Fisher R.E. J Nucl Med, 49: 899-906 (2008); Franklin, WA *et al. Int J Cancer*, Suppl 8: 89-95 (1994); Hartman L.C. *et al. Int J Cancer* 121: 938-942 (2007); Iwakiri S *et al. Annals of Surgical Oncology*, 15(3): 889-899; Parker N. *et al. Analytical Biochemistry*, 338: 284-293 (2005); Weitman, SD *et al. Cancer Res* 52: 3396-3401 (1992); Saba N.F. *et al. Head Neck*, 31(4): 475-481 (2009); Yang R *et al. Clin Cancer Res* 13: 2557-2567 (2007). In some types of cancers (*e.g.*, squamous cell carcinoma of the head and neck), a higher level of FRα expression is associated with a worse prognosis, whereas in other types of cancers (*e.g.*, non-small-cell lung cancers), a higher level of FRα expression is associated with a better prognosis. See, *e.g.*, Iwakiri S *et al. Annals of Surgical Oncology*, 15(3): 889-899; Saba N.F. *et al. Head Neck*, 31(4): 475-481 (2009).

Earlier detection of cancer improves survival rates and quality of life. To improve the likelihood of early detection and treatment, a pressing need exists for non-invasive methods for diagnosing cancer, for determining the level of risk of developing cancer, and for predicting the progression of cancer. The present invention satisfies these needs for FRα-expressing cancers.

SUMMARY

The present disclosure provides methods of assessing whether a subject is afflicted with FRα-expressing cancers such as lung or ovarian cancer, methods of assessing the progression of FRα-expressing cancers such as lung or ovarian cancer in a subject afflicted with the FRα-expressing cancers, methods of stratifying an FRα-expressing cancer subject into one of at least four cancer therapy groups, methods of assessing the efficacy of MORAb-003 treatment of ovarian cancer or lung cancer and kits for assessing whether a subject is afflicted with FRα-expressing cancers such as lung or ovarian cancer or for assessing the progression of FRα-expressing cancers such as lung or ovarian cancer in a subject.

Methods of Assessing Whether a Subject is Afflicted with an FRα Expressing Cancer

In a first example, the present disclosure provides a method of assessing whether a subject is afflicted with an FRα-expressing cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample, wherein a difference between the level of FRα in

the sample derived from the subject and the level of FRα in the control sample is an indication that the subject is afflicted with an FRα-expressing cancer; wherein the level of FRα in the sample derived from the subject is assessed by contacting the sample with an antibody that binds FRα. In a particular example, the sample is either urine, serum, plasma or ascites.

In one aspect, the present disclosure refers to a method of assessing whether a subject is afflicted with ovarian or lung cancer, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample;

identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample; and

determining that the subject is afflicted with ovarian or lung cancer based on said increase.

In another example, the present disclosure is directed to a method of assessing whether a subject is afflicted with an FRα-expressing cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the urine sample derived from the subject with the level of FRα in a control sample, wherein a difference between the level of FRα in the urine sample derived from the subject and the level of FRα in the control sample is an indication that the subject is afflicted with an FRα-expressing cancer. In a further example, the present disclosure provides a method of assessing whether a subject is afflicted with a cancer that expresses FRα, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the serum sample derived from the subject with the level of FRα in a control sample, wherein a difference between the level of FRα in the serum sample derived from the subject and the level of FRα in the control sample is an indication that the subject is afflicted with an FRα-expressing cancer.

In another aspect, the present disclosure refers to a method of assessing whether a subject is afflicted with folate receptor alpha (FRα)-expressing ovarian cancer or lung cancer, the method comprising

determining the level of FRα which is not bound to a cell in a serum or plasma sample derived from said subject; and

comparing the level of FRα which is not bound to a cell with the level of FRα in a control sample,

identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample; and

determining that the subject is afflicted with ovarian cancer or lung cancer based upon said increase,

wherein the level of FRα which is not bound to a cell in the serum or plasma sample derived from said subject is assessed by contacting the serum or plasma sample with a pair of antibodies that bind FRα in a two-antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA).

In various examples of the foregoing examples of the disclosure, the FRα-expressing cancer is selected from the group consisting of lung cancer, mesothelioma, ovarian cancer, renal cancer, brain cancer, cervical cancer, nasopharyngeal cancer, squamous cell carcinoma of the head and neck, endometrial cancer, breast cancer, bladder cancer, pancreatic cancer, bone cancer, pituitary cancer, colorectal cancer and medullary thyroid cancer. In a particular example, the FRα-expressing cancer is ovarian cancer. In another example, the FRα-expressing cancer is non-small cell lung cancer, such as an adenocarcinoma.

In another example, the present disclosure is directed to methods of assessing whether a subject is afflicted with ovarian cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject, wherein the presence of FRα which is not bound to a cell in the urine sample at

a concentration of greater than about 9100 pg/ml is an indication that the subject is afflicted with ovarian cancer.

In various examples of the foregoing examples of the disclosure, the presence of FRα in the urine sample at a concentration of greater than about 9500 pg/mL, about 10,000 pg/mL, about 11,000 pg/mL, about 12,000 pg/mL, about 13,000 pg/mL, about 14,000 pg/mL, about 15,000 pg/mL, about 16,000 pg/mL, about 17,000 pg/mL, about 18,000 pg/mL, about 19,000 pg/mL, or about 20,000 pg/mL is an indication that the subject is afflicted with ovarian cancer.

In various examples, the level of FRα is determined by contacting the sample with an antibody that binds FRα. For example, the antibody is selected from the group consisting of:

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that binds the same epitope as the 6D398 antibody;

(i) an antibody that binds the same epitope as the 26B3 antibody;

(j) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1 , SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3;

(k) the 26B3 antibody;

(l) an antibody that binds the same epitope as the 19D4 antibody;

(m) an antibody comprising SEQ ID NO:39 (HPYMH) as CDRH1, SEQ ID NO:40 (RIDPANGNTKYDPKFQG) as CDRH2, SEQ ID NO:41 (EEVADYTMDY) as CDRH3, SEQ ID NO:35 (RASESVDTYGNNFIH) as CDRL1, SEQ ID NO:36 (LASNLES) as CDRL2 and SEQ ID NO:37 (QQNNGDPWT) as CDRL3;

(n) the 19D4 antibody;

(o) an antibody that binds the same epitope as the 9F3 antibody;

(p) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3;

(q) the 9F3 antibody;

(r) an antibody that binds the same epitope as the 24F12 antibody;

(s) an antibody comprising SEQ ID NO:47 (SYAMS) as CDRH1, SEQ ID NO:48 (EIGSGGSYTYYPDTVTG) as CDRH2, SEQ ID NO:49 (ETTAGYFDY) as CDRH3, SEQ ID NO:43 (SASQGINNFLN) as CDRL1, SEQ ID NO:44 (YTSSLHS) as CDRL2 and SEQ ID NO:45 (QHFSKLPWT) as CDRL3;

(t) the 24F12 antibody;

(u) an antibody that comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16);

(v) an antibody that comprises a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21);

(w) an antibody that comprises the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16);

(x) an antibody that comprises the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); and

(y) an antibody that comprises the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the antibody binds the same epitope as the MORAb-003 antibody. In another example, the antibody includes SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as

CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3. In another example, the antibody is the MOV18 antibody. In yet another example, the antibody binds the same epitope as the MOV18 antibody. In a further example, the antibody comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16). Alternatively or in combination, the antibody includes a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21). In certain examples, the antibody includes (i) the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); or the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the level of FRα in the sample derived from said subject is assessed by contacting the sample with a pair of antibodies selected from the group consisting of (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody; (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody; (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody; and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody.

In certain examples, the antibody is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody. Alternatively, or in combination, the antibody is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In certain examples, the level of FRα is determined by using a technique selected from the group consisting of western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion,

solution phase assay, electrochemiluminescence immunoassay (ECLIA) and ELISA assay.

In various examples of the foregoing examples of the disclosure, the control sample is a standardized control level of FRα in a healthy subject.

In certain examples, the sample is treated with guanidine prior to determining the level of FRα in the sample. Alternatively or in combination, the sample is diluted prior to determining the level of FRα in the sample. Alternatively, or in combination, the sample is centrifuged, vortexed, or both, prior to determining the level of FRα in the sample.

In yet another example, the present disclosure is directed to a method of assessing whether a subject is afflicted with ovarian cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the sample with the level of FRα in a control sample, wherein a difference between the levels of FRα in the sample derived from the subject and in the control sample is an indication that the subject is afflicted with ovarian cancer; wherein the level of FRα in the sample derived from the subject is assessed by contacting the sample with (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody, (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody, (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody, and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody. For example, the sample may be urine, serum, plasma or ascites.

Methods of Assessing the Progression of an FRα Expressing Cancer in a Subject

In a further example, the present disclosure is directed to a method of assessing the progression of an FRα-expressing cancer in a subject afflicted with an FRα-expressing cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample, wherein an increase in the level of FRα in the sample derived from the subject as compared with the level of FRα in the control sample is an indication that the cancer will progress rapidly; and wherein a decrease in the level of FRα in the sample derived from the subject as compared with the level of FRα in the control sample is an indication that

the cancer will progress slowly or will regress, thereby assessing the progression of the FRα-expressing cancer in the subject; wherein the level of FRα which is not bound to a cell in the sample derived from the subject is assessed by contacting the sample with an antibody that binds FRα. In a particular example, the sample is urine, serum, plasma or ascites.

In another aspect, the present disclosure refers to a method of assessing the progression of ovarian cancer in a subject afflicted with ovarian cancer, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress rapidly based on said increase; or

(ii) identifying a decrease in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress slowly based on said decrease.

In another example, the present disclosure provides a method of assessing the progression of an FRα-expressing cancer in a subject afflicted with an FRα-expressing cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the urine sample derived from the subject with the level of FRα in a control sample, wherein an increase in the level of FRα in the urine sample derived from the subject as compared with the level of FRα in the control sample is an indication that the cancer will progress rapidly; and wherein a decrease in the level of FRα in the urine sample derived from the subject as compared with the level of FRα in the control sample is an indication that the cancer will progress slowly or will regress, thereby assessing the progression of the FRα-expressing cancer in the subject.

In a further example, the present disclosure provides methods of assessing the progression of an FRα-expressing cancer in a subject afflicted with an

FRα-expressing cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the serum sample derived from the subject with the level of FRα in control sample, wherein an increase in the level of FRα in the serum sample derived from the subject as compared with the level of FRα in the control sample is an indication that the cancer will progress rapidly; and wherein a decrease in the level of FRα in the serum sample derived from the subject as compared with the level of FRα in the control sample is an indication that the cancer will progress slowly or will regress, thereby assessing the progression of the FRα-expressing cancer in the subject.

In another aspect, the present disclosure refers to a method of assessing the progression of ovarian cancer in a subject afflicted with ovarian cancer, the method comprising

determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum or plasma sample derived from said subject by performing a two antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA);

comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress rapidly based on said increase; or

(ii) identifying a decrease in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress slowly based on said decrease.

In various examples of the foregoing examples of the disclosure, the FRα-expressing cancer is selected from the group consisting of lung cancer, mesothelioma, ovarian cancer, renal cancer, brain cancer, cervical cancer, nasopharyngeal cancer, squamous cell carcinoma of the head and neck, endometrial cancer, breast cancer,

bladder cancer, pancreatic cancer, bone cancer, pituitary cancer, colorectal cancer and medullary thyroid cancer. In a particular example, the FRα-expressing cancer is ovarian cancer. In another example, the FRα-expressing cancer is non-small cell lung cancer, such as an adenocarcinoma.

In another example, the present disclosure is directed to methods of assessing whether a subject is afflicted with ovarian cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject, wherein the presence of FRα which is not bound to a cell in the urine sample at a concentration of greater than about 9100 pg/ml is an indication that the subject is afflicted with ovarian cancer.

In various examples of the foregoing examples of the disclosure, the presence of FRα in the urine sample at a concentration of greater than about 9500 pg/mL, about 10,000 pg/mL, about 11,000 pg/mL, about 12,000 pg/mL, about 13,000 pg/mL, about 14,000 pg/mL, about 15,000 pg/mL, about 16,000 pg/mL, about 17,000 pg/mL, about 18,000 pg/mL, about 19,000 pg/mL, or about 20,000 pg/mL is an indication that the subject is afflicted with ovarian cancer.

In various examples, the level of FRα is determined by contacting the sample with an antibody that binds FRα. For example, the antibody is selected from the group consisting of:

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that binds the same epitope as the 6D398 antibody;

(i) an antibody that binds the same epitope as the 26B3 antibody;

(j) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as

(x) an antibody that comprises the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); and

(y) an antibody that comprises the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the antibody binds the same epitope as the MORAb-003 antibody. In another example, the antibody includes SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3. In another example, the antibody is the MOV18 antibody. In yet another example, the antibody binds the same epitope as the MOV18 antibody. In a further example, the antibody comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16). Alternatively or in combination, the antibody includes a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21). In certain examples, the antibody includes (i) the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); or the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the level of FRα in the sample derived from said subject is assessed by contacting the sample with a pair of antibodies selected from the group consisting of (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody; (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody; (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody; and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody.

In certain examples, the antibody is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody. Alternatively, or in combination, the antibody is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In certain examples, the level of FRα is determined by using a technique selected from the group consisting of western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, solution phase assay, electrochemiluminescence immunoassay (ECLIA) and ELISA assay.

In various examples of the foregoing examples of the disclosure, the control sample is a standardized control level of FRα in a healthy subject. In another example, the control sample is a sample previously obtained from the subject.

In certain examples, the sample is treated with guanidine prior to determining the level of FRα in the sample. Alternatively or in combination, the sample is diluted prior to determining the level of FRα in the sample. Alternatively, or in combination, the sample is centrifuged, vortexed, or both, prior to determining the level of FRα in the sample.

In a further example, the present disclosure provides methods of assessing the progression of ovarian cancer in a subject afflicted with ovarian cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the sample with the level of FRα in a control sample, wherein an increase in the level of FRα in the sample derived from the subject as compared with the level of FRα in the control sample is an indication that the ovarian cancer will progress rapidly; and wherein a decrease in the level of FRα in the sample derived from the subject as compared with the level of FRα in the control sample is an indication that the ovarian cancer will progress slowly or will regress, thereby assessing the progression of ovarian cancer in the subject; wherein the level of FRα in the sample derived from the subject is assessed by contacting the sample with (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody, (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody, (c) 26B3 antibody immobilized to a solid

support and labeled 19D4 antibody, and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody. For example, the sample may be urine, serum, plasma or ascites.

Methods of Stratifying an FRα Expressing Cancer into Cancer Therapy Groups

In a further example, the present disclosure provides a method of stratifying a subject afflicted with an FRα-expressing cancer into one of at least four cancer therapy groups by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a sample derived from the subject; and stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell; wherein the level of FRα which is not bound to a cell in the sample derived from the subject is assessed by contacting the sample with an antibody that binds FRα. For example, the sample is selected from the group consisting of urine, serum, plasma or ascites.

In another aspect, the present disclosure refers to a method of stratifying a subject afflicted with ovarian cancer into one of at least four cancer therapy groups comprising:

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell.

In another aspect, the present disclosure refers to a method of stratifying a subject afflicted with ovarian cancer into one of at least four cancer therapy groups comprising:

determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a serum or plasma sample derived from said subject by performing a two antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA); and

stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell.

In yet another example, the present disclosure provides a method of stratifying a subject afflicted with an FRα-expressing cancer into one of at least four cancer therapy groups by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject; and stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell in the sample. In a further example, the present disclosure is directed to methods of stratifying a subject afflicted with an FRα-expressing cancer into one of at least four cancer therapy groups by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum sample derived from the subject; and stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell in the serum sample.

In various examples of the foregoing examples of the disclosure, the FRα-expressing cancer is selected from the group consisting of lung cancer, mesothelioma, ovarian cancer, renal cancer, brain cancer, cervical cancer, nasopharyngeal cancer, squamous cell carcinoma of the head and neck, endometrial cancer, breast cancer, bladder cancer, pancreatic cancer, bone cancer, pituitary cancer, colorectal cancer and medullary thyroid cancer. In a particular example, the FRα-expressing cancer is ovarian cancer. In another example, the FRα-expressing cancer is non-small cell lung cancer, such as an adenocarcinoma.

In another example, the present disclosure is directed to methods of assessing whether a subject is afflicted with ovarian cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject, wherein the presence of FRα which is not bound to a cell in the urine sample at a concentration of greater than about 9100 pg/ml is an indication that the subject is afflicted with ovarian cancer.

In various examples of the foregoing examples of the disclosure, the presence of FRα in the urine sample at a concentration of greater than about 9500 pg/mL, about 10,000 pg/mL, about 11,000 pg/mL, about 12,000 pg/mL, about 13,000 pg/mL, about 14,000 pg/mL, about 15,000 pg/mL, about 16,000 pg/mL, about 17,000 pg/mL, about 18,000 pg/mL, about 19,000 pg/mL, or about 20,000 pg/mL is an indication that the subject is afflicted with ovarian cancer.

In various examples, the level of FRα is determined by contacting the sample with an antibody that binds FRα. For example, the antibody is selected from the group consisting of:

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that binds the same epitope as the 6D398 antibody;

(i) an antibody that binds the same epitope as the 26B3 antibody;

(j) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1 , SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3;

(k) the 26B3 antibody;

(l) an antibody that binds the same epitope as the 19D4 antibody;

In a particular example, the antibody binds the same epitope as the MORAb-003 antibody. In another example, the antibody includes SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3. In another example, the antibody is the MOV18 antibody. In yet another example, the antibody binds the same epitope as the MOV18 antibody. In a further example, the antibody comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16). Alternatively or in combination, the antibody includes a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21). In certain examples, the antibody includes (i) the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); or the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the level of FRα in the sample derived from said subject is assessed by contacting the sample with a pair of antibodies selected from the group consisting of (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody; (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody; (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody; and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody.

In certain examples, the antibody is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody. Alternatively, or in combination, the antibody is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In certain examples, the level of FRα is determined by using a technique selected from the group consisting of western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, solution phase assay, electrochemiluminescence immunoassay (ECLIA) and ELISA assay.

In various examples of the foregoing examples of the disclosure, the control sample is a standardized control level of FRα in a healthy subject.

In certain examples, the sample is treated with guanidine prior to determining the level of FRα in the sample. Alternatively or in combination, the sample is diluted prior to determining the level of FRα in the sample. Alternatively, or in combination, the sample is centrifuged, vortexed, or both, prior to determining the level of FRα in the sample.

In a particular example, the subject is stratified in Stage I, Stage II, Stage III or Stage IV ovarian cancer.

In a further example, the present disclosure provides a method of stratifying an ovarian cancer subject into one of at least four cancer therapy groups by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell in the sample; wherein the level of FRα in the sample derived from the subject is assessed by contacting the sample with (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody, (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody, (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody, and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody. For example, the sample may be urine, serum, plasma or ascites.

Methods of Monitoring the Efficacy of MORAb-003 Treatment of Ovarian Cancer or Lung Cancer

In one example, the present disclosure provides a method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer or lung cancer in a subject suffering from ovarian cancer or lung cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a sample derived from the subject, wherein the subject has been previously administered MORAb-003; and comparing the level of folate

receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample, wherein an increase in the level of FRα in the sample derived from the subject as compared with the level of FRα in the control sample is an indication that the MORAb-003 treatment is not efficacious; and wherein a decrease in the level of FRα in the sample derived from the subject as compared with the level of FRα in the control sample is an indication that the MORAb-003 treatment is efficacious. In particular examples, the level of FRα which is not bound to a cell in the sample derived from the subject is assessed by contacting the sample with an antibody that binds FRα. For example, the sample may be urine, serum, plasma or ascites.

In another aspect, the present disclosure refers to a method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer in a subject suffering from ovarian cancer, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample, wherein said subject has been previously administered MORAb-003;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is not efficacious; or

(ii) identifying a decrease in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is efficacious.

In a further example, the present disclosure provides a method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer or lung cancer in a subject suffering from ovarian cancer or lung cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject, wherein the subject has been previously administered MORAb-003; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the urine sample derived from the subject with the level of FRα in a control sample, wherein an increase in the level of FRα in the urine sample derived from the subject as compared

with the level of FRα in the control sample is an indication that the MORAb-003 treatment is not efficacious; and wherein a decrease in the level of FRα in the urine sample derived from the subject as compared with the level of FRα in the control sample is an indication that the MORAb-003 treatment is efficacious.

In yet another example, the present disclosure is directed to a method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer or lung cancer in a subject suffering from ovarian cancer or lung cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum sample derived from the subject, wherein the subject has been previously administered MORAb-003; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the serum sample derived from the subject with the level of FRα in a control sample, wherein an increase in the level of FRα in the serum sample derived from the subject as compared with the level of FRα in the control sample is an indication that the MORAb-003 treatment is not efficacious; and wherein a decrease in the level of FRα in the serum sample derived from the subject as compared with the level of FRα in the control sample is an indication that the MORAb-003 treatment is efficacious.

In another aspect, the present disclosure refers to a method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer in a subject suffering from ovarian cancer, the method comprising

determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum or plasma sample derived from said subject by performing a two antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA), wherein said subject has been previously administered MORAb-003;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said serum or plasma sample derived from said subject with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is not efficacious; or

(ii) identifying a decrease in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is efficacious.

In various examples, the level of FRα is determined by contacting the sample with an antibody that binds FRα. For example, the antibody is selected from the group consisting of:

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that binds the same epitope as the 6D398 antibody;

(i) an antibody that binds the same epitope as the 26B3 antibody;

(j) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1 , SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3;

(k) the 26B3 antibody;

(l) an antibody that binds the same epitope as the 19D4 antibody;

(m) an antibody comprising SEQ ID NO:39 (HPYMH) as CDRH1, SEQ ID NO:40 (RIDPANGNTKYDPKFQG) as CDRH2, SEQ ID NO:41 (EEVADYTMDY) as CDRH3, SEQ ID NO:35 (RASESVDTYGNNFIH) as CDRL1, SEQ ID NO:36 (LASNLES) as CDRL2 and SEQ ID NO:37 (QQNNGDPWT) as CDRL3;

(n) the 19D4 antibody;

(o) an antibody that binds the same epitope as the 9F3 antibody;

(p) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3;

(q) the 9F3 antibody;

(r) an antibody that binds the same epitope as the 24F12 antibody;

(s) an antibody comprising SEQ ID NO:47 (SYAMS) as CDRH1, SEQ ID NO:48 (EIGSGGSYTYYPDTVTG) as CDRH2, SEQ ID NO:49 (ETTAGYFDY) as CDRH3, SEQ ID NO:43 (SASQGINNFLN) as CDRL1, SEQ ID NO:44 (YTSSLHS) as CDRL2 and SEQ ID NO:45 (QHFSKLPWT) as CDRL3;

(t) the 24F12 antibody;

(u) an antibody that comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16);

(v) an antibody that comprises a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21);

(w) an antibody that comprises the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16);

(x) an antibody that comprises the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); and

(y) an antibody that comprises the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the antibody binds the same epitope as the MORAb-003 antibody. In another example, the antibody includes SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3. In another example, the antibody is the MOV18 antibody. In yet another example, the antibody binds the same epitope as the MOV18 antibody. In a further example, the antibody comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16). Alternatively or in combination, the antibody includes a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH

FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21). In certain examples, the antibody includes (i) the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); or the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the level of FRα in the sample derived from said subject is assessed by contacting the sample with a pair of antibodies selected from the group consisting of (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody; (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody; (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody; and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody.

In certain examples, the antibody is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody. Alternatively, or in combination, the antibody is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In certain examples, the level of FRα is determined by using a technique selected from the group consisting of western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, solution phase assay, electrochemiluminescence immunoassay (ECLIA) and ELISA assay.

In various examples of the foregoing examples of the disclosure, the control sample is a standardized control level of FRα in a healthy subject. In another example, the control sample is a sample previously obtained from the subject.

In certain examples, the sample is treated with guanidine prior to determining the level of FRα in the sample. Alternatively or in combination, the sample is diluted prior to determining the level of FRα in the sample. Alternatively, or in

combination, the sample is centrifuged, vortexed, or both, prior to determining the level of FRα in the sample.

Methods of Predicting Whether a Subject Will Respond to MORAb-003 treatment

In one example, the present disclosure provides a method for predicting whether a subject suffering from an FRα expressing cancer, such as ovarian cancer or lung cancer, will respond to treatment with MORAb-003, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the sample derived from the subject with the level of FRα in a control sample, wherein a difference between the level of FRα in the sample derived from the subject and the level of FRα in the control sample is an indication that the subject will respond to treatment with MORAb-003.

In another aspect, the present disclosure refers to a method for predicting whether a subject suffering from ovarian cancer will respond to treatment with MORAb-003, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the subject will respond to treatment with MORAb-003.

In one example, the present disclosure provides a method for predicting whether a subject suffering from an FRα expressing cancer, such as ovarian cancer or lung cancer, will respond to treatment with MORAb-003, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the urine sample derived from the subject with the level of FRα in a control sample, wherein a difference between the level of FRα in the urine sample

derived from the subject and the level of FRα in the control sample is an indication that the subject will respond to treatment with MORAb-003.

In a further example, the present disclosure provides a method for predicting whether a subject suffering from an FRα expressing cancer, such as ovarian cancer or lung cancer, will respond to treatment with MORAb-003, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the serum sample derived from the subject with the level of FRα in a control sample, wherein a difference between the level of FRα in the serum sample derived from the subject and the level of FRα in the control sample is an indication that the subject will respond to treatment with MORAb-003.

In another aspect, the present disclosure refers to a method for predicting whether a subject suffering from ovarian cancer will respond to treatment with MORAb-003, the method comprising

determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum or plasma sample derived from said subject,

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the serum or plasma sample derived from said subject with the level of FRα in a control sample,

identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the subject will respond to treatment with MORAb-003,

wherein the level of FRα which is not bound to a cell in the serum or plasma sample derived from said subject is assessed by contacting the serum or plasma sample with a pair of antibodies that bind FRα in a two-antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA).

In further examples, the FRα-expressing cancer is selected from the group consisting of lung cancer, mesothelioma, ovarian cancer, renal cancer, brain cancer,

cervical cancer, nasopharyngeal cancer, squamous cell carcinoma of the head and neck, endometrial cancer, breast cancer, bladder cancer, pancreatic cancer, bone cancer, pituitary cancer, colorectal cancer and medullary thyroid cancer. In a particular example, the FRα-expressing cancer is ovarian cancer. In another example, the FRα-expressing lung cancer is non-small cell lung cancer, such as adenocarcinoma.

In a further example, the present disclosure provides methods for predicting whether a subject suffering from ovarian cancer will respond to treatment with MORAb-003, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject, wherein the presence of FRα which is not bound to a cell in the urine sample at a concentration of greater than about 9100 pg/ml is an indication that the subject will respond to treatment with MORAb-003.

In various examples of the foregoing examples of the disclosure, the presence of FRα in the urine sample at a concentration of greater than about 9500 pg/mL, about 10,000 pg/mL, about 11,000 pg/mL, about 12,000 pg/mL, about 13,000 pg/mL, about 14,000 pg/mL, about 15,000 pg/mL, about 16,000 pg/mL, about 17,000 pg/mL, about 18,000 pg/mL, about 19,000 pg/mL, or about 20,000 pg/mL is an indication that the subject is afflicted with ovarian cancer.

In various examples of the foregoing examples of the disclosure, the level of FRα is determined by contacting the sample with an antibody that binds FRα. For example, the antibody is selected from the group consisting of:

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that binds the same epitope as the 6D398 antibody;

(i) an antibody that binds the same epitope as the 26B3 antibody;

(x) an antibody that comprises the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); and

(y) an antibody that comprises the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the antibody binds the same epitope as the MORAb-003 antibody. In another example, the antibody includes SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3. In another example, the antibody is the MOV18 antibody. In yet another example, the antibody binds the same epitope as the MOV18 antibody. In a further example, the antibody comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16). Alternatively or in combination, the antibody includes a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21). In certain examples, the antibody includes (i) the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); or the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the level of FRα in the sample derived from said subject is assessed by contacting the sample with a pair of antibodies selected from the group consisting of (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody; (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody; (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody; and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody.

In certain examples, the antibody is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody. Alternatively, or in combination, the antibody is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In certain examples, the level of FRα is determined by using a technique selected from the group consisting of western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, solution phase assay, electrochemiluminescence immunoassay (ECLIA) and ELISA assay.

In various examples of the foregoing examples of the disclosure, the control sample is a standardized control level of FRα in a healthy subject.

In certain examples, the sample is treated with guanidine prior to determining the level of FRα in the sample. Alternatively or in combination, the sample is diluted prior to determining the level of FRα in the sample. Alternatively, or in combination, the sample is centrifuged, vortexed, or both, prior to determining the level of FRα in the sample.

In a further example, the present disclosure provides a method for predicting whether a subject suffering from an FRα expressing cancer, such as ovarian cancer or lung cancer, will respond to treatment with MORAb-003, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the sample with the level of FRα in a control sample, wherein a difference between the levels of FRα in the sample derived from the subject and in the control sample is an indication that the subject will respond to treatment with MORAb-003; wherein the level of FRα in the sample derived from the subject is assessed by contacting the sample with (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody, (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody, (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody, and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody. For example, the sample may be urine, serum, plasma or ascites.

In various examples of the foregoing examples of the disclosure, the MORAb-003 for treatment is (a) an antibody that comprises the heavy chain amino acid sequence as set forth in SEQ ID NO:7 and the light chain amino acid sequence as set forth in SEQ ID NO:8; (b) an antibody that binds the same epitope as the MORAb-003 antibody; or (c) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3.

Methods of Treating a Subject Having Ovarian Cancer or Lung Cancer

In another example, the present disclosure provides methods of treating a subject having ovarian cancer or lung cancer by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a sample derived from said subject (for example, urine, serum, plasma or ascites); and comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample, wherein a difference between the level of FRα in the sample derived from said subject and the level of FRα in the control sample is an indication that the subject is afflicted with ovarian cancer or lung cancer; and administering a therapeutically effective amount of MORAb-003 to said subject.

In another example, the present disclosure provides methods of treating a subject having ovarian cancer or lung cancer by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a urine sample derived from said subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample, wherein a difference between the level of FRα in the urine sample derived from said subject and the level of FRα in the control sample is an indication that the subject is afflicted with ovarian cancer or lung cancer; and administering a therapeutically effective amount of MORAb-003 to said subject.

In another example, the present disclosure provides methods of treating a subject having ovarian cancer or lung cancer by determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a serum sample derived from said subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample, wherein a difference between the level of FRα in the serum sample derived from said subject and the level of FRα in the control sample is an

indication that the subject is afflicted with ovarian cancer or lung cancer; and administering a therapeutically effective amount of MORAb-003 to said subject.

In a further example, the present disclosure provides methods for treating a subject suffering from ovarian cancer by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a urine sample derived from the subject, wherein the presence of FRα which is not bound to a cell in the urine sample at a concentration of greater than about 9100 pg/ml is an indication that the subject will respond to treatment with MORAb-003; and administering a therapeutically effective amount of MORAb-003 to said subject.

In particular examples, the level of FRα which is not bound to a cell in the sample derived from said subject is assessed by contacting the sample with an antibody that binds FRα.

In various examples of the foregoing examples of the disclosure, the presence of FRα in the urine sample at a concentration of greater than about 9500 pg/mL, about 10,000 pg/mL, about 11,000 pg/mL, about 12,000 pg/mL, about 13,000 pg/mL, about 14,000 pg/mL, about 15,000 pg/mL, about 16,000 pg/mL, about 17,000 pg/mL, about 18,000 pg/mL, about 19,000 pg/mL, or about 20,000 pg/mL is an indication that the subject is afflicted with ovarian cancer.

In various examples of the foregoing examples of the disclosure, the level of FRα is determined by contacting the sample with an antibody that binds FRα. For example, the antibody is selected from the group consisting of:

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that binds the same epitope as the 6D398 antibody;

(i) an antibody that binds the same epitope as the 26B3 antibody;

(x) an antibody that comprises the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); and

(y) an antibody that comprises the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the antibody binds the same epitope as the MORAb-003 antibody. In another example, the antibody includes SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3. In another example, the antibody is the MOV18 antibody. In yet another example, the antibody binds the same epitope as the MOV18 antibody. In a further example, the antibody comprises a variable region light chain selected from the group consisting of LK26HuVK (SEQ ID NO: 13); LK26HuVKY (SEQ ID NO: 14); LK26HuVKPW (SEQ ID NO: 15); and LK26HuVKPW,Y (SEQ ID NO: 16). Alternatively or in combination, the antibody includes a variable region heavy chain selected from the group consisting of LK26HuVH (SEQ ID NO: 17); LK26HuVH FAIS,N (SEQ ID NO: 18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21). In certain examples, the antibody includes (i) the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); or the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In a particular example, the level of FRα in the sample derived from said subject is assessed by contacting the sample with a pair of antibodies selected from the group consisting of (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody; (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody; (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody; and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody.

In certain examples, the antibody is selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, SMIP, affibody, avimer, versabody, nanobody, and a domain antibody. Alternatively, or in combination, the antibody is labeled, for example, with a label selected from the group consisting of a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In certain examples, the level of FRα is determined by using a technique selected from the group consisting of western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, solution phase assay, electrochemiluminescence immunoassay (ECLIA) and ELISA assay.

In various examples of the foregoing examples of the disclosure, the control sample is a standardized control level of FRα in a healthy subject.

In certain examples, the sample is treated with guanidine prior to determining the level of FRα in the sample. Alternatively or in combination, the sample is diluted prior to determining the level of FRα in the sample. Alternatively, or in combination, the sample is centrifuged, vortexed, or both, prior to determining the level of FRα in the sample.

In a further example, the present disclosure provides a method for treating a subject suffering from ovarian cancer or lung cancer, by determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the sample with the level of FRα in a control sample, wherein a difference between the levels of FRα in the sample derived from the subject and in the control sample is an indication that the subject will respond to treatment with MORAb-003; wherein the level of FRα in the sample derived from the subject is assessed by contacting the sample with (a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody, (b) 9F3 antibody immobilized to a solid support and labeled 24F12 antibody, (c) 26B3 antibody immobilized to a solid support and labeled 19D4 antibody, and (d) 9F3 antibody immobilized to a solid support and labeled 26B3 antibody. For example, the sample may be urine, serum, plasma or ascites.

In various examples of the foregoing examples of the disclosure, the MORAb-003 for treatment is (a) an antibody that comprises the heavy chain amino acid sequence

as set forth in SEQ ID NO:7 and the light chain amino acid sequence as set forth in SEQ ID NO:8; (b) an antibody that binds the same epitope as the MORAb-003 antibody; or (c) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3.

Kits of the Disclosure

In one example, the present disclosure provides a kit for assessing whether a subject is afflicted with an FRα-expressing cancer or for assessing the progression of an FRα-expressing cancer in a subject, the kit including means for determining the level of folate receptor alpha (FRα) which is not bound to a cell in a sample derived from the subject; and instructions for use of the kit to assess whether the subject is afflicted with an FRα-expressing cancer or to assess the progression of an FRα-expressing cancer. For example, the FRα-expressing cancer is selected from the group consisting of lung cancer, mesothelioma, ovarian cancer, renal cancer, brain cancer, cervical cancer, nasopharyngeal cancer, squamous cell carcinoma of the head and neck, endometrial cancer, breast cancer, bladder cancer, pancreatic cancer, bone cancer, pituitary cancer, colorectal cancer and medullary thyroid cancer. In a particular example, the FRα-expressing cancer is ovarian cancer. In yet another example, the FRα-expressing cancer is non-small cell lung cancer, for example, adenocarcinoma. In a further example, the sample is either urine, serum, plasma or ascites.

In a further example, the means includes a folate receptor alpha (FRα) binding agent, for example, an antibody. In a further example, the antibody is selected from the group consisting of

(a) an antibody that binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

18); LK26HuVH SLF (SEQ ID NO: 19); LK26HuVH I,I (SEQ ID NO: 20); and LK26KOLHuVH (SEQ ID NO: 21);

(w) an antibody that comprises the heavy chain variable region LK26KOLHuVH (SEQ ID NO: 21) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16);

(x) an antibody that comprises the heavy chain variable region LK26HuVH SLF (SEQ ID NO: 19) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16); and

(y) an antibody that comprises the heavy chain variable region LK26HuVH FAIS,N (SEQ ID NO: 18) and the light chain variable region LK26HuVKPW,Y (SEQ ID NO: 16).

In certain examples, the antibody is labeled including, but not limited to, a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, or an enzyme-label.

In yet another example, the kit includes a means for obtaining a sample from the subject.

The present disclosure is further illustrated by the following detailed description and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic depiction of an electrochemiluminescence immunoassay (ECLIA) method for assessing the FRα in urine as described in the Examples. MOV18 antibody attached to solid supports bound FRα in urine. The FRα was subsequently detected by binding to Ru-labeled MORAb-003 antibody.

Figure 2 shows the distribution of FRα levels in the urine of ovarian cancer subjects and normal control subjects as measured by ECLIA (see Example 1).

Figure 3 depicts the detection of FRα in urine of ovarian cancer patients (pale band on lane 1, clear band on lane 2) using immunoblotting (see Example 5).

Figure 4 shows the distribution of FRα levels in the urine of ovarian cancer subjects and normal control subjects as measured by ECLIA after the urine was treated with guanidine, as described in Example 7.

Figure 5 depicts an ROC curve showing the sensitivity and specificity of the ECLIA measurement of FRα levels in urine after the urine was treated with guanidine,

CLAIMS

What is claimed:

1. A method of assessing whether a subject is afflicted with ovarian or lung cancer, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample;

identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample; and

determining that the subject is afflicted with ovarian or lung cancer based on said increase.

2. The method of claim 1, wherein the subject is identified as being afflicted with ovarian cancer.

3. The method of claim 1, wherein the subject is identified as being afflicted with lung cancer.

4. The method of claim 3, wherein the lung cancer is non-small cell lung cancer.

5. The method of claim 4, wherein the non-small cell lung cancer is adenocarcinoma.

6. The method of claim 1, wherein the presence of FRα in said urine sample derived from said subject at a concentration of greater than 9500 pg/mL, 10,000 pg/mL, 11,000 pg/mL, 12,000 pg/mL, 13,000 pg/mL, 14,000 pg/mL, 15,000 pg/mL, 16,000 pg/mL, 17,000 pg/mL, 18,000 pg/mL, 19,000 pg/mL, or 20,000 pg/mL is an indication that the subject is afflicted with ovarian cancer.

7. The method of claim 1, wherein the antibody is:

(a) an antibody that specifically binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that specifically binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that specifically binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that specifically binds the same epitope as the 6D398 antibody;

(i) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 58 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:54;

(j) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1 , SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3;

(k) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 58 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:54;

(l) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:38;

(m) an antibody comprising SEQ ID NO:39 (HPYMH) as CDRH1, SEQ ID NO:40 (RIDPANGNTKYDPKFQG) as CDRH2, SEQ ID NO:41 (EEVADYTMDY) as CDRH3, SEQ

ID NO:35 (RASESVDTYGNNFIH) as CDRL1, SEQ ID NO:36 (LASNLES) as CDRL2 and SEQ ID NO:37 (QQNNGDPWT) as CDRL3;

(n) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:38;

(o) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 34 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:30;

(p) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3;

(q) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 34 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:30;

(r) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 50 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:46;

(s) an antibody comprising SEQ ID NO:47 (SYAMS) as CDRH1, SEQ ID NO:48 (EIGSGGSYTYYPDTVTG) as CDRH2, SEQ ID NO:49 (ETTAGYFDY) as CDRH3, SEQ ID NO:43 (SASQGINNFLN) as CDRL1, SEQ ID NO:44 (YTSSLHS) as CDRL2 and SEQ ID NO:45 (QHFSKLPWT) as CDRL3;

(t) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 50 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:46;

(u) an antibody that comprises a variable region light chain of SEQ ID NO: 13; SEQ ID NO: 14; SEQ ID NO: 15; or SEQ ID NO: 16;

(v) an antibody that comprises a variable region heavy chain of SEQ ID NO: 17; SEQ ID NO: 18; SEQ ID NO: 19; SEQ ID NO: 20; or SEQ ID NO: 21;

(w) an antibody that comprises the heavy chain variable region SEQ ID NO: 21 and the light chain variable region SEQ ID NO: 16;

(x) an antibody that comprises the heavy chain variable region SEQ ID NO: 19 and the light chain variable region SEQ ID NO: 16; or

(y) an antibody that comprises the heavy chain variable region SEQ ID NO: 18 and the light chain variable region SEQ ID NO: 16.

8. The method of claim 1, wherein the antibody is a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, nanobody™, or a domain antibody.

9. The method of claim 1, wherein the antibody is labeled.

10. The method of claim 9, wherein the antibody is labeled with a label that is a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, an ECL label or an enzyme-label.

11. The method of claim 1, wherein the level of FRα is determined by using a technique that is western blot analysis, radioimmunoassay, immunofluorimetry, immunoprecipitation, equilibrium dialysis, immunodiffusion, solution phase assay, electrochemiluminescence immunoassay (ECLIA) or ELISA assay.

12. The method of claim 1, wherein the control sample comprises a standardized control level of FRα in a healthy subject.

13. The method of claim 1, wherein the urine sample derived from said subject is treated with guanidine prior to determining the level of FRα.

14. The method of claim 1, wherein the urine sample derived from said subject is diluted prior to determining the level of FRα.

15. The method of claim 1, wherein the urine sample derived from said subject is centrifuged, vortexed, or both, prior to determining the level of FRα.

16. The method of claim 1, wherein the level of FRα in the urine sample derived from said subject is assessed by contacting the urine sample derived from said subject with a pair of antibodies that are

(a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody,

(b) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3 immobilized to a solid support and a labeled antibody comprising SEQ ID NO:47 (SYAMS) as CDRH1, SEQ ID NO:48 (EIGSGGSYTYYPDTVTG) as CDRH2, SEQ ID NO:49 (ETTAGYFDY) as CDRH3, SEQ ID NO:43 (SASQGINNFLN) as CDRL1, SEQ ID NO:44 (YTSSLHS) as CDRL2 and SEQ ID NO:45 (QHFSKLPWT) as CDRL3,

(c) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1, SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3 immobilized to a solid support and a labeled antibody comprising SEQ ID NO:39 (HPYMH) as CDRH1, SEQ ID NO:40 (RIDPANGNTKYDPKFQG) as CDRH2, SEQ ID NO:41 (EEVADYTMDY) as CDRH3, SEQ ID NO:35 (RASESVDTYGNNFIH) as CDRL1, SEQ ID NO:36 (LASNLES) as CDRL2 and SEQ ID NO:37 (QQNNGDPWT) as CDRL3, or

(d) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3 immobilized to a solid support and a labeled antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1, SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3.

17. A method of assessing the progression of ovarian cancer in a subject afflicted with ovarian cancer, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress rapidly based on said increase; or

(ii) identifying a decrease in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress slowly based on said decrease.

18. A method of stratifying a subject afflicted with ovarian cancer into one of at least four cancer therapy groups comprising:

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell.

19. The method of claim 18, wherein the subject is stratified in Stage I, Stage II, Stage III or Stage IV ovarian cancer.

20. A method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer in a subject suffering from ovarian cancer, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample, wherein said subject has been previously administered MORAb-003;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is not efficacious; or

(ii) identifying a decrease in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is efficacious.

21. A method for predicting whether a subject suffering from ovarian cancer will respond to treatment with MORAb-003, the method comprising

contacting a urine sample derived from said subject with an antibody that binds FRα, thereby determining the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said urine sample derived from said subject with the level of FRα in a control sample; and

identifying an increase in the level of FRα in the urine sample derived from said subject as compared to the level of FRα in the control sample and determining that the subject will respond to treatment with MORAb-003.

22. A method of assessing whether a subject is afflicted with folate receptor alpha (FRα)-expressing ovarian cancer or lung cancer, the method comprising

determining the level of FRα which is not bound to a cell in a serum or plasma sample derived from said subject; and

comparing the level of FRα which is not bound to a cell with the level of FRα in a control sample,

identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample; and

determining that the subject is afflicted with ovarian cancer or lung cancer based upon said increase,

wherein the level of FRα which is not bound to a cell in the serum or plasma sample derived from said subject is assessed by contacting the serum or plasma sample with a pair of antibodies that bind FRα in a two-antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA).

23. The method of claim 22, wherein the subject is identified as being afflicted with ovarian cancer.

24. The method of claim 22, wherein the subject is identified as being afflicted with lung cancer.

25. The method of claim 24, wherein the lung cancer is non-small cell lung cancer.

26. The method of claim 25, wherein the non-small cell lung cancer is adenocarcinoma.

27. The method of claim 22, wherein the antibodies that bind FRα are selected from the group consisting of:

(a) an antibody that specifically binds the same epitope as the MORAb-003 antibody;

(b) an antibody comprising SEQ ID NO:1 (GFTFSGYGLS) as CDRH1, SEQ ID NO:2 (MISSGGSYTYYADSVKG) as CDRH2, SEQ ID NO:3 (HGDDPAWFAY) as CDRH3, SEQ ID NO:4 (SVSSSISSNNLH) as CDRL1, SEQ ID NO:5 (GTSNLAS) as CDRL2 and SEQ ID NO:6 (QQWSSYPYMYT) as CDRL3;

(c) the MOV18 antibody;

(d) an antibody that specifically binds the same epitope as the MOV18 antibody;

(e) the 548908 antibody;

(f) an antibody that specifically binds the same epitope as the 548908 antibody;

(g) the 6D398 antibody;

(h) an antibody that specifically binds the same epitope as the 6D398 antibody;

(i) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 58 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:54;

(j) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1 , SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3;

(k) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 58 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:54;

(l) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:38;

(m) an antibody comprising SEQ ID NO:39 (HPYMH) as CDRH1, SEQ ID NO:40 (RIDPANGNTKYDPKFQG) as CDRH2, SEQ ID NO:41 (EEVADYTMDY) as CDRH3, SEQ ID NO:35 (RASESVDTYGNNFIH) as CDRL1, SEQ ID NO:36 (LASNLES) as CDRL2 and SEQ ID NO:37 (QQNNGDPWT) as CDRL3;

(n) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 42 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:38;

(o) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 34 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:30;

(p) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3;

(q) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 34 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:30;

(r) an antibody that specifically binds the same epitope as an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 50 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:46;

(s) an antibody comprising SEQ ID NO:47 (SYAMS) as CDRH1, SEQ ID NO:48 (EIGSGGSYTYYPDTVTG) as CDRH2, SEQ ID NO:49 (ETTAGYFDY) as CDRH3, SEQ ID NO:43 (SASQGINNFLN) as CDRL1, SEQ ID NO:44 (YTSSLHS) as CDRL2 and SEQ ID NO:45 (QHFSKLPWT) as CDRL3;

(t) an antibody having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 50 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:46;

(u) an antibody that comprises a variable region light chain of SEQ ID NO: 13; SEQ ID NO: 14; SEQ ID NO: 15; or SEQ ID NO: 16;

(v) an antibody that comprises a variable region heavy chain of SEQ ID NO: 17; SEQ ID NO: 18; SEQ ID NO: 19; SEQ ID NO: 20; or SEQ ID NO: 21;

(w) an antibody that comprises the heavy chain variable region SEQ ID NO: 21 and the light chain variable region SEQ ID NO: 16;

(x) an antibody that comprises the heavy chain variable region SEQ ID NO: 19 and the light chain variable region SEQ ID NO: 16; and

(y) an antibody that comprises the heavy chain variable region SEQ ID NO: 18 and the light chain variable region SEQ ID NO: 16.

28. The method of claim 22, wherein the antibodies that bind FRα are selected from the group consisting of a murine antibody, a human antibody, a humanized antibody, a bispecific antibody, a chimeric antibody, a Fab, Fab'2, ScFv, nanobody™, and a domain antibody.

29. The method of claim 22, wherein the level of FRα is determined by electrochemiluminescence immunoassay (ECLIA).

30. The method of claim 22, wherein the control sample comprises a standardized control level of FRα in a healthy subject.

31. The method of claim 22, wherein (i) the serum or plasma sample derived from the subject is treated with guanidine prior to determining the level of FRα, (ii) the serum or plasma sample derived from the subject is diluted prior to determining the level of FRα, and/or (iii) the serum or plasma sample derived from the subject is centrifuged, vortexed, or both, prior to determining the level of FRα.

32. The method of claim 22, wherein the pair of antibodies is selected from the group consisting of:

(a) MOV18 antibody immobilized to a solid support and labeled MORAB-003 antibody,

(b) an antibody comprising SEQ ID NO:31 (SGYYWN) as CDRH1, SEQ ID NO:32 (YIKSDGSNNYNPSLKN) as CDRH2, SEQ ID NO:33 (EWKAMDY) as CDRH3, SEQ ID NO:27 (RASSTVSYSYLH) as CDRL1, SEQ ID NO:28 (GTSNLAS) as CDRL2 and SEQ ID NO:29 (QQYSGYPLT) as CDRL3 immobilized to a solid support and a labeled antibody comprising SEQ ID NO:47 (SYAMS) as CDRH1, SEQ ID NO:48 (EIGSGGSYTYYPDTVTG) as CDRH2, SEQ ID NO:49 (ETTAGYFDY) as CDRH3, SEQ ID NO:43 (SASQGINNFLN) as CDRL1, SEQ ID NO:44 (YTSSLHS) as CDRL2 and SEQ ID NO:45 (QHFSKLPWT) as CDRL3, and

(c) an antibody comprising SEQ ID NO:55 (GYFMN) as CDRH1, SEQ ID NO:56 (RIFPYNGDTFYNQKFKG) as CDRH2, SEQ ID NO:57 (GTHYFDY) as CDRH3, SEQ ID NO:51 (RTSENIFSYLA) as CDRL1 , SEQ ID NO:52 (NAKTLAE) as CDRL2 and SEQ ID NO:53 (QHHYAFPWT) as CDRL3 immobilized to a solid support and a labeled antibody comprising SEQ ID NO:39 (HPYMH) as CDRH1, SEQ ID NO:40 (RIDPANGNTKYDPKFQG) as CDRH2, SEQ ID NO:41 (EEVADYTMDY) as CDRH3, SEQ ID NO:35 (RASESVDTYGNNFIH) as CDRL1, SEQ ID NO:36 (LASNLES) as CDRL2 and SEQ ID NO:37 (QQNNGDPWT) as CDRL3.

33. A method of assessing the progression of ovarian cancer in a subject afflicted with ovarian cancer, the method comprising

determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum or plasma sample derived from said subject by performing a two antibody sandwich assay,

wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA);

comparing the level of folate receptor alpha (FRα) which is not bound to a cell with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress rapidly based on said increase; or

(ii) identifying a decrease in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the ovarian cancer will progress slowly based on said decrease.

34. A method of stratifying a subject afflicted with ovarian cancer into one of at least four cancer therapy groups comprising:

determining the level of folate receptor alpha (FRα) which is not bound to a cell, in a serum or plasma sample derived from said subject by performing a two antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA); and

stratifying the subject into one of at least four cancer therapy groups based on the level of folate receptor alpha (FRα) which is not bound to a cell.

35. The method of claim 34, wherein the subject is stratified into Stage I, Stage II, Stage III or Stage IV ovarian cancer.

36. A method of monitoring the efficacy of MORAb-003 treatment of ovarian cancer in a subject suffering from ovarian cancer, the method comprising

determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum or plasma sample derived from said subject by performing a two antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA), wherein said subject has been previously administered MORAb-003;

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in said serum or plasma sample derived from said subject with the level of FRα in a control sample; and

(i) identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is not efficacious; or

(ii) identifying a decrease in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the MORAb-003 treatment is efficacious.

37. A method for predicting whether a subject suffering from ovarian cancer will respond to treatment with MORAb-003, the method comprising

determining the level of folate receptor alpha (FRα) which is not bound to a cell in a serum or plasma sample derived from said subject,

comparing the level of folate receptor alpha (FRα) which is not bound to a cell in the serum or plasma sample derived from said subject with the level of FRα in a control sample,

identifying an increase in the level of FRα in the serum or plasma sample derived from said subject as compared to the level of FRα in the control sample and determining that the subject will respond to treatment with MORAb-003,

wherein the level of FRα which is not bound to a cell in the serum or plasma sample derived from said subject is assessed by contacting the serum or plasma sample with a pair of antibodies that bind FRα in a two-antibody sandwich assay, wherein the two antibody-sandwich assay is an electrochemiluminescence assay (ECLIA) or enzyme immunoassay (EIA).

38. The method of claim 22, wherein at least one of the antibodies that bind FRα is labeled.

39. The method of claim 38, wherein the label is a radio-label, a biotin-label, a chromophore-label, a fluorophore-label, an ECL label or an enzyme-label.