Rapid Cycle Analysis of Respiratory Syncytial Virus Vaccines in Older Adults in VSD (VSD Study #1363)

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Background

RSV infection in older adults (≥65 yrs) in the US is common and serious

- 60,000-160,000 hospitalizations per year
- 6,000-10,000 deaths per year

Two RSV vaccines were approved for use in older adults (≥60 yrs) in 2023

- GSK (Arexvy) and Pfizer (Abrysvo)

Objectives

- Monitor RSV vaccine uptake among older adults
- Monitor occurrence of pre-specified outcomes following RSV vaccination
- Conduct near real-time surveillance using rapid cycle analysis methods

Methods

Study design and population

- Prospective cohort of persons ≥60 years old who received an RSV vaccine at 9 VSD sites
- Surveillance period: 8/1/2023 thru 5/31/2025
- Vaccinated concurrent comparators

Exposure groups (n=4)

- GSK (Arexvy) / Pfizer (Abrysvo)
  - With and without simultaneous vaccination

Prespecified outcomes (n=14)

- Primary risk interval: 1-21 days (12 outcomes)
  - Comparison intervals: 43-63 days (primary), 22-42 days (secondary)
  - Secondary risk interval: 1-42 days (12 outcomes)
- Selected outcomes and signals chart reviewed
- Anaphylaxis and CIDP are descriptively monitored only with risk intervals of 0-1 and 1-84 days, respectively

Sequential analysis

- Biweekly analyses (began in March 2024)
- Sequential test of 1-sided H_0: vaccine does not increase the risk of the outcome in risk interval
- Signals when P value is < threshold (0.014)
- Rate ratios computed with nominal 95% confidence intervals
- Adjusted for age group, sex, race/ethnicity, VSD site, and calendar day

Results

Table 1. RSV Vaccines Administered by Manufacturer, 8/1/2023 – 4/13/2024

Manufacturer	N	%
GSK	322233	88.1
Pfizer	43353	11.9
Unspecified[1]	148	0.0
Total	365734	100.0

[1]All subsequent analyses **exclude** the 'Unspecified' category

- 88% of RSV vaccines were GSK
- 25% of RSV vaccines administered simultaneously with other vaccines
  - Mostly COVID-19 and influenza

Figure 1. RSV Vaccinations by Manufacturer and Week of Administration, 8/1/2023 – 4/13/2024

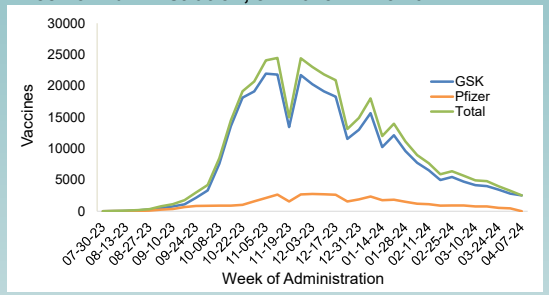

Table 2. Summary of Sequential Analysis Outcomes and Signals, 4/13/2024

Outcome	Setting[1]	Signal
Acute disseminated encephalomyelitis	E, I	No
Acute myocardial infarction	E, I	No
Atrial fibrillation	E, I, O, T	No
Bell's palsy	E, I, O, T	No
Deep vein thrombosis	E, I	No
Encephalitis / myelitis	E, I	No
Guillain-Barré syndrome (GBS)	E, I	No
Immune thrombocytopenia (ITP)	E, I, O, T	Yes
Myocarditis / pericarditis	E, I	No
Stroke	E, I	No
Transverse myelitis	E, I	No
Pulmonary embolism	E, I	No

[1]E = emergency department, I = inpatient, O = outpatient, T = telehealth

Safety signal for ITP in 1st sequential analysis run (Tables 2 and 3)

- Quick chart review of 19 ITP cases in 1-21 day risk interval
  - 15/19 (79%) not incident ITP or ITP preceded RSV vaccination
- Quick chart review of ITP cases in the comparison intervals is ongoing

No other safety signals noted, including for GBS

- 8 cases of GBS identified and confirmed by chart review
  - 6 cases following GSK vaccine
  - 2 cases following Pfizer vaccine

Table 3. Sequential Analysis for ITP – Run #1, 8/1/2023 – 3/16/2024

Analysis Parameters				Signal Information and Informative Counts					Nominal Analysis			Sequential Test
Outcome Event	Risk Interval Days	Comp Interval Days	Vaccine Type	Signaled in a Prior Run[1]	New Sequential Analysis Signal[2]	Events in Risk Interval	Events in Comp Interval	Adjusted Expected Events in Risk Interval	Adjusted Rate Ratio[3]	95% Confidence Interval	2-sided P Value	1-sided P Value[4]
ITP	1-21	43-63	GSK w simul	n/a	No	2	1	0.6	3.08	0.23-92.44	0.408	0.347
			GSK wo simul	n/a	No	19	8	8.1	2.35	0.99-5.97	0.054	0.040
			Pfizer w simul	n/a	No	0	1	0.2	0.00	0.00-81.18	0.810	0.810
			Pfizer wo simul	n/a	No	2	2	1.8	1.10	0.11-11.27	0.931	0.659
		22-42	GSK w simul	n/a	No	3	2	1.4	2.21	0.31-19.61	0.432	0.340
			GSK wo simul	n/a	Yes	19	6	6.3	3.04	1.22-8.47	0.016	0.012
			Pfizer w simul	n/a	No	0	1	1.1	0.00	0.00-16.74	0.468	0.468
			Pfizer wo simul	n/a	No	2	1	0.7	2.67	0.20-78.89	0.472	0.394
	1-42	43-84	GSK w simul	n/a	No	4	7	4.3	0.93	0.22-3.42	0.931	0.662
			GSK wo simul	n/a	No	25	14	15.6	1.60	0.80-3.28	0.186	0.121
			Pfizer w simul	n/a	No	1	3	3.5	0.29	0.01-4.25	0.428	0.957
			Pfizer wo simul	n/a	No	3	3	3.4	0.88	0.14-5.47	0.888	0.718

[1]n/a = not applicable
[2]No prior signal, at least 2 events in the risk interval, 1-sided P value <0.014
[3]Adjusted for calendar date, VSD site, age category, sex, and race/ethnicity
[4]Red: new sequential analysis signal

Limitations

- Low uptake of RSV vaccines limits power to detect associations, especially for the Pfizer product
- Near real-time data can be unstable
- RSV vaccines are recommended under shared clinical decision-making; this increases uncertainty regarding who should be vaccinated and their baseline risk of adverse events

Conclusions

- 366,000 doses of RSV vaccines administered to older adults in VSD since August 2023
  - 88% were GSK vaccine
- Statistical signal identified for ITP in persons administered GSK RSV vaccine without simultaneous vaccination
  - 79% of ITP cases were misclassified or not temporally related to RSV vaccination
  - Additional chart review underway
- **No other signals have been observed after 3 biweekly sequential analyses**

Next Steps

- Surveillance will continue through May 2025, including chart review of all cases of GBS
- Continued investigation into ITP signal

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