AnteMEL test report

A polygenic risk score test for skin melanoma

Name	**POTTER, JOHN**		
Id	12345678910	**Sample Id**	TS406
Age	37	**Sample material**	Buccal swab
Date of birth	14.03.1985	**Analysis method**	Illumina Global Screening Array-24
Ethnic descent	European	**Report Id**	176557-2024-07-17
Country	United Kingdom	**Time of result**	29.04.2024

Genotyping: University of Tartu Core Facility of Genomics
Processing and interpretation of analysis results: Antegenes

Result		Explanation
Polygenic risk score (z-score)	2.73 SD	**Your polygenic risk score is higher than the population average.** The result shows that the skin melanoma polygenic risk score is 2.73 standard deviation units higher than the population average.
Percentile	100	More than 99% of men have a lower risk than the patient.
Absolute risk (10 years)	0.22% (0.26–0.19%)	Your personal risk of developing melanoma in the next 10 years is **0.22%** (0.26–0.19%). The general population risk of melanoma among 37-year-old men in United Kingdom is **0.09%** (0.09–0.09%).
Relative risk	2.43	This means that the risk of developing melanoma in the next 10 years is 2.43 times higher than the 10-year genetic risk among 37-year-old men.

Time of evaluation of the result: 29.04.2024
The results were confirmed: Dr. Neeme Tõnisson, D07099.
Healthcare professional speciality: E190 Laboratory medicine.
Name of test manufacturer: OÜ Antegenes.

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AnteMEL test general information

AnteMEL is a genetic test that estimates a patient's risk of developing melanoma. AnteMEL test is based on the methodology of polygenic risk scores, which enables early detection and prevention of melanoma.

In addition to the patient's genetics, age, gender and ancestry, risk calculations also take into account the United Kingdom population average morbidity and mortality rates. As the risk of cancer increases with age, each patient is compared with people of the same age when evaluating the test results.

Genetic variants used in the AnteMEL test are distributed throughout the genome. The AnteMEL test includes a total of 28 genetic variants that can increase or decrease the risk of melanoma.

The result of the AnteMEL is given as units of standard deviation (SD) that characterizes the patient's genetic risk compared to the population average taking into account patient's ancestry (European, African, East Asian, South Asian or Mixed ancestry). For example, an outcome that exceeds 2.326 SD units corresponds to the highest level of risk in the 99th percentile. A result lower than -2.326 SD units corresponds to the lowest level of risk in the 1st percentile.

In case the patient's age exceeds the actual recommended starting age for screening or any other procedures, the report will state the patient's age for the start time.

AnteMEL test limitations

- AnteMEL cannot be used to diagnose melanoma.
- The risks identified by the AnteMEL test take into account the polygenic risk, but do not consider other risk factors (see section Health behavior).
- An elevated risk estimated by the AnteMEL test does not mean that the patient will develop melanoma during their lifetime. Also, a moderate or low-risk score does not mean that the patient will not develop skin melanoma.
- AnteMEL test is patient-specific, it does not give any information about the risk of developing a disease in the patient's family or close relatives, i.e. polygenic risk score-based disease risks may not be transmitted directly from parents to children.
- AnteMEL test does not analyze rare risk increasing mutations in single genes, e.g., *CDKN2A*, *MC1R*, *CDK4*, *TP53*, *PTEN*, *BAP1*, *POT1*, *ACD*, *PARK2*, *TERF2IP*, *TERT*, *BRCA1*, *BRCA2*, *RB1*, etc. Therefore, we recommend testing of rare risk increasing mutations in single genes if the following criteria are met:
    1. History of multiple cases of melanoma in biological relatives;
    2. Presence of rare variants that increase tumor risk in biological relatives.
- The AnteMEL test is based on up-to-date scientific data. However, the field of genetics is constantly evolving which may lead to changes in the risk assessments in the future as additional information becomes available. Therefore, also the clinical recommendations based on the test results may change.
- Different polygenic risk score models of the same trait may give different estimates to the individual's risks due to differences in the genetic variants included in the model and their weights.
- The result of this test should be applied in context with other relevant clinical data. In addition to the possible genetic predisposition, other risk factors also affect the risk of developing melanoma.

AnteMEL Test Clinical Recommendations

Based on the skin melanoma polygenic risk score test results, Antegenes' Clinic recommends:

- Watch for abnormal moles and perform a skin self-exam every month for any new changes. If you spot anything that just doesn't look right, get it checked by a dermatologist as soon as possible.
- Limit your exposure to ultraviolet (UV) radiation: protect your skin by using a broad-spectrum sunscreen with an SPF 30 or higher.
- Avoid using tanning beds and sunlamps.
- See a dermatologist once a year for a full-body skin exam.

For the patient - what should be done next?

In order to implement our clinical recommendations, you can contact a doctor that suits you (GP, family doctor, dermatologist).

Polygenic risk score assessment as an innovation in healthcare may not be yet in use in all medical practices, but doctors can use clinical recommendations and rationales provided in this report.

In addition to the polygenic component used by the AnteMEL test, there are also other melanoma risk factors to be considered.

For the doctor and the medical team

The clinical recommendations accompanying the AnteMEL test are based only on the patient's age and polygenic risk results and do not consider other possible risk factors. Therefore, taking into account other risk factors, it is possible to modify the current recommendations if necessary.

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Skin type

Fair skin unable to tan or tans minimally even when trying to tan, blue or green eyes, blond or red hair, freckles, multiple moles are signs of an increased risk of melanoma.

Health behaviour

- Sunburn, especially in childhood, significantly increases the risk of melanoma.
- Using tanning beds increases the risk of melanoma.
- Staying in areas with intense sunlight (near the equator, high mountains) increases risk.
- People with weakened immune systems have a higher risk of developing melanoma.

Body awareness

We recommend you to be aware of your body and skin conditions and possible changes.

If you notice any of the symptoms listed below, we recommend that you seek dermatologist consultation. These may indicate the development of melanoma:

- The irregular shape of the mole or asymmetry – One-half of a mole does not have the same shape as the other half;
- The edge of a mole is uneven (irregular). It can look jagged, notched or blurred edge;
- The color of a mole is uneven – There are different shades in one birthmark;
- There is a change in the size, shape, color of the mole over a short period of time;
- Itchy skin or bleeding;
- New onset of skin changes over 40 years of age.

More info at https://www.euromelanoma.org

Rationale for Current Clinical Recommendations

For individuals in the general population who are not identified as being in a high-risk category, screening is not warranted; however, evaluation of any suspicious lesions identified by a clinician or patient is warranted. Screening for melanoma is recommended for high-risk patients – annual full-body skin exam by a dermatologist. In addition to phenotype risk factors and family history, polygenic risk score testing identifies additional high-risk persons.

AnteMEL explanatory information and post-test counselling

The AnteMEL test includes a total of 28 positions. By analyzing all risk positions in the patient's genome, we estimated that the patient's risk score for developing melanoma is 2.73 SD units. The risk score is higher than in 99% of 37-year-old men. In other words, the patient's melanoma risk score is placed in the 100th percentile of 37-year-old men.

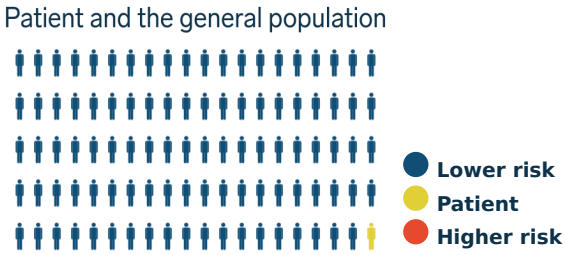

Figure 1: The patient's skin melanoma polygenic risk position compared to other men of the same age.

AnteMEL test considers the patient's nationality, gender, age, and the demographic background of melanoma. The patient's risk of developing melanoma within the next 10 years is 0.22% (0.26–0.19%). About 22 men out of 10,000 will develop the disease.

At the same time, the risk of melanoma among 37-year-old men in United Kingdom is 0.09% (0.09–0.09%) meaning that the expected rate of developing the disease is 9 men out of 10 000.

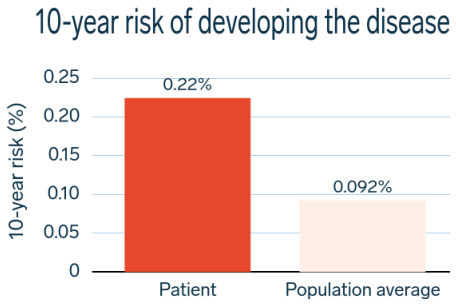

Figure 2: The patient's breast cancer polygenic risk over next 10 years compared to the population average

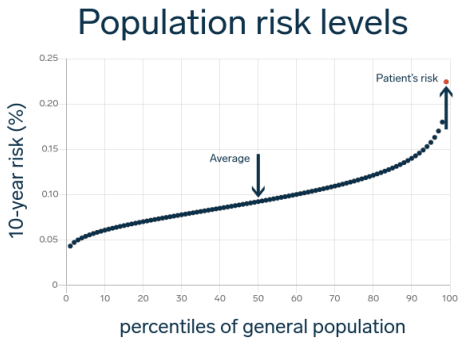

Figure 3: Location of the patient's 10-year polygenic risk on the population risk distribution curve

Contact

OÜ Antegenes (Licence L05386)
Registry code: 14489312
info@antegenes.com
Phone: +372 53 778 141 (Mon-Fri 9.00-17.00)
www.antegenes.com