

Supplementary appendix

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Text S1. Inclusion and exclusion criteria

The volunteers had to meet all following inclusion and exclusion criteria to be eligible for the study.

Inclusion criteria

1. Age 50 years or older on the day of enrollment, regardless of gender, and able to provide legal identification.
2. Able to understand the trial procedures, voluntarily agree to participate in the study, and sign the "Informed Consent Form."
3. Female subjects are not pregnant or lactating. Female subjects with childbearing potential should take reliable contraceptive measures, and have no pregnancy and fertility plan within 8 months;
4. Axillary temperature $\leq 37.0^{\circ}\text{C}$ on the day of enrollment.
5. Able to attend all scheduled follow-up visits and able to comply with protocol requirements.

Exclusion criteria

1. History of herpes zoster within the past 5 years.
2. Previous vaccination with varicella vaccine or zoster vaccine (including use of registered products or participation in clinical trials for varicella or zoster vaccines).
3. Allergy to any component of the study vaccine: Previous allergy to any recombinant vaccine derived from CHO cells (such as recombinant hepatitis B vaccine [CHO cells]), polysorbates, or a history of severe allergic reactions to any vaccination. (Severe allergic reactions: Anaphylactic shock, allergic laryngeal edema, allergic purpura, thrombocytopenic purpura, localized allergic necrotic reaction (Arthus reaction), severe urticaria, etc.
4. Diagnosis of immune deficiency diseases (such as congenital or acquired immunodeficiency, HIV infection, etc.), or receiving immunosuppressive/cytotoxic treatment (e.g., chemotherapy, organ transplantation, or planned treatment during the clinical trial within 6 months before vaccination).

5. Subjects who received immunosuppressive therapy within 3 months before vaccination, or planning to receive such treatment within 1 month after full immunization (e.g., long-term use of systemic glucocorticoids for ≥ 14 days, dose ≥ 2 mg/kg/day or ≥ 20 mg/day prednisone or equivalence);
6. Receiving an inactivated vaccine, recombinant vaccine, or mRNA vaccine within 14 days or any live vaccine within 28 days prior to vaccination;
7. Subjects with acute illness or in the acute phase of a chronic disease within 3 days prior to vaccination.
8. Asplenia or splenectomy.
9. Subjects who receive blood products or immunoglobulin therapy within 3 months before vaccination, or planning to use such products within 2 months after vaccination.
10. Participating in other clinical studies of investigational or un-registered products (drugs, vaccines or devices, etc.), or planning to participate in other clinical studies before the end of this clinical study.
11. Any significant underlying medical condition (e.g., life-threatening diseases that may limit survival to less than 4 years) or other conditions that the investigator believes may interfere with the completion of the study.

Text S2. Measurement of gE-Specific Antibody Concentrations

The levels of gE-specific IgG antibodies were determined by ELISA. gE protein (Sino Biological, Inc., Beijing, China) was diluted with coating buffer to a final concentration of 2 µg/mL and then used to coat 96-well microplates. After washing 3 times with phosphate-buffered saline-Tween (PBS-T) solution, the plates were blocked with 200 µL/well solution (1% bovine serum albumin [BSA] in phosphate-buffered saline [PBS]) at 37 °C for 1 h. After removing the blocking solution, the plates were incubated in threefold-diluted human serum (100 µL/well) starting at 50-fold at 37 °C for 1 h. After washing 4 times, horseradish peroxidase (HRP)-labeled anti-human IgG antibody was added to each well, and plates were incubated at 37 °C for 1 h. After washing 5 times, 3,3',5,5'-tetramethylbenzidine (TMB substrate (BD Biosciences, San Diego, CA, USA)) was added to the plate. Eight minutes later, the reaction was stopped, and the absorbance was measured at 450 nm with a microplate reader. The standard curve between antibody concentration and absorbance OD value was obtained by using varicella-zoster virus (VZV) antibody standard. The absorbance values of each well of the sample were substituted into the standard curve to calculate the antibody concentration in each well. If the deviation of antibody concentration between successive dilutions of the same sample did not exceed 30%, the mean value was used as the final antibody concentration. Anti-gE antibody cut-off value is 100 milli-International Units (mIU)/mL.

Text S3. Flow Cytometry Analysis

Cryopreserved PBMCs were rapidly thawed at 37°C, resuspended in pre-warmed complete medium, and centrifuged (800 rpm, 10 min). Cell viability was determined using trypan blue exclusion, and density was adjusted to 2.0×10^6 cells/mL. PBMCs (2×10^6 cells/mL) were plated in 24-well plates (500 µL/well) and stimulated with

recombinant VZV gE-His protein (200 µg/mL) or medium (unstimulated control) for 20 h at 37°C under 5% CO₂. Single-color controls (CD3, CD4, CD8, CD40L), fluorescence minus one (FMO) controls, and unstimulated blanks were prepared using pooled PBMCs. Protein Transport Inhibitor (containing Brefeldin A, 1 µL/well) was added to test samples 4 h prior to harvest. Leukocyte Activation Cocktail (BD GolgiPlug™, 2 µL/well) was used for positive controls. Cells were incubated with Human BD Fc Block™ (1:50 dilution) for 15 min at 4°C. Cell surface stained with anti-CD3-PE, CD4-FITC, CD8-APC-Cy7, and CD40L-BB700 antibodies (30 min, 4°C). Cells were fixed using BD Cytofix/Cytoperm™ solution (20 min, 4°C), followed by two washes with Perm/Wash buffer. Intracellular stained with anti-IFN-γ-BV650, IL-2-PE-Cy7, and TNF-α-BV421 antibodies (30 min, 4°C). Stained cells were analyzed on a BD FACSCanto™ II flow cytometer equipped with FACSDiva™ software (v8.0.1). Finally, the cells were gated (FSC/SSC), and 10⁵ T cells were analyzed with a FACS Canto™ flow cytometer (BD Biosciences, USA) and FlowJo X 10.0.7 R2 (Tree Star Inc., San Carlos, CA, USA). Recombinant gE was supplied by Beijing Luzhu Biotechnology Co., Ltd., Beijing, China.

Table S1. The proportion of participants with gE-specific CD4+ T-cell responses producing 1 or any combination of 2, 3, or 4 cytokines 30 days after vaccination

		LZ901 group n (%)	HZ/su group n (%)	<i>p</i> value
N		141	136	
4 cytokines	IFN- γ + IL-2 + TNF- α + CD40L	38 (27.0)	13 (9.6)	0.0002
3 cytokines	IFN- γ + IL-2 + TNF- α	43 (30.5)	55 (40.4)	
	IFN- γ + IL-2 + CD40L	9 (6.4)	2 (1.5)	
	IFN- γ + TNF- α + CD40L	4 (2.8)	0	
	IL-2 + TNF- α + CD40L	2 (1.4)	1 (0.7)	
	total	58 (41.1)	58 (42.6)	0.7987
2 cytokines	IFN- γ + IL-2	21 (14.9)	9 (6.6)	
	IFN- γ + TNF- α	6 (4.3)	8 (5.9)	
	IFN- γ + CD40L	4 (2.8)	1 (0.7)	
	IL-2 + TNF- α	7 (5.0)	16 (11.8)	
	IL-2 + CD40L	1 (0.7)	1 (0.7)	
	TNF- α + CD40L	1 (0.7)	2 (1.5)	
	total	40 (28.4)	37 (27.2)	0.8290
1 cytokines	IFN- γ	1 (0.7)	3 (2.2)	
	IL-2	3 (2.1)	8 (5.9)	
	TNF- α	1 (0.7)	6 (4.4)	
	CD40L	0	6 (4.4)	
	total	5 (3.5)	23 (16.9)	0.0002
0 cytokine	None	0	5 (3.7)	
≥ 2 cytokines		136 (96.5)	108 (79.4)	<0.0001

N= the number of samples analyzed; n=the number of of participants with gE-specific CD4+ T-cell responses expressing any combination of immune markers; %=the proportion of participants with gE-specific CD4+ T-cell responses expressing any combination of immune markers; A active response was defined as a statistically significant increase in the proportion of cytokine-secreting T cells postvaccination compared with that of pre-immunization ($p < 0.05$); IFN- γ , interferon- γ ; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α ; CD40L, cluster of differentiation 40 ligand.

Table S2. The proportion of participants with gE-specific CD8⁺ T-cell responses producing 1 or any combination of 2, 3, or 4 cytokines 30 days after vaccination

		LZ901 group n (%)	HZ/su group n (%)	<i>p</i> value
N		141	136	
4 cytokines	IFN- γ + IL-2 + TNF- α + CD40L	8 (5.7)	0	0.0071
3 cytokines	IFN- γ + IL-2 + TNF- α	24 (17.0)	3 (2.2)	
	IFN- γ + IL-2 + CD40L	14 (9.9)	0	
	IFN- γ + TNF- α + CD40L	5 (3.5)	4 (2.9)	
	IL-2 + TNF- α + CD40L	3 (2.1)	0	
	total	46 (32.6)	7 (5.1)	<0.0001
2 cytokines	IFN- γ + IL-2	19 (13.5)	4 (2.9)	
	IFN- γ + TNF- α	5 (3.5)	9 (6.6)	
	IFN- γ + CD40L	5 (3.5)	0	
	IL-2 + TNF- α	6 (4.3)	2 (1.5)	
	IL-2 + CD40L	9 (6.4)	6 (4.4)	
	TNF- α + CD40L	0	3 (2.2)	
	total	44 (31.2)	24 (17.6)	0.0088
1 cytokine	IFN- γ	7 (5.0)	2 (1.5)	
	IL-2	21 (14.9)	17 (12.5)	
	TNF- α	1 (0.7)	4 (2.9)	
	CD40L	3 (2.1)	15 (11.0)	
	total	32 (22.7)	38 (27.9)	0.3152
0 cytokine	None	11 (7.8)	67 (49.3)	
≥ 2 cytokines		98 (69.5)	31 (22.8)	<0.0001

N= the number of samples analyzed; n=the number of participants with gE-specific CD8⁺ T-cell responses expressing any combination of immune markers; %=the proportion of participants with gE-specific CD8⁺ T-cell responses expressing any combination of immune markers; A active response was defined as a statistically significant increase in the proportion of cytokine-secreting T cells postvaccination compared with that of pre-immunization ($p < 0.05$); IFN- γ , interferon- γ ; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α ; CD40L, cluster of differentiation 40 ligand.

Table S3. The frequencies of cytokine-producing T cells per 10⁵ CD4⁺ T cells

	LZ901 group				HZ/su group				p value (LZ901 vs. HZ/su)	
	Day 0	Day 30	Fold increase	p value	Day 0	Day 30	Fold increase	p value	Day 0	Day 30
IFN-γ										
All ages	76.0 (49.0, 99.0)	198.0 (148.0, 261.0)	2.68 (2.09, 3.78)	<0.0001	87.0 (64.0, 120.0)	165.0 (114.0, 226.0)	1.84 (1.11, 2.77)	<0.0001	0.0254	0.0007
50~59 years	73.0 (49.0, 99.0)	200.0 (157.0, 242.0)	2.66 (2.01, 3.98)	<0.0001	87.0 (67.0, 115.0)	161.0 (108.0, 215.0)	1.76 (1.20, 2.56)	<0.0001	0.0417	0.0077
60~69 years	78.5 (56.5, 104.5)	197.0 (148.0, 290.0)	2.68 (2.20, 3.69)	<0.0001	88.0 (54.0, 132.0)	170.5 (124.0, 229.0)	1.87 (1.07, 3.62)	<0.0001	0.4065	0.0301
≥ 70 years	74.5 (42.5, 97.5)	178.0 (116.0, 264.5)	2.69 (2.03, 3.42)	<0.0001	87.0 (68.0, 117.0)	134.0 (113.0, 250.0)	2.32 (1.08, 3.02)	0.0044	0.4138	0.5817
IL-2										
All ages	66.0 (45.0, 105.0)	219.0 (142.0, 308.0)	3.35 (2.18, 4.83)	<0.0001	79.0 (48.0, 111.0)	210.5 (126.0, 288.0)	2.71 (1.43, 4.92)	<0.0001	0.4038	0.3132
50~59 years	84.0 (50.0, 118.0)	238.0 (138.0, 312.0)	3.22 (2.05, 4.40)	<0.0001	83.5 (48.0, 115.0)	218.0 (143.0, 294.0)	2.86 (1.42, 5.09)	<0.0001	0.9631	0.7055
60~69 years	58.5 (38.5, 84.0)	222.0 (153.5, 309.5)	3.80 (2.76, 5.29)	<0.0001	74.0 (46.0, 97.0)	203.0 (122.0, 289.0)	2.69 (2.04, 4.21)	<0.0001	0.1583	0.4110
≥ 70 years	85.5 (49.5, 127.0)	190.0 (119.0, 256.0)	2.65 (2.01, 4.23)	0.0033	83.0 (63.0, 134.0)	165.0 (95.0, 227.0)	1.71 (0.984, 3.00)	0.0397	0.8709	0.4024
TNF-α										
All ages	129.0 (90.0, 186.0)	266.0 (187.0, 364.0)	2.18 (1.26, 3.03)	<0.0001	147.5 (102.0, 193.0)	277.5 (206.5, 458.0)	2.07 (1.24, 3.06)	<0.0001	0.1269	0.0769
50~59 years	128.0 (90.0, 190.0)	265.0 (180.0, 354.0)	2.29 (1.40, 2.98)	<0.0001	151.5 (102.0, 197.0)	286.0 (202.0, 459.0)	2.06 (1.11, 2.94)	<0.0001	0.1279	0.1637

60~69 years	128.5 (87.0, 163.0)	264.0 (182.5, 403.5)	2.13 (1.17, 3.37)	<0.0001	150.0 (102.0, 206.0)	275.0 (225.0, 467.0)	2.02 (1.28, 3.07)	<0.0001	0.1887	0.1266
≥70 years	156.5 (118.0, 188.0)	300.0 (249.0, 354.5)	1.97 (1.65, 3.00)	0.0005	127.0 (81.0, 150.0)	248.0 (211.0, 387.0)	2.18 (1.79, 3.05)	0.0003	0.1986	0.6899
CD40L										
All ages	42.0 (29.0, 66.0)	58.0 (35.0, 103.0)	1.47 (0.92, 2.08)	0.0003	49.5 (29.0, 83.0)	51.5 (33.5, 89.0)	0.96 (0.72, 1.22)	0.7513	0.3774	0.0227
50~59 years	43.0 (26.0, 72.0)	52.0 (36.0, 94.0)	1.41 (0.92, 2.08)	0.0140	49.0 (29.0, 85.0)	49.0 (33.0, 95.0)	0.96 (0.74, 1.54)	0.5543	0.4343	0.2529
60~69 years	40.5 (31.0, 64.0)	59.0 (31.5, 104.5)	1.55 (1.03, 1.88)	0.0196	57.0 (36.0, 85.0)	54.0 (38.0, 85.0)	0.97 (0.68, 1.14)	0.7465	0.1060	0.2785
≥70 years	46.0 (38.0, 68.0)	76.0 (46.0, 119.0)	1.71 (0.82, 2.23)	0.1932	35.0 (18.0, 44.0)	34.0 (19.0, 52.0)	1.07 (0.93, 1.14)	0.7467	0.0151	0.0129

Data shows the median, and error bars indicate interquartile range (IQR); Fold increase indicates the median fold of the frequencies of cytokine-producing CD4⁺ T cells day 30 postvaccination to that baseline; Differences between groups were analyzed using t test after log-transformed T-cell frequency. Day 0, baseline before vaccination; Day 30, day 30 after the second dose. IFN- γ , interferon- γ ; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α ; CD40L, cluster of differentiation 40 ligand; PBMCs, peripheral blood mononuclear cells.

Table S4. The frequencies of cytokine-producing T cells per 10⁵ CD8⁺ T cells

	LZ901 (n=141)				HZ/su (n=136)				p value (LZ901 VS HZ/su)	
	Day 0	Day 30	Fold increase	p value	Day 0	Day 30	Fold increase	p value	Day 0	Day 30
IFN-γ										
All ages	197.0 (130.0,289.0)	347.0 (222.0,495.0)	1.90 (1.08,2.52)	<0.0001	216.5 (151.0,326.0)	213.0 (154.5,328.5)	0.995 (0.792,1.15)	0.8221	0.0697	<0.0001
50~59 years	202.0 (137.0,311.0)	340.0 (217.0,523.0)	1.88 (1.07, 2.41)	<0.0001	229.5 (151.0,351.0)	242.0 (163.0,348.0)	0.992 (0.823,1.10)	0.9706	0.0649	0.0030
60~69 years	196.0 (131.5,286.0)	358.5 (243.0,486.0)	1.82 (1.11, 2.55)	0.0002	198.0 (153.0,299.0)	200.5 (151.0,306.0)	0.998 (0.773, 1.22)	0.7488	0.9300	0.0002
≥ 70 years	158.0 (117.0,244.5)	328.0 (251.0,468.5)	2.35 (1.51, 2.70)	0.0003	177.0 (140.0,359.0)	185.0 (154.0,403.0)	1.04 (0.773, 1.12)	0.8714	0.2132	0.1368
IL-2										
All ages	97.0 (50.0, 164.0)	235.0 (140.0,376.0)	2.57 (1.61, 3.71)	<0.0001	110.5 (79.0, 152.0)	136.5 (83.5, 204.0)	1.12 (0.92, 1.54)	0.0024	0.1380	<0.0001
50~59 years	92.0 (50.0, 164.0)	268.0 (149.0,377.0)	2.92 (1.95, 3.93)	<0.0001	108.0 (84.0, 156.0)	150.0 (109.0,220.0)	1.61 (1.01, 1.70)	0.0065	0.0597	<0.0001
60~69 years	107.5 (55.0, 179.5)	225.0 (134.5,363.0)	2.23 (1.33, 3.42)	<0.0001	120.0 (68.0, 154.0)	134.5 (79.0, 186.0)	1.08 (0.89, 1.28)	0.1097	0.8562	<0.0001
≥ 70 years	89.5 (63.0, 163.5)	182.5 (123.5,265.5)	2.21 (1.05, 3.04)	0.0058	80.0 (53.0, 134.0)	82.0 (79.0, 135.0)	1.01 (0.768, 1.76)	0.6601	0.9650	0.0504
TNF-α										
All ages	514.0 (345.0,827.0)	598.0 (418.0,882.0)	1.01 (0.834,1.66)	0.1908	563.0 (395.0,906.0)	505.5 (331.5,746.0)	0.894 (0.612, 1.07)	0.0210	0.0652	0.0830
50~59 years	554.0 (347.0,811.0)	525.0 (330.0,803.0)	0.989 (0.791, 1.33)	0.9925	594.0 (395.0,986.0)	501.0 (306.0,756.0)	0.797 (0.561, 1.04)	0.0143	0.0583	0.6270
60~69 years	533.5 (348.5,840.0)	710.5 (461.5,1016.0)	1.03 (0.862, 1.92)	0.1433	555.0 (395.0,719.0)	542.5 (389.0,737.0)	0.948 (0.741, 1.06)	0.5399	0.6754	0.0905

≥70 years	452.5 (306.0,865.5)	675.0 (523.5, 865.5)	1.26 (0.943, 1.90)	0.2049	506.0 (416.0,1117.0)	464.0 (343.0,704.0)	0.925 (0.505, 1.57)	0.7501	0.5989	0.3502
CD40L										
All ages	68.0 (45.0, 120.0)	92.0 (46.0, 165.0)	1.41 (0.902, 1.98)	0.0108	67.0 (40.0, 114.0)	76.5 (38.0, 132.0)	0.993 (0.697, 1.59)	0.8007	0.9111	0.0298
50~59 years	74.0 (40.0, 115.0)	96.0 (49.0, 162.0)	1.52 (0.927, 2.00)	0.0224	67.5 (40.0, 119.0)	84.0 (42.0, 147.0)	1.01 (0.741, 1.82)	0.3815	0.9828	0.1732
60~69 years	70.5 (45.5, 127.5)	83.0 (44.5, 173.0)	1.34 (0.873, 1.87)	0.3039	64.0 (42.0, 107.0)	73.5 (35.0, 131.0)	0.956 (0.726, 1.32)	0.8563	0.4043	0.1448
≥70 years	53.0 (47.5, 91.5)	80.5 (35.5, 152.5)	1.43 (0.855, 1.86)	0.4303	83.0 (51.0, 142.0)	51.0 (38.0, 99.0)	0.758 (0.32, 1.59)	0.2656	0.2995	0.3272

Data shows the median, and error bars indicate interquartile range (IQR); Fold increase indicates the median fold of the frequencies of cytokine-producing CD8+ T cells day 30 postvaccination to that baseline; Differences between groups were analyzed using t test after log-transformed T-cell frequency. Day 0, baseline before vaccination; Day 30, day 30 after the second dose. IFN- γ , interferon- γ ; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α ; CD40L, cluster of differentiation 40 ligand; PBMCs, peripheral blood mononuclear cells.

Table S5. Multivariable Analysis of anti-gE antibody and CD4⁺/CD8⁺ T cells expressing cytokines 30 days after vaccination

Variables	D30 IgG		D30 IFN- γ ⁺ CD4 ⁺		D30 IL-2 ⁺ CD4 ⁺		D30 TNF- α ⁺ CD4 ⁺		D30 CD40L ⁺ CD4 ⁺		D30 IFN- γ ⁺ CD8 ⁺		D30 IL-2 ⁺ CD8 ⁺		D30 TNF- α ⁺ CD8 ⁺		D30 CD40L ⁺ CD8 ⁺	
	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value	β (SE)	P value
Sex(reference: female)	0.004 (0.073)	0.955	0.034 (0.056)	0.543	-0.002 (0.068)	0.980	0.077 (0.061)	0.208	-0.017 (0.077)	0.829	0.041 (0.062)	0.51 0	-0.002 (0.063)	0.979	0.089 (0.065)	0.17 1	0.001 (0.083)	0.987
Age (reference:50-59 years)																		
60-69 years	0.022 (0.077)	0.777	0.092 (0.059)	0.121	0.005 (0.072)	0.941	0.059 (0.064)	0.359	-0.036 (0.082)	0.659	-0.012 (0.066)	0.85 4	-0.151 (0.067)	0.025	0.188 (0.068)	0.00 6	-0.108 (0.088)	0.217
≥70 years	-0.111 (0.121)	0.360	0.014 (0.093)	0.882	-0.215 (0.113)	0.057	0.170 (0.101)	0.092	-0.043 (0.128)	0.736	0.068 (0.104)	0.51 4	-0.287 (0.105)	0.007	0.224 (0.107)	0.03 8	-0.341 (0.137)	0.014
Vaccine group (reference: HZ/su)	-0.815 (0.072)	<0.0 01	0.267 (0.055)	<0.00 1	0.141 (0.067)	0.036	0.060 (0.060)	0.320	0.255 (0.076)	<0.00 1	0.437 (0.062)	<0.0 01	0.640 (0.062)	<0.00 1	0.199 (0.064)	0.00 2	0.197 (0.082)	0.016
Log(D0 IgG)	0.163 (0.041)	<0.0 01	0.053 (0.031)	0.093	0.043 (0.038)	0.262	-0.0009 (0.034)	0.980	0.021 (0.043)	0.634	0.039 (0.035)	0.26 4	0.099 (0.035)	0.005	0.003 (0.036)	0.93 1	0.022 (0.046)	0.638
Log(D0 IFN- γ ⁺ CD4 ⁺)	-0.040 (0.075)	0.598	0.291 (0.058)	<0.00 1	0.019 (0.070)	0.790	-0.0009 (0.063)	0.989	-0.135 (0.080)	0.093	-0.074 (0.064)	0.25 2	0.055 (0.065)	0.399	-0.107 (0.067)	0.10 9	-0.202 (0.086)	0.019
Log(D0 IL-2 ⁺ CD4 ⁺)	-0.012 (0.055)	0.827	0.037 (0.042)	0.379	0.340 (0.051)	<0.00 1	0.002 (0.046)	0.972	-0.026 (0.058)	0.659	0.085 (0.047)	0.07 2	0.102 (0.048)	0.033	0.110 (0.049)	0.02 5	0.033 (0.625)	0.596
Log(D0 TNF- α ⁺ CD4 ⁺)	0.046 (0.070)	0.510	0.070 (0.054)	0.195	-0.058 (0.065)	0.379	0.316 (0.058)	<0.00 1	0.005 (0.074)	0.949	-0.034 (0.060)	0.57 5	-0.088 (0.061)	0.151	-0.065 (0.062)	0.29 6	0.044 (0.080)	0.581

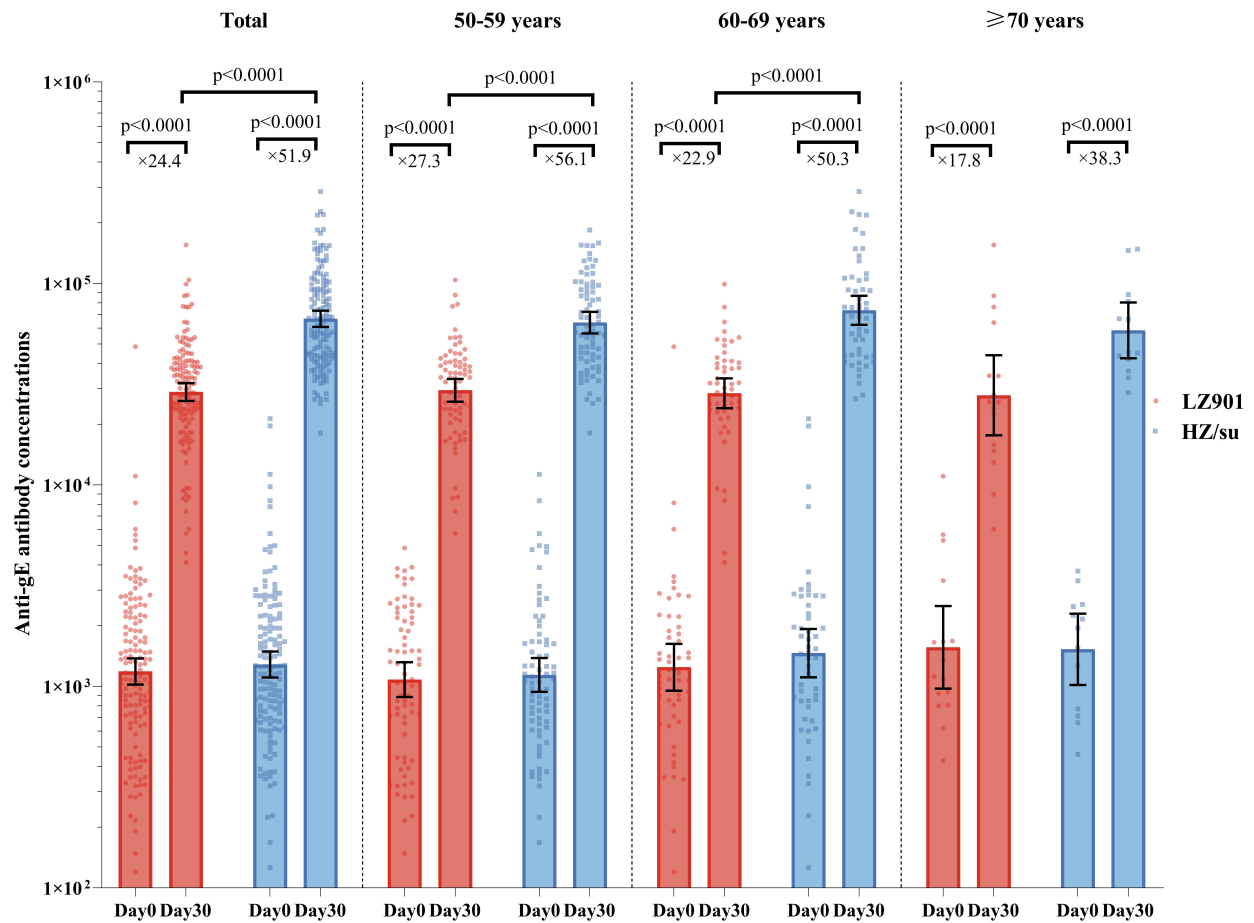
Log(D0 CD40L ⁺ CD 4 ⁺)	0.066 (0.056)	0.242	0.024 (0.043)	0.585	0.042 (0.053)	0.427	0.059 (0.047)	0.212	0.683 (0.060)	<0.00 1	0.023 (0.048)	0.63 7	-0.012 (0.049)	0.809	0.055 (0.050)	0.27 0	-0.041 (0.064)	0.522
Log(D0 IFN- γ ⁺ CD8 ⁺)	0.019 (0.092)	0.839	0.086 (0.071)	0.223	-0.006 (0.086)	0.949	0.032 (0.077)	0.679	-0.061 (0.098)	0.535	0.487 (0.079)	<0.0 01	-0.007 (0.080)	0.927	-0.050 (0.082)	0.54 0	-0.129 (0.104)	0.221
Log(D0 IL-2 ⁺ CD8 ⁺)	-0.013 (0.056)	0.810	-0.016 (0.043)	0.711	0.102 (0.052)	0.049	-0.047 (0.046)	0.313	-0.058 (0.059)	0.327	0.028 (0.048)	0.56 0	0.511 (0.048)	<0.00 1	-0.069 (0.049)	0.16 6	0.003 (0.063)	0.958
Log(D0 TNF- α ⁺ CD 8 ⁺)	0.0003 (0.078)	0.997	-0.066 (0.060)	0.275	0.061 (0.073)	0.404	-0.069 (0.065)	0.291	0.086 (0.083)	0.302	0.073 (0.067)	0.27 8	0.102 (0.068)	0.133	0.693 (0.069)	<0.0 01	0.146 (0.089)	0.102
Log(D0 CD40L ⁺ CD 8 ⁺)	-0.034 (0.051)	0.507	-0.807 (0.039)	0.039	-0.036 (0.047)	0.447	-0.0007 (0.042)	0.987	-0.039 (0.054)	0.474	0.012 (0.043)	0.79 0	-0.026 (0.044)	0.563	0.080 (0.045)	0.07 6	0.659 (0.058)	<0.0 01

Day 0, baseline before vaccination; Day 30, day 30 after the second dose. IFN- γ , interferon- γ ; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α ; CD40L, cluster of differentiation 40 ligand.

Table S6. List of severe adverse events

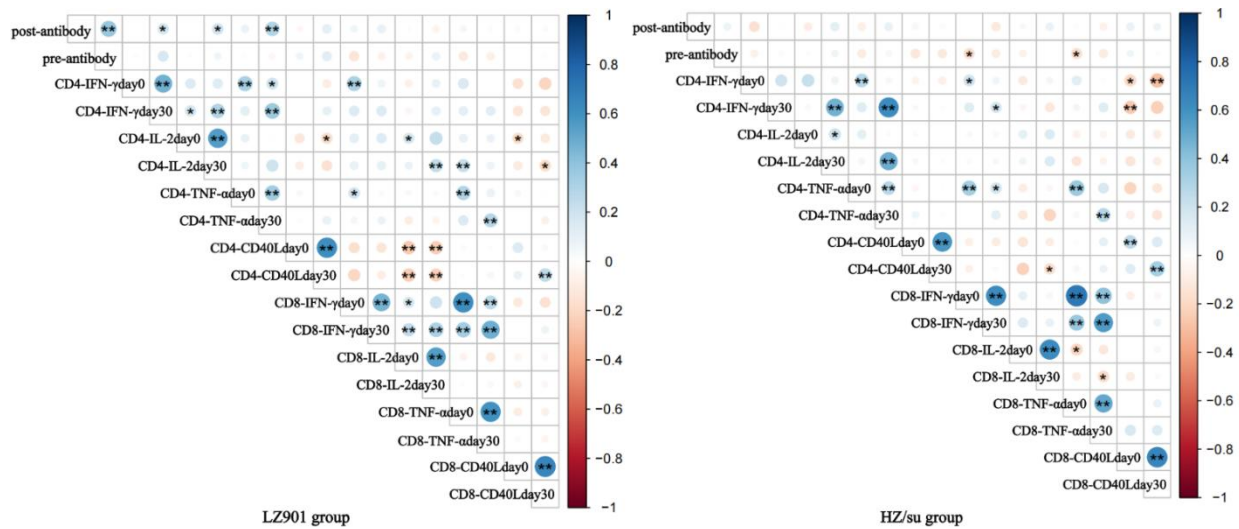
Group	Disease	Time of vaccination	Start time	End time	Outcome	Correlation with vaccination
LZ901	Bronchiectasis with infection, candida pneumonia, type II respiratory failure	2023/12/25	2024/2/4	2024/2/16	Improvement	NO
LZ901	Hepatocellular carcinoma	2023/12/26	2024/5/9	2024/8/28	Improvement	NO
LZ901	Incarcerated inguinal hernia	2023/12/27	2024/5/10	2024/5/18	Recovery	NO
LZ901	Coronary atherosclerotic cardiopathy	2023/12/29	2024/3/27	2024/4/2	Improvement	NO
HZ/su	hypohepatia	2023/12/26	2024/8/5	2024/8/20	Recovery	NO
HZ/su	Lung abscess	2023/12/26	2024/1/29	2024/5/20	Recovery	NO
HZ/su	Polypofcolon	2023/12/27	2024/7/17	2024/7/23	Recovery	NO
HZ/su	Enign tumor of hepatic flexure of colon	2023/12/28	2024/7/20	2024/7/25	Recovery	NO

Figure S1. gE-specific IgG antibody concentrations according to age



The number under p value indicate that geometric mean fold increase (GMFI) of gE-specific IgG antibody day 30 after the second dose to that baseline. Day 0, baseline before vaccination; Day 30, day 30 after the second dose.

Figure S2. Correlation matrices of antibody levels with cell-mediated immunity responses to LZ901 vaccine and HZ/su vaccine.



*P < .05; **P < .01; blank cells: P > .05. Day 0, baseline before vaccination; Day 30, day 30 after the second dose. IFN- γ , interferon- γ ; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α ; CD40L, cluster of differentiation 40 ligand.

Figure S3. Solicited adverse reactions that occurred within 30 days after each dose

