

LADIRATUZUMAB VEDOTIN

An investigational antibody-drug conjugate directed to LIV-1

Anti-LIV-1 antibody

Humanized monoclonal antibody that binds to LIV-1

MMAE

Microtubule-disrupting agent

Protease-cleavable mc-vc linker

Covalently attaches MMAE to the antibody and releases agent within the target cell



Target: LIV-1

- Expressed in >90% of all clinical subtypes of metastatic breast cancer, with limited to no expression in normal tissues as assessed by immunohistochemistry¹⁻³

Proposed Mechanism of Action^{6-10,a}

- Direct cytotoxicity
- Bystander effect
- Immunogenic cell death

 Expression in tumors is linked with malignant progression and lymph node involvement^{4,5}

mc-vc: maleimidocaproyl-valine-citrulline; **MMAE**: monomethyl auristatin E

^aBased on preclinical data

1. Forero A et al. Cancer Res. 2016: Abstract P3-14-05. 2. Forero-Torres A et al. Cancer Res. 2017: Abstract P6-12-04. 3. Modi S et al. SABCS 2017: Abstract PD3-14. 4. Yamashita S et al. Nature. 2004: 298-302. 5. Hogstrand C et al. Biochem J. 2013: 229-37. 6. Sussman D et al. Mol Cancer Ther. 2014: 2991-3000. 7. Specht J et al. ESMO 2018: Abstract 286PD. 8. Li F et al. Cancer Res. 2016: 2710-9. 9. Cao A et al. Cancer Res. 2018: Abstract 2742. 10. Pusztai L et al. SITC virtual 2020: Abstract 323.

The safety and efficacy of this agent(s), or use in this setting, has not been established or is subject to confirmation. For an agent(s) whose safety and efficacy has not been established or confirmed, future regulatory approval or commercial availability is not guaranteed.





Proposed Mechanism of Action^{1-5,a}



Binds to LIV-1



3

4

Complex is internalized and traffics to lysosome



Microtubule LIV-1

Direct cytotoxicity

3

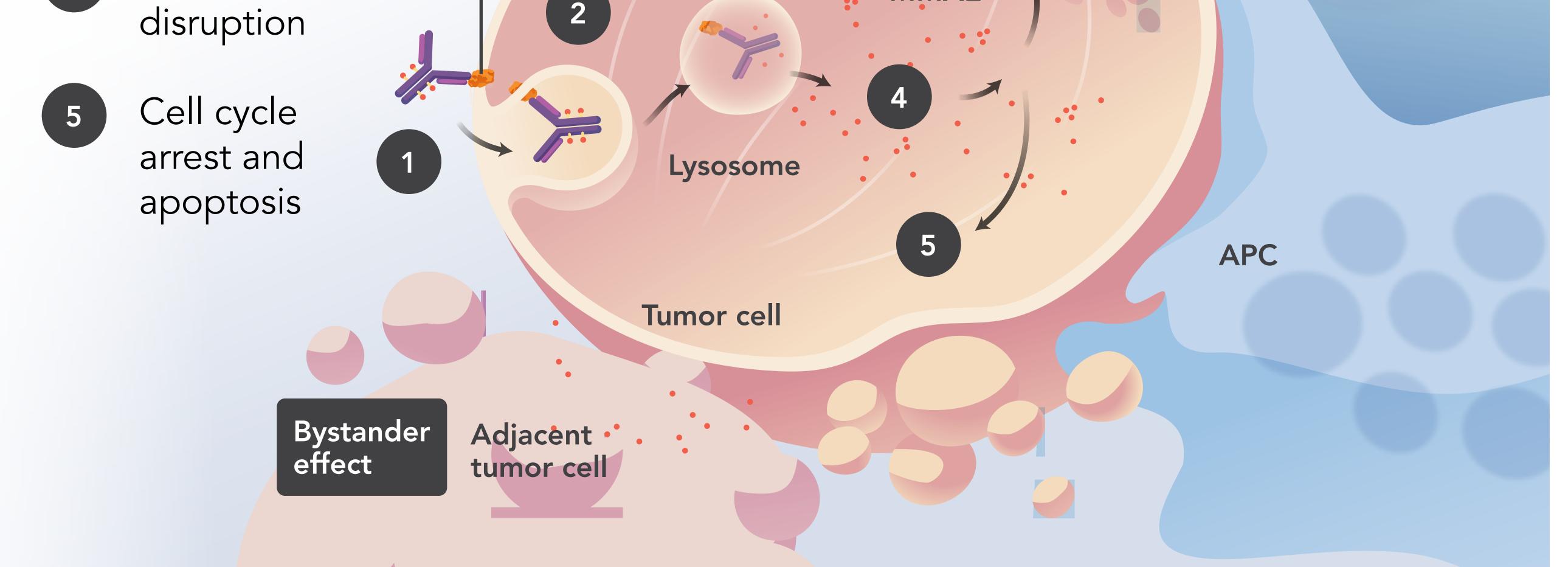
Endoplasmic reticulum stress

- MMAE

Activated T cell

9

Immunogenic cell death



^aBased on preclinical data

1. Cao A et al. Cancer Res. 2018: Abstract 2742. 2. Spect J et al. Ann Oncol. 2018: viii90-121. 3. Pusztai L et al. SITC virtual 2020: Abstract 323. 4. Li F et al. Cancer Res. 2016: 2710-9. 5. Sussman D et al. Mol Cancer Ther. 2014: 2991-3000.

Clinical Trials ^a Phase 1		ase 2	Phase 3	
	RECRUITING	SGNLVA-005: Locally advanced or metastatic solid tumors (NCT04032704) Ladiratuzumab vedotin		
	RECRUITING	SGNLVA-002/KEYNOTE-721 ^b : First-line locally advanced or metastatic triple-negative breast cancer (NCT03310957) Ladiratuzumab vedotin + pembrolizumab		
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^aProgram being co-developed with Merck Sharp & Dohme LLC ^bPhase 1b/2

Clinical trial information retrieved from clinicaltrials.gov, accessed Apr 2023.

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