(such as single or double-stranded DNA breaks) or indirect damage (such as by-stander or crossfire effects) to the biomolecules that constitute a cell. The present disclosure combines radioimmunoconjugates targeted to cancer cells with checkpoint inhibition to induce or improve an immune response to a tumor. In some embodiments, disclosed combination therapies ameliorate or treat cancer.

[0007] In one aspect, provided are methods of treating a patient having cancer, said method comprising administering to the patient a therapeutically effective amount of an [^{225}Ac]-radioimmunoconjugate, which comprises ^{225}Ac chelated with a compound having the formula: A-L^1-X-L^2-Z-B,

wherein A is a chelating moiety selected from DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid), DOTMA (1R,4R,7R,10R)-α, α', α", α'"-tetramethyl-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid, DOTAM (1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane), DO3AM-acetic acid (2-(4,7,10-tris(2-amino-2-oxoethyl)-1,4,7,10-tetraazacyclododecan-1-yl)acetic acid), DOTP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonic acid)), DOTA-4AMP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(acetamido-methylenephosphonic acid), NOTA (1,4,7-triazacyclononane-1,4,7-triacetic acid), and HP-DO3A (hydroxypropyltetraazacyclododecanetriacetic acid);

L^1 is optionally substituted C_{1-6} alkyl or C_{1-6} heteroalkyl;

X is C=O(NR^1), NR^1C=O(O), NR^1C=O(NR^1), CH_2PhC=O(NR^1), O, or NR^1, each R^1 independently being H or C_{1-6} alkyl;

L^2 is optionally substituted C_{1-50} alkyl or C_{1-50} heteroalkyl;

Z is C=O, CH_2, OC=O, NR^2C=O, or NR^2, each R^2 independently being H or C_{1-6} alkyl; and

B is a targeting moiety,

wherein the patient has received or is receiving one or more checkpoint inhibitors, and wherein the [^{225}Ac]-radioimmunoconjugate is administered at a dose of about 10 kBq to about 400 kBq/kg of body weight of said patient or is administered as a unitary dosage of about 1-30 MBq to said patient.

[0007a] In another aspect, provided herein is the use of a [^{225}Ac]-radioimmunoconjugate in the manufacture of a medicament for treating a patient having cancer, wherein the patient is being co-administered one or more checkpoint inhibitors:

wherein the [^{225}Ac]-radioimmunoconjugate comprises ^{225}Ac chelated with a compound having the formula: A-L^1-X-L^2-Z-B, wherein:

A is a chelating moiety selected from the group consisting of DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid), DOTMA (1R,4R,7R,10R)-α, α', α", α'"-tetramethyl-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid, DOTAM (1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane), DO3AM-acetic acid (2-(4,7,10-tris(2-amino-2-oxoethyl)-1,4,7,10-tetraazacyclododecan-1-yl)acetic acid), DOTP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonic acid)), DOTA-4AMP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(acetamido-methylenephosphonic acid), NOTA (1,4,7-triazacyclononane-1,4,7-triacetic acid), and HP-DO3A (10-(2-hydroxypropyl)-1,4,7-tetraazacyclododecane-1,4,7-triacetic acid);

L^1 is a bond or optionally substituted C_{1-6} alkyl or C_{1-6} heteroalkyl;

X is –C(O)NR^1–*, –NR^1C(O)–*, –OC(O)NR^1–*, –NR^1C(O)O–*, –NR^1C(O)NR^1–, –CH_2–Ph–C(O)NR^1–*, –NR^1C(O)–Ph–CH_2–*, –O–, or –NR^1–, wherein "*" indicates the attachment point to L^2, and each R^1 is independently hydrogen or C_{1-6} alkyl;

L^2 is optionally substituted C_{1-50} alkyl or C_{1-50} heteroalkyl;

Z is –C(O)–, –CH_2–, –OC(O)–#, –C(O)O–#, –NR^2C(O)–#, –C(O)NR^2–#, or –NR^2–, wherein "#" indicates the attachment point to B, and each R^2 is independently hydrogen or C_{1-6} alkyl; and

B is a targeting moiety,

and wherein the [^{225}Ac]-radioimmunoconjugate is to be administered at a dose of 10 kBq to 400 kBq/kg of body weight of said patient or is to be administered as a unitary dosage of 1-30 MBq to said patient.

[0008] In some embodiments, the above compound has the chelating moiety being DOTA.

[0009] In some embodiments, the compound has formula I: