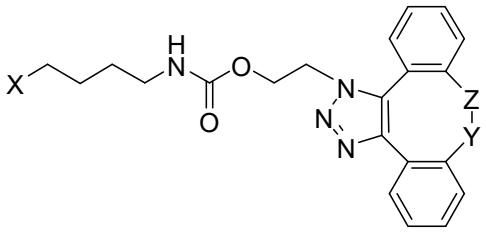
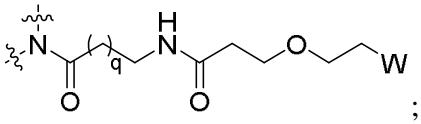
CLAIMS

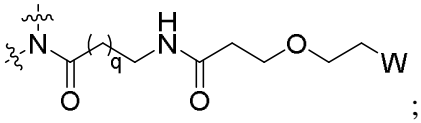
1. Use of an IL-2 conjugate for the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the IL-2 conjugate comprises the amino acid sequence of SEQ ID NO: 3 in which at least one amino acid residue in the IL-2 conjugate is replaced by the structure of Formula (I):

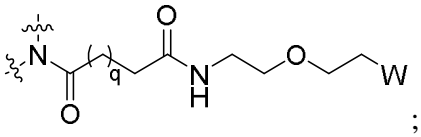


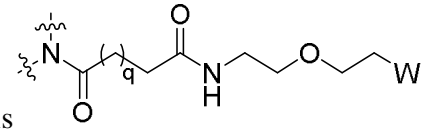
(I)

wherein:

Z is CH_2 and Y is  ;

Y is CH_2 and Z is  ;

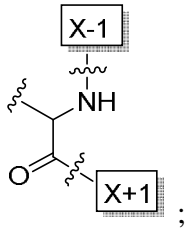
Z is CH_2 and Y is  ; or

Y is CH_2 and Z is  ;

W is a PEG group having an average molecular weight of about 5 kDa, 10 kDa, 15 kDa, 20 kDa,

25 kDa, 30 kDa, 35 kDa, 40 kDa, 45 kDa, 50 kDa, or 60 kDa; and

X is an L-amino acid having the structure:



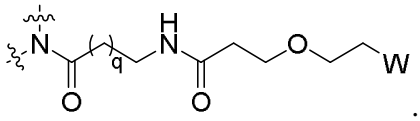
;

X-1 indicates the point of attachment to the preceding amino acid residue; and

X+1 indicates the point of attachment to the following amino acid residue;

wherein the position of the structure of Formula (I) in the amino acid sequence of the IL-2 conjugate is selected from K34, F41, F43, K42, E61, P64, R37, T40, E67, Y44, V68, and L71; and wherein the treatment comprises administering to the subject a therapeutically effective amount of (a) the IL-2 conjugate, and (b) an anti-EGFR antibody.

2. The use of claim 1, wherein in the IL-2 conjugate Z is CH_2 and Y is



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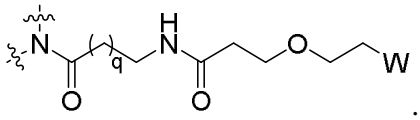
3. The use of claim 1, wherein in the IL-2 conjugate Y is CH_2 and Z is



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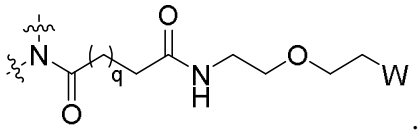
4. The use of claim 1, wherein in the IL-2 conjugate Z is CH_2 and Y is



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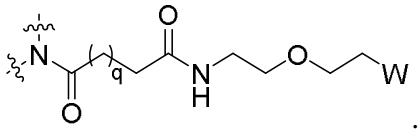
5. The use of claim 1, wherein in the IL-2 conjugate Y is CH_2 and Z is



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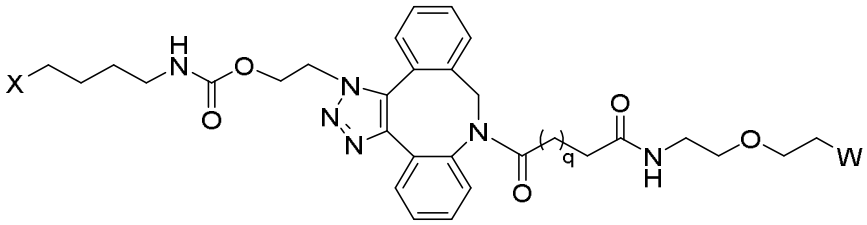
6. The use of any one of claims 1-5, wherein in the IL-2 conjugate the PEG group has an

average molecular weight of about 25 kDa, 30 kDa, or 35 kDa.

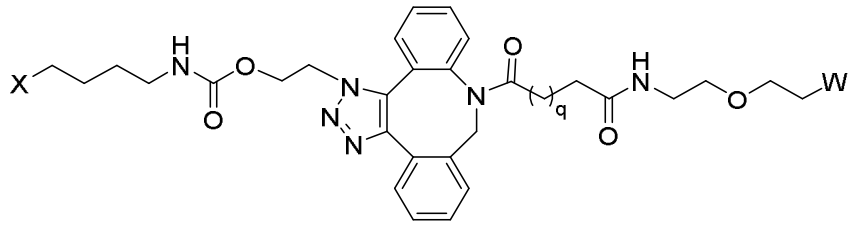
7. The use of claim 6, wherein in the IL-2 conjugate the PEG group has an average molecular weight of about 30 kDa.

8. The use of any one of claims 1-7, wherein the position of the structure of Formula (I) in the amino acid sequence of the IL-2 conjugate is P64.

9. The use of claim 1, wherein the structure of Formula (I) has the structure of Formula (IV) or Formula (V), or is a mixture of the structures of Formula (IV) and Formula (V):



(IV)



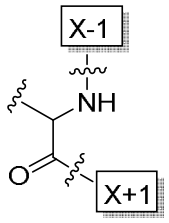
(V)

wherein:

W is a PEG group having an average molecular weight of about 25 kDa, 30 kDa, or 30 kDa;

q is 1, 2, or 3;

X is an L-amino acid having the structure:



;

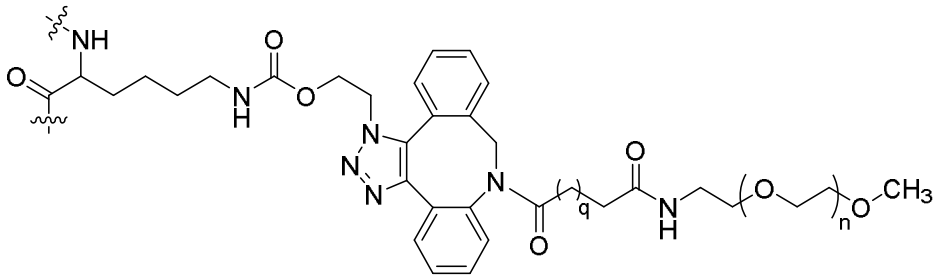
X-1 indicates the point of attachment to the preceding amino acid residue; and

X+1 indicates the point of attachment to the following amino acid residue.

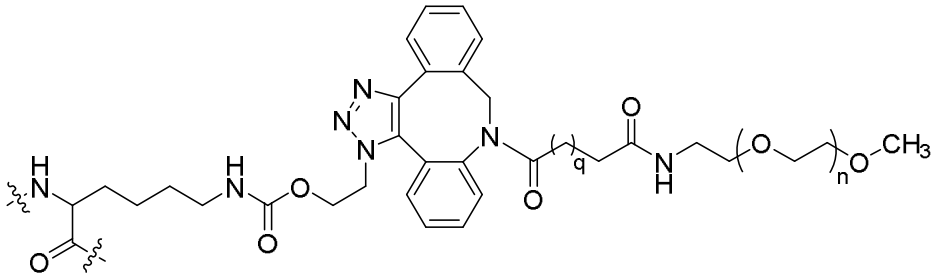
10. The use of claim 9, wherein the position of the structure of Formula (IV) or Formula (V) in the amino acid sequence of the IL-2 conjugate is P64.

11. The use according to any one of claims 1-10, wherein the anti-EGFR antibody is cetuximab.

12. Use of an IL-2 conjugatefor the manufacture of a medicament for the treatment of a cancer in a subject in need thereof, wherein the IL-2 conjugate comprises the amino acid sequence of SEQ ID NO: 50, wherein [AzK_L1_PEG30kD] has the structure of Formula (XII) or Formula (XIII), or is a mixture of the structures of Formula (XII) and Formula (XIII):



(XII)



(XIII)

wherein:

n is an integer n is an integer such that -$(OCH_2CH_2)_n$-OCH_3 has a molecular weight of about 30 kDa;

q is 1, 2, or 3; and

the wavy lines indicate covalent bonds to amino acid residues within SEQ ID NO: 50 that are not replaced;

and wherein the treatment comprises administering to the subject a therapeutically effective amount of (a) the IL-2 conjugate, and (b) cetuximab.

13. The use of any one of claims 1-12, wherein q is 1.

14. The use of any one of claims 1-12, wherein q is 2.

15. The use of any one of claims 1-12, wherein q is 3.

16. The use of any one of claims 1-15, wherein the average molecular weight is a number average molecular weight.

17. The use of any one of claims 1-15, wherein the average molecular weight is a weight average molecular weight.

18. The use of any one of claims 1-17, wherein the IL-2 conjugate is a pharmaceutically acceptable salt, solvate, or hydrate.

19. The use according to any one of claims 1-18, wherein the IL-2 conjugate is to be administered to the subject about once every two weeks, about once every three weeks, or about once every 4 weeks.

20. The use according to any one of claims 1-19, wherein the anti-EGFR antibody is to be administered to the subject about once every week, about once every two weeks, about once every three weeks, or about once every 4 weeks.

21. The use according to any one of claims 1-20, wherein the IL-2 conjugate is to be administered to the subject by intravenous administration.

22. The use according to any one of claims 1-21, wherein the IL-2 conjugate and the anti-EGFR antibody are to be administered separately.

23. The use of claim 23, wherein the IL-2 conjugate and the anti-EGFR antibody are to be administered sequentially.

24. The use according to any one of claims 1-23, wherein the cancer is selected from renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), head and neck squamous cell cancer (HNSCC), classical Hodgkin lymphoma (cHL), primary mediastinal large B-cell lymphoma (PMBCL), urothelial carcinoma, microsatellite unstable cancer, microsatellite stable

cancer, gastric cancer, colon cancer, colorectal cancer (CRC), cervical cancer, hepatocellular carcinoma (HCC), Merkel cell carcinoma (MCC), melanoma, small cell lung cancer (SCLC), esophageal, esophageal squamous cell carcinoma (ESCC), glioblastoma, mesothelioma, breast cancer, triple-negative breast cancer, prostate cancer, castrate-resistant prostate cancer, metastatic castrate-resistant prostate cancer, or metastatic castrate-resistant prostate cancer having DNA damage response (DDR) defects, bladder cancer, ovarian cancer, tumors of moderate to low mutational burden, cutaneous squamous cell carcinoma (CSCC), squamous cell skin cancer (SCSC), tumors of low- to non-expressing PD-L1, tumors disseminated systemically to the liver and CNS beyond their primary anatomic originating site, and diffuse large B-cell lymphoma.

25. The use of any one of claims 1-24, wherein about 16 μg/kg of the IL-2 conjugate is to be administered to the subject.

26. The use of any one of claims 1-24, wherein about 24 μg/kg of the IL-2 conjugate is to be administered to the subject.

27. The use of any one of claims 1-10 or 12-26, wherein the anti-EGFR antibody is selected from panitumumab (Vectibix), necitumumab (Portrazza), JNJ-61186372 (Amivantamab), IMC-C225, ABX-EGF, ICR62, and EMD 55900.