VZV vaccine (mRNA-1468)

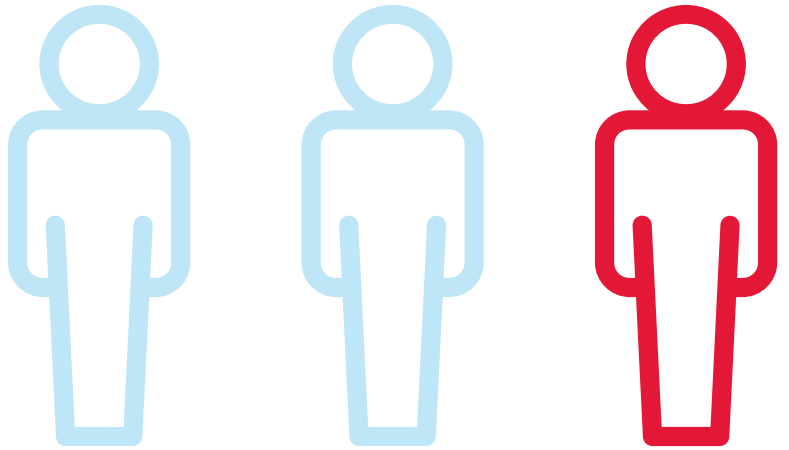
Last updated 5/2/24

Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial
Latent	**CMV vaccine**	mRNA-1647					
	EBV vaccine to prevent infectious mononucleosis	mRNA-1189					
	EBV vaccine to address EBV sequelae	mRNA-1195					
Infectious disease vaccines	**HSV vaccine**	mRNA-1608					
	VZV vaccine	mRNA-1468					
	HIV vaccines	mRNA-1644					
		mRNA-1574					
Enteric	**Norovirus vaccines**	mRNA-1403					
		mRNA-1405					
Bacterial	**Lyme vaccines**	mRNA-1975					
		mRNA-1982					
Public health	**Zika vaccine**	mRNA-1893					
	Nipah vaccine	mRNA-1215					
	Mpox vaccine	mRNA-1769					

Herpes zoster (shingles) disease overview

Herpes zoster is caused by **reactivation of latent varicella-zoster virus** (VZV)

Declining immunity in older adults decreases immunity against VZV, allowing reactivation of the virus from latently infected neurons, causing painful and itchy lesions



Herpes zoster occurs in **1 out of 3 adults in the U.S. in their lifetime** and incidence increases at approximately 50 years of age[1]

1. https://www.cdc.gov/shingles/about/index.html

VZV vaccine mRNA-1468 Phase 1/2 trial design

The Phase 1/2 was designed to test the safety and immunogenicity of mRNA-1468 in healthy adults ≥ 50

Design
Randomized 1:1:1:1:1, observer-blind, active-controlled study

Number of participants
500 medically stable adults ≥ 50 years of age without previous immunization against HZ or history of HZ in previous 10 years

At least 35% participants ≥ 70 years of age in each study arm

Vaccination schedule
2 doses of mRNA-1468 at 1 of 3 dose levels (Low, Medium, High) given at 0, 2 months, or

Single dose of mRNA-1468, given as placebo at month 0 and 1 dose of mRNA-1468 at month 2, or

2 doses of SHINGRIX given at 0, 2 months

Duration: 12-months
Study participants will be followed up for 12 months after study injection

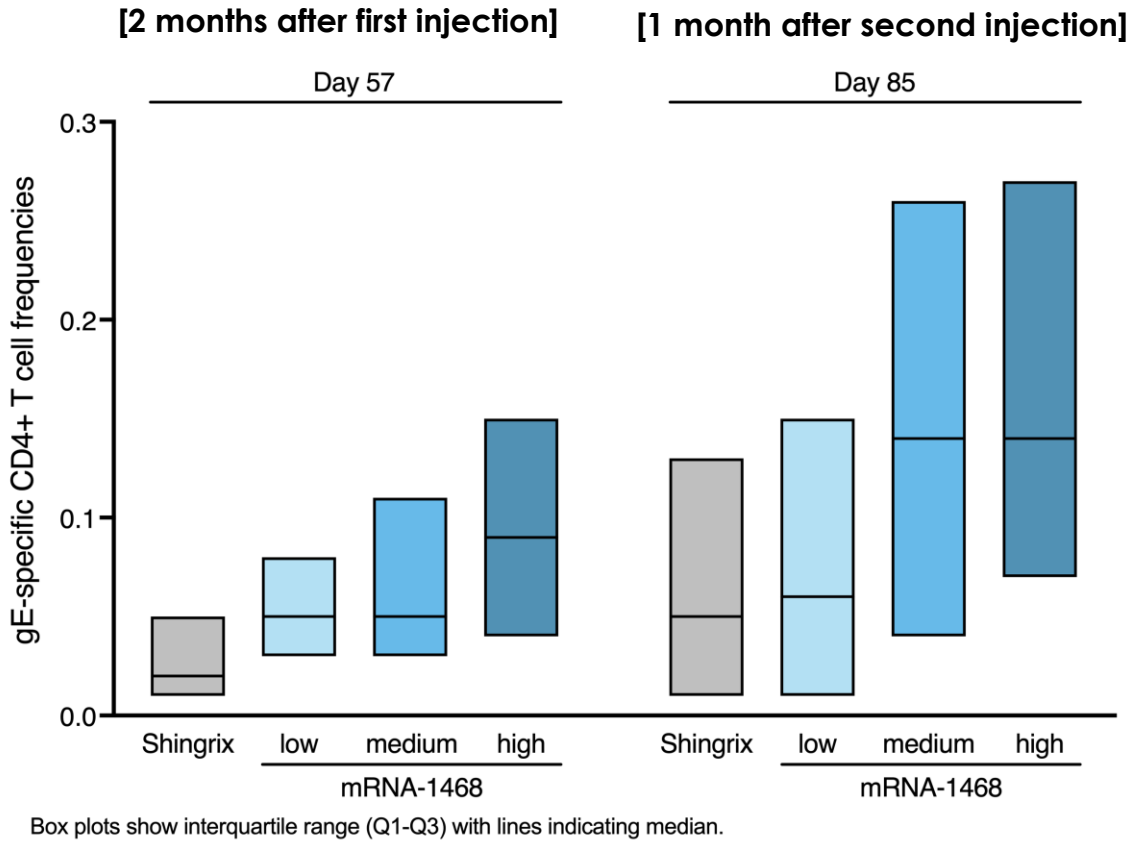
Site location
US

Total N = 500
Randomization = 1:1:1:1:1

Active comparator (SHINGRIX)
N=100
mRNA-1468 (2 doses, Low)
N=100
mRNA-1468 (2 doses, Medium)
N=100
mRNA-1468 (2 doses, High)
N=100
mRNA-1468 (1 dose, HIgh)
N=100

2 doses of mRNA-1468 elicited strong antigen-specific CD4+ T cell responses

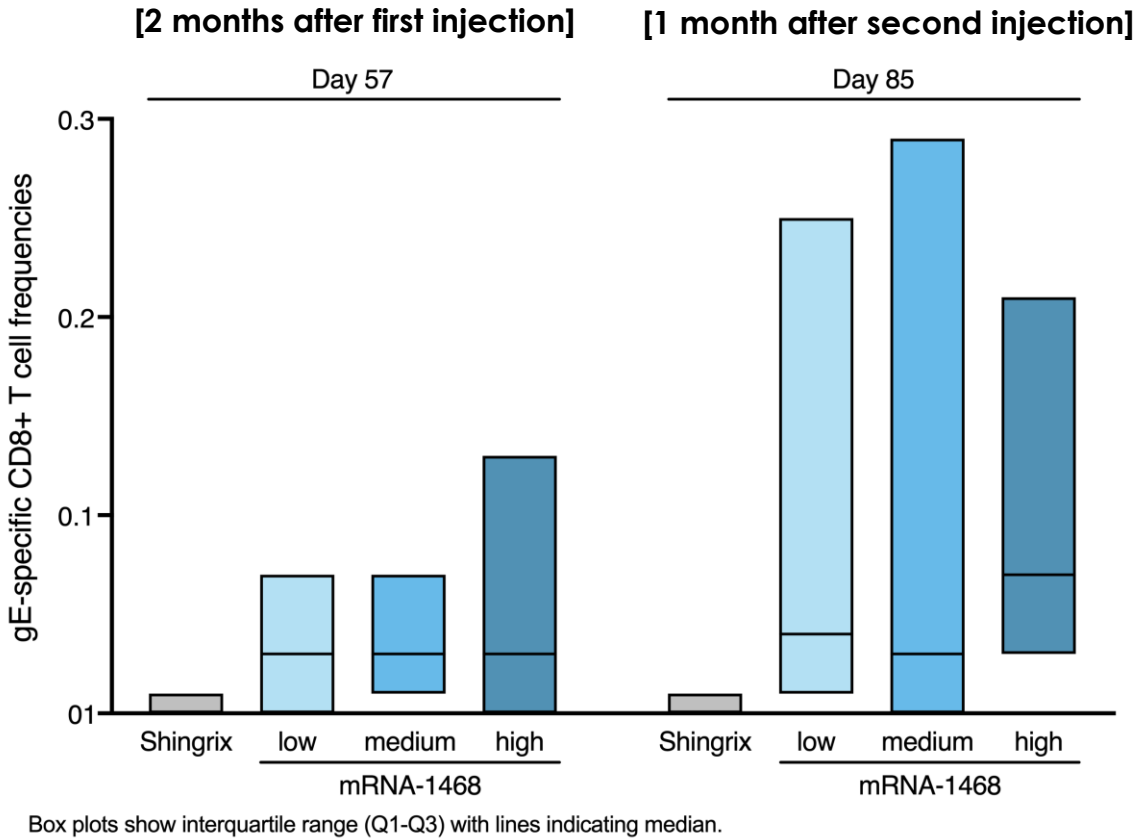
- CD4+ T cells defined as non-naïve gE-specific CD4+ T cells expressing 2 or more of the following markers: IFNγ, TNFα, IL-2, CD40L.
- Approximately 25 participants represented in each study arm at IA1.
- mRNA-1468 elicited comparable or higher CD4+ T cell responses relative to Shingrix after the first and second injection.



Box plots show interquartile range (Q1-Q3) with lines indicating median.

2 doses of mRNA-1468 elicited strong antigen-specific CD8+ T cell responses

- CD8+ T cells defined as non-naïve gE-specific CD8+ T cells expressing any of the following markers: IFNγ, TNFα, or IL-2.
- Approximately 25 participants represented in each study arm at IA1.
- mRNA-1468 elicited comparable or higher CD8+ T cell responses relative to Shingrix after the first and second injection.

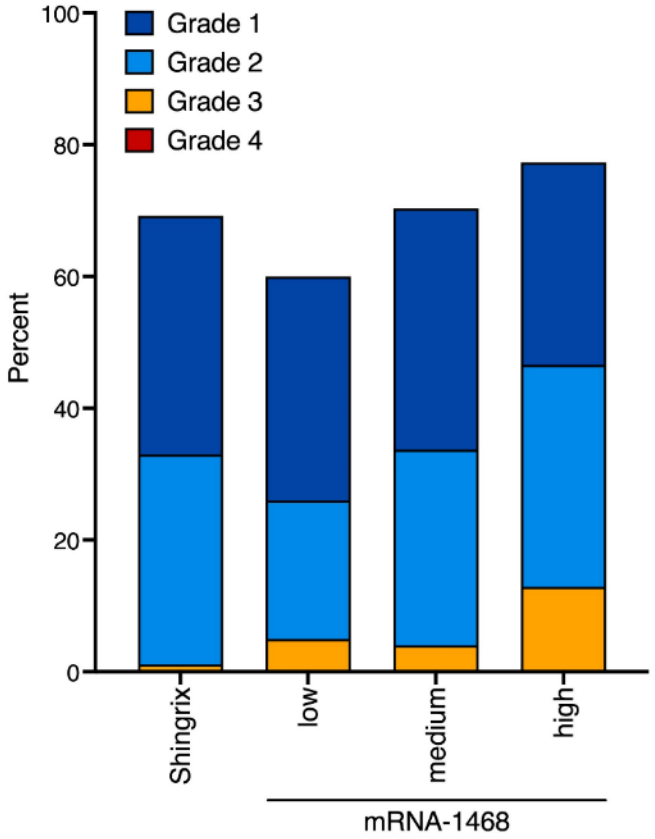


Box plots show interquartile range (Q1-Q3) with lines indicating median.

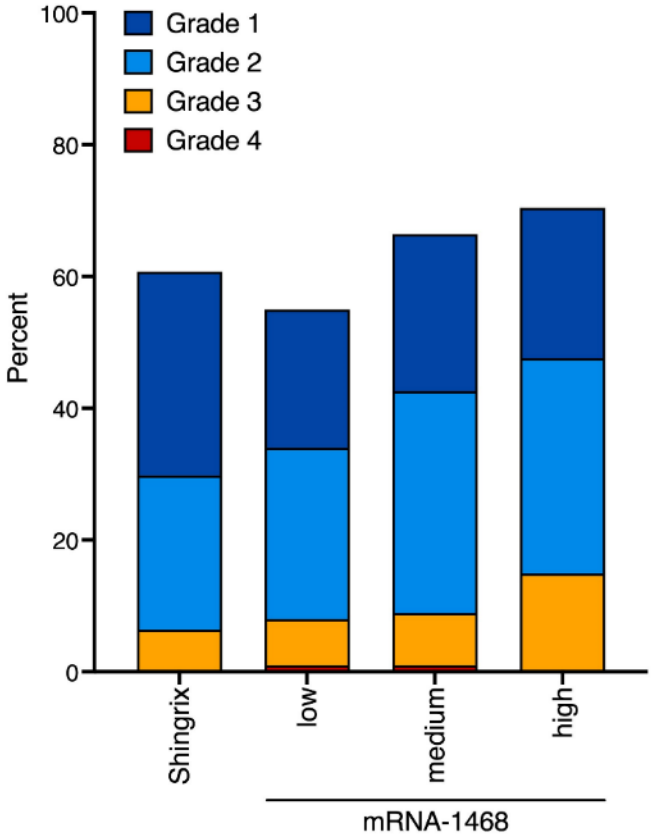
Reactogenicity profile of mRNA-1468 was comparable to Shingrix after any dose

- Reactogenicity of 2 doses of mRNA-1468 after any dose was comparable to Shingrix.
- 94-101 participants in each study arm.

Local Reactogenicity After Any Dose



Systemic Reactogenicity After Any Dose



*Reported grade 4 fever in mRNA-1468 25 µg and 50 µg arms verified as a reporting error and confirmed with subjects

VZV summary and next steps

Immunogenicity	• mRNA-1468 elicited comparable or higher CD4+ and CD8+ T cell responses relative to Shingrix
Safety	• mRNA-1468 was generally well tolerated across all dose levels tested
Next steps	• Additional results from the ongoing Phase 1/2 study will be available later this year, including persistence data • Advancing toward a pivotal Phase 3 trial

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