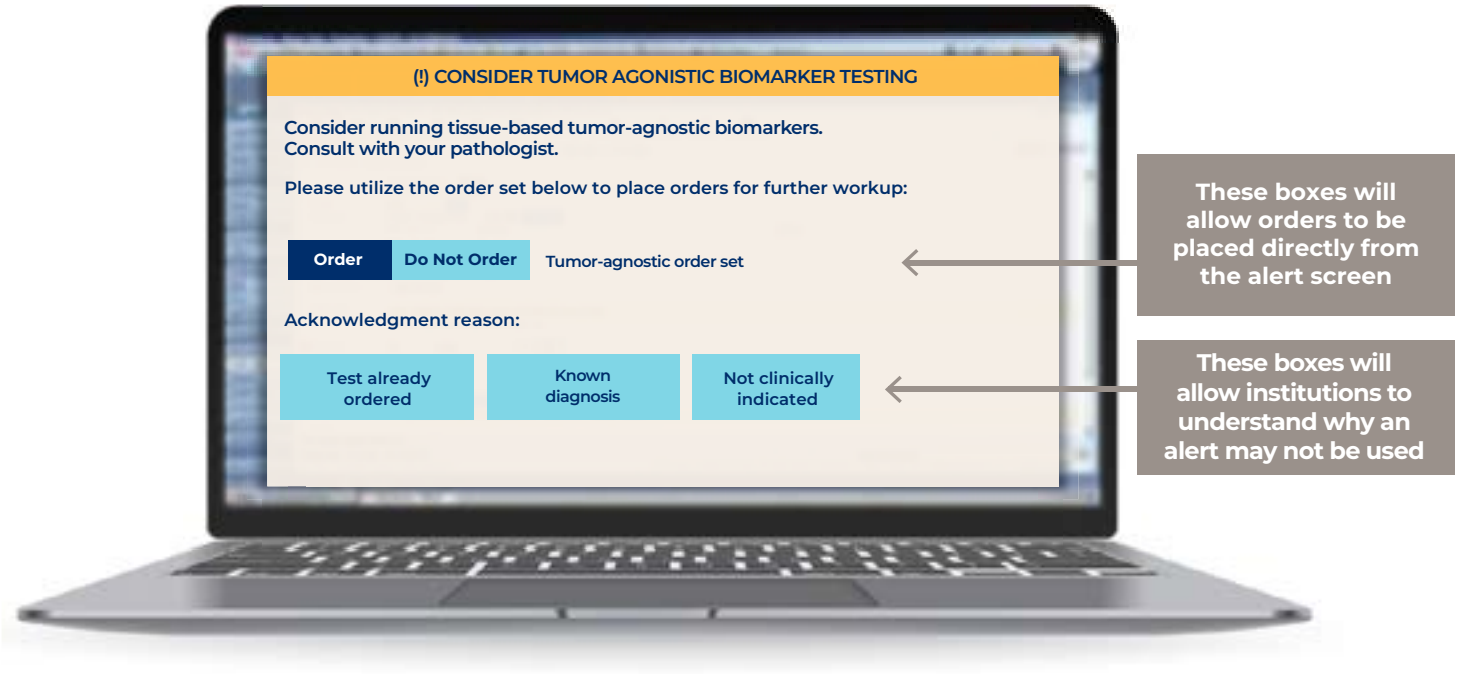
Some biomarkers may exist as part of a larger testing panel rather than as single order tests.

4

Best Practice Alerts to Help HCPs Triage Suspect Patients

Use Suspect Patient Criteria and Diagnostic Best Practices to Create Alerts

Using the data in the EHR to surface information in a patient's health record can be the first step in recognizing cancer patients who may need biomarker testing. Best practice alerts (BPAs) can be created using clinical criteria and the data in the EHR to help alert and guide an HCP in which diagnostic tests to run. The codes used to triage patients to the suspect patient list may also be used to develop BPAs. An example BPA can be found below.



Illustrative example. BPA should meet institutional guidelines and be specific based on criteria that led to the BPA. Consult with clinical and IT teams for effective implementation.

High-Level Technical Considerations for Generating BPAs

Automated BPAs may promote quality care by assisting HCPs in providing timely access to diagnostic best practices, reducing missed opportunities to biomarker test and delays in diagnosis. BPAs may also reduce inefficiency by decreasing the manual effort for HCPs in the diagnostic process.[34] Each EHR system is unique in how to establish automated BPAs, so you should engage with your healthcare organization's IT department. For example, in Epic EHR, a system is in place called "OurPractice Advisory (OPA)" that allows organizations to deliver HCPs messages through storyboard alerts, interruptive/active alerts, or passive alerts.[33*] These customized, practice-specific alerts can be programmed by the institution's IT team with assistance from clinical leadership to fire according to predetermined triggers, either individual or in combination, using inclusionary or exclusionary logic.[23] IT staff can be provided the suggested BPAs listed above triggered by patients meeting the suggested clinical criteria.

When making an IT request, clinical leaders should be involved in establishing the clinical criteria for BPAs. Consider including the following information to ensure that the suspect patient list is appropriately configured:

- The name for the alert
- The frequency of the alert based on established clinical guidelines
- Indication where the alert should be placed
- Identification of which providers should see the alert

Additional consideration for creating a BPA:

- Privileges on who can configure a BPA may be selective to specific users with security privileges or technical expertise (e.g., data scientists in the IT department); therefore, these stakeholders should be identified and engaged with as early as possible

Optimizing BPAs

Improving the visual design of clinical BPAs may help providers recognize medical conditions such as amyloidosis faster. Five presentation elements that have been suggested for EHR alerts include:

1. Physically organizing different information by placing it into bordered blocks
2. Consistency with visual cues (e.g. typeface fonts and colors)
3. Using typeface font size and "weight" to help organize and emphasize information
4. Applying color to the boxes used to organize the information
5. Consideration of the use of three-dimensional effects (to accommodate users who are color blind)

*It has been found that there is a **7.7x greater likelihood a BPA will be followed** by an HCP if the alert is active rather than passive.[34]

5

Additional Considerations

There are subtle differences between the various EHR systems. Each has similar functionality, but there may be differences such as the naming conventions of EHR system features. Additionally, organizations may have established protocols or patient portals for communicating sensitive health information identified by a BPA. The following section highlights some of these considerations.

The toolkit is provided for informational purposes only and does not substitute the internal review of your institution. Please coordinate with your institution's approval process before implementing an EHR build.

Naming Conventions

- Generating and maintaining suspect patient lists empowers organizations to surface patients who meet certain clinical and demographic criteria. These may also be named "worklists" depending on the system.
- BPAs allow organizations to notify providers when certain clinical activities should be prioritized for a particular patient. This functionality can account for a variety of clinical variables throughout the patient journey and may also be named "OurPractice Advisories (OPAs)" or "discern alerts".
- Standardized order sets allow providers to easily understand and order the most relevant tests and management options for patients who meet certain disease criteria or are being seen in a particular department. These may also be known as "power plans" depending on the system.

Each organization may also have its own vocabulary/terms allowed in drop-down lists, formulary, and lab codes. Engage with IT stakeholders at your organization to align on institution-specific variations.

Patient Communication Considerations

HCPs should follow established communication protocols, especially those related to communicating sensitive information to patients.

Note: EHR systems have patient portals that allow patients to stay in touch with their care teams, review their schedules, access personalized patient educational materials, and be more involved in managing their health. These portals may be one way to communicate the need for a follow-up appointment. Some examples of patient portals include:

» Epic MyChart
» Cerner® HealtheLife℠
» Meditech Health Portal
» Allscripts® FollowMyHealth®

The patient list and BPA functionality already exist in many EHR systems. AstraZeneca and Alexion did not sponsor, design, create, or otherwise modify this functionality in any manner. The instructions have not been designed to and are not tools and/or solutions for meeting Meaningful Use, Advancing Care information, and/or any other quality/accreditation requirement.

6

Implementing, Monitoring, and Maintaining a Program

The following section provides further guidance on how to implement the deciphEHRTM program in your healthcare organization as well as how to monitor and maintain the program. To assess the program, including surfaced suspect patients, you will need to monitor it on an ongoing basis. Remember, it will be essential to be clear about what you want to achieve and how you will measure it.

Step 1:

Establish a Clinical Program Lead

- It is important to establish a Clinical Program Lead for the project (a medical specialist with expertise in HER2+ cancer and biomarker testing, most likely an Oncologist/Pathologist) who can answer questions and help direct and oversee successful program implementation
- The Clinical Program Lead can communicate the value of the program to stakeholders throughout the healthcare organization by sharing the deciphEHR™ HER2+ Cancer Disease Overview
- The Clinical Program Lead can provide ongoing support, including monitoring the program and continuing to champion the use of EHR across multiple specialties for rapid testing of suspect HER2+ cancer patients
- Clinical Program Leads provide support to establish a diagnostic plan based on the clinical criteria for HER2+ cancer and suggestions for developing suspect patient lists, order sets, and BPAs to help HCPs triage and test suspected HER2+ cancer patients

Step 2:

Identify, engage, and communicate with organizational stakeholders*

- Identify and collaborate with relevant stakeholders within your healthcare organizations who are important in implementing the deciphEHR™ program and encouraging sustainable success
- Stakeholders may vary depending on the organization but may include:

Clinical Leadership

» Pathology, Specialty Medical Staff, and Multidisciplinary Team
» Pathology and Laboratory
» Pharmacy

Administrative Leadership

» IT/EHR Resource(s)
» Data Scientist (if available)
» Quality Director

*You may consider inviting input from representative medical staff during the initiation, implementation, and maintenance of this program.

For stakeholder involvement, see here.

Step 3:

Establish an implementation and support team

- Consider including the following members on your implementation and support team*:

  - » Clinical Program Lead†
  - » Specialty/Physician Representative(s)‡
  - » Implementation/Project Manager
  - » Super User
  - » EHR Analyst (EHR Builder, Suspect Patient List, BPA Builder)
  - » Workflow Redesign/ Process Engineer
  - » Report Writer/ Measurement and Tracking Lead

*Depending on the size and type of your organization, your organization may assign employees to more than one role.
†You may consider an additional stakeholder who has experience leading the implementation of BPAs.
‡For most applicable physicians, see here.

Step 4:

Develop and execute the implementation plan

- Engage relevant stakeholders and the implementation team to establish the adoption, scope, implementation, and rollout of the program
- Leverage the clinical criteria for HER2+ cancer (see Section 1) to create a suspect patient list for future clinical evaluation by (see Section 2 for technical considerations):
  - » Including recommended medical codes in the Appendix B
  - » Engaging clinical leadership and Super User with IT departments for most effective implementation
- Establish BPAs for HCPs based on clinical criteria (See Section 4 for technical considerations)
  - » Engage clinical leadership and Super User with IT departments for most effective implementation

Step 5:

Develop a monitoring and evaluation framework[35,36]

- The Measurement and Tracking Lead may be in charge of continuing to monitor and evaluate suspect HER2+ cancer patient lists on a routine (e.g., monthly, bimonthly) basis to assess the effectiveness of the program (the Super User may be engaged in this process)
- Effectiveness of the program should be measured based on defined metrics for success (for examples, see Step 6)
- The Clinical Program Lead and Super User can monitor and evaluate the BPA program to assess its usefulness and effectiveness in assisting HCPs (e.g., through HCP interview)

Note: While EHR systems may assist providers in generating suspect lists, it is the sole responsibility of the HCP to make a diagnosis based on in-person patient evaluation.

Step 6:

Measure success [35,36]

- Metrics for success should be determined at the start of implementation and should be continually measured to assess the success of the program. Metrics for success may include:
  - » Amount of time from suspect patient alert or on a report to the HCP for evaluation to rule in or rule out HER2+ cancer
  - » Number of times an HCP acts on a BPA
  - » Number of patients for which an alert helps the HCP to initiate biomarker testing
  - » Number of patients for which an alert helps the HCP to confirm a HER2+ cancer diagnosis

Step 7:

Ongoing improvement

- Engage with Clinical Program Lead to assess cancer biomarker testing criteria to ensure they are current
  - » Determine the appropriate timeframe for reassessment based on institutional standards (e.g., annually)
  - » Check deciphEHRoncology.com for updates
- Evaluate the effectiveness of HER2+ cancer suspect patient lists, order sets, and BPAs to triage suspect patients for biomarker testing
- In case of clinical concerns, reference your implementation and support team
- For EHR implementation troubleshooting and support, consider contacting your EHR provider

7

Appendix A: Medical Staff Considerations

Identify and collaborate with relevant stakeholders within your healthcare organizations who may see untested HER2+ cancer patients. See the list of possible clinicians below. Learn, understand, and comply with your institution's requirements for implementing.

Some clinicians to consider when rolling out the deciphEHR™ HER2+ Implementation Guide include, but are not limited to:

Medical Oncologist

Gynecologic Oncologist

Gastrointestinal Oncologist

Genitourinary Oncologist

Thoracic Oncologist

Pathologist

Surgeons

Other healthcare professionals involved in the diagnostic journey for HER2+ cancer patients include:

Nurses

Genetic Counselors

Laboratory Support Staff

7

Appendix B: Medical Codes to Support Suspect Patient Lists

The medical codes that represent criteria for identifying patients for pan-tumor biomarker testing and suggestions for how to best use these codes are found here in the appendix.

EHR Code Types

The EHR system contains multiple code types, each containing unique information. These codes can be used in combination to triage cancer patients for biomarker testing. Below are examples of code types that can be found in the EHR:

- **ICD-10:** International Classification of Diseases, tenth revision, a globally used diagnostic code for epidemiology, health management, and clinical purposes
- **SNOMED:** Systematized Nomenclature of Medicine Clinical Terms, a common language for systems to adopt for indexing, storing, retrieving, and aggregating clinical data
- **LOINC:** Logical Observation Identifiers Names and Codes, a database and universal standard for identifying medical laboratory observations

Suggestions for Leveraging EHR Codes

All codes are listed at the parent level. Determining level of specificity (e.g., specific codes within parent trees) is at the discretion of the institution. The institution is responsible for selection of codes based on the specific situation and patient needs.

- No one code has been found to have high specificity and sensitivity for HER2+ cancer; therefore, it is suggested that codes be used in combination to develop suspect patient lists
- Codes may change over time; please visit the respective code sites for up-to-date codes
  - » An Excel spreadsheet version is also available on the web page for your convenience
- The codes used to triage patients to the suspect patient list may also be used to develop BPAs

The included codes and suggested use cases for codes are illustrative. Any code implementation should be aligned with Clinical Leadership at your institution.

Suggested Codes for the Suspect Patient Lists Indicated in Section 2

These codes are helpful in triaging patients for biomarker testing. The decision on how to implement these codes should be aligned with your institution's Clinical Leadership.

Table 1: Recommended ICD-10 codes for patients to consider for HER2 biomarker testing

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Solid tumor cancer diagnosis				
ICD-10	Inclusion	C80.0	Disseminated malignant neoplasm, unspecified.	High priority code
ICD-10	Inclusion	C80	Malignant neoplasm without specification of site	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C24	Malignant neoplasm of other and unspecified parts of biliary tract	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C23	Malignant neoplasm of gallbladder	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C22.1	Intrahepatic bile duct carcinoma	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C67	Malignant neoplasm of bladder	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C54.1	Malignant neoplasm of endometrium	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C34	Malignant neoplasm of bronchus and lung	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C18	Malignant neoplasm of colon	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C20	Malignant neoplasm of rectum	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C56	Malignant neoplasm of ovary	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C53	Malignant neoplasm of cervix uteri	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C25	Malignant neoplasm of pancreas	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C50	Malignant neoplasm of breast	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C16	Malignant neoplasm of stomach	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C76.0	Malignant neoplasm of head, face and neck	High-priority code, may be used in combination with evidence of metastatic for more specificity
ICD-10	Inclusion	C52	Malignant neoplasm of vagina	High-priority code, may be used in combination with evidence of metastatic for more specificity

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Evidence of metastatic (to improve specificity)				
NOTE: Evidence of staging may be categorized in your EHR system. Any patient considered stage IV cancer can be considered metastatic.				
ICD-10	Inclusion to improve specificity	C79	Secondary malignant neoplasm of other and unspecified sites	May be used in combination with evidence of solid tumor for more specificity
ICD-10	Inclusion to improve specificity	C77	Secondary and unspecified malignant neoplasm of lymph nodes	May be used in combination with evidence of solid tumor for more specificity
ICD-10	Inclusion to improve specificity	C78	Secondary malignant neoplasm of respiratory and digestive organs	May be used in combination with evidence of solid tumor for more specificity
Evidence of previous HER2 testing				
LOINC	Exclusion	48676-1	Interpretation of FISH & Immune stain for Her-2/neu	Potential exclusion as this code indicates that IHC HER2 testing has been run
LOINC	Exclusion	18474-7	HER2 Ag [Presence] in Tissue by Immune stain	Potential exclusion as this code indicates that IHC HER2 testing has been run
LOINC	Exclusion	85319-2	HER2 [Presence] in Breast cancer specimen by Immune stain	Potential exclusion as this code indicates that IHC HER2 testing has been run
LOINC	Exclusion	85328-3	Cells. HER2 uniform intense membrane staining/100 cells in Breast cancer specimen by Immune stain	Potential exclusion as this code indicates that IHC HER2 testing has been run

Table 2: Recommended SNOMED codes for patients to consider for HER2 biomarker testing

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Solid tumor cancer diagnosis				
SNOMED	Inclusion	363415003	Malignant tumor of biliary tract	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	363353009	Malignant tumor of gallbladder	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	255066001	Carcinoma of genitourinary organ	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	399326009	Malignant neoplasm of urinary bladder	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	254878006	Endometrial carcinoma	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	188192002	Endometrial cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	254637007	Non-small cell lung cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	423121009	Non-small cell carcinoma of lung, TNM stage 4	High-priority code
SNOMED	Inclusion	1286877004	Malignant colorectal neoplasm	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	422985007	Carcinoma of colon, stage IV	High-priority code
SNOMED	Inclusion	363443007	Ovarian cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	285432005	Carcinoma of cervix	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	363354003	Cervical cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	363418001	Cancer of the pancreas	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	254837009	Malignant tumor of breast	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	363349007	Gastric cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	276809004	Microinvasive gastric cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	276810009	Late gastric cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	276811008	Gastric lymphoma	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	255052006	Malignant tumor of unknown origin	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	255056009	Head and neck cancer	High-priority code, may be used in combination with evidence of metastatic for more specificity
SNOMED	Inclusion	254893005	Vaginal carcinoma	High-priority code, may be used in combination with evidence of metastatic for more specificity

Code Type	Inclusion / Exclusion	Code	Code Description	Suggestions for Implementation
Evidence of metastatic (to improve specificity)				
NOTE: Evidence of staging may be categorized in your EHR system. Any patient considered stage IV cancer can be considered metastatic.				
SNOMED	Inclusion to improve specificity	2640006	Clinical stage IV (finding)	May be used in combination with evidence of solid tumor for more specificity
SNOMED	Inclusion to improve specificity	396535002	Stage IV: Distant metastasis or extension into other organs (adrenal cortical carcinoma)	May be used in combination with evidence of solid tumor for more specificity
SNOMED	Inclusion to improve specificity	452241000124100	Recurrent malignant neoplastic disease	May be used in combination with evidence of solid tumor for more specificity
SNOMED	Inclusion to improve specificity	128462008	Metastatic malignant neoplasm	May be used in combination with evidence of solid tumor for more specificity
SNOMED	Inclusion to improve specificity	405843009	Disseminated Malignant Neoplasm	May be used in combination with evidence of solid tumor for more specificity
Evidence of previous HER2 testing				
LOINC	Exclusion	48676-1	Interpretation of FISH & Immune stain for Her-2/neu	Potential exclusion as this code indicates that IHC HER2 testing has been run
LOINC	Exclusion	18474-7	HER2 Ag [Presence] in Tissue by Immune stain	Potential exclusion as this code indicates that IHC HER2 testing has been run
LOINC	Exclusion	85319-2	HER2 [Presence] in Breast cancer specimen by Immune stain	Potential exclusion as this code indicates that IHC HER2 testing has been run
LOINC	Exclusion	85328-3	Cells. HER2 uniform intense membrane staining/100 cells in Breast cancer specimen by Immune stain	Potential exclusion as this code indicates that IHC HER2 testing has been run

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