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Thyroid FNA Analysis

Poster #1162

Evaluation of Thyroid FNA Genomic Signatures (ENHANCE): A Unique Bio-repository for Advancing Science

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Evaluation of Thyroid FNA Genomic Signatures (ENHANCE): A Unique Bio-repository for Advancing Science

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BACKGROUND:

The Bethesda criteria and advances in cytopathology have facilitated the appropriate management of the majority of thyroid nodules. Nonetheless, 15-30% remain cytologically indeterminate (Cyto-I), predominantly in Bethesda classes III and IV. Genomics has provided additional clarity in these two classes for guiding the use and extent of diagnostic surgery. The mRNA 167 Gene Expression Classifier (GEC) is identified in the 2015 ATA and NCCN Guidelines with high NPV as a 'rule-out test' to assist informing diagnostic surgery decisions in cyto-I nodules. Extensive independent clinical utility publications have shown a marked reduction in the use of surgery among patients with benign 167 GEC results. Recently, certain DNA mutations have been suggested as a 'rule-in test'. Clinical utility for this latter approach in Cyto-I is unclear. Despite advances in genomic technology, opportunities remain for additional precision. The ENHANCE trial is intended as a unique comprehensively annotated bio-repository of paired genomic and histopathological samples, essential to further the understanding of genomic alterations and transcriptional expression in Cyto-I patients.

METHODS:

This is an IRB-approved study to accrue thyroid FNA samples and associated nucleic acid as well as associated clinical, radiological and histopathological data, if applicable, from patients who have already undergone either the Afirma Thyroid FNA Analysis, which includes cytopathology, or GEC only analysis. The study is comprised of 2 arms, Arm 1: patients who have been recommended surgery, Bethesda II-VI, or have undergone surgery, Arm 2: patients with either a benign GEC or benign cytopathology with a minimum of 2 years follow up (Figure 1). Histopathology for Arm 1 patients are centrally reviewed and assigned a guidelines-compliant pathology label by a panel of blinded expert pathologists (Figure 2).

RESULTS:

As of December 2015, 39 sites have been opened across the US of which 20% are academic centers, and 80% represent community practices. 650 of 700 planned patients have enrolled in the study. 80% of these patients fall under Arm 1 of the protocol and 20% under Arm 2 (Table 1). Centrally adjudicated pathology labels have been obtained for 200 patients (Table 2). Full genomic mutational and transcriptional data is being collected.

DISCUSSION:

As disease management and technology advance, bio-repositories are a critical resource for innovation and/or validation of new approaches to guide clinical care. Genomics rooted in the right clinical questions augments the understanding of pathophysiology which in turn benefits patients.

CONCLUSION:

This robust, rigorously annotated, bio-repository will serve as an invaluable resource to address critical future scientific and clinical questions.

FIGURE 1.
ENHANCE Study Design

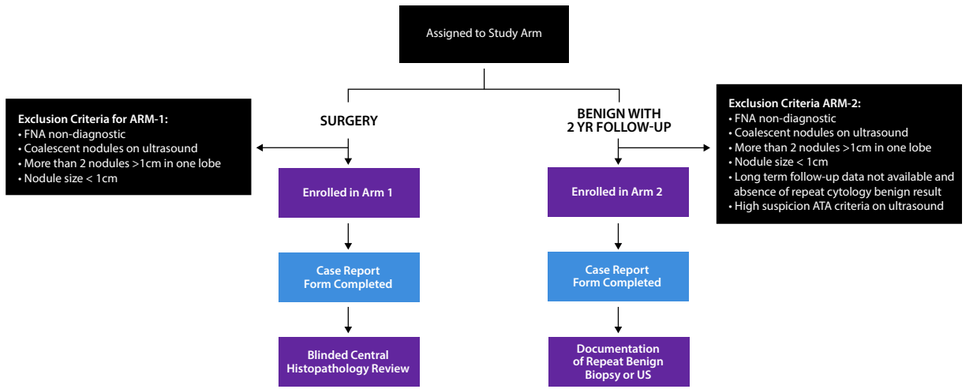

FIGURE 2.
Central Pathology Review Process

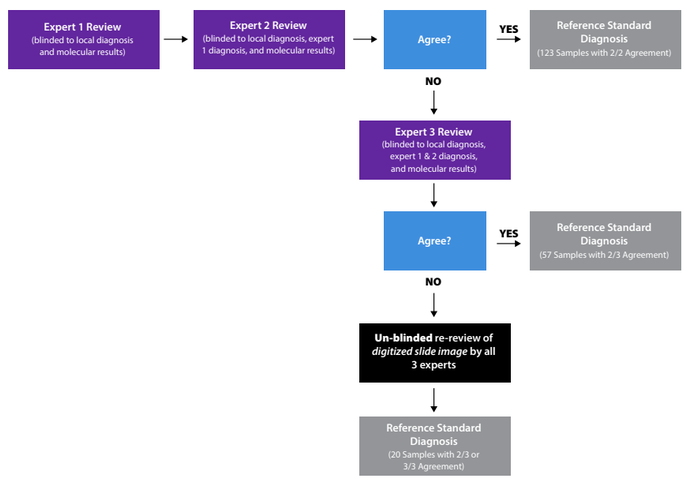

TABLE 1.
Baseline Demographic and Clinical Characteristics of the Study Cohort

Variable	Total Enrollment	Arm 1	Arm 2
Total no.			
Nodules	750	633	117
Patients	650	542	108
Type of study site - % of Patients			
Academic	20%	21.5%	9%
Community	80%	78.5%	91%
Age of patients—mean (range)	**54 (19-93)**	**54 (19-93)**	**55 (19-86)**
Sex—no. of patients (%)			
Male	140 (22%)	123 (19%)	20 (3%)
Female	507 (78%)	416 (64%)	91 (14%)
Nodule size – no. of nodules (%)			
1.0 – 1.9 cm	368 (49%)	293 (39%)	75 (10%)
2.0 – 2.9 cm	203 (27%)	180 (24%)	23 (3%)
3.0 – 3.9 cm	101 (13%)	90 (12%)	11 (1.5%)
≥ 4.0 cm	79 (11%)	75 (10%)	4 (0.5%)

TABLE 2.
Histopathological Subtypes in Study Cohort

	AUS/FLUS No. of Nodules	FN/SFN No. of Nodules
Benign		
Hyperplastic nodule*	13	6
Benign follicular nodule	13	3
Follicular adenoma	21	6
Hürthle cell adenoma	8	15
Chronic lymphocytic thyroiditis	3	—
Malignant		
Papillary thyroid carcinoma**	44	11
Hürthle cell carcinoma	4	4
Follicular carcinoma	3	2
Medullary thyroid carcinoma	3	3

* Hyperplastic nodule contains hyperplastic nodules and nodular hyperplasia
** Papillary thyroid carcinoma also contains PTC variants and NIFTP