NCT NUMBER: NCT03502213

STUDY TITLE: A PROSPECTIVE MULTICENTER OBSERVATIONAL TRIAL TO ASSESS PERSISTENCE ON ACTIVE SURVEILLANCE WHEN USING THE ONCOTYPE DX® PROSTATE CANCER ASSAY

DATE OF DOCUMENT 24APR2014

STUDY PROTOCOL

A PROSPECTIVE MULTICENTER OBSERVATIONAL TRIAL TO ASSESS PERSISTENCE ON ACTIVE SURVEILLANCE WHEN USING THE ONCO*TYPE* DX® PROSTATE CANCER ASSAY

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Development Study Number: 09-023

Medical Monitor: [redacted]

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A PROSPECTIVE MULTICENTER OBSERVATIONAL TRIAL TO ASSESS PERSISTENCE ON ACTIVE SURVEILLANCE WHEN USING THE ONCO*TYPE* DX® PROSTATE CANCER ASSAY

Genomic Health Approvals:

[redacted]

[redacted]

STUDY PROTOCOL

A PROSPECTIVE MULTICENTER OBSERVATIONAL TRIAL TO ASSESS PERSISTENCE ON ACTIVE SURVEILLANCE WHEN USING THE ONCO*TYPE* DX® PROSTATE CANCER ASSAY

Signature of Agreement for Protocol

I declare that I have read this protocol and I agree to conduct the study as described in the following document.

I will provide a copy of this protocol and all pertinent and relevant information to all those persons responsible for collaborating in the execution of the study. I will review and discuss the material with all of them in order to assure myself of their cognizant and complete information with respect to the study and its execution.

_____ _____

[redacted]

DOCUMENT HISTORY

Version	Date	Replaces	Description of Change
1.0		N/A	New issue

TABLE OF CONTENTS

DEFINITIONS AND ACRONYMS

Term	Definition
ADT	Androgen Deprivation Therapy
AS	Active Surveillance
ASCO	American Society of Clinical Oncology
AUA	American Urological Association
CaPSURE™	Cancer of the Prostate Strategic Urologic Research Endeavor
CI	Confidence Intervals
CRF	Case Report Form
DX	Diagnosis
EBRT	External Beam Radiation Therapy
ECOG	Eastern Cooperative Oncology Group
EDC	Electronic Data Capture
FDR	False Discovery Rate
GG	Gleason Grade
GHI	Genomic Health, Inc.
GPS	Genomic Prostate Score
GS	Gleason Score
IRB	Institutional Review Board
LND	Lymph Node Dissection
LTFU	Lost to Follow Up
NCCN	National Comprehensive Cancer Network
OR	Odds Ratio
PRO	Patient Reported Outcomes
PSA	Prostate Specific Antigen
QoL	Quality of Life
RNA	Ribonucleic Acid
RP	Radical Prostatectomy
RT-PCR	Reverse transcription polymerase chain reaction
UCSF-CAPRA	University of California San Francisco- Cancer of the Prostate Risk Assessment

1. BACKGROUND INFORMATION

1.1 Overview

Prostate cancer remains the most common solid organ malignancy in American men, with an estimated 238,590 new cases diagnosed in 2013 and an estimated 29,720 cancer-related deaths.[1] Prostate cancer screening through the use of prostate specific antigen (PSA) has dramatically increased the number of men diagnosed with prostate cancer annually, with most of the additional cases representing early stage disease. A large majority of men with early stage prostate cancer are receiving definitive treatment with radical prostatectomy (RP) or radiation therapy. Although some studies indicate that the early diagnosis and treatment of prostate cancer is associated with a decrease in prostate cancer specific mortality,[2] over 1,000 men had to be screened and 37 cancers detected to prevent a single death from prostate cancer.[3] This has led to controversy around over-treatment of many cases of indolent disease, resulting in needless morbidity and increased healthcare costs. These concerns regarding the over-diagnosis and over-treatment of early-stage prostate cancer have contributed to the recent recommendation by the US Preventive Task Force against PSA screening.[4]

Thus, many men diagnosed with prostate cancer in the PSA-screening era have a clinically indolent form of cancer that does not require immediate treatment and could instead be managed with active surveillance (AS) withholding treatment for curative intent if there are signs of progression. The uptake of this strategy, however, has been limited, with < 10 % of patients diagnosed with low-risk prostate cancer managed with AS according to a recent CaPSURE™ registry survey.[5] A significant limitation to the use of AS is the uncertainty amongst clinicians regarding the accuracy of the current tools used to identify patients with low-risk disease (see [6] for review). A major limitation is the limited nature of biopsy sampling with several studies demonstrating GS upgrading in a substantial proportion of cases (20-60%), from GS 6 on biopsy to GS 7 and even GS 8 at RP. [7-9]

There is clearly a need for the development of new clinical tools that will allow for identification of biological characteristics that translate to a more accurate risk assessment for an individual patient's prostate cancer. A tool to reliably identify patients with clinically indolent prostate cancer would improve selection of patients with low risk disease who can be confidently managed by AS, have greater confidence and improved persistence on AS, and avoid the potential side effects and complications of unnecessary interventions. Alternatively, men found to be at increased risk of harboring aggressive disease could be directed towards immediate treatment with curative intent.

1.2 Oncotype DX Prostate Cancer Assay Development and Validation

Genomic Health has applied the development approach from its prior breast and colon cancer programs to develop a biopsy-based genomic assay to discriminate clinically indolent from

aggressive prostate cancer [redacted]

Gene identification study

A study was conducted to identify genes whose expression was associated with clinical recurrence, biochemical recurrence and death from prostate cancer.[10] Of 2,641 subjects with clinical stage T1/T2 cancer who underwent RP at Cleveland Clinic from 1987 to 2004, a cohort sampling design was used to select 127 subjects with clinical recurrence (both local and metastatic) and 374 subjects without clinical recurrence after surgery. [redacted]

[redacted]

Gene refinement study in prostate biopsy specimens

[redacted]

[redacted]

2. OBJECTIVES

The primary goal of this prospective study is to assess the rate of persistence on Active Surveillance (AS) in men who choose AS after receiving the Oncotype DX Prostate Cancer GPS.

2.1 Primary Objective

2.1.1 To assess the rate of persistence on AS at 1 and 2 years after receiving the Oncotype DX Prostate Cancer GPS

[redacted]

3. PHYSICIAN AND PATIENT ELIGIBILITY

Prior to enrolling any patients into the study, the principal investigator (PI) and all participating investigators at each site must complete the Site PI Initiation Form (see Appendix A). The site PI must acknowledge and sign the Protocol Signature Page (see Appendix B). These forms must be completed at the beginning of the study.

3.1 Pre-Study Physician Requirements

In order to review the implications of GPS on treatment decisions at all sites regardless of prior use of GPS, each participating physician will be required to take part in a review of the clinical development and validation data of the assay and a detailed review of the protocol. After participating physicians have completed their training sign-off and have IRB approval, the site may begin to enroll patients in this study.

3.2 Patient Management Plan

3.2.1 **Identification of Potentially Eligible Subjects**: Patients with very low, low, and low-intermediate risk prostate cancer (as defined in section 3.3.2 below) may be eligible for this study.

3.3 Inclusion Criteria

3.3.1 **Physicians:** Each of the criteria in the following section must be met in order for a physician to be considered eligible for registration:

3.3.1.1 The physician is a urologist who makes primary treatment recommendations for patients with localized prostate cancer.

3.3.1.2 The physician must practice at a facility or group practice that consults on at least 25 newly diagnosed prostate cancer patients per year who are very low, low, or intermediate risk as per NCCN guidelines (NCCN V3, 2012)

3.3.1.3 The physician must practice in a group or setting that is experienced in offering AS. The Principal Investigator (PI) at each participating site must complete the Site Principal Investigator Initiation Form and Protocol signature page.

3.3.1.4 The physician must participate in a review of Oncotype DX Prostate Cancer Assay information and training materials, including assay development and validation data.

3.3.1.5 The physician and participating site staff (including pathology if available) must participate in a review of this protocol including patient eligibility and protocol related training materials.

3.3.2 **Patients:** Patients eligible for this study will have been newly diagnosed with prostate cancer within the last 3 months, with no treatment decision made, and

meet all Inclusion criteria and no Exclusion criteria. Eligible patients include those with:

- Clinical stage T1/T2
- PSA ≤ 20ng/mL
- Biopsy GS ≤ 6 with any number of cores positive, or Biopsy GS 3+4 disease with ≤3 positive cores or ≤ 33% positive cores
- The patient must be > 50 years of age
- The patient must have a life expectancy of > 10 years, based on the Social Security Actuarial Life Table (see Appendix C).
- The patient must be able to give consent in English or Spanish

3.4 Exclusion Criteria

3.4.1 Physicians are excluded from participating if they are:

3.4.1.1 Not responsible for the care of newly diagnosed prostate cancer patients who are candidates for AS

3.4.2 Patients are excluded from participating if they have/are any one of the following:

3.4.2.1 Clinical stage T3a or above

3.4.2.2 PSA > 20ng/mL

3.4.2.3 Biopsy GS 4+3 or ≥ 8

3.4.2.4 Known metastatic prostate cancer (bone, lymph node etc.)

3.4.2.5 Positive biopsy for prostate cancer > 3months ago

3.4.2.6 Treatment decision has already been made

3.4.2.7 Insufficient tumor in prostate biopsy tissue to perform the assay

3.4.2.8 Treatment with androgen deprivation therapy (ADT) prior to prostate biopsy

3.4.2.9 Diagnosis made by transurethral resection of prostate (TURP) shavings

3.4.2.10 Any psychiatric or psychological condition, such as depression or anxiety, that would impede the patient's ability to give informed consent

3.4.2.11 Contraindications to primary treatment according to physician's judgment

3.5 Target Enrollment

3.5.1 This study is targeted to enroll approximately 1200 patients, with no investigator contributing more than 50 patients.

3.6 Selection of Treatment Sites

This study will be conducted at approximately 25 large community based urology group practices and 5 academic sites in the United States. Site selection was based on:

3.6.1 Projected volumes of new prostate cancer cases per month who meet inclusion criteria

3.6.2 Experience with AS

3.6.3 The site's ability to conduct clinical studies in prostate cancer, including sufficient research personnel, experience, and infrastructure to obtain patient consent, manage questionnaires, and capture and transmit data to a central research coordinator

3.6.4 Expeditious contracting and IRB process

4. STUDY DESIGN

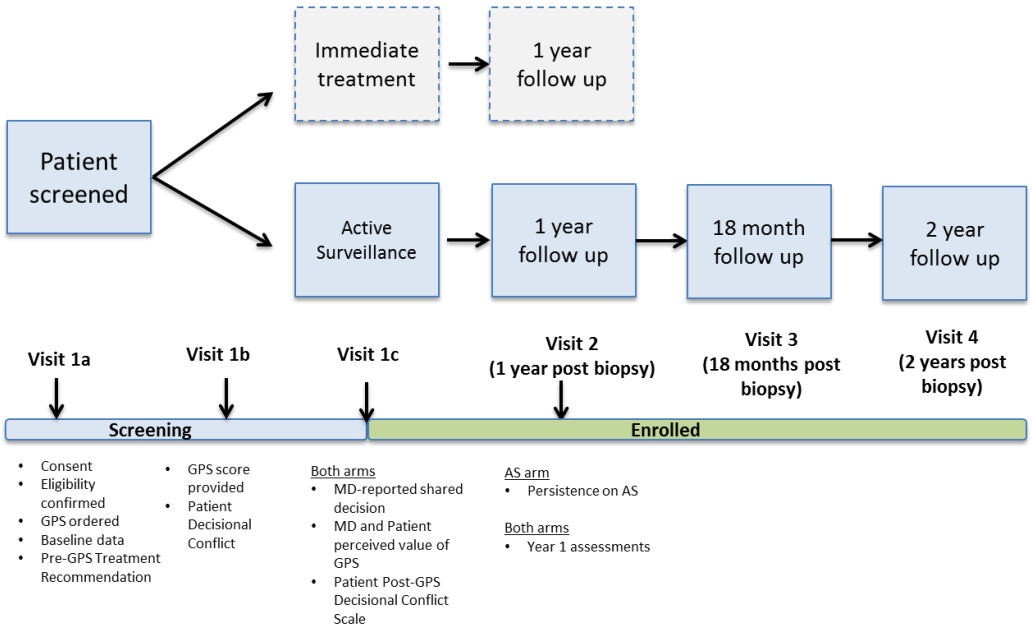
This is a multicenter observational study that evaluates eligible patients who will submit prostate cancer diagnostic biopsy tissues for Oncotype DX Prostate Cancer Assay testing. At visit 1a, the patient consents to the trial, a pre-assay physician treatment recommendation will be made along with additional assessments defined in Section 6, Table 1, and the assay is ordered. At Visit 1b, the physician will review clinical data, the GPS report and discuss treatment options with the patient. At the following visit, Visit 1c, a shared physician-patient treatment decision (immediate treatment or AS) will be made.

Men selecting immediate treatment will be contacted one year from date of diagnosis biopsy to document treatment received and to assess treatment satisfaction and Quality of Life (QoL) metrics.

Men selecting AS as primary treatment will be followed to assess persistence on AS. There is no required or standardized AS protocol for this study and the intensity of surveillance will be at the discretion of the investigator. Patients will not be required, but may undergo a standard TRUS guided surveillance biopsy at one year. In this study, the Oncotype DX Prostate Cancer Assay will be assessed on the diagnostic biopsy only and will not be assessed on subsequent biopsies. Patients will be queried at 12 and 24 months for assessment of decision satisfaction and Quality of Life metrics.

4.1 Duration of Study

Patients will be participating in the study from the time of consent until Visit 2 (Year 1) for those patients in the Immediate Treatment arm, and to Visit 4 (Year 2) for those patients in the AS arm. Patient questionnaires will be completed at those defined time points in the schedule of assessments for this study.



4.1.1 Early Termination/Withdrawal Procedures

The following patient situations will result in screen failures and these patients will not be included in any analysis:

- Patients who have signed a consent form, but for whom a sample was not sent to GHI
- Patients who have signed a consent form and had a sample submitted to GHI, but for whom no GPS was generated

Patients who sign a consent form and receive a valid GPS but do not choose either AS or immediate treatment at Visit 1c will be considered unevaluable.

Patients who enter the study on the AS arm, and who subsequently decide to undergo treatment, will be required to complete the End of Study (EOS) visit assessments. Those patients who are Lost to Follow Up (LTFU) will also have the EOS form completed. LTFU patients are defined as those that have had at least 3 contact attempts over a one-month period. Those patients who have been reported deceased or withdraw consent will also have the EOS form completed.

5. MATERIALS AND METHODS

The Oncotype DX Prostate Cancer Assay is a commercially available diagnostic test that is designed to aid in a physician's treatment recommendation to a newly diagnosed prostate cancer patient. All the necessary elements for the study (requisition forms, sample

preparation kits, shipping materials) will be provided by GHI and testing of all specimens will be performed at GHI at no charge to the patients or the clinical sites. Standard operating procedures will be followed at GHI when processing the specimens.

Patient Reported Outcomes (PROs) will be assessed at specified visits. These are questionnaire based, have been used in this disease state and include a pre and post GPS Decisional Conflict Scale, EPIC-CP; FACT-G and Decision Regret [12-15]. These are validated, self-administered, recall instruments and will be available in English and Spanish.

[redacted]

6. STUDY CALENDAR AND ASSESSMENTS

Site Specific Assessments and Forms:
The following forms will be collected during the course of the study: Site Principal Investigator Initiation Form, Site Principal Investigator Protocol Signature Page, Enrollment Log and Non-Enrollment Log. Instructions for the completion and submission of these forms will be provided by GHI.

Assessments and Forms for each Enrolled Patient:
After a patient consents to participate in this study, the assessments and forms listed in the table below will be completed by the treating physician and submitted to GHI as instructed. The Oncotype DX Prostate Cancer Assay is expected to report results within a 13-21 day turnaround time upon receipt of the tumor specimen at GHI's laboratory.

Completion of Forms for each Enrolled Patient:

- Data is expected to be entered into the EDC (Electronic Data Capture) system within 5 business days of the patient's visit.
- Queries are expected to be addressed and responded to within 5 days of issue.

Table 1: Study Schema

- Visits 1b and 1c may occur anytime within 4 months of consent (Visit 1a), as is suitable for the patient. Subsequent visits (Visits 2, 3 and 4) are based on the duration from the date of biopsy, not from Visit 1a.

Assessments	Visit 1a	1b	1c	2 M12	3 M18	4 M24	End of Study
Eligibility Criteria	X						
Informed consent	X						
GPS ordered	X						
Demographics	X						
Clinical T-Stage and Physician Risk Assessment	X						
Biopsy[1]	X			X	X	X	X
PSA[1]	X			X	X	X	X
DRE[1]	X			X	X	X	X
FACT-G	X			X		X	
EPIC-CP	X			X		X	
Decisional Conflict Scale		X[2]	X[3]				
Patient informed of GPS result		X					
Decisional aids provided	X[4]	X[5]					
Physician Treatment Recommendation	X[6]						
Physician –Patient Shared Decision			X				
Physician perceived value of GPS			X				
Patient perceived value of GPS			X				
Persistence on Active Surveillance				X	X	X	
Regret				X		X	
End of Study[7]							X
Surgical Pathology[8]				X			

[1] completed at Visit 1a and any subsequent visit, if new results are available since prior visit
[2] administered **before** the patient sees the physician and obtains the GPS report.
[3] administered at completion of the visit **after** discussing the treatment options with physician
[4] disease specific decisional aid provided (i.e. AUA Prostate Cancer Brochure)
[5] Oncotype DX specific decisional aid provided (i.e. GPS Patient Brochure)
[6] completed before ordering the Oncotype DX prostate cancer assay
[7] completed if a patient moves to immediate treatment, withdraws consent, does not get a valid GPS score, dies or is LTFU
[8] completed if surgery was performed on a patient who chose immediate treatment

7. STATISTICAL ANALYSIS METHODS

7.1 Risk group and endpoint definitions

7.1.1 NCCN-based risk groups

Clinical risk groups, based on the NCCN criteria (modification of NCCN V.3, 2012), are defined as follows:

Very Low: Gleason Score ≤6 and PSA<10 ng/ml and Clinical T1c and ≤2 positive cores and <50% tumor in any core and PSA density <0.15 ng/ml/g.

Low: Gleason Score ≤6 and PSA<10 ng/ml and Clinical T1c and not meeting criteria for Very Low

Low-Intermediate: Gleason Score 3+4 or PSA 10-20 ng/ml or Clinical T2 with either ≤3 positive cores or ≤33% positive cores.

7.1.2 Biological NCCN and GPS-based risk groups

Biological risk groups, based on NCCN and GPS, are defined as follows:

Very Low: probability of favorable pathology ≥79%

Low: probability of favorable pathology 68-78%

Low-Intermediate: probability of favorable pathology ≤67%

Note that the probability of favorable pathology will be rounded to the nearest whole percent.

7.1.3 Adverse RP pathology

RP pathology assessments will include Gleason score and pathologic T-stage. Adverse pathology is defined as high-grade and/or non-organ-confined disease as shown in the table below, where Gleason Score ≤ 3+3 or 3+4 and pT2 is the baseline category and all other categories are compared to the baseline category.

Table 1: Definition of Adverse Pathology

RP Gleason Score	Pathologic T2 Stage	Pathologic T3 Stage
≤3+3	Baseline Category	Non-organ confined Disease
3+4		
Major pattern 4 or any pattern 5	High-grade	High-grade and Non-organ confined Disease

High-grade disease at RP is defined as the presence of any major pattern 4 or any pattern 5 at RP.

Non-organ-confined disease is defined as pathologic T-stage (pT) pT3a or pT3b or nodal involvement where pT3a signifies extraprostatic extension (EPE) and pT3b signifies seminal vesicle involvement (SVI).

7.2 Statistical Analysis of Primary Endpoint

Persistence at 1 year will be described as the proportion of patients who remain on AS as of their 12 month visit. Specifically, this is defined as the number of patients who are documented as intervention-free at their 12-month visit (Visit 2) divided by the number of patients who chose AS at Visit 1c. Persistence at 2 years will be calculated in a similar manner. Additional analysis will exclude the subjects who were lost to follow-up or died before the 12-month (Visit 2) and 24-month (Visit 4) visits for analysis of the 1-year and 2-year persistence rates respectively. Exact 95% confidence intervals for proportions will be calculated using the *F*-distribution method [16].

Additionally, the proportion of men who experienced specific outcomes during surveillance, including definitive treatment, physician-reported biopsy findings, exit from the study, and death from all causes will be calculated as a crude proportion. Similar analyses will be conducted to estimate the proportion of patients who persist on AS by NCCN-based risk group (very low, low, and low-intermediate) and by biological risk group defined by NCCN and GPS (probability of favorable pathology ≥79%, 68-78%, ≤67%).

Kaplan-Meier methods will be used to estimate time on surveillance free of definitive treatment. Time zero will be defined as the diagnostic biopsy date and time on surveillance free of definitive treatment will be defined as time from diagnostic biopsy to definitive treatment. Patients who withdraw without evidence of definitive treatment or are lost to follow-up will be censored at the time of their last visit and those who died will be censored at the time of death.

The aforementioned methods have been used in prominent AS literature to assess persistence on AS [17]. Because patients lost to follow-up could be drop-outs due to seeking definitive treatment elsewhere, alternative methods that account for informative censoring will be explored to evaluate the consistency of results.

7.3 Statistical Analysis of the Impact of GPS on the Shared Decision

The primary assessment of the impact of GPS on the shared treatment decision will be performed in the NCCN Low-risk subset of the first 300 patients enrolled in the study with valid GPS results. The analysis will summarize the proportion of patients for whom the treatment recorded on the CRF changed from pre-assay to post-assay along

with a two-sided 95% confidence interval (CI). All treatment decision changes, including immediate treatment to AS and vice versa and changes in treatment modality will be characterized. Additional analysis of decision changes will include changes to and from AS only. Similar analysis will also be performed for all 300 patients to estimate an overall change rate across all NCCN risk groups. This analysis will be conducted as soon as 300 patients with valid GPS results and completed pre- and post-assay CRFs have been accrued.

[redacted]

[redacted]

7.5 Planned Interim Analyses

Planned Interim analysis will be conducted at two additional time points:

1. When all enrolled patients have completed Visit 1C, selection of AS versus immediate treatment will be analyzed. The impact of GPS on shared treatment decision, as described in Section 7.3 will be conducted on all enrolled patients at this time.
2. When all enrolled patients have completed Visit 2, persistence on AS at 1 year and quality of life measures will be analyzed.

8. SAMPLE SIZE JUSTIFICATION

The sample size was calculated with the intent of showing a drop-out rate on AS of 20% or less when GPS is incorporated into treatment decisions. A rate of 20-30% is what is reported in the literature [17,18]. Assuming a true drop-out rate of 17% by 2 years a sample size of 300 patients will be required to achieve 90% probability that the observed drop-out rate will be 20% or less. We expect that if 1200 patients are enrolled, approximately 30%, or 360 of the patients will choose active surveillance and after accounting for patients with insufficient tissue, approximately 300 will be evaluable for the primary endpoint.

[redacted]

9. DATA MANAGEMENT

9.1 Data Delivery

Forms capturing Patient Reported Outcomes (PRO) will be completed by patients on paper CRFs, and then entered into the Electronic Data Capture (EDC) system by study personnel, as per study conduct instructions provided by GHI. Other forms will be captured initially in site produced source documentation, and then entered into the EDC system by study personnel. Site personnel will be requested to enter data into the database within five business days of patient visits.

9.2 Data Administration

Study personnel will be trained in study procedures to ensure that all aspects of patient and data management are standardized throughout the duration of the study. All study data should be entered by study personnel using the collection methods designed for this study. Data will be validated in accordance with study-specific Data Management documentation.

9.3 Data Security

Whenever data is first recorded on a paper CRF, that document will be considered source documentation and will be stored at the study site in designated areas with secure locking systems. Data entered into the EDC system will be accessible to study personnel for the duration of their participation in the study. Study personnel will have access to study data only for their particular site. Study personnel with access to the EDC system will create their own password according to the instructions provided by GHI.

10. ETHICS AND REGULATORY ISSUES

10.1 Informed Consent

No patient will participate in the study until they have been duly informed, have had sufficient time to understand the implications of the study and their participation in it, and freely granted their consent to participate through the signed consent form, which will have been previously approved by the Institutional Review Board (IRB) at the participating institution. Informed consent must be obtained by a physician investigator or a designee who possesses the appropriate knowledge and expertise needed to obtain informed consent for this study. Each participant will receive a copy of the consent form and the site will keep the original that has been signed and dated by the patient, the witnesses, and the person who requested the consent.

10.2 Committees on Ethics and Research

The protocol must be approved in writing by the IRB of choice for the participating sites. The study will only be able to begin after this approval has been obtained. Before

beginning the study, it is the principal investigator's responsibility to provide a copy of the IRB's approval together with the approved documentation to GHI.

10.3 Protocol Amendments

Amendments to the protocol or changes to the informed consent must be approved by GHI and should be prepared in writing and submitted for approval to the IRB. All records of changes made by the IRB, both to the protocol and to documents related to the study, will be saved in the investigator's files and are subject to inspection by regulatory authorities. Copies of amended documents and approval letters must be provided to GHI.

10.4 Confidential Information

All information provided by GHI in association with this study and not previously published is considered confidential information. This information includes but is not limited to the protocol and other scientific data. Any data collected during the study is also considered confidential. This confidential information is the property of GHI, should not be divulged without written consent from GHI, and cannot be used, with the exception of use in the execution of this study.

Information developed during the course of this study is also considered confidential. In order to receive permission to use the information originating from this trial, the investigator is required to provide GHI with the complete results of and all data obtained during the study.

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APPENDIX A: SITE INVESTIGATOR INITIATION FORM

This form is to be completed by all the investigators on the study. This form should be submitted prior to enrolling any patients into the study.

List all the investigators at the site who are participating in the study below. All Investigators must have been trained and able to conduct the study as described in the protocol. No more than 6 physicians at the same site may participate in the study at any given time.
With this form you agree to offer this study to all patients who meet the protocol criteria.

Physician Printed Name	Physician Number	Date of Investigator Initiation	Date Completed or Dropped from Study
	01		
	02		
	03		
	04		
	05		
	06		

Site PI Printed Name_____ Site Number_____

Site PI Signature_____ Date:_____

APPENDIX B: PRINCIPAL INVESTIGATOR PROTOCOL SIGNATURE PAGE

STUDY PROTOCOL

A PROSPECTIVE MULTICENTER OBSERVATIONAL TRIAL TO ASSESS PERSISTENCE ON ACTIVE SURVEILLANCE WHEN USING THE ONCO*TYPE* DX® PROSTATE CANCER ASSAY

Signature of Agreement for Protocol

I declare that I have read this protocol and I agree to conduct the study as described in the following document.

I will provide a copy of this protocol and all pertinent and relevant information to all those persons responsible for collaborating in the execution of the study. I will review and discuss the material with all of them in order to assure myself of their cognizant and complete information with respect to the study and its execution.

_____ _____

Site Principal Investigator Signature Date

_____

Institution Name

APPENDIX C: ACTUARIAL LIFE TABLE

Life expectancy for men age 50-82 is presented below. Life expectancy for a given person can be adjusted, using the clinician's assessment of the patient's overall health.* Patients in the best quartile of health (exceptionally healthy) have a 50% longer life expectancy than patients of the same age in the middle two quartiles (of average health). Patients in the worst quartile of health (poor health) have a 50% shorter life expectancy than patients in the middle two quartiles.

The highlighted box in each of the columns represents the age below which all patients in that quartile of health have a life expectancy of greater than 10 years. Patients in the white and yellow boxes are eligible for this study. Patients in the red boxes have a life expectancy of less than 10 years and are not eligible for this study.

Males	**Adjusted Life Expectancy**** Based on clinician's assessment of overall health		
Exact age	**Best Quartile of Health**	**Middle Two Quartiles of Health**	**Worst Quartile of Health**
50	43.5	29.0	14.5
51	42.2	28.2	14.1
52	41.0	27.3	13.7
53	39.7	26.5	13.2
54	38.5	25.7	12.8
55	37.3	24.9	12.4
56	36.1	24.1	12.0
57	34.9	23.3	11.6
58	33.7	22.5	11.2
59	32.5	21.7	10.8
60	31.4	20.9	10.5
61	30.2	20.2	10.1
62	29.1	19.4	9.7
63	28.0	18.7	9.3
64	26.9	17.9	9.0
65	25.8	17.2	8.6
66	24.7	16.5	8.2
67	23.7	15.8	7.9
68	22.6	15.1	7.5
69	21.6	14.4	7.2
70	20.6	13.7	6.9
71	19.6	13.1	6.5
72	18.7	12.4	6.2
73	17.7	11.8	5.9
74	16.8	11.2	5.6
75	15.9	10.6	5.3
76	15.1	10.0	5.0
77	14.2	9.5	4.7
78	13.4	8.9	4.5
79	12.6	8.4	4.2
80	11.9	7.9	4.0
81	11.1	7.4	3.7
82	10.4	6.9	3.5

* NCCN Prostate Cancer Guidelines Version 3.2012.

** Modified from the Social Security Administration Actuarial Life Table, 2007 (http://www.ssa.gov/OACT/STATS/table4c6.html/).