



# Safety of Recombinant Zoster Vaccine: a Retrospective Study of 622 Rheumatology Patients

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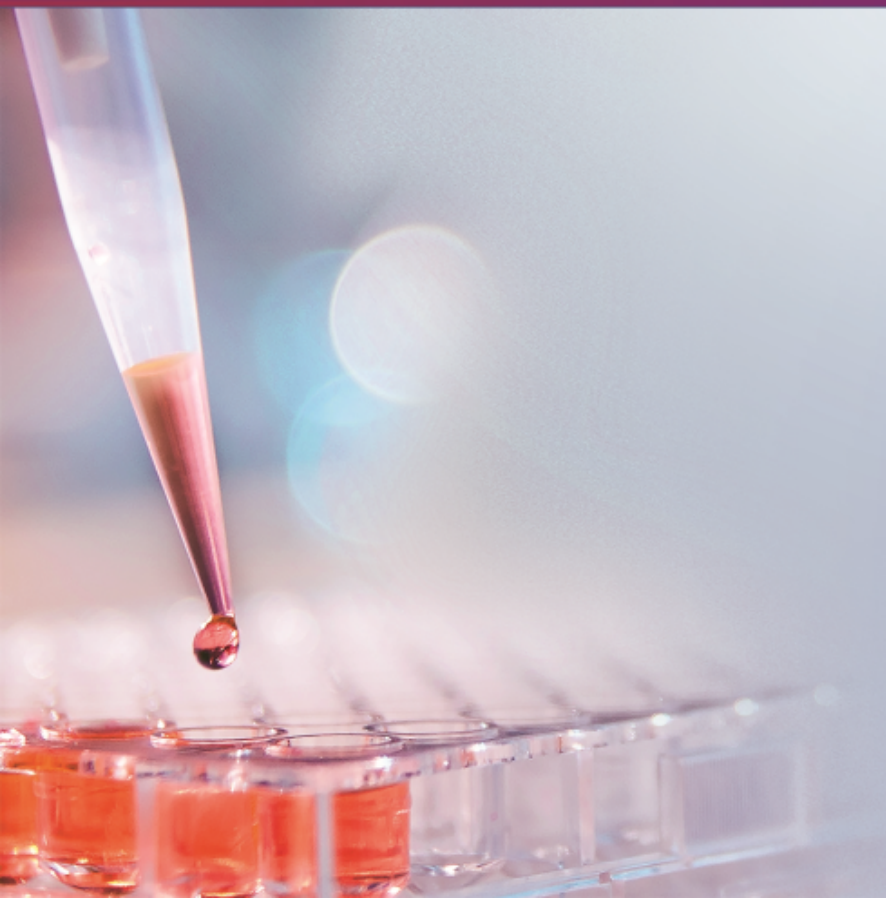
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#ACR20

# COI DISCLOSURE INFORMATION

Tiphaine Lenfant, MD



**I have no financial relationships to disclose.**







## Rationale

Recombinant Zoster Vaccine (RZV) and Immune Mediated Inflammatory Diseases (IMIDs)

# Rationale

- Higher risk of herpes zoster (HZ) in:
  - IMID patients (RA, SLE, etc.)
  - Immunosuppressive (IS) medications
- Recombinant Zoster Vaccine (RZV)
  - Novel adjuvant AS01B: highly immunogenic
  - Theoretical risk of IMID flares
- Are rheumatic diseases patients at higher risk of flare after RZV?

Yun H et al. Arthritis Rheumatol. 2016;68(9):2328-37.

Lal H et al. N Engl J Med. 2015;372(22):2087-96.

Lecrenier N et al. Expert Rev Vaccines. 2018;17(7):619-34.



## Patients and Methods



# Patients and Methods

## Study design

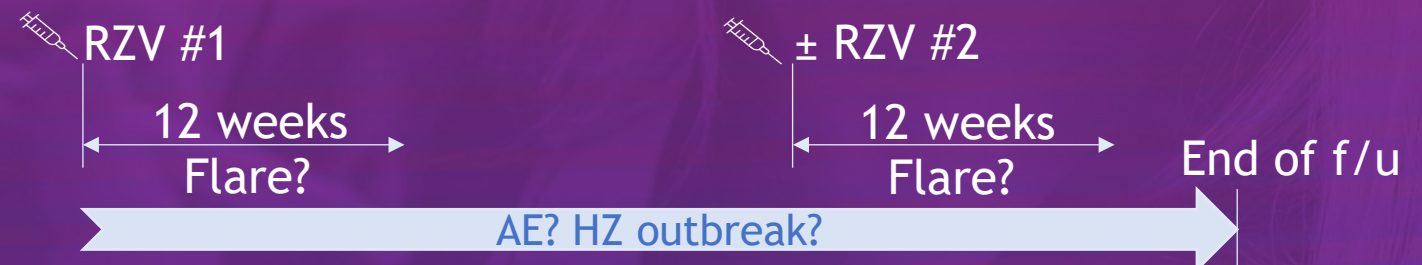
- Retrospective
- Single center
- Data collected from EMR

## Patients

- Rheumatic disease patients
  - IMIDs and non IMIDs
- Vaccinated by  $\geq 1$  dose of RZV
- February 2018  $\rightarrow$  May 2020

## Outcomes

- 1) Flares of the underlying IMID
  - Collected via chart review, office notes, new or higher prednisone prescription, treatment changes
  - In the 12-week period after each RZV
- 2) Adverse events and HZ outbreaks





## Results



# Results

n=622 patients, 359 IMIDs

- Median age 67, 67% female
- 77% received 2 RZV doses
- Median follow-up 36 weeks
- 359 IMID patients
  - RA n=88
  - Vasculitis n=50
  - PMR n=29
  - Gout n=28
  - SLE n=24
  - PsA n=20

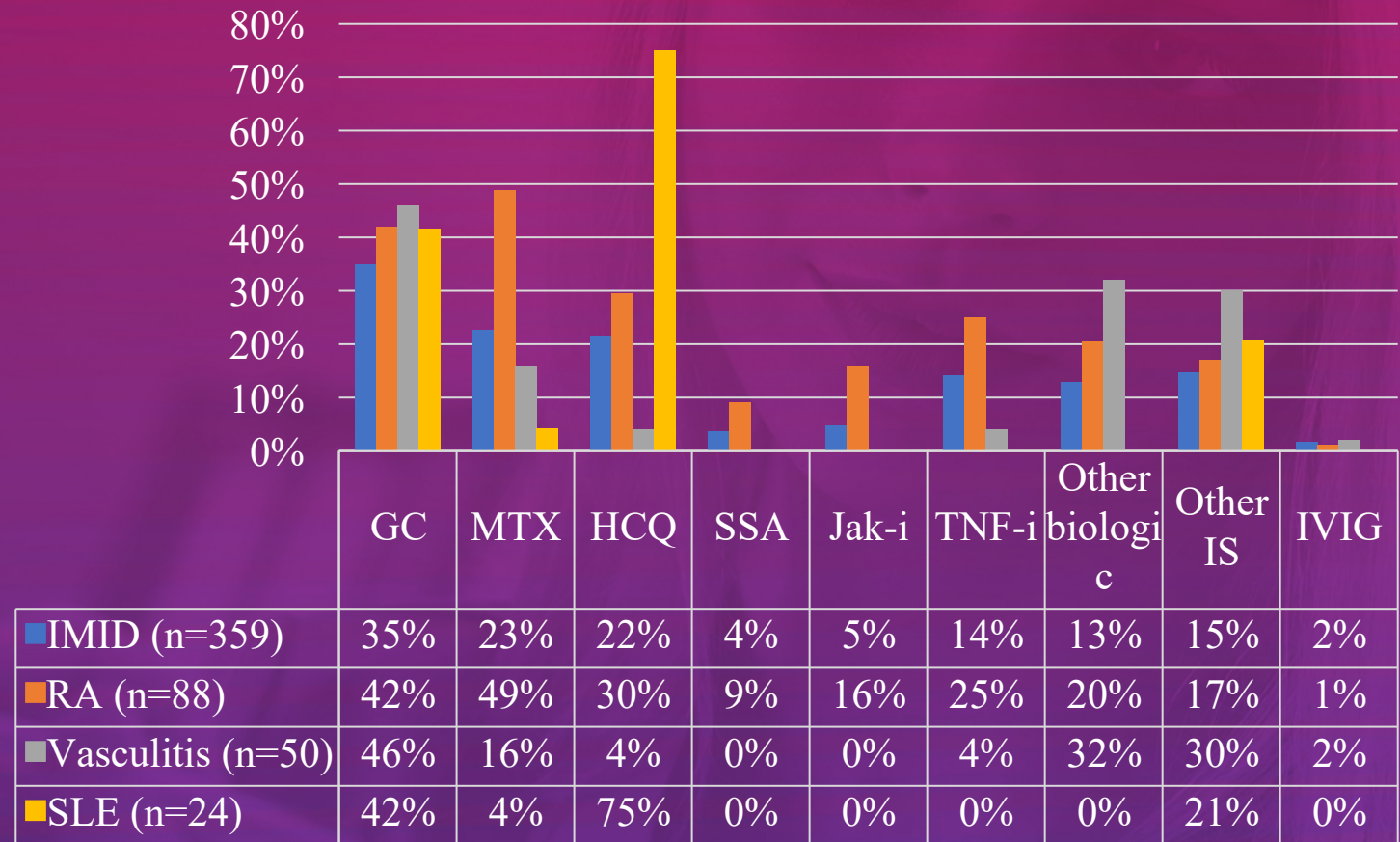


Figure 1: Panel of treatments received by IMID patients at the time of RZV



## Results (2): IMID flares

- Among 359 IMID patients,
- **59 flared after RZV (16%)**
  - 34 after 1<sup>st</sup> dose (median time to flare: 31 days)
  - 17 after 2<sup>nd</sup> dose (45 days)
  - 8 after both doses (17 & 40 days)

## Results (3): Flares

n=59 IMID flares after RZV

- RA patients had the highest flare rate (24%)
- Flares occurred in a temporal relation to a treatment change in 18 cases (31%)
- Management of flares:
  - Glucocorticoids (GC) (n=27, 45%)
  - Change in IS therapy (n=15, 25%)

IMID subgroups	Total IMID n=359 (100%)	On GC n=125 (35%)	≥1 Flare* n=59 (16%)
RA	88 (25%)	37 (42%)	<b>21 (24%)</b>
Vasculitis	50 (14%)	23 (46%)	5 (10%)
PMR	29 (8%)	21 (72%)	5 (17%)
Gout	28 (8%)	3 (11%)	5 (18%)
SLE	24 (7%)	10 (42%)	4 (17%)
PsA	20 (6%)	6 (30%)	2 (10%)
Inflammatory arthritis	19 (5%)	5 (26%)	3 (16%)
Sjögren	18 (5%)	0 (0%)	2 (11%)
SpA	17 (5%)	2 (12%)	2 (12%)
CPPD	14 (4%)	2 (14%)	3 (21%)
Myositis	9 (3%)	3 (33%)	2 (22%)
Scleroderma	9 (3%)	1 (11%)	0 (0%)
IBD related arthritis	8 (2%)	1 (13%)	1 (13%)
Other	26 (7%)	11 (42%)	4 (15%)

Table 1: Proportion of IMID patients, GC regimen and flares



## Results (4)

### Risk factors for IMID flares

- Multivariate model of logistic regression:
- Controlling for Jak-inhibition and RA
- Only GC use at the time of vaccine remained significantly associated with IMID flares
- OR = 2.31 [1.3-4.1] p=0.004

	No flare (n=300)	Flare (n=59)	Univ analysis p value	Multivariate analysis adjusted for significant factors Adjusted OR [IC95%] p value	
Median age (years)	67	67	0.962		
Gender (female)	66%	63%	0.592		
Ethnicity (white)	84%	86%	0.445		
RA(vs others)	n=67 22%	n=21 36%	0.030	1.57 [0.8-2.98]	0.173
<b>Glucocorticoids</b>	31%	53%	0.002	<b>2.31 [1.3-4.1]</b>	<b>0.004</b>
Jak-inhibitors	4%	10%	0.032	2.09 [0.64-6.34]	0.203
Hydroxychloroquine	21%	25%	0.416		
Methotrexate	22%	25%	0.565		
TNF inhibitors	14%	17%	0.509		
Other biologic	12%	15%	0.539		
Other immunosuppressant	14%	19%	0.358		

Table 2: Risk factors of IMID flares in a cohort of 359 IMID patients vaccinated with RZV

*No significant association with laboratory findings (CRP, ESR, ANA, ENA, RF, CCP)*

# Results (5): Time-to-flare

Multivariate Cox-model (n=359 IMID patients)

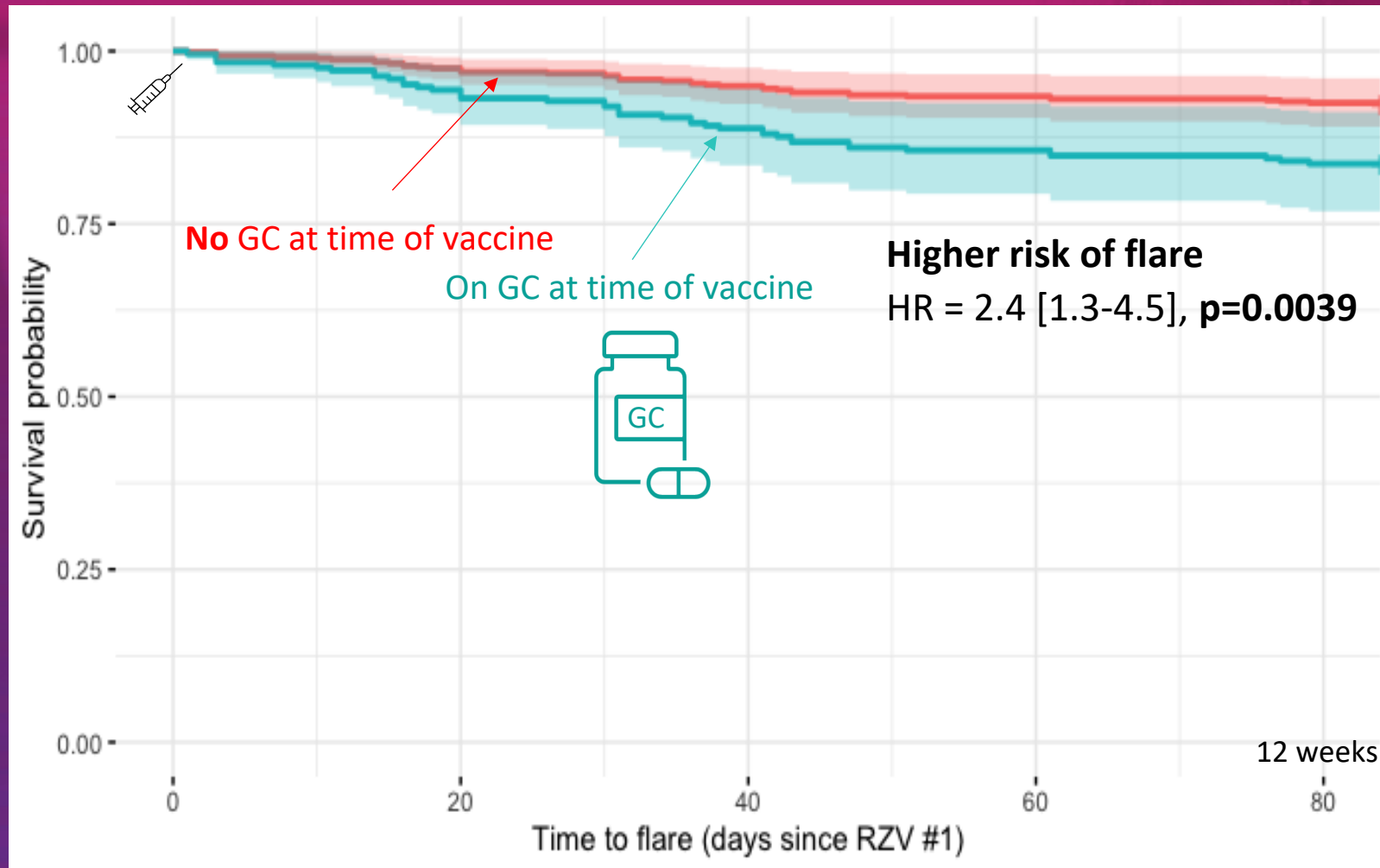


Figure 2A. Survival analysis of the time to flare in the 12-week time period following the first dose of RZV in 359 IMID patients (multivariate Cox-model)



# Results (5): Time-to-flare

Multivariate Cox-model (n=263 that received 2 RZV doses)

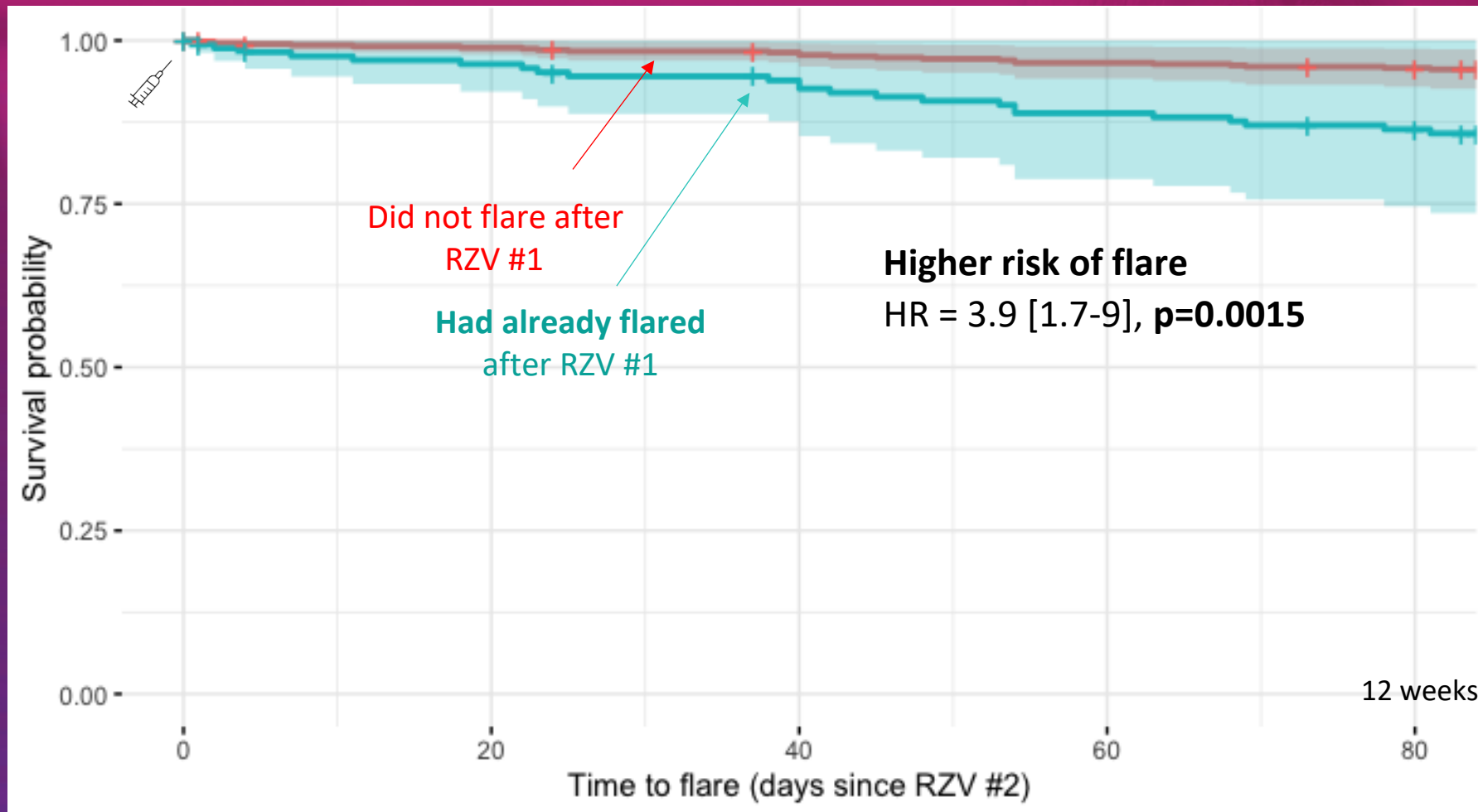


Figure 2B. Survival analysis of the time to flare in the 12-week time period following the second dose of RZV in 263 IMiD patients having received both doses (multivariate Cox-model).

# Key take away points

- Use of RZV appears safe in IMiD patients
- Mild flares were not uncommon in the first 12 weeks after RZV
- GC use at the time of RZV administration was associated with a significantly higher rate of flares in IMiD patients
- Having flared after the first dose was associated with a higher risk of flare after the second dose.



## 1. Rationale



IMiD patients / IMiD treatments = higher risk of zoster  
Recombinant Zoster Vaccine: available, high efficacy, new adjuvant  
Adjuvant → **Theoretical risk of flares after vaccine**



Are rheumatology patients at **higher risk of flares** after RZV?



## 2. Study



Retrospective single-center study (Rheumatology, CCF, USA)  
Inclusion: ≥1 RZV dose between Feb. 2018 and May 2020  
Data extracted from Electronic Medical Records

- Flares in the 12-week period after each dose? Risk factors?
- Adverse events? Zoster outbreak?



## 3. Results



**n=622** rheumatology patients  
**n=359** IMiD patients

67% female  
Median age 67 yo  
77% received 2 doses  
8.7% adverse events  
Median f/u = 36 weeks

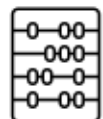
Which IMiD/treatment? Flared after RZV?



Description

**Flares: n=59**

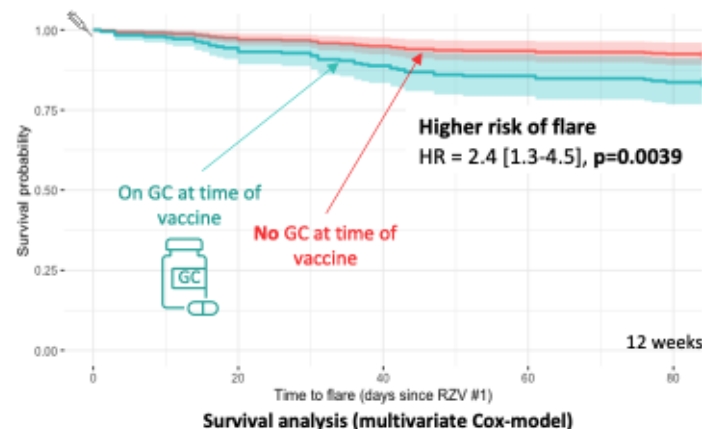
A change in IS  
treatment was  
needed in 25%



Logistic regression

IMiD subgroups	Total from IMiD (n=359)	On GC n=125 (35%)	≥1 Flare n=59 (16%)
RA	88 (25%)	37 (42%)	21 (24%)
Vasculitis	50 (14%)	23 (46%)	5 (10%)
PMR	29 (8%)	21 (72%)	5 (17%)
Gout	28 (8%)	3 (11%)	5 (18%)
SLE	24 (7%)	10 (42%)	4 (17%)

Risk factor	No flare (n=300)	Flare (n=59)	Univariate p-value	Multivariate OR [IC95]	p-value
RA	67 (22%)	21 (36%)	0.030	1.57 [0.8-3]	0.173
GC	31%	53%	0.002	2.31 [1.3-4]	0.004
Jak-i	4%	10%	0.032	2.09 [0.6-6]	0.203



## Key messages



- ✓ RZV appears safe in IMiD patients
- ✓ GC at time of vaccine = higher risk of flare
- ✓ Patient + Provider discussion
- ✓ Informed consent
- ✓ Benefits / Risks Balance







Thank  
You!

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