Regional Medical Laboratory
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MEMORANDUM

To: All RML Clients
From: Charity Maulsby, MT(ASCP), Director of Anatomical Pathology
Michael R. Harvey, MD, Chief of Anatomical Pathology
Ryan Hendren, MD, Chief of Cytology
Date: May 3rd, 2017
Subject: Memo for ThyGenX and ThyraMIR rev 4

Regional Medical Laboratory (RML) has partnered with Interpace Diagnostics in order to offer predictive molecular testing in thyroid fine needle aspirations. The combination of routine cytologic evaluation and two molecular testing platforms will adjudicate clinical management options on Bethesda categories III and IV; i.e., atypia undetermined and follicular lesion of undetermined significance (AUS/FLUS) and follicular neoplasm or suspicious for a follicular neoplasm respectively (FN/SFN).

With your request for routine cytologic evaluation on fine needle aspiration specimen of the thyroid and the reflex to molecular testing, our pathologists will evaluate the material and report the cytologic findings. Specimens with AUS/FLUS or FN/SFN interpretation will be reflexed and sent to Interpace for molecular testing.

Molecular testing will be performed in an algorithmic fashion. ThyGenX is a next gen sequencing (NGS) assay that evaluates for the presence of mutations in the BRAF, HRAS, KRAS and NRAS genes, PIK3CA and fusions of PAX8-PPARG, RET-PTC1 and RET-PTC3. ThyGenX is considered a "rule in," test and a positive result with strong oncogenes (BRAF, RET-PTC1, RET-PTC3 and PIK3CA) has a high risk of malignancy and is sufficient to predict the presence of cancer. Surgery is indicated in this scenario and testing is stopped. If the ThyGenX result is a weaker oncogene (HRAS, NRAS, KRAS, PAX8-PPARG) or is negative, then reflex testing using the ThyraMIR miRNA gene expression classifier, a "rule out test," is performed to evaluate for the expression levels of 10 miRNAs that are associated with thyroid malignancy. A negative result using the ThyraMIR assay following negative ThyGenX confers a 94% likelihood of benignancy in indeterminate thyroid nodules. Conversely a positive result for the ThyraMIR assay confers a 74% chance of malignancy and, therefore, indicates the need for surgery. The results will be reported in an addendum to the original cytology report.

RML is proud to offer this in partnership with Interpace Diagnostics as we believe the data shows significant improvement in management of patients with indeterminate thyroid nodules. It is also important to note that your patient's thyroid aspirates will be evaluated locally by Pathology Laboratory Associates' (PLA) board certified pathologists, allowing you direct access to your local pathologists who can assist in the care of your patients. Financial assistance is available to patients that meet the qualifications.

Literature describing the use of the molecular assays as a reflex to indeterminate cytology exams is available upon request or on www.RMLonline.com; see download section.

Please feel free to contact Michael R. Harvey, MD, or Ryan Hendren, MD, with questions regarding these new assays at 918-744-2553.

Mark or indicate the following test order on the requisition:

FNA Thyroid Cytology with reflex to ThyGenX with reflex to ThyraMIR

FNA Thyroid Cytology: CPT Code 88173, optional 88305
ThyGenX: CPT codes 81210, 81275, 81404, 81403, 81404, 81401, 81479
ThyraMir: CPT code 81479

FNA Specimen Requirement:

FNA Kit with RNA Retain vial is available from RML Materials Management.

Prepare smears from the thyroid aspirate, add aspirate material to the cytology preservative and add a small amount of aspirate to the RNA Retain vial – stable at room temperature for 6 weeks. Label all containers and slides with patient name and second identifier such as birth date, MRN or other unique identifier. Include patient history and location of the nodules on the requisition.