

Human growth hormone (hGH) has never been described in this context. It is only known that relatively elevated levels of plasma hGH in the normal population (especially in males) are associated with an increased risk for the development of incident adverse cardiac events in WO/2014/108396.

5

Here we describe that elevated levels of plasma hGH, and/or its isoforms in subjects are associated with the success of therapy with hypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins), whereas such therapy is not  
10 efficacious in patients with relatively low levels of plasma hGH, and/or its isoforms. Thus, measurement of hGH, and/or its isoforms in subjects is a suitable to stratify patients for pharmacological therapy.

15

The present disclosure relates to a method of determining whether a subject has a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) comprising the steps:

20

25

30

- determining the level of hGH, and/or its isoforms in a blood sample of said subject and
- comparing the determined level of hGH, and/or its isoforms in said blood sample with a pre-determined threshold and
- wherein in case the determined level of hGH, and/or its isoforms is above said pre-determined threshold then the subject is identified as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) and
- wherein in case the determined level of hGH, and/or its isoforms is below said pre-determined threshold then the subject is identified as not having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins).

In one aspect, the present disclosure relates to a method of determining whether a subject has a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) comprising the steps:

- determining the level of hGH, and/or its isoforms in a blood sample of said subject and
- comparing the determined level of hGH, and/or its isoforms in said blood sample with a pre-determined threshold and
- wherein in case the determined level of hGH, and/or its isoforms is above said pre-determined threshold then the subject is identified as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) and
- wherein in case the determined level of hGH, and/or its isoforms is below said pre-determined threshold then the subject is identified as not having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) and
- wherein said isoforms of hGH is selected from the group consisting of: hGH isoform 1, hGH isoform 2, hGH isoform 3 and hGH isoform 4.

In another aspect, the present disclosure relates to the use of an antihypertensive drug (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) in the manufacture of a medicament, for preventing a major cardiovascular event and/or a cardiovascular disease in a subject whose determined level of hGH, and/or its isoforms is above said pre-determined threshold and wherein said subject is identified according to the methods as disclosed herein as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs.

In a further aspect, the present disclosure relates to the use of an antihypertensive drug (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) in the manufacture of a

medicament, for preventing a major cardiovascular event and/or a cardiovascular disease in a subject whose determined level of hGH, and/or its isoforms is above said pre-determined threshold and wherein said subject is identified according to the methods as disclosed herein as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs wherein said subject does not have hypertension.

In yet another aspect, the present disclosure relates to a method for monitoring the therapy response of a subject at vascular risk that is treated with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) comprising the steps:

- determining the level of hGH, and/or its isoforms in a blood sample of said subject taken at a time point X1 with antihypertensive drugs and
- determining the level of hGH, and/or its isoforms in a blood sample of said subject taken at a time point X2 with antihypertensive drugs, and
- wherein time point X1 is either before the beginning of therapy or after starting the therapy but in any event earlier than time point X2, and
- wherein time point X2 is after starting the therapy and in any event later than time point X1
- comparing the determined level of hGH, and/or its isoforms in said blood sample taken at point X1 with the determined level of hGH, and/or its isoforms in said blood sample taken at time point X2
- wherein a lower level of hGH, and/or its isoforms in said blood sample taken at time point X2 compared to the level of hGH, and/or its isoforms in said blood sample taken at time point X1 indicates a therapy response.

## Claims

- 5 1) Method of determining whether a subject has a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) comprising the steps:

  - 10 • determining the level of hGH, and/or its isoforms in a blood sample of said subject and
  - 15 • comparing the determined level of hGH, and/or its isoforms in said blood sample with a pre-determined threshold and
  - 20 • wherein in case the determined level of hGH, and/or its isoforms is above said pre-determined threshold then the subject is identified as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) and
  - 25 • wherein in case the determined level of hGH, and/or its isoforms is below said pre-determined threshold then the subject is identified as not having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) and
  - 30 • wherein said isoforms of hGH is selected from the group consisting of: hGH isoform 1, hGH isoform 2, hGH isoform 3 and hGH isoform 4.
- 25 2) Method of determining whether a subject has a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs according to claim 1, wherein said subject does not have hypertension (at least >140mmHG (systolic) to 90 mmHG (diastolic)).
- 30 3) Method of determining whether a subject has a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs according to claim 1 or 2 wherein the blood sample is taken from a subject that has not yet treated with antihypertensive drugs.