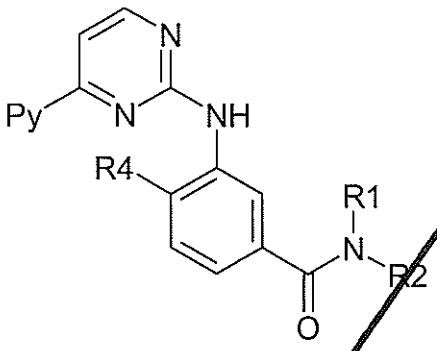
We claim:

1. A method of treating a proliferative disorder or other pathological conditions mediated by Bcr-Abl, c-Kit, DDR1, DDR2 or PDGF-R kinase activity comprising oral administration of an effective dose of a pyrimidylaminobenzamide of formula (I):



(I),

wherein

(a) Py denotes 3-pyridyl,

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, *N*-mono- or *N,N*-di-substituted carbamoyl, amino, mono- or di-substituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bi-cyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; or

R_1 and R_2, together, represent alkylene with 4, 5 or 6 carbon atoms optionally mono- or di-substituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or di-substituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with 4 or 5 carbon atoms; oxaalkylene with 1 oxygen and 3 or 4 carbon atoms; or azaalkylene with 1 nitrogen and 3 or 4 carbon atoms, wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, *N*-mono- or *N,N*-di-substituted carbamoyl-lower alkyl, cycloalkyl,

lower alkoxycarbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl or pyrazinyl;

R_4 represents hydrogen, lower alkyl or halogen;

or

(b) Py denotes 5-pyrimidyl, R_1 is hydrogen, R_2 is [[(3S)-3-(dimethylamino)- 1-pyrrolidinyl]-methyl]-3-(trifluoromethyl)phenyl and R_4 is methyl;

or a pharmaceutically acceptable salt thereof, and, optionally, pharmaceutically acceptable carriers, dispersed in a fruit preparation, to a human patient in need thereof.

2. The method according to claim 1, wherein the pyrimidylaminobenzamide is 4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(4-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)-phenyl] benzamide.

3. The method according to claim 2, wherein the pyrimidylaminobenzamide is employed in the form of its hydrochloride monohydrate.

4. The method according to any one of claims 1 to 3, wherein the proliferative disorder or other pathological condition is selected from melanoma, breast cancer, cancer of the colon, lung cancer, cancer of the prostate or Kaposi's sarcoma, gastrointestinal stromal tumors (GIST), acute myeloid leukemia (AML), leukemia which responds to an inhibition of the Abl tyrosine kinase activity, mesothelioma, systemic mastocytosis, hypereosinophilic syndrome (HES), fibrosis, rheumatoid arthritis, polyarthritis, scleroderma, lupus erythematosus, graft-versus host diseases, neurofibromatosis, pulmonary hypertension, Alzheimer's disease, seminomas and dysgerminomas and psoriasis.

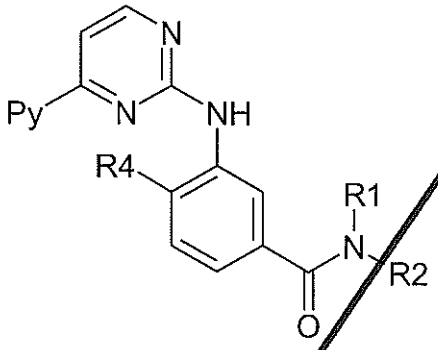
5. The method according to any one of claims 1 to 3, wherein the proliferative disorder or other pathological condition is selected from GIST, CML, Ph+ ALL, systemic mastocytosis, HES, fibrosis, scleroderma, neurofibromatosis and pulmonary arterial hypertension.

6. The method according to claim 1, wherein the human patient is a elderly or a pediatric patient.

7. The method according to claim 1, wherein the fruit preparation is a juice, sauce or puree prepared from fruits.

8. The method according to claim 1, wherein the fruit preparation is applesauce.

9. A commercial package containing a pyrimidylaminobenzamide of formula I



(I)

wherein

(a) Py denotes 3-pyridyl,

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amino, mono- or disubstituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising zero, one, two or three ring nitrogen atoms and zero or one oxygen atom and zero or one sulfur atom, which groups in each case are unsubstituted or mono- or polysubstituted;

or wherein R_1 and R_2 together represent alkylene with four, five or six carbon atoms optionally mono- or disubstituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or disubstituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with four or five carbon atoms; oxaalkylene with one oxygen and three or four carbon atoms; or azaalkylene with one nitrogen and three or four carbon atoms wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, N-mono- or N,N-

disubstituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxycarbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl, or pyrazinyl;

R_4 represents hydrogen, lower alkyl, or halogen;

wherein the prefix "lower" denotes a radical having up to and including a maximum of 7 carbon atoms,

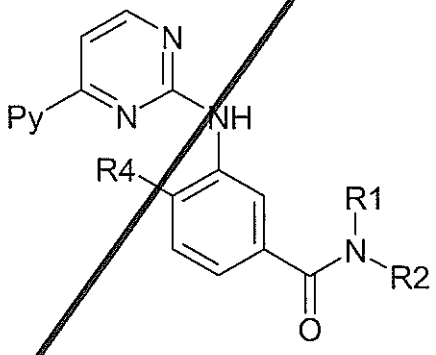
or

(b) Py denotes 5-pyrimidyl, R_1 is hydrogen, R_2 is [[(3S)-3-(dimethylamino)- 1-pyrrolidinyl]-methyl]-3-(trifluoromethyl)phenyl and R_4 is methyl;

or a pharmaceutically acceptable salt thereof, respectively,

together with instructions to disperse the compound of formula I or a pharmaceutically acceptable salt thereof in a fruit preparation.

10. A pyrimidylaminobenzamide of formula I



(I),

wherein

(a) Py denotes 3-pyridyl,

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, *N*-mono- or *N,N*-di-substituted carbamoyl, amino, mono- or di-substituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bi-cyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; or

R_1 and R_2, together, represent alkylene with 4, 5 or 6 carbon atoms optionally mono- or di-substituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or di-substituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with 4 or 5 carbon atoms; oxaalkylene with 1 oxygen and 3 or 4 carbon atoms; or azaalkylene with 1 nitrogen and 3 or 4 carbon atoms, wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, *N*-mono- or *N,N*-di-substituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxycarbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl or pyrazinyl;

R_4 represents hydrogen, lower alkyl or halogen;

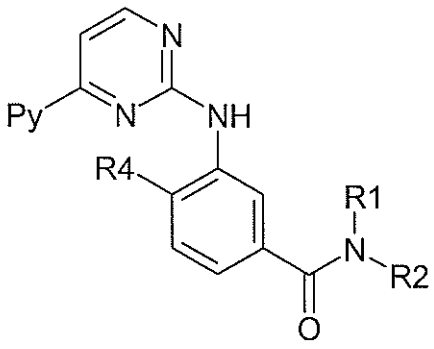
or

(b) Py denotes 5-pyrimidyl, R_1 is hydrogen, R_2 is [[(3S)-3-(dimethylamino)- 1-pyrrolidinyl]-methyl]-3-(trifluoromethyl)phenyl and R_4 is methyl;

or a pharmaceutically acceptable salt thereof, for the treatment of a proliferative disorder or other pathological conditions mediated by Bcr-Abl, c-Kit, DDR1, DDR2 or PDGF-R kinase activity, wherein the compound of formula (I) or a pharmaceutically acceptable salt thereof and, optionally, pharmaceutically acceptable carriers, are dispersed in a fruit preparation.

Claims

1. An effective dose for oral administration of a pyrimidylaminobenzamide comprised of formula (I):



(I),

wherein

(a) Py denotes 3-pyridyl,

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, *N*-mono- or *N,N*-di-substituted carbamoyl, amino, mono- or di-substituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bi-cyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; or

R_1 and R_2, together, represent alkylene with 4, 5 or 6 carbon atoms optionally mono- or di-substituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or di-substituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with 4 or 5 carbon atoms; oxaalkylene with 1 oxygen and 3 or 4 carbon atoms; or azaalkylene with 1 nitrogen and 3 or 4 carbon atoms, wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, *N*-mono- or *N,N*-di-substituted carbamoyl-lower alkyl, cycloalkyl,

lower alkoxycarbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl or pyrazinyl;

R_4 represents hydrogen, lower alkyl or halogen;

or

(b) Py denotes 5-pyrimidyl, R_1 is hydrogen, R_2 is [[(3S)-3-(dimethylamino)- 1-pyrrolidinyl]-methyl]-3-(trifluoromethyl)phenyl and R_4 is methyl;

or a pharmaceutically acceptable salt thereof, for the treatment of a proliferative disorder or other pathological conditions mediated by Bcr-Abl, c-Kit, DDR1, DDR2 or PDGF-R kinase activity, wherein the compound of formula (I) or a pharmaceutically acceptable salt thereof and, optionally, pharmaceutically acceptable carriers, are dispersed in a fruit preparation.

2. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to claim 1, wherein the pyrimidylaminobenzamide is 4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(4-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl] benzamide.

3. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to claim 2, wherein the pyrimidylaminobenzamide is employed in the form of its hydrochloride monohydrate.

4. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein the proliferative disorder or other pathological condition is selected from melanoma, breast cancer, cancer of the colon, lung cancer, cancer of the prostate or Kaposi's sarcoma, gastrointestinal stromal tumors (GIST), acute myeloid leukemia (AML), leukemia which responds to an inhibition of the Abl tyrosine kinase activity, mesothelioma, systemic mastocytosis, hypereosinophilic syndrome (HES), fibrosis, rheumatoid arthritis, polyarthritis, scleroderma, lupus erythematosus, graft-versus host diseases, neurofibromatosis, pulmonary hypertension, Alzheimer's disease, seminomas and dysgerminomas and psoriasis.

5. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein the proliferative disorder or other pathological condition is selected from GIST, CML, Ph+ ALL, systemic mastocytosis, HES, fibrosis, scleroderma, neurofibromatosis and pulmonary arterial hypertension.

6. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to claim 1, wherein the human patient is a elderly or a pediatric patient.

7. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to claim 1, wherein the fruit preparation is a juice, sauce or puree prepared from fruits.

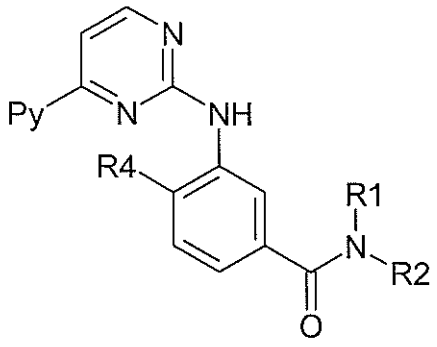
8. The pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof according to claim 1, wherein the fruit preparation is applesauce.

9. A kit comprising:

- a commercial package containing a pyrimidylaminobenzamide or a pharmaceutically acceptable salt thereof as claimed in claim 1,
- together with instructions to disperse the compound or a pharmaceutically acceptable salt thereof in a fruit preparation;

for use in the treatment of a proliferative disorder or other pathological conditions mediated by Bcr-Abl, c-Kit, DDR1, DDR2 or PDGF-R kinase activity.

10. The use of a pyrimidylaminobenzamide comprised of formula (I):



(I),

wherein

(a) Py denotes 3-pyridyl,

R_1 represents hydrogen, lower alkyl, lower alkoxy-lower alkyl, acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, or phenyl-lower alkyl;

R_2 represents hydrogen, lower alkyl, optionally substituted by one or more identical or different radicals R_3, cycloalkyl, benzcycloalkyl, heterocyclyl, an aryl group, or a mono- or bicyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen

atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; and

R_3 represents hydroxy, lower alkoxy, acyloxy, carboxy, lower alkoxycarbonyl, carbamoyl, *N*-mono- or *N,N*-di-substituted carbamoyl, amino, mono- or di-substituted amino, cycloalkyl, heterocyclyl, an aryl group, or a mono- or bi-cyclic heteroaryl group comprising 0-, 1-, 2- or 3-ring nitrogen atoms and 0 or 1 oxygen atom and 0 or 1 sulfur atom, which groups in each case are unsubstituted or mono- or poly-substituted; or

R_1 and R_2, together, represent alkylene with 4, 5 or 6 carbon atoms optionally mono- or di-substituted by lower alkyl, cycloalkyl, heterocyclyl, phenyl, hydroxy, lower alkoxy, amino, mono- or di-substituted amino, oxo, pyridyl, pyrazinyl or pyrimidinyl; benzalkylene with 4 or 5 carbon atoms; oxaalkylene with 1 oxygen and 3 or 4 carbon atoms; or azaalkylene with 1 nitrogen and 3 or 4 carbon atoms, wherein nitrogen is unsubstituted or substituted by lower alkyl, phenyl-lower alkyl, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkyl, carbamoyl-lower alkyl, *N*-mono- or *N,N*-di-substituted carbamoyl-lower alkyl, cycloalkyl, lower alkoxycarbonyl, carboxy, phenyl, substituted phenyl, pyridinyl, pyrimidinyl or pyrazinyl;

R_4 represents hydrogen, lower alkyl or halogen;

or

(b) Py denotes 5-pyrimidyl, R_1 is hydrogen, R_2 is [[(3S)-3-(dimethylamino)- 1-pyrrolidinyl]-methyl]-3-(trifluoromethyl)phenyl and R_4 is methyl;

or a pharmaceutically acceptable salt thereof, and, optionally, pharmaceutically acceptable carriers, dispersed in a fruit preparation, to a human patient in need thereof; in the manufacture of a medicament in the form of an effective dose by oral administration for the treatment of a proliferative disorder or other pathological conditions mediated by Bcr-Abl, c-Kit, DDR1, DDR2 or PDGF-R kinase activity, wherein the proliferative disorder or other pathological condition is selected from melanoma, breast cancer, cancer of the colon, lung cancer, cancer of the prostate or Kaposi's sarcoma, gastrointestinal stromal tumors (GIST), acute myeloid leukemia (AML), leukemia which responds to an inhibition of the Abl tyrosine kinase activity, mesothelioma, systemic mastocytosis, hypereosinophilic syndrome (HES), fibrosis, rheumatoid arthritis, polyarthritis, scleroderma, lupus erythematosus, graft-versus host diseases, neurofibromatosis, pulmonary hypertension, Alzheimer's disease, seminomas and dysgerminomas and psoriasis.

11. The use of either the pyrimidylaminobenzamide or the pharmaceutically acceptable salt

thereof according to claim 10, wherein the pyrimidylaminobenzamide is 4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-*N*-[5-(4-methyl-1H-imidazol-1-yl)-3-(trifluoromethyl)phenyl] benzamide.

12. The use of either the pyrimidylaminobenzamide or the pharmaceutically acceptable salt thereof according to claim 11, wherein the pyrimidylaminobenzamide is employed in the form of its hydrochloride monohydrate.

13. The use of either the pyrimidylaminobenzamide or the pharmaceutically acceptable salt thereof according to any one of claims 10 to 12, wherein the proliferative disorder or other pathological condition is selected from GIST, CML, Ph+ ALL, systemic mastocytosis, HES, fibrosis, scleroderma, neurofibromatosis and pulmonary arterial hypertension.

14. The use of either the pyrimidylaminobenzamide or the pharmaceutically acceptable salt thereof according to claim 10, wherein the human patient is a elderly or a pediatric patient.

15. The use of either the pyrimidylaminobenzamide or the pharmaceutically acceptable salt thereof according to claim 10, wherein the fruit preparation is a juice, sauce or puree prepared from fruits.

16. The use of either the pyrimidylaminobenzamide or the pharmaceutically acceptable salt thereof according to claim 10, wherein the fruit preparation is applesauce.