Product Data Sheet

Product Name: Trastuzumab deruxtecan
Cat. No.: GC61473

Chemical Properties

Cas. No.	1826843-81-5		
SMILES	[Trastuzumab deruxtecan]		
Formula		M.Wt	146298.97
Solubility	Soluble in acetonitrile	Storage	-80°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	Trastuzumab deruxtecan		

Protocol

Cell experiment [1]:

Cell lines	KPL-4 cells
Preparation Method	KPL-4 cells were treated with Trastuzumab deruxtecan (10μg/mL), anti-HER2 Ab (10μg/mL), and DXd (10nM) for 72h. Several proteins were detected by Western blotting.
Reaction Conditions	10μg/mL; 72h
Applications	Trastuzumab deruxtecan induced the phosphorylations of Chk1 and Histone H2A.X, and PARP cleavage in KPL-4 cells.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Animal experiment [2]:

Animal models	BALB/c mice
Preparation Method	Mice were inoculated with CT26.WT-hHER2 cells suspended in saline into the right flank by s.c. injection. When the average volume of tumors reached approximately 100 to 200mm^3, the mice were divided into control and treatment groups based on tumor volumes by using the randomized block method, and treatment was initiated (day 0). Trastuzumab deruxtecan (10mg/kg), anti-hHER2 antibody (10mg/kg), and anti–PD-1 antibody (5mg/kg) were administered i.v. at a volume of 10mL/kg to mice. As a control, ABS buffer (10mM Acetate Buffer, 5% sorbitol, and pH5.5) was administered at the same volume as the Trastuzumab deruxtecan. Trastuzumab deruxtecan and anti-hHER2 antibody were administered on days 0 and 7. Anti–PD-1 antibody was administered on days 0, 3, 7, and 10.
Dosage form	10mg/kg , once a week, twice; i.v.
Applications	Compared with anti-hHER2 antibody, Trastuzumab deruxtecan showed a significant antitumor effect.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

References:

[1]Ogitani Y, Aida T, Hagihara K, et al. DS-8201a, a novel HER2-targeting ADC with a novel DNA topoisomerase I inhibitor, demonstrates a promising antitumor efficacy with differentiation from T-DM1[J]. Clinical Cancer Research, 2016, 22(20): 5097-5108.

[2]Iwata T N, Ishii C, Ishida S, et al. A HER2-targeting antibody–drug conjugate, trastuzumab deruxtecan (DS-8201a), enhances antitumor immunity in a mouse model[J]. Molecular cancer therapeutics, 2018, 17(7): 1494-1503.

Background

Trastuzumab deruxtecan is a human epidermal growth factor receptor 2 (HER2)-targeted

antibody-drug conjugate (ADC) composed of a humanized anti-human HER2 (anti-hHER2) antibody, an enzymatically cleavable peptide linker, and a topoisomerase I inhibitor (DX-8951 derivative)[1]. Trastuzumab deruxtecan has shown sustained antitumor activity in a population of patients with previously treated HER2-positive metastatic breast cancer[2]. The primary mechanism of action of Trastuzumab deruxtecan is antibody-dependent cell-mediated cytotoxicity (ADCC) through binding to FcγRIII on immune effector cells[3].

In vitro, Trastuzumab deruxtecan (10μg/mL) treatment of KPL-4 cells for 72h induced Chk1 and histone H2A.X phosphorylation and PARP cleavage, and induced DNA damage and apoptosis[4]. Trastuzumab deruxtecan (0-100μg/mL) treatment of SK-BR-3 cells for 24h induced downregulation of intracellular pAkt in a dose-dependent manner[4]. Trastuzumab deruxtecan (0.2μg/mL) treatment of N87 parental cells and N87 T-DM1-resistant (TDMR) cells for 15 days, significantly inhibited cell proliferation[5].

In vivo, Trastuzumab deruxtecan (10mg/kg, once a week) was intravenously injected into CT26.WT-hHER2 cell xenograft mice for 2 weeks, significantly inhibiting tumor growth in mice and forming immune memory[6].

References:
[1] Nakada T, Sugihara K, Jikoh T, et al. The latest research and development into the antibody–drug conjugate,[fam-] trastuzumab deruxtecan (DS-8201a), for HER2 cancer therapy[J]. Chemical and Pharmaceutical Bulletin, 2019, 67(3): 173-185.
[2] Modi S, Saura C, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-positive breast cancer[J]. New England Journal of Medicine, 2020, 382(7): 610-621.
[3] Mandó P, Rivero S G, Rizzo M M, et al. Targeting ADCC: A different approach to HER2 breast cancer in the immunotherapy era[J]. The Breast, 2021, 60: 15-25.
[4] Ogitani Y, Aida T, Hagihara K, et al. DS-8201a, a novel HER2-targeting ADC with a novel DNA topoisomerase I inhibitor, demonstrates a promising antitumor efficacy with differentiation from T-DM1[J]. Clinical Cancer Research, 2016, 22(20): 5097-5108.
[5] Takegawa N, Nonagase Y, Yonesaka K, et al. DS-8201a, a new HER2-targeting antibody–drug conjugate incorporating a novel DNA topoisomerase I inhibitor, overcomes HER2-positive gastric cancer T-DM1 resistance[J]. International journal of cancer, 2017, 141(8): 1682-1689.
[6] Iwata T N, Ishii C, Ishida S, et al. A HER2-targeting antibody–drug conjugate,

trastuzumab deruxtecan (DS-8201a), enhances antitumor immunity in a mouse model[J]. Molecular cancer therapeutics, 2018, 17(7): 1494-1503.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA