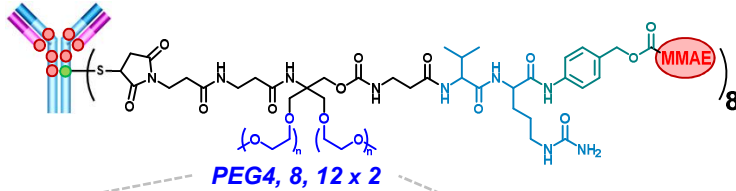


Features

ADC preparation and Characterization of ADCs by HIC*

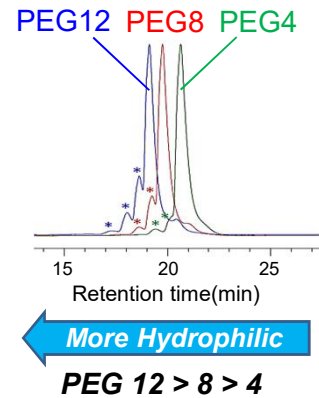
Preparation of DAR8-ADCs



PEG4	PEG8	PEG12
DAR 7.9	DAR 7.8	DAR 7.6

Drug: MMAE
Antibody: Trastuzumab

HIC analysis of DAR8-ADCs



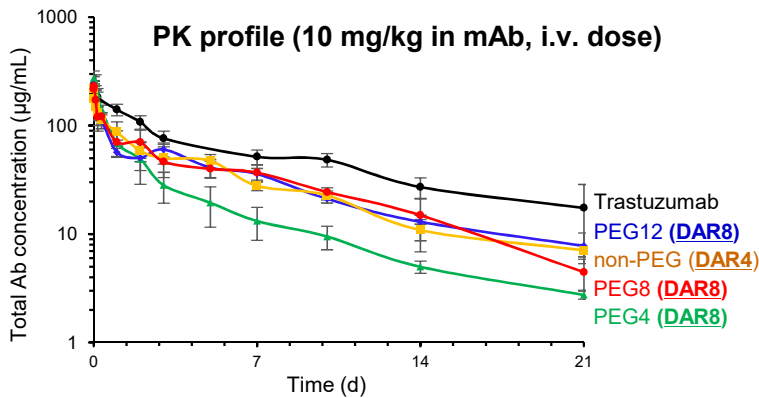
PEGylated ADCs were successfully synthesized without aggregation.

Longer PEGs improved the hydrophilicity of ADCs more effectively.

*HIC=Hydrophobic Interaction Chromatography

PK profile of ADCs

The cleavable pendant type PEG linkers improve pharmacokinetics of DAR8-ADCs in comparison with a conventional non-PEG linker.

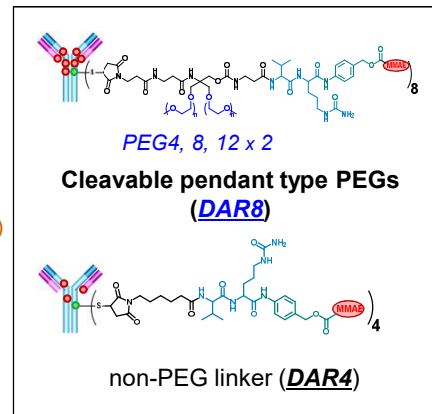


Half-life of each ADCs in days

$t_{1/2 \beta}$ (d)	(DAR4)		(DAR8)			TRS
	non-PEG	PEG4	PEG8	PEG12		
	3.7	2.9	5.1	6.2	8.0	

Shorter half life ← half life → Longer half life

Longer PEG-ADCs showed good PK profile.

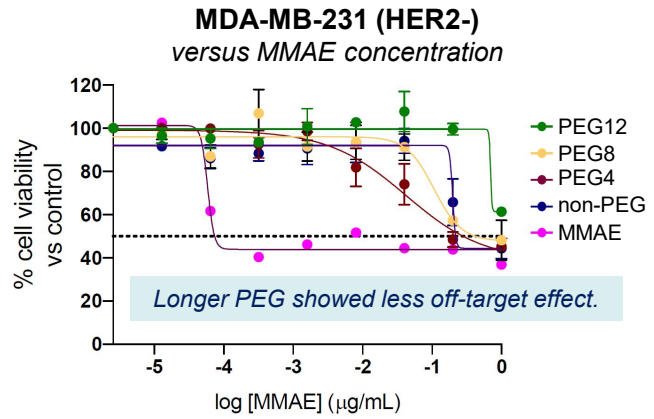
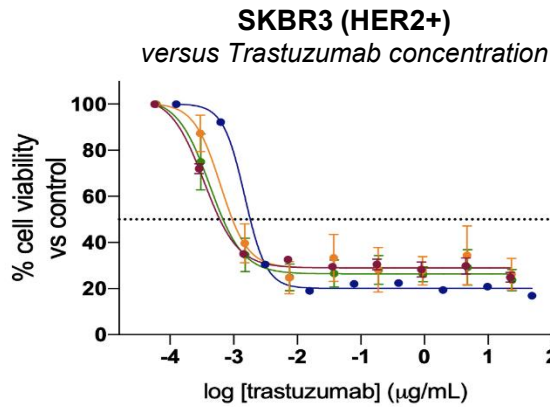


Drug: MMAE
Antibody: Trastuzumab

mAb concentrations in blood were measured by ELISA.

Features

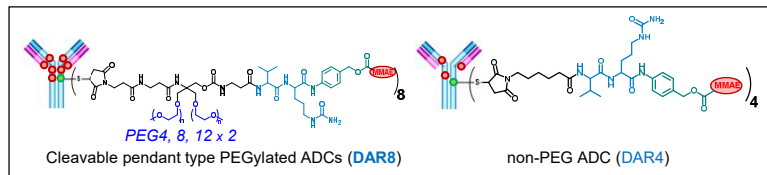
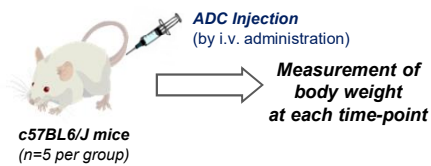
In vitro Cytotoxicity of ADCs



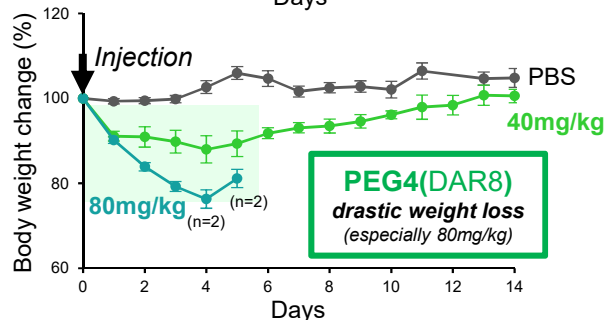
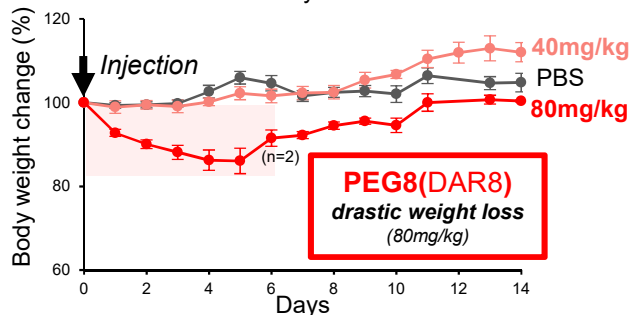
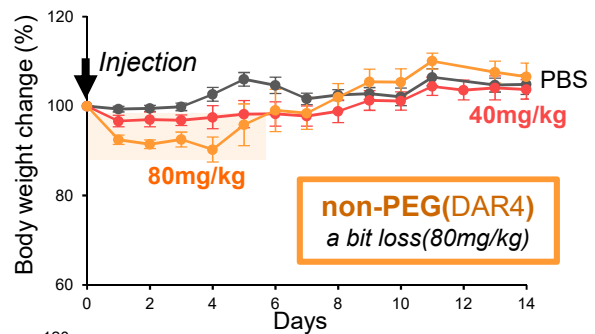
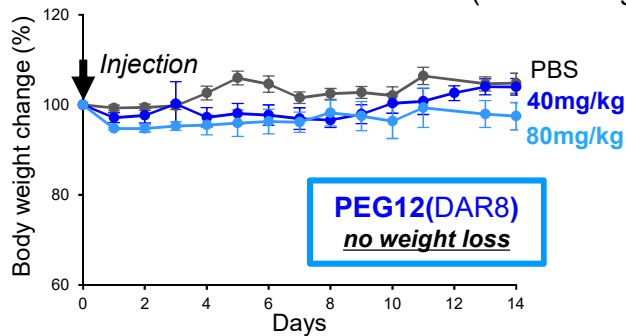
IC ₅₀ (ng/mL) [Trastuzumab]	(DAR4)		(DAR8)		
	non-PEG	PEG4	PEG8	PEG12	
	1.49	0.42	0.63	0.34	

PEGylated DAR8-ADCs showed cytotoxicity depending on DAR and are specific on HER2+ cell lines.

In vivo Single dose mice tolerability of ADCs



Single dose body weight change on c57BL6/J mice (n=5 per group) (40 or 80 mg/kg, i.v. dose)

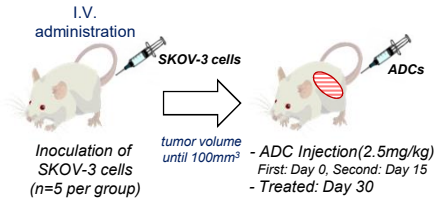


DAR8-ADC bearing PEG12 showed the highest tolerability.

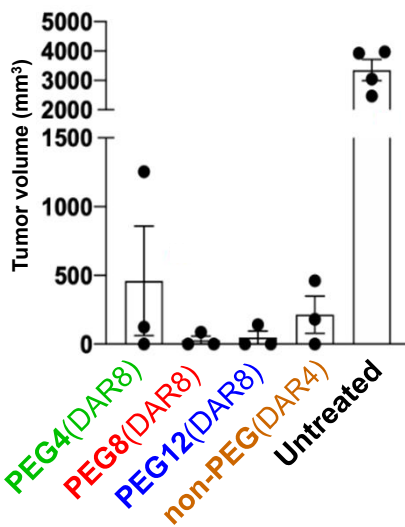
Features

In vivo Anti-tumor activity of ADCs

Experimental design

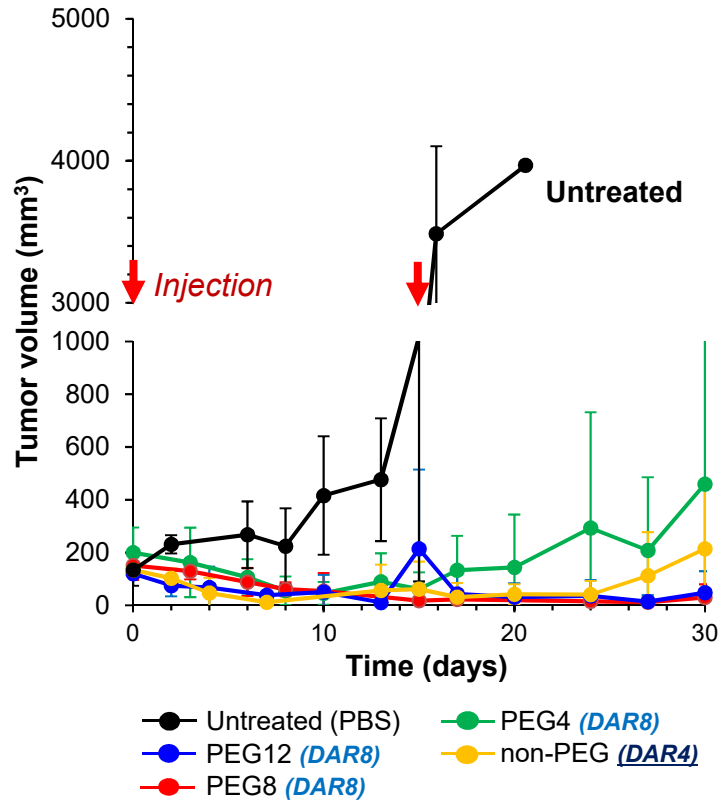


Tumor volume in Day 30



In vivo activity on the SKOV-3 mice xenograft model

(2.5mg/kg, i.v. dose)



DAR8-ADCs bearing PEG8 and 12 had a close profile and were stronger activity among all the ADCs.

The ADC using cleavable pendant type PEG linkers showed higher efficacy and lower toxicity than the non-PEG linker.

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