

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.

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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.

In one aspect, the present disclosure relates to a method of determining whether a subject has
15 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 • 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-
25 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-
30 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 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.

comprising heart failure, atherosclerosis, hypertension, cardiomyopathy, myocardial infarction and stroke.

16) Method of determining whether a subject has a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs according to any of the preceding claims wherein the method further comprises:

- recommendation of administration of antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) to a subject whose determined level of hGH, and/or its isoforms is above said pre-determined threshold and who is identified as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs or
- recommendation of withholding with antihypertensive drugs (e.g. Angiotensin converting enzyme inhibitor (ACE inhibitor), Angiotensin Receptor Blocker (ARB), Beta-Adrenoreceptor Blocker (Beta-blocker) and/or statins) to a subject whose determined level of hGH, and/or its isoforms is below said pre-determined threshold and who is identified as not having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs.

- 17) 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 of any of claims 1-16 as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs.
- 18) 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 of any of claims 1-16 as having a vascular risk that can be reduced by blood pressure lowering therapy with antihypertensive drugs wherein said subject does not have hypertension.
- 19) 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.

20) 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) according to claim 19 wherein the determined level of hGH, and/or its isoforms in said blood sample taken at point X1 is above a pre-determined threshold and the subject has been 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).

21) 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) according to claim 19 or 20 wherein the time point X1 is before starting the therapy.

22) 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) according to any of claims 19 to 21 wherein time point X2 is 12 months, 24 Months, or 36 months after time point X1.