[0004] Treatment options for cancer patients often include surgery, radiotherapy, chemotherapy, hormone therapy, or a combination thereof. The compound ABDNAZ described in, for example, U.S. Patent Nos. 7,507,842; 8,299,053; and 8,927,527 has been studied in multiple clinical trials for use in treating cancer. ABDNAZ is typically formulated as a mixture with water, dimethylacetamide, and a poly(ethylene glycol) for intravenous infusion to the patient suffering from cancer. In clinical trials, patients receiving the aforementioned mixture of ABDNAZ by intravenous infusion have complained of significant pain at the site of infusion due to the ABDNAZ mixture. The significant pain at the site of infusion due to the ABDNAZ mixture has required medical personnel to reduce the rate at which the ABDNAZ mixture is administered to the patient, sometimes requiring infusion times up to eight hours. The long infusion times and slow rate of administration has, in some instances, limited the amount of ABDNAZ that can be administered to a patient when the ABDNAZ is used in combination with radiation therapy to be performed the same day as administration of ABDNAZ.

[0005] The present invention provides a new formulation containing ABDNAZ that can be rapidly administered to the patient without causing any significant pain at the site of infusion and has other advantages as described herein below.

SUMMARY

[0005a] In an aspect of the present disclosure, there is provided a formulation for intravenous administration to a patient suffering from cancer in order to treat the cancer, comprising:

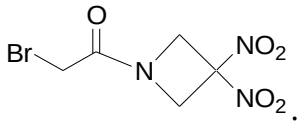
a. whole blood in an amount of at least 60% v/v of the formulation;

b. at least 10 μg/mL of ABDNAZ; and

c. an anticoagulant.

[0006] The disclosure provides compositions and methods for intravenous administration of 2-bromo-1-(3,3-dinitroazetidin-1-yl)ethanone (ABDNAZ), including formulations containing autologous whole blood and ABDNAZ that can be rapidly administered to a patient by intravenous infusion. The compositions and methods provide the further advantage that rapid administration of the formulation does not result in any significant pain at the site of

intravenous infusion due to the administration. The compound ABDNAZ has the following chemical structure:



[0007] The ABDNAZ formulations contain whole blood (preferably autologous whole blood), ABDNAZ, and an anticoagulant. The formulations and methods are particularly useful for

administering ABDNAZ to a patient suffering from cancer. The ABDNAZ formulations can be administered intravenously to the patient at a rate of, for example, at least 5 mL/hour, 10 mL/hour, 30 mL/hour, or higher rates. The rapid rate of administration reduces the time required to administer a therapeutically effective amount of ABDNAZ for treating cancer, and has particular advantages when large doses of ADBDNAZ need to be administered to the patient during the same day as the patient receives radiation therapy. The methods can be further characterized according to the magnitude of pain experienced by the patient at the site of administering the ABDNAZ formulation, wherein the magnitude of any pain experienced by the patient is small. The disclosure having been generally described is explained in more detail in the examples and examples below and in the detailed description.

[0008] One example of the disclosure provides a method for intravenous administration of an ABDNAZ formulation to a patient suffering from cancer in order to treat the cancer. The method comprises intravenously administering to the patient in need thereof a therapeutically effective amount of an ABDNAZ formulation described herein (such as a formulation comprising whole blood, ABDNAZ, and an anticoagulant) in order to treat the cancer. The ABDNAZ formulation may be administered at a rate of, for example, at least 5 mL/hour or at least 10 mL/hour. The method provides the advantage of being able to rapidly administer ABDNAZ without causing undue pain at the site of administering the ABDNAZ formulation, and any such pain may be characterized according to, for example, the feature that any such pain is no greater than Grade 1 pain.

[0009] Another example of the disclosure provides a method for rapid intravenous administration of an ABDNAZ formulation to a patient while minimizing injection site pain experienced by the patient, wherein the method comprises intravenously administering to the patient at a rate of, for example, at least 10 mL/hour, an ABDNAZ formulation described herein (such as a formulation comprising whole blood, ABDNAZ, and an anticoagulant), wherein any pain experienced by the patient at the site of intravenous administration of the ABDNAZ formulation due to intravenous administration of the ABDNAZ formulation is no greater than Grade 2. The ABDNAZ formulation may be further characterized according to the concentration of ABDNAZ in the

formulation, such as where the formulation contains ABDNAZ at a concentration of, for example, at least 10 μg/mL, at least 20 μg/mL, at least 50 μg/mL, at least 100 μg/mL, or at least 150 μg/mL.

[0010] Another example of the disclosure provides an intravenous formulation containing ABDNAZ for intravenous administration to a patient, wherein the formulation comprises: (a) whole blood in an amount of at least 60% v/v of the formulation; (b) a polyethylene glycol at a concentration of from about 0.4 μL/mL to about 30 μL/mL in the formulation; (c) N,N-dimethylacetamide at a concentration of from about 0.2 μL/mL to about 15 μL/mL in the formulation; (d) ABDNAZ at a concentration of at least 10 μg/mL in the formulation; (e) water; and (f) an anticoagulant. The intravenous formulations are suited for use in the methods described herein, and provide the advantage of being able to be rapidly administered to the patient by intravenous infusion without causing any significant pain at the site of administration.

[0011] Another example of the disclosure provides a kit for intravenous administration of an ABDNAZ formulation to a patient suffering from cancer in order to treat the cancer. The kit comprises: (i) a formulation comprising ABDNAZ, and (ii) instructions for intravenous administration of an ABDNAZ formulation to a patient suffering from cancer in order to treat the cancer according to procedures described herein. One benefit of the kit is that it provides an ABDNAZ formulation capable of being rapidly administered to the patient by intravenous infusion without causing any significant pain at the site of administration.

[0012] Another example of the disclosure provides a kit for rapid intravenous administration of an ABDNAZ formulation to a patient while minimizing injection site pain experienced by the patient. The kit comprises: (i) a formulation comprising ABDNAZ, and (ii) instructions for rapid intravenous administration of an ABDNAZ formulation to a patient while minimizing injection site pain experienced by the patient according to procedures described herein.

DETAILED DESCRIPTION

[0013] The invention provides compositions and methods for intravenous administration of 2-bromo-1-(3,3-dinitroazetidin-1-yl)ethanone (ABDNAZ), including formulations containing autologous whole blood and ABDNAZ that can be rapidly administered to a patient by intravenous

Adverse Event	10 mg/m^2 Dose ABDNAZ (n=6)		16.7 mg/m^2 Dose ABDNAZ (n=3)		24.6 mg/m^2 Dose ABDNAZ (n=3)		33 mg/m^2 Dose ABDNAZ (n=4)		55 mg/m^2 Dose ABDNAZ (n=3)		83 mg/m^2 Dose ABDNAZ (n=6)	
	Grade 1-2	Grade 3	Grade 1-2	Grade 3	Grade 1-2	Grade 3	Grade 1-2	Grade 3	Grade 1-2	Grade 3	Grade 1-2	Grade 3
Infusion-site pain	4 (67%)	0	3 (100%)	0	1 (33%)	0	3 (75%)	1 (25%)	3 (100%)	0	6 (100%)	0
Arm swelling or oedema	0	0	1 (33%)	0	0	0	1 (25%)	0	2 (67%)	0	4 (67%)	0
Vein hardening	0	0	0	0	0	0	1 (25%)	0	1 (33%)	0	5 (83%)	0
Dyspnoea or wheezing	1 (17%)	0	0	0	0	0	0	0	1 (33%)	0	3 (50%)	0
Mouth tingling or burning	0	0	0	0	0	0	0	0	2 (67%)	0	2 (33%)	0

What is claimed is:

1. A formulation for intravenous administration to a patient suffering from cancer in order to treat the cancer, comprising:
    a. whole blood in an amount of at least 60% v/v of the formulation;
    b. at least 10 μg/mL of ABDNAZ; and
    c. an anticoagulant.
2. The formulation of claim 1, wherein the formulation further comprises polyethylene glycol, and the polyethylene glycol has a number average molecular weight in the range of about 200 g/mol to about 600 g/mol.
3. The formulation of claim 1, wherein the formulation further comprises polyethylene glycol, and the polyethylene glycol has a number average molecular weight of about 400 g/mol.
4. The formulation of any one of claims 1-3, wherein the anticoagulant is a solution comprising an alkali metal citrate salt, dextrose, and water.
5. The formulation of any one of claims 1-4, wherein the whole blood constitutes from about 60% wt./wt. to about 99% wt./wt. of the formulation.
6. The formulation of any one of claims 1-5, wherein the formulation comprises from about 90 mL to about 110 mL of whole blood.
7. The formulation of any one of claims 1-5, wherein the formulation comprises about 10 mL to about 20 mL of whole blood.
8. The formulation of any one of claims 1-5, wherein the formulation is in a form of a unit dose having a volume in a range from about 50 mL to about 200 mL.
9. The formulation of any one of claims 1-5, wherein the formulation is in a form of a unit dose having a volume in a range from about 10 mL to about 30 mL.
10. The formulation of any one of claims 1-9, wherein the formulation further comprises polyethylene glycol, and the polyethylene glycol is present at a concentration from about 0.4 μL/mL to about 4 μL/mL in the formulation.
11. The formulation of any one of claims 1-10, wherein the formulation further comprises N,N-dimethylacetamide, and the N,N-dimethylacetamide is present at a concentration from about 0.2 μL/mL to about 2 μL/mL in the formulation.
12. The formulation of any one of claims 1-11, wherein the formulation comprises 10 μg/mL to 2 mg/mL of ABDNAZ.

13. The formulation of any one of claims 1-12, wherein the formulation comprises 10 µg/mL to 1 mg/mL of ABDNAZ.

14. The formulation of any one of claims 1-12, wherein the formulation comprises 2 mg/mL of ABDNAZ.