Breast Cancer Molecular Testing – Oncologist

Applicability This document applies to all Oncologist personnel of AHS, the Lamont Health Centre and administered by Covenant Health.

Purpose This document provides instruction on how to order Breast Cancer Molecular Tests (Prosigna™ or Oncotype Dx™) in Alberta.

Background Breast cancer is a heterogeneous disease with at least two endocrine sensitive (estrogen receptor positive – ER+) subtypes. Although the majority of ER+ patients have a low relapse risk and benefit largely from endocrine therapy alone, approximately 15-30% of these patients will recur and may benefit from the addition of chemotherapy. Gene expression profiling tests can provide prognostic information that reduces the use of adjuvant chemotherapy, restricting it to only those patients who are most likely to benefit.

Oncotype Dx™ (Genomic Health Inc., Redwood City, CA, USA) was the first gene expression test available. Oncotype Dx™ assesses the mRNA expression of 5 housekeeping and 16 key genes (including ER, progesterone receptor, HER2 and Ki67) using reverse transcriptase polymerase chain reaction on formalin fixed paraffin embedded material and provides a Recurrence Score (RS) and Risk Category for recurrence (low RS< 18; intermediate 18-30; or high RS≥ 31).

Prosigna™ (Nanostring Technologies, Seattle, WA, USA) is a newer gene expression test that uses a novel technology to assess a 50 gene expression profile and identifies intrinsic subtype, reports a Risk of Recurrence Score (ROR) and assigns patients to a predefined risk group (see table). These results involve a proprietary algorithm based on the PAM50 gene signature, intrinsic subtype and clinical variables including tumour size and nodal status. The Prosigna™ test can be performed in any laboratory using a Health Canada and FDA approved kit and assay platform. The American Society of Clinical Oncologists (ASCO) has given equal evidentiary ratings to the two tests.

As this is an area of active research, the molecular test protocols will be re-examined periodically. Until October 2018, the Oncotype Dx™ test can be requested but requires prior approval from the *Oncotype Approval Committee*. This document establishes a provincial testing policy to capture all molecular testing in the province to standardize testing and to facilitate future comparison and validation of any alternative test.

Risk Groups and Probability of Distant Recurrence (DR) Associated with Prosigna's Risk of Recurrence (ROR) Score for Node Negative (NN) and Node Positive (NP) women.

Risk Group	ROR Score (NN)	Probability of DR (NN) Average	Probability of DR (NN) 95% CI	ROR Score (NP)	Probability of DR (NP) Average	Probability of DR (NP) 95% CI
Low	0 to 40	4%	3% – 5%	0 to 15	8%	2% - 29%
Intermediate	41 to 60	11%	8% - 14%	16 to 40	10%	6% - 15%
High	61 to 100	22%	18% - 27%	41 to 100	28%	23% - 34%

Procedure

Step	Responsible Person and Action	Detail
1.	Oncologist or designate completes: Breast Molecular Request Form (Appendix A) and submits it with the necessary approval (for Oncotype Dx™ requests see Details) to the laboratory that performed the original Biomarker testing.	**IF:** the Oncologist is requesting Oncotype Dx™ before October 2018 **THEN**: a copy of the completed Breast Molecular Request Form must be e-mailed to the *Oncotype Approval Committee* (listed on AHS Global e-mail contact list). Subsequent e-mail approval from the committee must be included with the submitted requisition. **Note**: In the event of a laboratory submission without attached approval for *Oncotype* testing, the laboratory will hold testing and follow-up with the requestor via email indicating the following: • We have received your request for Oncotype Dx™ molecular testing on this patient. • As per the September 2017 AHS Lab Bulletin regarding the *Prosigna™ Breast Cancer Prognostic Gene Signature Assay*, Oncotype Dx™ testing requires prior approval from the "Oncotype Approval Committee" (found on AHS Global Contact list). • Please resubmit this form with an attached approval to allow us to proceed with Oncotype Dx. • If you would prefer to proceed with Prosigna™ we could facilitate that testing immediately without any further approval. • Please note that duplicate testing with Prosigna and Oncotype Dx is not permitted. In Calgary: Consult Desk, Dept. of Pathology, Peter Laugheed Hospital In Edmonton: Edmonton Zone IHC Lab, Dept of Lab Med, Cross Cancer Institute
2.	Anatomical Pathology Laboratory: • Confirms ordering Oncologist is on approved list* • Retrieves block from pre-emptive files or contacts the original laboratory and requests a designated block.	**IF:** the requesting physician is not on the approved list **THEN**: the request is sent to the Medical Lead of the Provincial Breast Cancer Program** and the requesting physician is notified by the laboratory.
3.	Block is obtained, material sent to Molecular Pathology at UAH (Prosigna™) or Genomic Health (Oncotype Dx™)	• More details in Breast Cancer Molecular Testing and Reporting SOP
4.	Molecular Path UAH or Genomic Health: • Faxes molecular test results to Biomarker Lab	
5.	Biomarker Pathologist: • Compares result to previous pathology data	• Supplementary Report issued as a Biomarker (HR# in Edmonton) or Surgical (Calgary) report.

	• Dictates Supplementary Report • Authorizes Supplementary Report	• Supplementary Report authorized and transferred to NetCare. Full Prosigna™ and Genomic Health reports are filed in the Molecular Path (UAH) or Biomarker Labs respectively.

A list of Approved Medical Oncologists will be supplied to the two Biomarker Laboratories by the Provincial Breast Cancer Program. This list will be reviewed and updated annually.

***For the current Program Lead see:** http://www.albertahealthservices.ca/cancerguidelines.asp

Related Documents

Appendix A. Oncotype Dx Request Form – Oncologist
Appendix B: Process Flow-Chart (Oncologists)
Breast Cancer Molecular Testing and Reporting – Laboratory procedure

Appendix A: Breast Molecular Request Form – Authorized Oncologist only

BREAST MOLECULAR REQUEST (Oncologist)

□ Prosigna™ □ Oncotype Dx™ (requires approval, see *)

☐ Original Biomarker Testing Laboratory in Calgary:

Send to:
Consult Desk, Department of Pathology,
Peter Lougheed Center
3500 26 Avenue NE
Calgary, AB T2N 2T9
Phone: 403-943-5642 OR 403-943-4783 (Dr. Sienko)
Fx:403-292-2931

☐ Original Biomarker Testing Laboratory in Edmonton:

Send to:
Edmonton Zone IHC Lab
Dept of Lab Med, Cross Cancer Inst.,
Rm: 1484, 11560 University Avenue
Edmonton, AB T6G 1Z2
Phone. 780-432-8587
Fax. 780-432-8455

ORDERING PHYSICIAN (PLEASE PRINT): _____ DATE: _____

FAX NUMBER: _____ TELEPHONE NUMBER: _____

PATIENT NAME: _____

PHN: _____ DOB (DD/MM/YYYY): _____

**Molecular testing criteria: ERpos, HER2neg, Node neg (N0, $N0_{ITC}$ or N1mi), Grade 2 or Grade 3*

REQUESTING ONCOLOGIST TO COMPLETE THE FOLLOWING *(prior to form submission)*:

1. ***Based upon current available clinic-pathologic information (pre-Molecular test result) how would you categorize this patient's risk of recurrence?***
   ☐ ***Low*** ☐ ***Intermediate*** ☐ ***High***

2. ***Would you currently recommend adjuvant chemotherapy to your patient (pre-Molecular test result)?***
   ☐ ***Yes*** ☐ ***No*** ☐ ***Unsure***

3. ***Patient Clinicopathologic Data:***
   ER: ☐ ***pos*** ☐ ***neg, HER2:*** ☐ ***pos*** ☐ ***neg, Grade*** ☐ ***1*** ☐ ***2*** ☐ ***3, Tumour Size:*** ☐ ***≤1cm*** ☐ ***1 to ≤ 2cm*** ☐ **>2cm**
   Positive Nodes: ☐ ***zero*** ☐ ***ITC only*** ☐ ***Micrometastases only*** ☐ ***At least 1 metastasis > 2mm,***

4. *****Comment (Must specify reason if Oncotype Dx™ is being requested):***

_____

_____

_____ **DATE: _____**

Oncologist Signature

****For Oncotype Dx™ a scanned copy of this form should be e-mailed to "Oncotype Approval Committee" (OAC) found on AHS Global with the subject line "Request for Oncotype Approval". OAC approval must be attached to this form.**
Medical Oncology (Dr. Marc Webster, Dr. Karen King, Dr. Sasha Lupichuk) Pathology (Dr. Hua Yang, Dr. Gilbert Bigras, Dr. Judith Hugh)

DATE Received in Lab: _____

Appendix B: Process Flow-Chart (Oncologists)