Armune BioScience®

APIFINY®
Non-PSA blood test

PHYSICIAN REFERENCE

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FORM: CT-027 Rev. 03 02/23/16

What is the basis of the Apifiny Test?
Apifiny is a cancer specific, non-PSA blood test designed to aid in the risk assessment of prostate cancer. The Apifiny technology is based on the measurement of eight prostate cancer specific autoantibodies in human serum. These autoantibodies are produced and replicated (amplified) by the immune system in response to the presence of prostate cancer cells. The autoantibodies are stable and, because of their amplification, are likely to be abundant and easy to detect, especially at low tumor burdens characteristic of early stage cancer. The use of Apifiny results may supplement other information in the risk assessment for prostate cancer.

The autoantibody markers span a range of biological functions integral to prostate cancer progression. Cell cycle, structure and cellular signaling pathways are all represented.

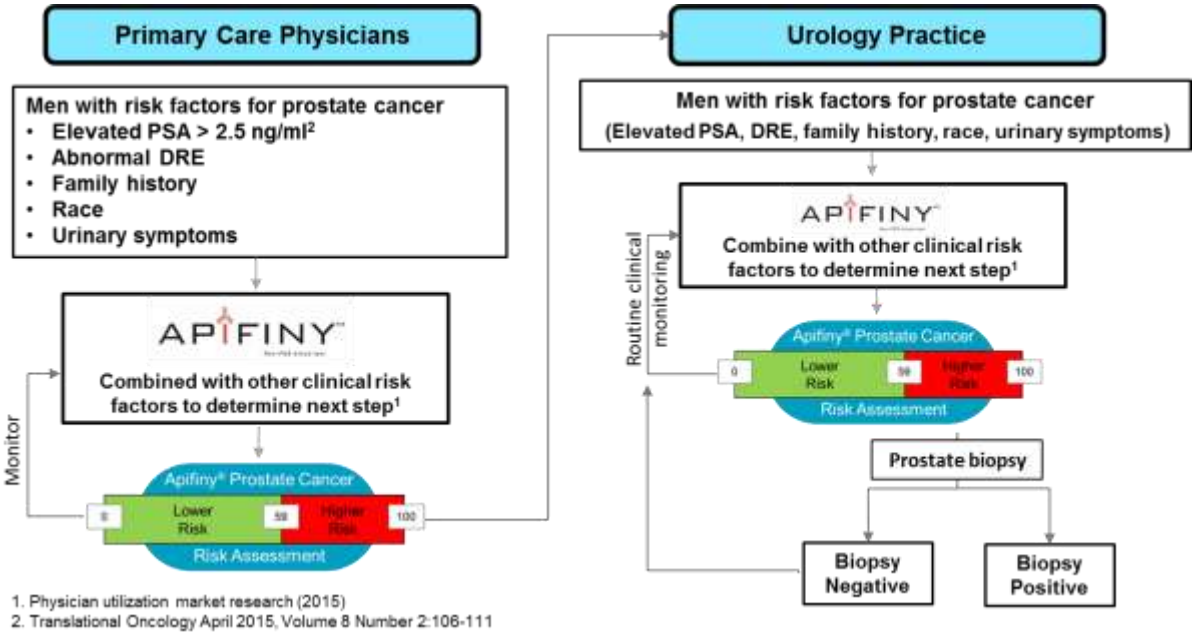
How do the Apifiny biomarkers relate to each other?
Statistical analysis shows there is an interdependence among the biomarkers which is further confirmed by their biological functions. Three of the biomarkers are associated with androgen response regulation, and four are related to cellular structural integrity. The eighth biomarker has been implicated in prostate cancer progression and a variety of cellular functions ranging from cellular signaling for numerous protein kinases to regulating cell cycle and cellular division. This eighth biomarker appears to be a potential bridge between the biomarkers in the other two general biochemical areas. More information about the biomarkers can be found in Translational Oncology 2015:8 (2):106-11 (Schipper M, Wang G, Giles N, Ohrnberger J. Novel prostate cancer biomarkers derived from autoantibody signatures).

How is the Apifiny assay performed?
The Apifiny test process is performed in part using a qualitative immunoassay technique and in part using flow cytometry. The laboratory data generated by these methodologies are then subjected to a proprietary algorithmic analysis that generates a cancer risk score. The Apifiny Test Directory has more information about the assay, test score reference range, laboratory turn-around, and other test details.

How should Apifiny be used?
Apifiny is designed to aid in the risk assessment of prostate cancer and should be used in combination with other accepted methods of patient management. Since Apifiny is based on a simple blood draw, it should be easily tolerated by most men. Apifiny score reporting was designed to optimize the identification of patients at lower risk. When combined with other patient information (i.e. PSA level, PSA velocity, DRE, race, family history, etc.) patients with lower risk Apifiny scores may be placed on a routine clinical monitoring program (i.e., semi-annual or annual checkup) with other accepted methods to assess the ongoing risk of prostate cancer. Men with higher Apifiny scores may require a more specific risk assessment plan which may include referral to a specialist and/or a prostate biopsy.

How do I order Apifiny?
Download, fill out, and sign the Apifiny Test Requisition and patient insurance/payment information. If you are using an Apifiny sample collection/mailer kit, the kit will contain Test Requisition Forms, sample collection materials, and directions. For more information about sample collection, handling, and shipment, refer to the Apifiny User Guide.

How might Apifiny fit within the clinical management process for my patients?
Apifiny is designed to aid in the risk assessment of prostate cancer.



1. Physician utilization market research (2015)
2. Translational Oncology April 2015, Volume 8 Number 2:106-111

What clinical studies have been completed on Apifiny?
Two studies have been completed. The first, a biomarker selection / algorithm development study, established the appropriate components for the assay. The second was a clinical validation study.

The assay biomarkers and the classifier algorithm were "locked down" in advance of the validation analysis using entirely independent samples. 519 samples were used in the biomarker selection / algorithm development study and 259 different samples were used in the clinical validation study. Samples were sourced from the University of Michigan, Johns Hopkins University, and Bioreclamation, a commercial sample provider. These studies fully complied with the recommendations of the 2012 report from the Institute of Medicine Committee on Omics-Based Predictive Tests, "Evolution of Translational Omics: Lessons Learned and Path Forward"; National Academy Press, Washington, DC. Results of the studies were analyzed by independent biostatisticians. These two studies were published in Translational Oncology 2015:8 (2):106-11 (Schipper M, Wang G, Giles N, Ohrnberger J. Novel prostate cancer biomarkers derived from autoantibody signatures).

How are the results of Apifiny interpreted?
Based on the studies and on the design intent of Apifiny, a cut point of 59 was chosen to optimize the identification of patients at lower risk. Scores below 59 are lower risk, while scores at or above 59 are higher risk. Apifiny test score ranges and potential decisions are summarized below. In addition, some interpretive comments and potential "talking points" are provided to support the physician – patient interaction on the discussion of results.

Lower risk of prostate cancer. Score not consistent with prostate cancer.

"In the most recent peer-reviewed published study on Apifiny[1], approximately 9 out of 10 men like you, with a score of less than 59, were cancer free."

Potential clinical decision[2]: Combine with other clinical information to determine next steps. Continue routine clinical monitoring.

Higher risk of prostate cancer. Score consistent with prostate cancer.

"In the most recent peer-reviewed published study on Apifiny[1], approximately 1 out 3 men like you, with a score of 59 or above, had prostate cancer. You may be at higher risk."

Potential clinical decision[2]: Combine with other clinical information to determine next steps. Develop an individualized patient management plan and consider a prostate biopsy

1. Translational Oncology, April 2015, Volume 8 Number 2: 106-111
2. Physician utilization market research (2015)

Is there a range of risk within the lower-risk or higher-risk scores?
Additional information on the performance of Apifiny is contained in the published validation study (Translational Oncology April 2015: 8 (2):106-11).

Further analysis of the data from the validation study demonstrates a false positive rate of approximately 20% at the 59 cut point and a false positive rate of approximately 4% at scores above 90. More study is required, but this may demonstrate a trend towards greater risk as Apifiny scores increase.

Does a patient's age have an impact on the Apifiny result?
Armune continues to assess the potential impact of age on Apifiny scores. In the published data on Apifiny, there was no observed impact of age on Apifiny scores (average age was 63 with the maximum age of a study participant being 90 years old)

The impact of ages above 90 on an Apifiny score is unknown.

Does a patient's race have an impact on the Apifiny result?
Armune continues to assess the potential impact of race on Apifiny scores. In the published data on Apifiny, there was no observed impact of race on Apifiny scores. In addition, in the ongoing clinical assessment of commercial samples of Apifiny, there does not appear to be an impact of race on the scores for Apifiny.

Do certain drug therapies or "herbal-natural" therapies have an impact on the score of Apifiny?
Armune continues to assess the potential impact of therapies on Apifiny scores.

For patients on immune-suppressant therapies and/or high dose steroids such as prednisone, Armune recommends to postpone testing with Apifiny until the course of therapy is complete.

Based on published data, ongoing clinical research, and the company's internal assessment of patient data, Apifiny scores do not appear to be impacted by common therapies for benign prostatic hyperplasia (BPH) such as finasteride or dutasteride, erectile dysfunction therapies, and testosterone replacement therapies. Although there is limited information on the impact of these therapies on Apifiny results, there is no known biological reason why these therapies could impact the result of Apifiny.

Additional clinical programs are in development to further assess the potential impact of therapies on Apifiny scores.

Can Apifiny be used to monitor disease progression in men on active surveillance and/or assess the recurrence of disease after local or systemic therapy?
Apifiny was not developed to be utilized in monitoring disease progression or recurrence of disease. However, in the initial research on Armune BioScience's autoantibody technology published in the New England Journal of Medicine (2005; 353:1224-1235 and Appendix), the autoantibodies demonstrated, in limited patient samples, the potential to be used to assess disease progression and recurrence.

Additional studies are being planned by Armune BioScience and in collaboration with pharmaceutical companies to further assess the potential of autoantibody technology to be used in these important areas.

Can a urinary tract infection, prostatitis, or recent ejaculation impact an Apifiny result?
Based on published research on Armune BioScience's autoantibody technology, there has not been an observed impact of these conditions on the scores of Apifiny. Armune's ongoing clinical development program will help to more definitively answer these clinical questions.

After a negative prostate biopsy, how long should a patient wait before being tested with Apifiny?
There is currently no evidence to suggest a certain clinical window needs to be maintained after a biopsy before testing with Apifiny. Armune recommends that a physician take into account several clinical factors in negative biopsy patients and test with Apifiny when it is appropriate to provide additional insight into the patient's overall risk assessment for prostate cancer.

How often should my patients get an Apifiny test?
Apifiny is the only cancer specific, non-PSA blood test designed to aid in the risk assessment for prostate cancer. Apifiny may be used as part of a routine clinical monitoring program (i.e., semi-annual or annual checkup) to assess a patient's ongoing risk of prostate cancer.

Should a patient use the results of Apifiny to delay or cancel other tests or treatment?
No. Apifiny is a risk assessment tool and should be used in conjunction with all the other detection and risk assessment tools at a physician's disposal. Prostate biopsy currently is the primary detection method and should be utilized following a physician's recommendation. Apifiny results may indeed encourage greater compliance with follow up biopsies by men who are identified at higher risk of having prostate cancer.

Is Apifiny a genetic test?
Apifiny does not produce genetic information about the patient, and there are no tests for DNA sequences or gene mutations included in the Apifiny assay. The test measures only the level of certain autoantibody proteins in blood serum.

Who developed the Apifiny test?
The Apifiny technology is derived from basic research performed at the University of Michigan. Armune BioScience continues to conduct further research and development of the assay for commercial use. Armune BioScience is privately owned.

How does the Apifiny technology compare with other tests available to assess a patient's risk of prostate cancer?
Apifiny technology is the only cancer specific, non-PSA blood test available to aid in the risk assessment for prostate cancer. Apifiny has no dependence on PSA, and may directly indicate potential cancer activity in prostate tissue based on the measurement of 8 prostate cancer specific serum autoantibodies created and amplified by the body's own immune system. Apifiny's advantages also include easy blood draw sample collection, low assay rejection rates, and competitive lab turn around and pricing compared to many other alternative tests.

How can I get more information?
Review Armune's website (www.armune.com), email CustomerService@armune.com, or call 844-4Armune (844-427-6863) for more information about Armune BioScience, the Apifiny technology, or the Armune BioScience Laboratory.