PCOS STRATIFICATION

Field of the Invention

The invention relates to a method of stratifying test subjects with Polycystic Ovary Syndrome (PCOS). The invention also relates to a computer system and a computer program for implementing the method according to the invention.

Background of the Invention

Polycystic ovary syndrome (PCOS) affects at least 10% of women worldwide. PCOS is diagnosed based on the presence of clinical and/or biochemical signs of androgen excess, chronic anovulation/irregular menstrual cycles, and polycystic appearance of the ovaries on ultrasound. According to the widely accepted Rotterdam criteria, at least two out of those three criteria need to be present to make a diagnosis of PCOS, in addition to exclusion of other rare possible underlying causes.

PCOS was previously mainly perceived as a disorder affecting women of reproductive age and the by far most common cause of female infertility. However, over recent years it has become clear that PCOS is a lifelong metabolic disorder and multiple studies have demonstrated that women with PCOS have a 2-3-fold increased risk of type 2 diabetes, hypertension, fatty liver disease and cardiovascular disease. Thus, women with PCOS represent a major risk group for the development of metabolic disease and associated co-morbidities and mortality. However, due to the large number of affected women, health care systems struggle to manage this risk effectively, and there are currently no tools for metabolic risk stratification, an urgent unmet clinical need. The present invention seeks to address these problems.

Summary

In one aspect, the present disclosure provides for a method of stratifying test subjects with Polycystic Ovary Syndrome (PCOS) into those that are expected to respond to therapeutic treatment with an inhibitor of hypothalamic-pituitary-adrenal axis activity, those that are expected to respond to therapeutic treatment with an AKR1C3 inhibitor, and those that are expected to respond to therapeutic treatment with a 5alpha-reductase inhibitor, the method comprising: (a) providing a test sample from a test subject with

PCOS; (b) determining the concentration/level in the test sample of at least one ovarian androgen steroid and/or a derivative thereof, and at least one adrenal steroid and/or derivative thereof; and (c) using the results from (b) to predict if the subject will respond to therapeutic treatment with an inhibitor of hypothalamic-pituitary-adrenal axis activity, therapeutic treatment with an AKR1C3 inhibitor, or therapeutic treatment with a 5alpha-reductase inhibitor.

In another aspect, the present disclosure provides for a method of stratifying test subjects with PCOS into those that are expected to respond to therapeutic treatment with an inhibitor of hypothalamic-pituitary-adrenal axis activity, those that are expected to respond to therapeutic treatment with an AKR1C3 inhibitor, and those that are expected to respond to therapeutic treatment with a 5alpha-reductase inhibitor, the method comprising: (a) providing a test sample from a test subject with PCOS; (b) determining the concentration/level in the test sample of at least one ovarian androgen steroid or derivative thereof comprising DHT, and at least six adrenal steroids and/or derivatives thereof comprising pregnenolone, 17-hydroxypregnenolone, DHEA, 11KT, 17OHP, S, F, DOC, B and Aldo; and (c) using the results from (b) to predict if the subject will respond to therapeutic treatment with an inhibitor of hypothalamic-pituitary-adrenal axis activity, therapeutic treatment with an AKR1C3 inhibitor, or therapeutic treatment with a 5alpha-reductase inhibitor.

In another aspect, the present disclosure provides for a method of stratifying test subjects with PCOS into those that are expected to respond to therapeutic treatment with an inhibitor of hypothalamic-pituitary-adrenal axis activity, those that are expected to respond to therapeutic treatment with an AKR1C3 inhibitor, and those that are expected to respond to therapeutic treatment with a 5alpha-reductase inhibitor, the method comprising: (a) providing a test sample from a test subject with PCOS; (b) determining the concentration/level in the test sample of at least three ovarian androgen steroids and/or derivatives thereof comprising testosterone, DHT and 5adione, and at least six adrenal steroids and/or derivatives thereof comprising DHEAS, DHEA, 11OHA4, 11KA4, 11KT and 11OHT; and (c) using the results from (b) to predict if the subject will respond to therapeutic treatment with an inhibitor of hypothalamic-pituitary-adrenal axis activity, therapeutic treatment with an AKR1C3 inhibitor, or therapeutic treatment with a 5alpha-reductase inhibitor.

Detailed Description

The inventors believe but do not wish to be bound by the theory that an increase of steroid hormones, particularly androgens, in women with PCOS is responsible for causing PCOS and metabolic disorders that are known to be associated with PCOS. However, in some women with PCOS, there is also an increase in the ratio of the concentration/level of hormones synthesised in the adrenal glands compared to the concentration/level of hormones synthesised in the ovaries e.g., ovarian androgens. The inventors believe but do not wish to be bound by the theory that this relative increase