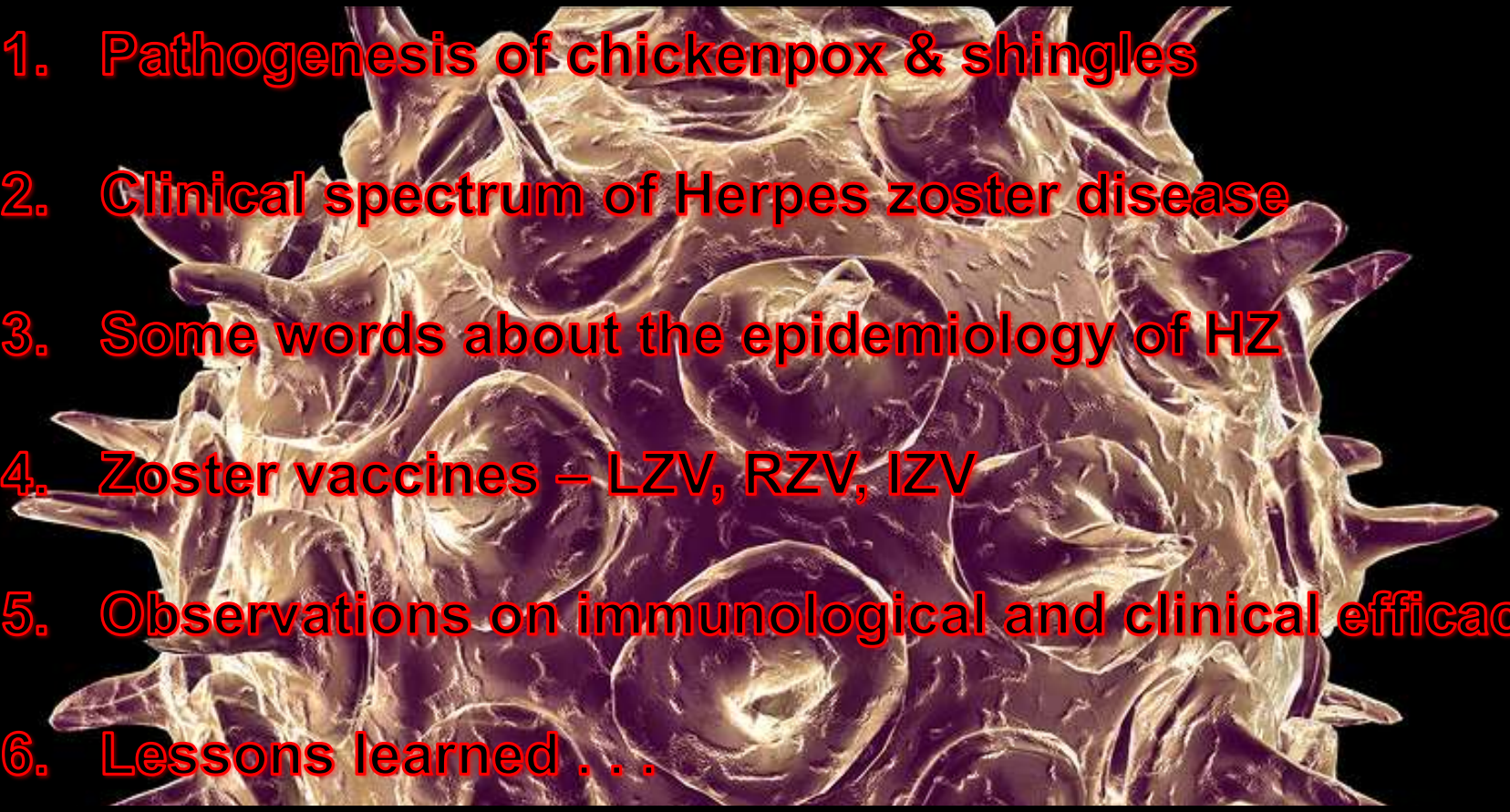
VARICELLA-ZOSTER VIRUS –

Herpes zoster is An Ever-present Risk for Cancer Patients. . .

VARICELLA-ZOSTER VIRUS

A focus on Herpes zoster . . .



1. Pathogenesis of chickenpox & shingles
2. Clinical spectrum of Herpes zoster disease
3. Some words about the epidemiology of HZ
4. Zoster vaccines – LZV, RZV, IZV
5. Observations on immunological and clinical efficacy
6. Lessons learned . . .

PATHOGENESIS OF HERPES-ZOSTER V

Infection of host
respiratory epithelial cells

Infection of host
immune cells –
dendritic cells

T-cell 2° viraemia:
Transport to skin cells

DRG

Sensory
nerve
"Latency"

Spinal
cord

1°Viraemia: Transport to local lymph nodes and reticuloendothelial system with infection of T-cells . . . 2 weeks (10-21 days)

HERPES ZOSTER IN CANCER PATIENTS

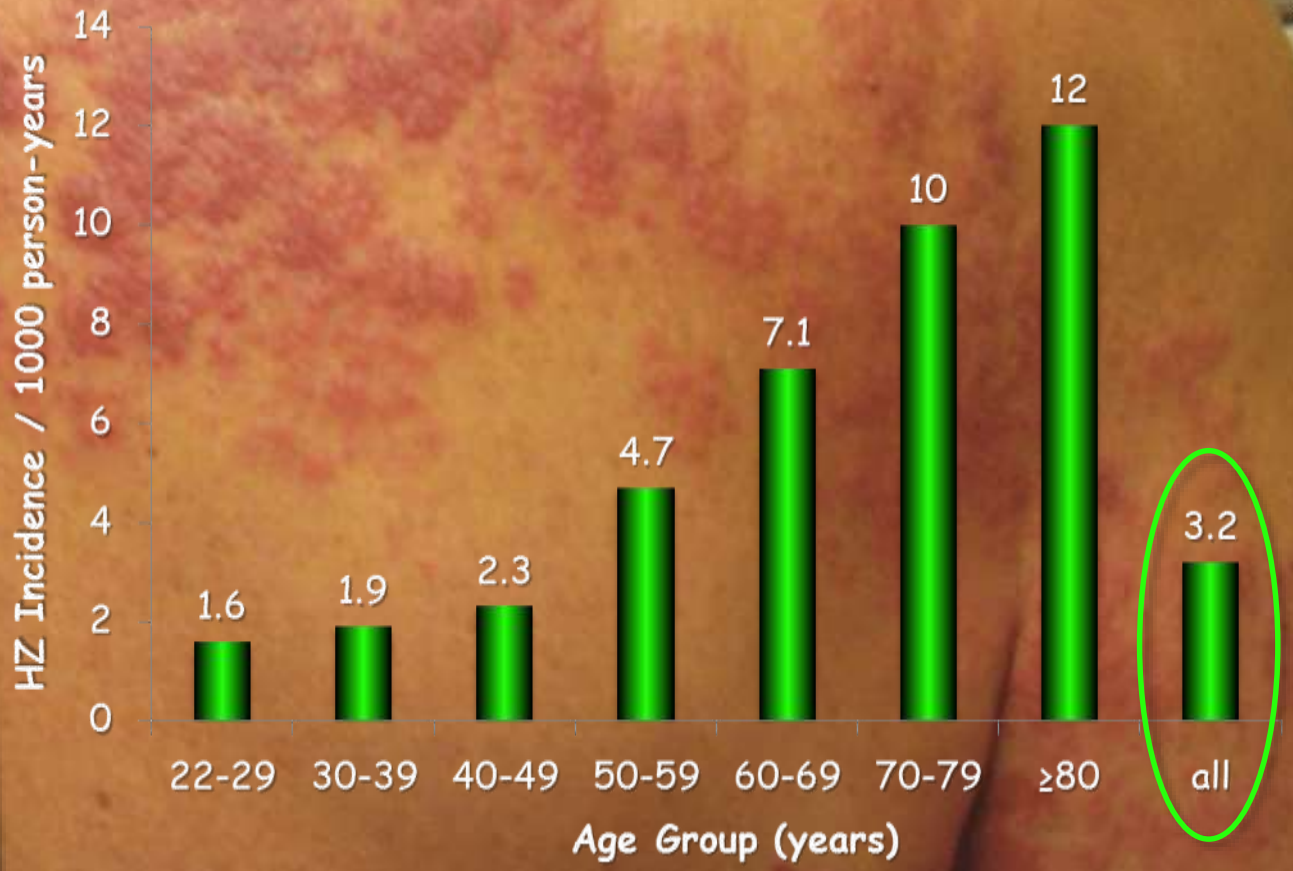
Clinical Spectrum of Herpes Zoster (Shingles)

- Cutaneous Zoster
  - Localized dermatomal (contiguous)
  - Disseminated (non-contiguous)
- Visceral
  - Brain
  - Lungs
  - Liver
- Atypical syndromes (Abdominal pain)
- Bacterial superinfection
- Post-herpetic neuralgia
- Zoster ophthalmicus

HERPES ZOSTER IN IMMUNOCOMPETENT PATIENTS

Incidence by Age Extrapolated to the US Population

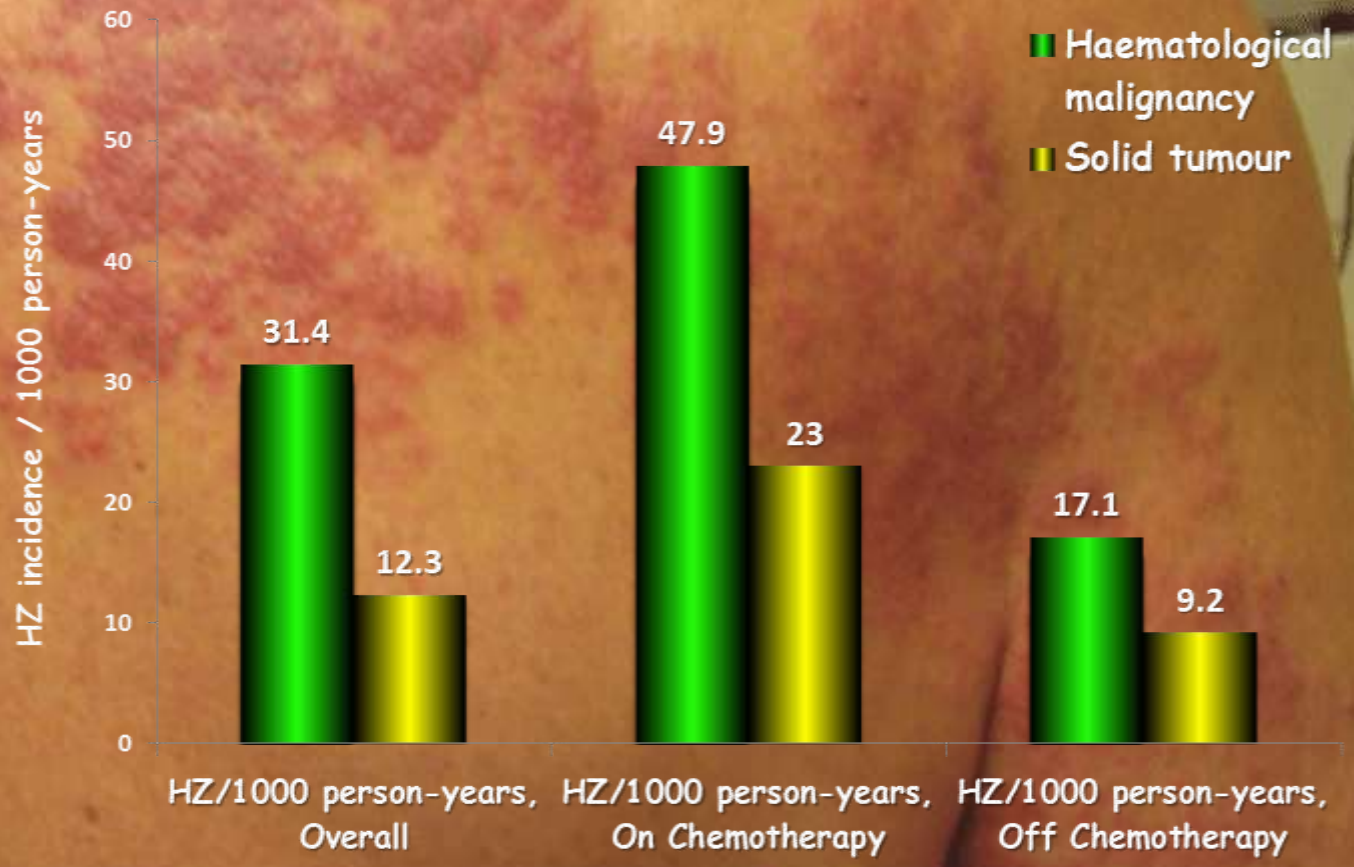
Yawn BP *et al.* (Olmsted Medical Center, Rochester, NY) Mayo Clin Proc 2007;82(11):1341-1349



HERPES ZOSTER IN CANCER PATIENTS

Incidence by Tumour Type & Chemotherapy

Habel LA *et al.* (Kaiser Permanente, Northern California) Cancer Epidemiol Biomarkers Prev 2013;22(1):82-90

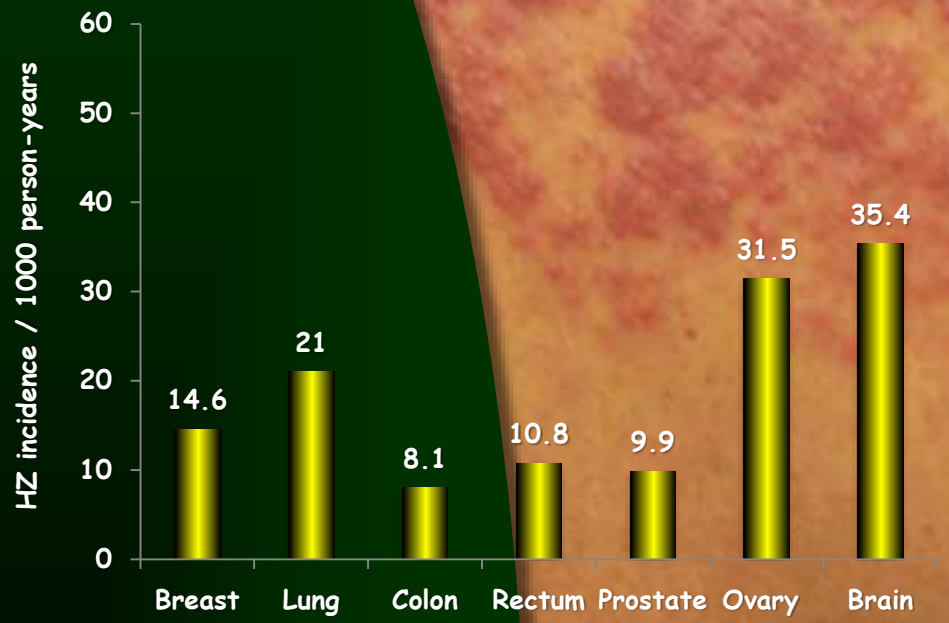


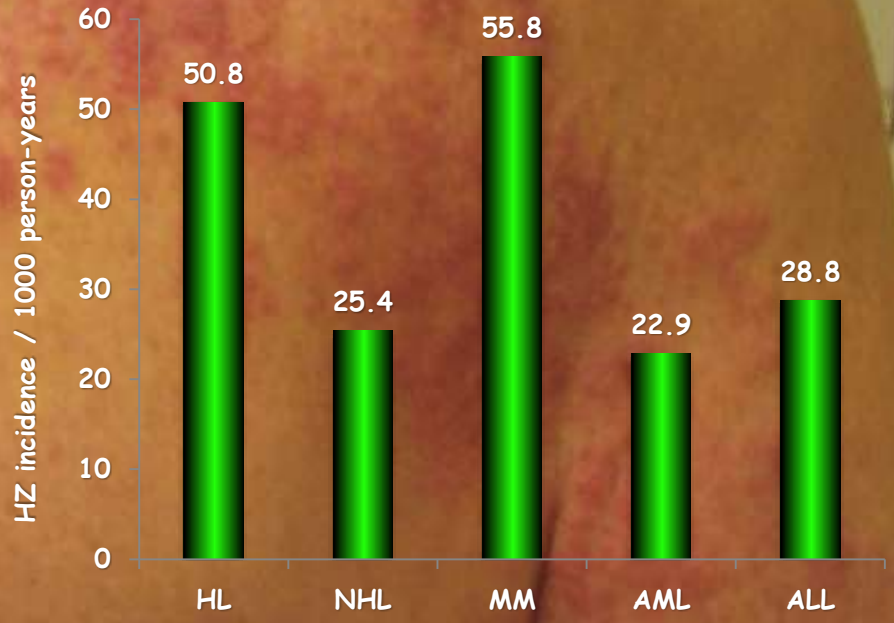
HERPES ZOSTER IN CANCER PATIENTS

Incidence by Diagnosis:

Solid Tumour vs Haematological Malignancy

Habel LA *et al.* (Kaiser Permanente, Northern California) Cancer Epidemiol Biomarkers Prev 2013;22(1):82-90





IMMUNIZATION IN CANCER PATIENTS

Zoster (Shingles) Vaccines

Live Attenuated VZV (LZV)

- OKA/Merck Strain
- Zostavax™
- 0.65 mL SC

Inactivated VZV (IZV)

- OKA/Merck Strain
- Heat inactivated or Gamma irradiated
- 4 doses, 0.5 mL SC each

Recombinant Adjuvanted VZV (RZV)

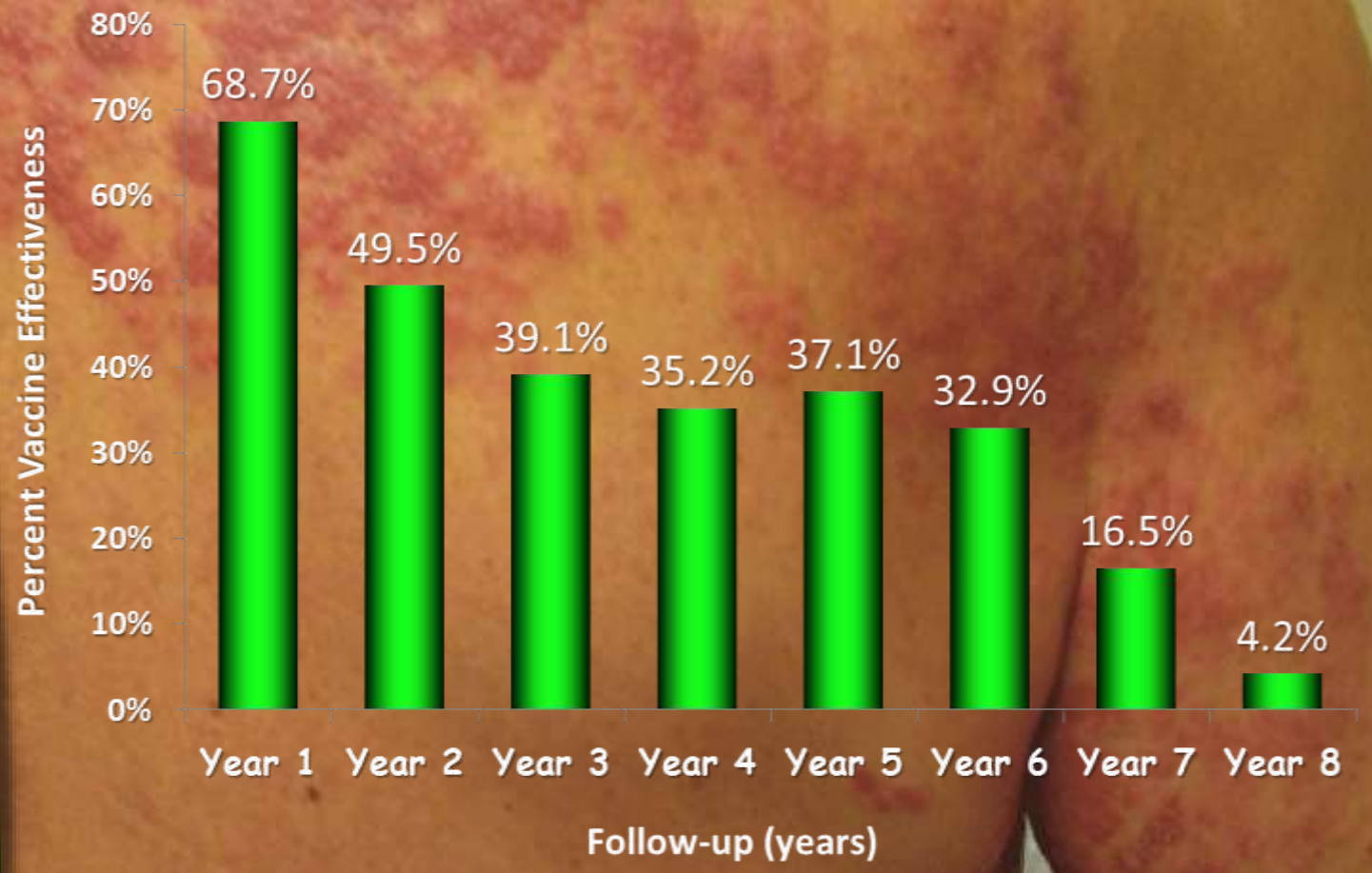
- Glycoprotein-E Ag
- $ASO1_B$ adjuvant system
- Shingrix™
- 2 doses, 0.5 mL IM each

IMMUNIZATION IN HEALTHY ADULTS ≥ 60 YRS

Live Attenuated Zoster Vaccine:

Waning Effectiveness after 7 Years

Tseng HF *et al.* (Kaiser Permanente) J Infect Dis 2016:213:1872-5

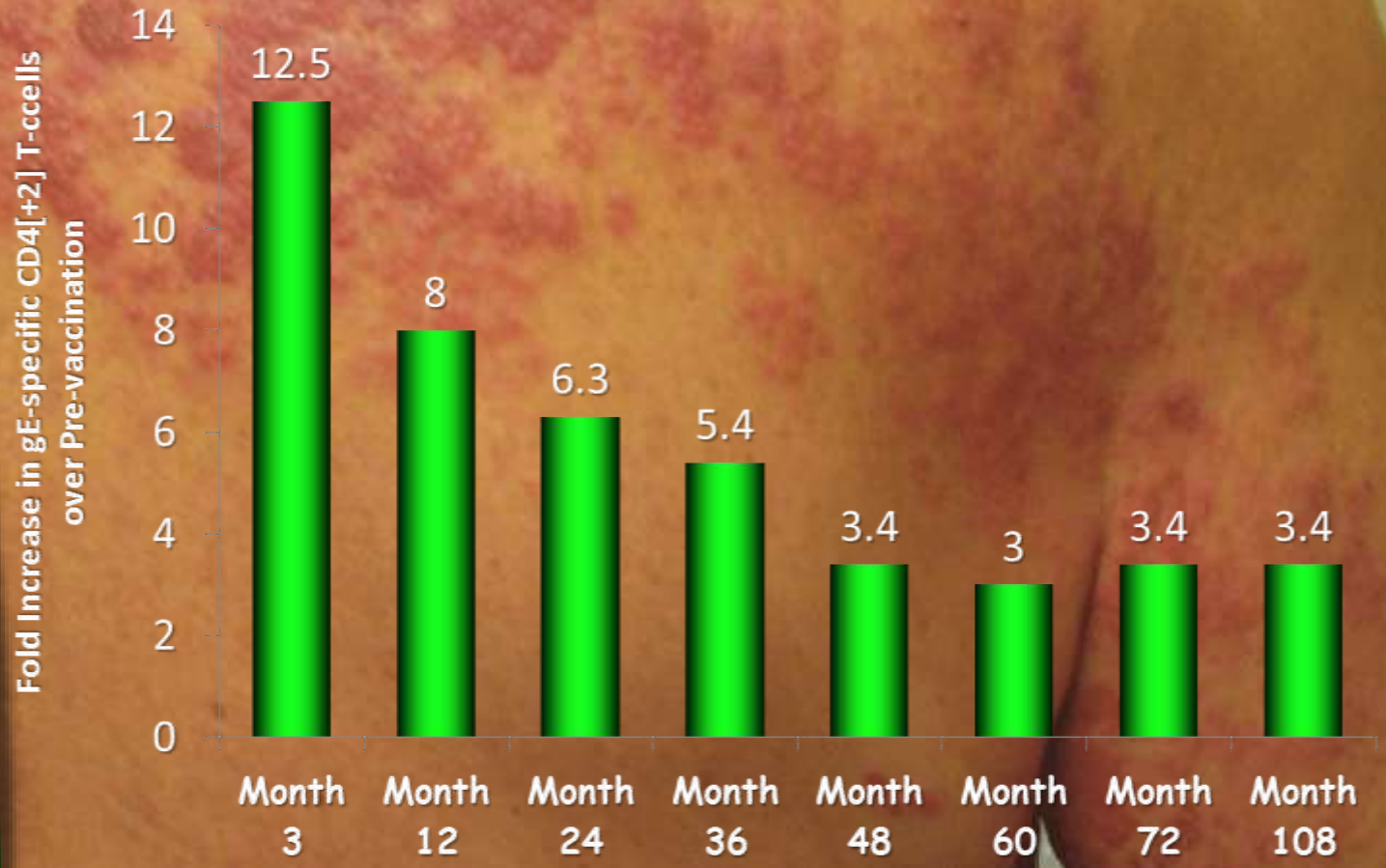


IMMUNIZATION IN HEALTHY ADULTS ≥ 60 YRS

Recombinant Zoster Vaccine:

Persistence of Cellular Immune Response ≥ 9 Yrs

Pauksens K *et al.* IDSA Week 2017:Abstract #1342



IMMUNIZATION AGAINST HERPES ZOSTER

Relative Efficacy of the Live Attenuated Compared to Recombinant Zoster (Shingles) Vaccines in Otherwise Healthy Older Adults

	Herpes Zoster	Incidence rate$^{-1000\ P\text{-}Y}$	Vaccine Efficacy (1-IRR)[6]
Oxman, 2005[1]			
LZV[2]	315 / 19254 (1.6%)	5.4	51.3%
PLA[3]	642 / 19247 (3.3%)	11.1	(44.2-57.6%)
Lal, 2015[4]			
RZV[5]	6 / 7698 (0.08%)	0.3	97.2%
PLA[3]	210 / 7713 (2.7%)	9.1	(93.7-99.0%)

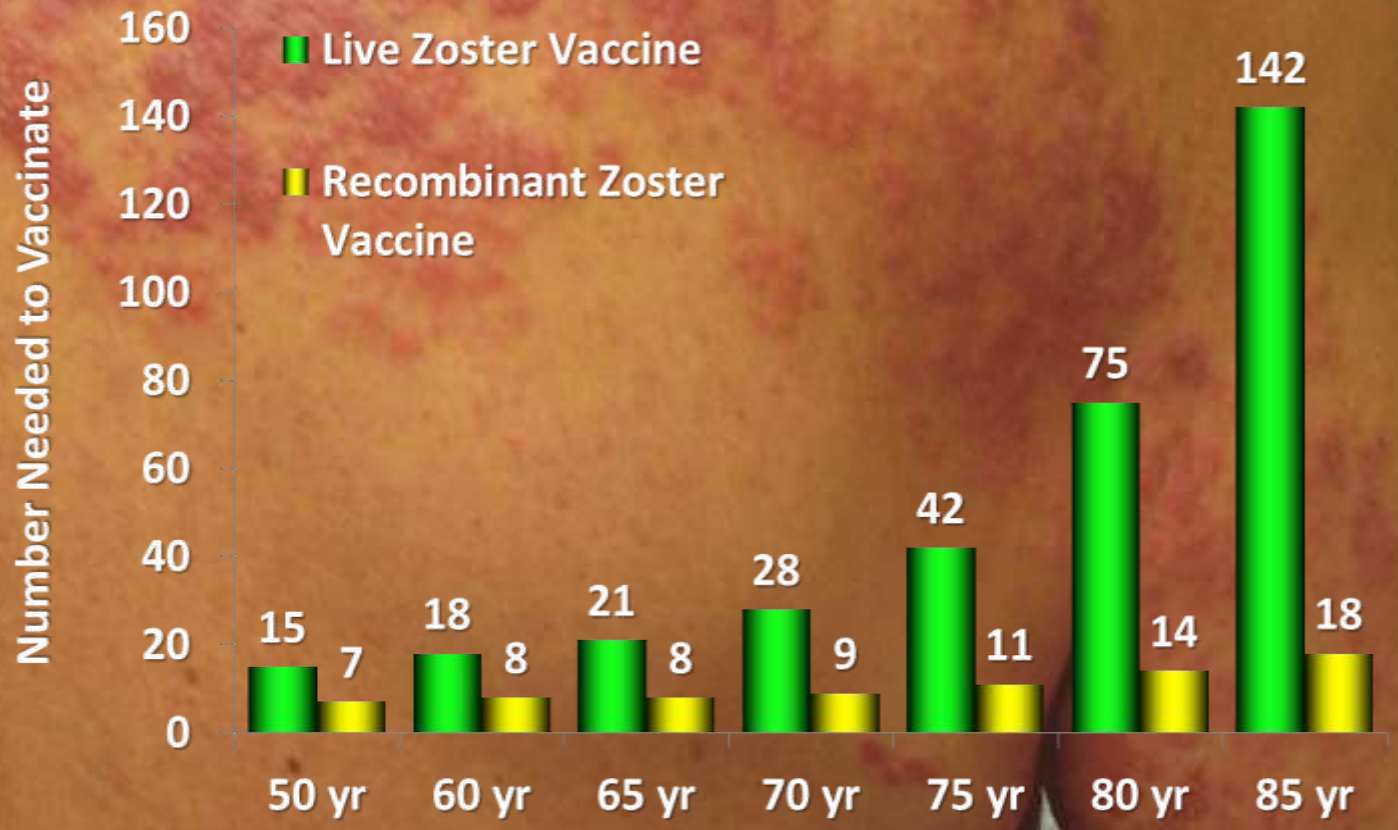
1. Oxman MN *et al.* (Shingles Prevention Grp) NEJM 2005;352(22):2271-84. RRR = 52%, NNT = 59.
2. Live attenuated zoster vaccine
3. Placebo
4. Lal, H. *et al.* (ZOE-50 Study) NEJM 2015;372 (22):2087-96. RRR = 70%, NNT = 38.
5. Recombinant zoster vaccine
6. Incidence rate ratio

IMMUNIZATION IN HEALTHY ADULTS ≥ 50 YRS

Live vs Recombinant Zoster Vaccine:

Number Needed to Vaccinate to Prevent a Case of Zoster

Drolet M *et al.* (L'Université de Quebec, Université Laval, Institute National de Santé Publique du Québec)
CMAJ 2019:191(34):E932-9



IMMUNIZATION IN IMMUNOSUPPRESSED PATIENTS

RZV Efficacy Against Herpes Zoster in Patients with Immune-mediated Diseases (GSK ZOE-50/70 Studies)

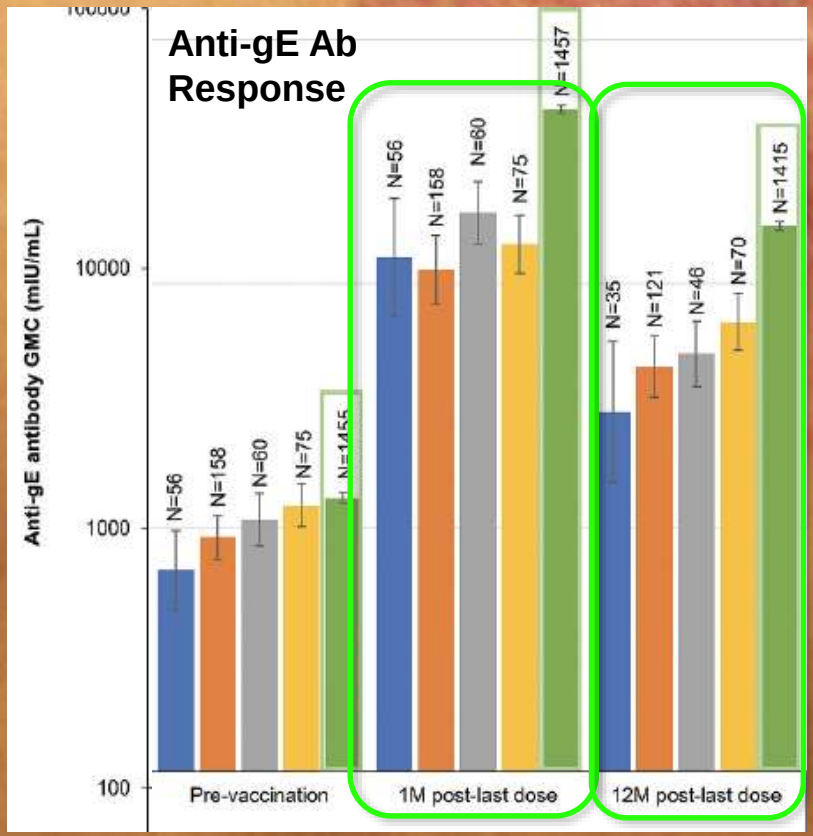
Dagnew AF (GSK) *et al.* Rheumatology 2021;60(3):1226-33

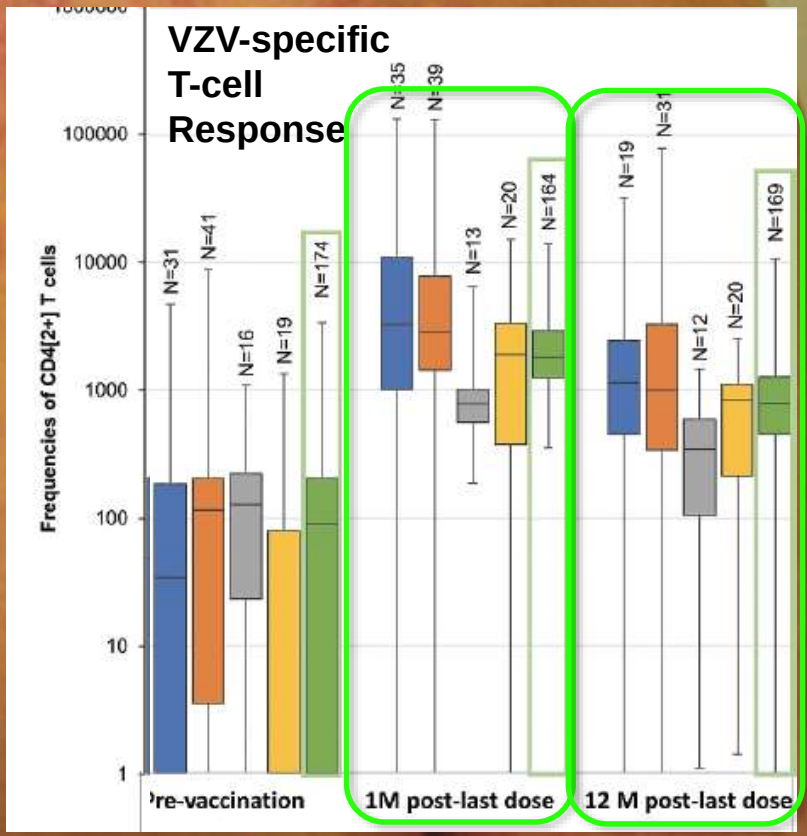
	RZV				Placebo				Vaccine efficacy[b], % (95% CI)
	n	No. of confirmed HZ cases	Sum of follow-up years[a]	Incidence per 1000 person-years	*n*	No. of confirmed HZ cases	Sum of follow-up years[a]	Incidence per 1000 person-years	
Overall	936	4	3611.7	1.1	923	38	3408.8	11.1	90.5 (73.5, 97.5)
50–59 YOA	222	1	885.6	1.1	201	11	775.6	14.2	92.8 (50.5, 99.8)
60–69 YOA	159	0	638.3	0.0	151	8	588.8	13.6	100 (54.9, 100)
70–79 YOA	427	2	1623.0	1.2	450	13	1647.3	7.9	84.4 (30.8, 98.3)
≥80 YOA	128	1	464.8	2.2	121	6	397.0	15.1	86.2 (-13.5, 99.7)

IMMUNIZATION IN IMMUNOSUPPRESSED PATIENTS

Humoral and Cellular Response to RZV in Oncology and Renal Transplant Patients in GSK Clinical Trials

Dagnew AF (GSK) *et al.* Hum Vaccin Immunother 2021;17(11):432-43





AutoSCT Recipients | HM Patients | ST Patients | Renal allograft | Immunocompetent Controls

IMMUNIZATION IN CANCER PATIENTS

Zoster (Shingles) Vaccines in AutoSCT

	Herpes Zoster	Person-years	Incidence rate[-1000 P-Y]	Vaccine Efficacy (1-IRR)[6]
Winston, 2018[1]				
IZV[2]	42/538 (7.8%)	1277	32.9	64%
PLA[3]	113/535 (21.1%)	1230	91.9	(48-75%)
Bastidas, 2019[4]				
RZV[5]	49/870 (5.6%)	1633	30.0	64%
PLA[3]	135/851 (15.9%)	1432	94.3	(56-78%)

1. Winston D *et al.* (V212 Protocol 001 Trial) Lancet 2018;391(10135):2116-27. RRR = 63%, NNT = 8.
2. Inactivated zoster vaccine
3. Placebo
4. Bastidas A, *et al.* (ZOE-HSCT Study) JAMA 2019;322(2):123-33. RRR = 65%, NNT = 10.
5. Recombinant zoster vaccine
6. Incidence rate ratio

IMMUNIZATION IN CANCER PATIENTS

Impact of Zoster Vaccines on Post-herpetic Neuralgia in AutoSCT

	Post-Herpetic neuralgia	Person-years	Incidence rate$^{-1000\ P\text{-}Y}$	Vaccine Efficacy (1-IRR)[6]
Winston, 2018[1]				
IZV[2]	3/538 (0.6%)	1277	2.3	84%
PLA[3]	18/535 (3.4%)	1230	14.6	(45-95%)
Bastidas, 2019[4]				
RZV[5]	1/870 (0.1%)	1898	0.5	89%
PLA[3]	9/851 (1.1%)	1833	4.9	(22-100%)

1. Winston D *et al.* (V212 Protocol 001 Trial) Lancet 2018;391(10135):2116-27. RRR = 82%, NNT = 36
2. Inactivated zoster vaccine, 4 doses: d-30 pre-SCT, d+30, d+60, d+90
3. Placebo
4. Bastidas A, *et al.* (ZOE-HSCT Study) JAMA 2019;322(2):123-33. RRR = 91%, NNT = 100.
5. Recombinant zoster vaccine, 2 doses: d+50 to +70, then d+1 to 2 months later
6. Incidence rate ratio

IMMUNIZATION IN CANCER PATIENTS

Impact of Recombinant Zoster Vaccine on Pain and Functional Quality of Life after AutoSCT

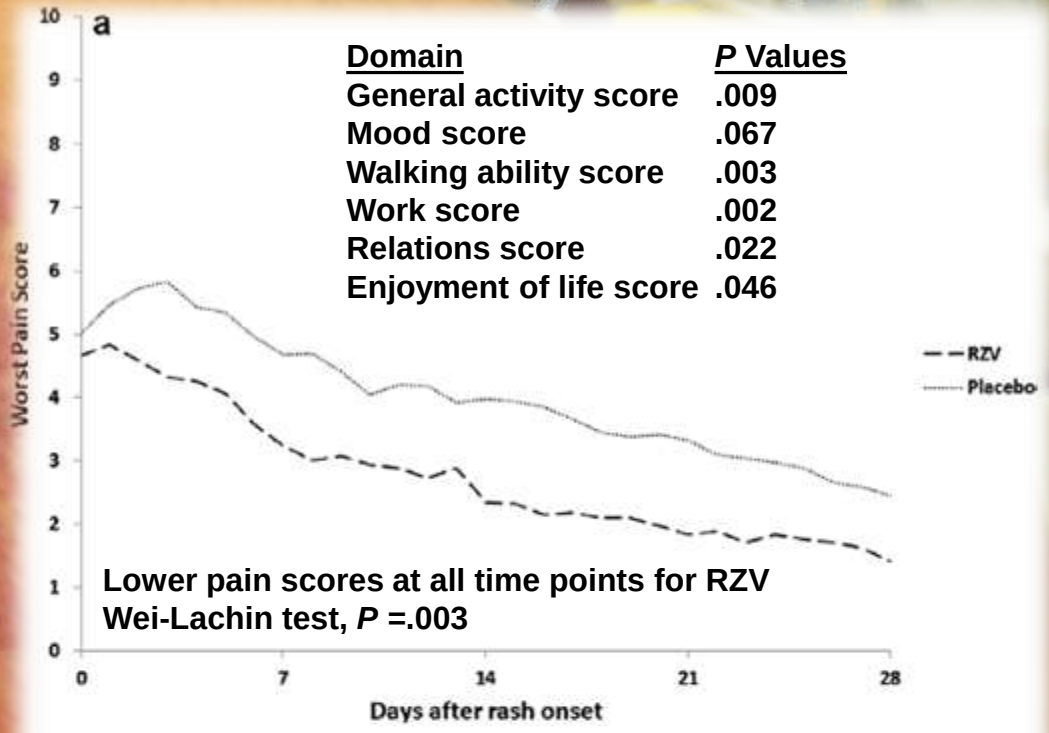
Curran D *et al.* Biol Blood Marrow Transpl 2019;25(12):2474-81

A. Mean Pain Score (Zoster Brief Pain Inventory) - Impact of HZ pain (0-10) on 7 domains:

1. General activity
2. Mood
3. Walking ability
4. Work
5. Relation with others
6. Sleep
7. Enjoyment of life

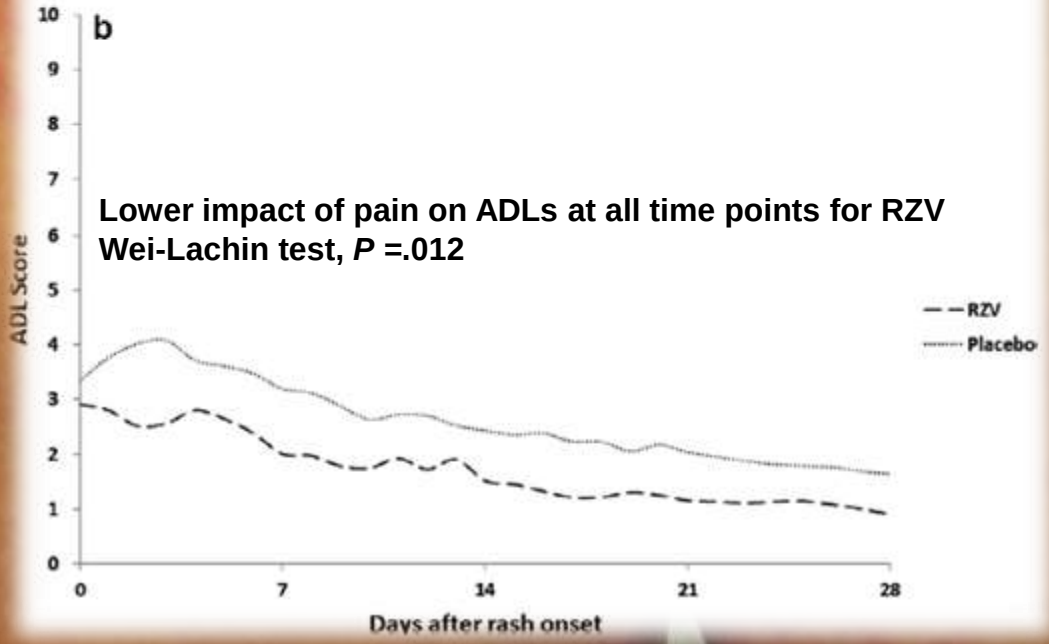
B. Mean Activities of Daily Living Score - Impact of HZ pain (None, some, severe) on 5 dimensions:

1. Mobility
2. Self care
3. Usual activities
4. Pain or discomfort
5. Anxiety or depression



Domain	*P* Values
General activity score	.009
Mood score	.067
Walking ability score	.003
Work score	.002
Relations score	.022
Enjoyment of life score	.046

Lower pain scores at all time points for RZV
Wei-Lachin test, *P* =.003



Lower impact of pain on ADLs at all time points for RZV
Wei-Lachin test, *P* =.012

IMMUNIZATION IN CANCER PATIENTS

Injection Site Adverse Events Associated with Zoster Vaccines in AutoSCT

Inactivated Zoster Vaccine[1]	Placebo[1]	Recombinant Zoster Vaccine[2]	Placebo[2]
191/657 (29.1%)[3,5]	113/535 (6.4%)[3]	773/901 (85.8%)[4,5]	93/892 (10.4%)[4]

1. Winston D *et al.* (V212 Protocol 001 Trial) Lancet 2018;391(10135):2116-27. RRI = 3.5x, NNH = 4.
2. Bastidas A, *et al.* (ZOE-HSCT Study) JAMA 2019;322(2):123-33. RRI = 7.3x, NNH = 1.
3. P < .0001
4. P < .0001
5. IZV vs RZV, P < .0001

ZOSTER IMMUNIZATION IN CANCER PATIENTS

Lessons from Published Reports

1. Incidence of HZ in cancer patients is 2-to-14-fold higher than the general population at risk for HZ.
2. A minority of eligible cancer patients (2-8%) receive Zoster vaccine
3. HZ, PHN, ZO can be prevented by vaccination in immunocompetent patients > age 60 and in immunosuppressed cancer patients at risk including autologous stem cell transplant recipients, solid tumour patients, and to a lesser degree haematological malignancies.
4. Live attenuated zoster vaccine (LZV) has modest efficacy over placebo. LZV remains contraindicated in the immunocompromised.
5. Recombinant adjuvant zoster vaccine (RZV) is significantly more effective than either placebo or LZV, but there are more injection site-related Aes (> 7-fold more) . . .

VARICELLA-ZOSTER VIRUS

A focus on Herpes zoster . . .

Thank you . . .