Patent Claims

1.) Use of Abituzumab for the manufacture of a medicament for treating a bone metastasis disease which is cancer or is derived from cancer in a subject, wherein said subject has been determined to have
a) high levels of one protein in at least one body fluid of said subject, selected from whole blood, blood serum, blood plasma, exudate, lymph, mucus, peritoneal fluid, saliva, sputum, tears and urine, wherein said one protein is:
DCN (UniProt ID: P07585);
and optionally
b) low levels of one or more proteins in at least one body fluid of said subject, wherein said one or more proteins are selected from the group consisting of:
ANG (UniProt ID: P03950),
IL1B (UniProt ID: P01584),
LEPR (UniProt ID: P48357),
MAP2K2 (UniProt ID: P36507),
MAPK11 (UniProt ID: Q15759),
RGMB (UniProt ID: Q6NW40), and
TNFRSF17 (UniProt ID: Q02223);
and/or proteins that have at least 95% sequence identity to said proteins, wherein said protein level is
(i) classified as high, if the respective specific protein level in said at least one body fluid is at least 2 % higher than the median threshold for the respective specific protein, and
(ii) classified as low, if the respective specific protein level in said at least one body fluid is at least 2 % lower than the median threshold for the respective specific protein.

2.) Use according to claim 1, wherein said subject has been determined to have

a) high levels of one protein in said at least one body fluid of said subject, wherein said one protein is:

DCN (UniProt ID: P07585);

and

b) low levels of one or more proteins in said at least one body fluid of said subject, wherein said one or more proteins are selected from the group consisting of:

ANG (UniProt ID: P03950),
IL1B (UniProt ID: P01584),
LEPR (UniProt ID: P48357),
MAP2K2 (UniProt ID: P36507),
MAPK11 (UniProt ID: Q15759),
RGMB (UniProt ID: Q6NW40), and
TNFRSF17 (UniProt ID: Q02223);

and/or proteins that have at least 99% sequence identity to said proteins.

3.) Use according to claim 1, wherein said cancer is selected from prostate cancer, breast cancer and/or lung cancer.

4.) Use according to claim 1, 2 and/or 3, wherein the level of said specific protein in said at least one body fluid of said subject is

a) classified as high, if the respective specific protein level in said at least one body fluid is at least 5% higher, at least 10% higher or at least 25% higher than the median threshold determined for the respective specific protein,

and/or

b) classified as low, if the respective specific protein level in said at least one body fluid is at least 5% lower, at least 10% lower or at

least 25% lower than said median threshold for the respective specific protein.

5.) Use according to claim 1, 2, 3 and/or 4, wherein said median thresholds are determined in a subject population having said bone metastasis disease.

6.) Use according to one or more of the preceding claims, wherein said subject has been determined to have a high level of the protein DCN (UniProt ID: P07585) and/or a protein having at least 99% sequence identity to said protein, wherein said protein level is classified as high, if the respective specific protein level in said at least one body fluid is at least 2 % higher than the median threshold for the respective specific protein.

7.) Use according to one or more of the preceding claims, wherein said subject has been determined to have the respective levels of one or more proteins having at least 99% sequence identity to said one or more proteins according to claim 1.

8.) Use according to one or more of the preceding claims, wherein said body fluid is selected from the group consisting of blood plasma, blood serum and whole blood.

9.) Use according to one or more of the preceding claims, wherein said high levels and/or low levels of one or more of said proteins are present and/or determined prior to said Abituzumab is to be administered.

10.) Use according to one or more of the preceding claims, wherein said high levels and/or low levels of one or more of said proteins are

present and/or determined during or after said Abituzumab is to be administered.

11.) Use according to one or more of the preceding claims, wherein the bone metastasis disease is derived from prostate cancer, breast cancer and/or lung cancer.

12.) Use according according to one or more of the preceding claims, wherein the bone metastasis disease is derived from prostate cancer or castrate-resistant prostate cancer.

13.) Use according to one or more of the preceding claims, wherein said threshold or median threshold for the respective specific protein is determined from the body fluid of a plurality of subjects being part of a diseased subject population suffering from the respective bone metastasis disease.

14.) Use according to one or more of the preceding claims, wherein said Abituzumab is to be administered to said subject in an amount of 100 mg to 3000 mg per month.

15.) Use according to one or more of the preceding claims, wherein said Abituzumab is to be administered to said subject in an amount of 500 to 2000 mg every week, every second week or every fourth week.

16.) Use according to one or more of the preceding claims, wherein said Abituzumab is to be administered to said subject in an amount of 500 mg +/- 10% per week, 750 mg +/- 10% per week, 1000 mg +/- 10% per week or 1500 mg +/- 10% per week, optionally every week, every second week or every fourth week.

17.) Use according to one or more of the preceding claims, wherein said

Abituzumab is to be administered in combination with one or more agents or chemotherapeutic agents,
a) selected from the group consisting of Leuproreline, Leuproreline acetate, bicalutamide, nilutamide, triptoreline, gosereline, flutamide, cyproterone, busereline and degarelix,
b) selected from the group consisting of Zoledronic acid,Pamidronic acid, Clodronate disodium, Alendronic acid and Ibandronic acid, and/or
c) selected from the group consisting of Abiraterone, Abiraterone acetate, Prednisone, Enzalutamide, Radium Ra 223 dichloride, Docetaxel, Sipuleucel-T, Cabazitaxel and Mitoxantrone;
and/or the pharmaceutically acceptable derivatives and/or salts thereof.

18.) Use according to one or more of the preceding claims, wherein said Abituzumab is to be administered in combination with, or additionally in combination with, one or more chemotherapeutic agents, selected from the group consisting of cetuximab, Panitumumab, irinotecan, vinorelbine, capecitabine, leucovorine, oxaliplatin, cisplatin, carboplatin, 5-fluorouracil (5-FU), bevacizumab, aflibercept and regorafenib.

19.) Use according to one or more of the preceding claims, wherein said Abituzumab is to be administered in combination with one or more agents or chemotherapeutic agents, selected from the group consisting of
a) Leuproreline, Leuproreline acetate, bicalutamide, nilutamide, triptoreline, gosereline, flutamide, cyproterone, busereline and degarelix,
and/or the pharmaceutically acceptable derivatives and/or salts thereof; and/or
b) Zoledronic acid, Pamidronic acid, Clodronate disodium, Alendronic

acid and Ibandronic acid,
and/or the pharmaceutically acceptable derivatives and/or salts thereof.

20.) A method to identify tumours in a subject likely to benefit from treatment with Abituzumab, said method comprising
a) determining the levels of one or more proteins, selected from the group consisting of DCN (UniProt ID: P07585)
in at least one body fluid sample of said subject, selected from whole blood, blood serum, blood plasma, exudate, lymph, mucus, peritoneal fluid, saliva, sputum, tears and urine, wherein
a) a high level of:
DCN (UniProt ID: P07585);
and optionally
b) low levels of one or more proteins in said at least one body fluid sample of said subject, wherein said one or more proteins are selected from the group consisting of:
ANG (UniProt ID: P03950),
IL1B (UniProt ID: P01584),
LEPR (UniProt ID: P48357),
MAP2K2 (UniProt ID: P36507),
MAPK11 (UniProt ID: Q15759),
RGMB (UniProt ID: Q6NW40), and
TNFRSF17 (UniProt ID: Q02223);
identify a tumour likely to benefit from the treatment with Abituzumab, wherein said protein level is
(i) classified as high, if the respective specific protein level in said at least one body fluid sample is at least 2 % higher than the median threshold for the respective specific protein, and
(ii) classified as low, if the respective specific protein level in said at least one body fluid sample is at least 2 % lower than the median threshold for the respective specific protein.

21.) A method to identify tumours in a subject likely to benefit from treatment with Abituzumab, said method comprising determining the level of the protein DCN (UniProt ID: P07585), and/or a protein having at at least 99% sequence identity to DCN, in one or more body fluid samples, selected from whole blood, blood serum, blood plasma, exudate, lymph, mucus, peritoneal fluid, saliva, sputum, tears and urine, of said subject, wherein a high level thereof identify a tumour likely to benefit from the treatment with Abituzumab, and wherein said protein level is classified as high, if the respective specific protein level in said at least one body fluid sample is at least 2 % higher than the median threshold for the respective specific protein.

22.) The method according to one or more of the preceding claims and especially according to claim 20 and/or 21, wherein the level of protein in said one or more body fluid samples is
a) classified as high, if the respective protein level in said one or more body fluid sample is at least 5% higher, at least 10% higher or at least 25% higher than the median threshold determined for the respective protein,
and/or
b) classified as low, if the respective protein level in said one or more body fluid samples is at least 5% lower, at least 10% lower or at least 25% lower than said median threshold for the respective protein.

23.) The method according to claim 20, 21 and/or 22, wherein the one or more body fluid samples comprise a blood plasma or consist of blood plasma.

24.) The method according to claim 20, 21, 22 and/or 23, wherein the one or more body fluid samples consist of blood plasma.

25.) A method to identify a subject that is suffering from a bone metastasis disease which is cancer or is derived from cancer to be responsive to treatment with Abituzumab, comprising

a) determining the levels of one or more proteins, comprising of DCN (UniProt ID: P07585)

in at least one body fluid sample of said subject, wherein

a) a high level one or more proteins selected from the group consisting of:

DCN (UniProt ID: P07585),

and optionally

b) low levels of one or more proteins in at least one body fluid sample of said subject, wherein said one or more proteins are selected from the group consisting of:

ANG (UniProt ID: P03950),
IL1B (UniProt ID: P01584),
LEPR (UniProt ID: P48357),
MAP2K2 (UniProt ID: P36507),
MAPK11 (UniProt ID: Q15759),
RGMB (UniProt ID: Q6NW40), and
TNFRSF17 (UniProt ID: Q02223);

identify a subject responsive to treatment with said Abituzumab, wherein said protein level is

(i) classified as high, if the respective specific protein level in said at least one body fluid sample is at least 2 % higher than the median threshold for the respective specific protein, and

(ii) classified as low, if the respective specific protein level in said at least one body fluid sample is at least 2 % lower than the median threshold for the respective specific protein.