[0006b] In another aspect of the present disclosure, there is provided a system for differentially diagnosing Cushing's Disease from Ectopic Cushing's Syndrome in a patient with an established diagnosis of ACTH-dependent Cushing's Syndrome, the system comprising:

a processor;

a memory coupled with the processor via an interconnect;

a communications interface coupled with the interconnect and adapted to receive a first set of values and a second set of values corresponding to analytical results from blood samples obtained from the patient;

a comparison engine communicatively coupled with the processor, wherein the comparison engine is configured to:

receive the first set of values, which represent a set of pre administration blood sample values corresponding to a baseline cortisol level and baseline adrenocorticotropic hormone (ACTH) or a baseline ratio of the baseline cortisol level to the baseline ACTH level;

receive the second set values, which represent a set of post administration blood sample values corresponding to a cortisol level and an ACTH level or a ratio of the cortisol to the ACTH level of the patient after a minimum of 6 weeks of mifepristone administration in an amount of 5 – 20 mg/kg effective to raise cortisol levels in a healthy individual by at least two-fold; and

compare the first set of values and the second set of values to determine a differential relationship between the pre administration values and the post administration values; and

an output module communicatively coupled with the processor and configured to output an indication, wherein the indication represents a positive diagnosis for Ectopic Cushing's Syndrome if the differential relationship represents a decrease of the mifepristone-exposed levels by greater than 50% as compared to the baseline levels and the indication represents a positive diagnosis for Cushing's Disease if the differential relationship represents an increase by greater than 50% of the mifepristone-exposed levels as compared to the baseline levels.

[0006c] In a further aspect of the present disclosure, there is provided a method of differentially diagnosing Cushing's Disease from Ectopic Cushing's Syndrome in a patient with an established diagnosis of ACTH-dependent Cushing's Syndrome, the method comprising:

obtaining, with a computing system associated with a treating physician, a first set of values representing a baseline cortisol level and a baseline ACTH level or a baseline ratio between the baseline cortisol and ACTH levels corresponding to one or more pre mifepristone administration blood samples from the patient;

obtaining, with the computing system, a second set of values representing a mifepristone-exposed cortisol level and a mifepristone-exposed ACTH level or a ratio between the mifepristone-exposed cortisol and ACTH levels corresponding to one or more post administration blood samples from the patient obtained after undergoing mifepristone administration according to a predetermined protocol comprising daily mifepristone administration at a daily dose of 5 mg/kg, increasing the mifepristone daily dose over a period of 10 weeks up to a daily mifepristone dose of 20 mg/kg;

determining, with the computing system, a differential relationship between the first and second set of values; and

outputting to a user, with the computing system, an indication representing a positive diagnosis for Ectopic Cushing's Syndrome, if the differential relationship represents a decrease of the mifepristone-exposed levels by greater than 50% as compared to the baseline levels; and

outputting to a user, with the computing system, an indication representing a positive diagnosis for Cushing's Disease, if the differential relationship represents an increase of the mifepristone-exposed levels by greater than 50% as compared to the baseline levels.

[0007] In some embodiments, the GRA is a non-steroidal GRA. In some embodiments, GRA is mifepristone. In some embodiments, the GRA is selected from the group consisting of

- (R)-4a-(ethoxymethyl)-1-(4-fluorophenyl)-6-((4-(trifluoromethyl)phenyl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinoline;
- 6-((1r,4r)-4-phenylcyclohexyl)-5-(3-(trifluoromethyl)benzyl)pyrimidine-2,4(1H,3H)-dione;
- (R)-(1-(4-fluorophenyl)-6-((4-(trifluoromethyl)phenyl)sulfonyl)-4,4a,5,6,7,8-hexahydro1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(thiazol-2-yl)methanone;

WHAT IS CLAIMED IS:

1. A method of differentially diagnosing Cushing's Disease from Ectopic Cushing's Syndrome in a patient with an established diagnosis of ACTH-dependent Cushing's Syndrome, wherein:

(i) determining a baseline cortisol level and a baseline adrenocorticotropic hormone (ACTH) level from one or more blood samples obtained from the patient prior to administration of mifepristone to the patient;

(ii) determining a second ACTH level and a second cortisol level from one or more second blood samples obtained from the patient after administration of mifepristone to the patient for a period of not less than 6 weeks and in an amount of 5 – 20 mg/kg effective to raise ACTH levels in a healthy individual by at least two-fold;

(iii) calculating a baseline ratio of cortisol to ACTH using the baseline levels of cortisol and ACTH, and calculating a mifepristone exposed ratio of cortisol to ACTH using the second cortisol and ACTH levels; and,

(iv) diagnosing Ectopic Cushing's Syndrome in the patient if the mifepristone exposed ratio of cortisol to ACTH has decreased by greater than 50% compared to the baseline ratio, or diagnosing Cushing's Disease in the patient if the mifepristone exposed ratio of cortisol to ACTH has increased by greater than 50% compared to the baseline ratio.

2. The method of claim 1 wherein the one or more second samples are taken from the patient after mifepristone has been administered for a minimum of 6 weeks and on a daily basis equal to between 5-20 mg/kg of the patient.

3. The method of claim 1 where in the determining of the second ACTH and cortisol levels is after administration of mifepristone for a period of between 6 and 10 weeks.

4. The method of claim 1 where the pretreatment samples and second samples are from plasma and measured in μg/dl.

5. A system for differentially diagnosing Cushing's Disease from Ectopic Cushing's Syndrome in a patient with an established diagnosis of ACTH-dependent Cushing's Syndrome, the system comprising:

a processor;

a memory coupled with the processor via an interconnect;

a communications interface coupled with the interconnect and adapted to receive a first set of values and a second set of values corresponding to analytical results from blood samples obtained from the patient;

a comparison engine communicatively coupled with the processor, wherein the comparison engine is configured to:

receive the first set of values, which represent a set of pre administration blood sample values corresponding to a baseline cortisol level and baseline adrenocorticotropic hormone (ACTH) or a baseline ratio of the baseline cortisol level to the baseline ACTH level;

receive the second set values, which represent a set of post administration blood sample values corresponding to a cortisol level and an ACTH level or a ratio of the cortisol to the ACTH level of the patient after a minimum of 6 weeks of mifepristone administration in an amount of 5 – 20 mg/kg effective to raise cortisol levels in a healthy individual by at least two-fold; and

compare the first set of values and the second set of values to determine a differential relationship between the pre administration values and the post administration values; and

an output module communicatively coupled with the processor and configured to output an indication, wherein the indication represents a positive diagnosis for Ectopic Cushing's Syndrome if the differential relationship represents a decrease of the mifepristone-exposed levels by greater than 50% as compared to the baseline levels and the indication represents a positive diagnosis for Cushing's Disease if the differential relationship represents an increase by greater than 50% of the mifepristone-exposed levels as compared to the baseline levels.

6. The system of claim 5, wherein the comparison engine is further configured such that comparing the first and second set of values comprises determining which of the set of post-treatment values have changed from the set of pre-treatment values, and

wherein the output module is further configured output another indication to the user representing which of the set of post-treatment values have changed from the set of pre-treatment values, wherein the values are labeled in terms of post and pre-treatment values and wherein an increase in the ratio of cortisol to ACTH predicts a positive diagnosis for Cushing's Disease and wherein a decrease in the ratio of cortisol to ACTH predicts a positive diagnosis for Ectopic Cushing's Syndrome.

7. The system of claim 5, wherein the output module communicates said indication to the user in terms of a positive diagnosis of either Cushing's Disease or Ectopic Cushing's Syndrome.

8. The system of claim 5, further comprising:

an analytic device for measuring cortisol and ACTH levels in patient samples where the device is coupled to the processor in a manner permitting the output of the levels to the processor as one or more values.

9. A method of differentially diagnosing Cushing's Disease from Ectopic Cushing's Syndrome in a patient with an established diagnosis of ACTH-dependent Cushing's Syndrome, the method comprising:

obtaining, with a computing system associated with a treating physician, a first set of values representing a baseline cortisol level and a baseline ACTH level or a baseline ratio between the baseline cortisol and ACTH levels corresponding to one or more pre mifepristone administration blood samples from the patient;

obtaining, with the computing system, a second set of values representing a mifepristone-exposed cortisol level and a mifepristone-exposed ACTH level or a ratio between the mifepristone-exposed cortisol and ACTH levels corresponding to one or more post administration blood samples from the patient obtained after undergoing mifepristone administration according to a predetermined protocol comprising daily mifepristone administration at a daily dose of 5 mg/kg, increasing the mifepristone daily dose over a period of 10 weeks up to a daily mifepristone dose of 20 mg/kg;

determining, with the computing system, a differential relationship between the first and second set of values; and

outputting to a user, with the computing system, an indication representing a positive diagnosis for Ectopic Cushing's Syndrome, if the differential relationship represents a decrease of the mifepristone-exposed levels by greater than 50% as compared to the baseline levels; and

outputting to a user, with the computing system, an indication representing a positive diagnosis for Cushing's Disease, if the differential relationship represents an increase of the mifepristone-exposed levels by greater than 50% as compared to the baseline levels.

10. The method of claim 9, wherein in the pre-determined adminstration protocol, mifepristone is to be administered to the patient in an amount effective to raise ACTH and cortisol levels in a healthy individual by at least two-fold.

11. The method of claim 9, wherein obtaining the baseline ratio comprises receiving, with the computing system, each of a baseline cortisol level and a baseline ACTH level and determining the baseline ratio therefrom.

12. The method of claim 9, wherein obtaining the first set of values comprises storing, in a memory of the computing system, the first set of values designated as corresponding to baseline levels of the patient and

obtaining the second set of values comprises storing the second set of values, in the memory, designated as corresponding to mifepristone-exposed levels of the patient.

13. The method of claim 9, wherein obtaining the baseline ratio comprises receiving, with the computing system, each of a baseline cortisol level and a baseline ACTH level and determining the baseline ratio therefrom.

14. The method of claim 9, wherein obtaining the first and second set of values comprises accessing the first and second set of values remotely through a server of a medical facility or laboratory associated with the patient.