Short term safety profile of respiratory syncytial virus vaccine in adults aged ≥ 60 years in Australia

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Arexvy®, a recombinant respiratory syncytial virus (RSV) pre-fusion F protein vaccine for prevention of lower respiratory tract disease caused by RSV, has been available for use in adults aged ≥60 years in Australia on the private market since February 2024, outside the government-funded National Immunisation Program (NIP) and requiring out-of-pocket purchase. A Phase 3 clinical trial of Arexvy conducted in 17 countries reported mostly mild-to-moderate adverse events within 30 days of vaccination, most commonly pain at injection site (60·9%), fatigue (33·6%), myalgia (28·9%) and headache (27·2%).[1] Post-marketing data from the US active vaccine surveillance system (V-safe) found 48·6% of adults aged ≥60 years reported at least one symptom post-vaccination, with 0·5% seeking medical care between day 0–7 following vaccination.[2] No systematic post-marketing safety data on Arexvy administered concomitantly with other vaccines has been reported.

Australia's active vaccine safety surveillance system AusVaxSafety monitors a number of vaccines, including Arexvy, by reporting on solicited adverse events following immunisation (AEFI) through an online survey sent to vaccinees 3 days post-vaccination as previously described.[3] Here we report on survey responses from adults aged ≥60 years receiving Arexvy at primary healthcare practices or pharmacies, who responded to the survey by day 7 post-vaccination.

We examined the proportions of respondents reporting: any AEFI 0–3 days following vaccination; local adverse events (pain, redness, swelling, itching), systemic symptoms (fever, chills, fatigue, headache, myalgia, arthralgia), gastrointestinal symptoms, those seeking medical attention (at primary healthcare practices or hospital emergency department), and any impact on daily activities, by demographic characteristics and medical history, comparing respondents receiving Arexvy alone and those who received it with another vaccine(s) in the same visit. The point estimate probability of reported medical attendance following vaccination with 95% credible interval (CrI) was calculated using Bayesian logistic regression.[4] Analyses were conducted in R Statistical Software (v4.4.1).[5] Ethics approval was obtained from the Sydney Children's Hospitals Network (HREC/16/SCHN/19). The National Centre for Immunisation Research and Surveillance operates under the governance and infrastructure support of Kids Research, Sydney Children's Hospitals Network.

There were 2013 respondents aged ≥60 years who received Arexvy between 29 February 2024 and 27 September 2024 (response rate 68·6%). The median age was 75 years (interquartile range 70–80 years), 1247 (62%) were women. Of respondents, 274 (13·6%) received Arexvy with other vaccines, most commonly with one vaccine: COVID-19 mRNA (88, 4·4%), influenza (69, 3·4%), pertussis (28, 1·4%), pneumococcal conjugate (27, 1·3%), and recombinant zoster (26, 1·3%) vaccines. Only 24 (1·2%) received more than two vaccines concomitantly with Arexvy.

Overall, 36·8% of respondents reported an AEFI following Arexvy vaccination with higher rates in women and those who reported chronic medical conditions, with rates varying by condition (Table 1). The most frequently reported symptoms were pain at the injection site, fatigue, myalgia, and headache. Respondents receiving concomitant vaccines reported higher AEFI rates across all demographics and symptom types (Table 1; 43% vs. 36% for any AEFI; Supplementary Figure S1). AEFI rates were lower in older age groups (Supplementary Figure S1).

The estimated probability of medical attendance following vaccination was 0·45% (CrI: 0·21–0·78); all seeking care with primary healthcare providers only. Due to the low number of medical attendances reported, no subgroup analysis was conducted. The rate of any impact on daily activity was low (4·2%), with 66% of respondents reporting an impact of one day or less (Table 1). Slightly higher rates of impact on daily activity (7·3%) were reported in respondents who received concomitant vaccines, but the number of days impacted was similar between groups.

Our study population was slightly older (median age 75 vs. 72 years) and included a higher proportion of

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	All Arexvy doses, n/N (%)	Arexvy administered alone, n/N (%)	Arexvy administered concomitantly, n/N (%)
Any adverse event rate (all respondents)	741/2013 (37%)	622/1739 (36%)	119/274 (43%)
Local adverse event rate[a]	605 (30%)	504 (29%)	101 (37%)
Local pain	518 (26%)	429 (25%)	89 (32%)
Local itching	91 (4·5%)	73 (4·2%)	18 (6·6%)
Local redness	204 (10%)	175 (10%)	29 (11%)
Local swelling	223 (11%)	180 (10%)	43 (16%)
Systemic adverse event rate[a]	527 (26%)	436 (25%)	91 (33%)
Fever[b]	98 (4·9%)	81 (4·7%)	17 (6·2%)
Chills	154 (7·7%)	131 (7·5%)	23 (8·4%)
Fatigue	416 (21%)	348 (20%)	68 (25%)
Headache	237 (12%)	198 (11%)	39 (14%)
Myalgia	252 (13%)	199 (11%)	53 (19%)
Arthralgia	163 (8·1%)	139 (8·0%)	24 (8·8%)
Gastrointestinal[a,c]	104 (5·2%)	86 (4·9%)	18 (6·6%)
Other[a,d]	65 (3·2%)	57 (3·3%)	8 (2·9%)
Any adverse event rate (by respondent characteristics)			
Age group (years)			
60–69	228/446 (51·1%)	185/372 (49·7%)	43/74 (58·1%)
70–79	390/1042 (37·4%)	330/907 (36·4%)	60/135 (44·4%)
≥80	112/469 (23·9%)	98/413 (23·7%)	14/56 (25%)
Sex			
Male	234/758 (30·9%)	196/647 (30·3%)	38/111 (34·2%)
Female	503/1247 (40·3%)	422/1085 (38·9%)	81/162 (50%)
Unknown	4/8 (50%)	4/7 (57·1%)	0/1 (0%)
Any chronic medical condition			
Yes	418/1032 (40·5%)	352/898 (39·2%)	66/134 (49·3%)
No	323/981 (32·9%)	270/841 (32·1%)	53/140 (37·9%)
Specific chronic medical condition[e,f]			
Chronic cardiovascular disease[g]	101/281 (35·9%)	90/247 (36·4%)	11/34 (32·4%)
Diabetes	85/196 (43·4%)	74/172 (43%)	11/24 (45·8%)
Lung disease	110/313 (35·1%)	96/283 (33·9%)	14/30 (46·7%)
Cancer[h]	43/120 (35·8%)	39/108 (36·1%)	4/12 (33·3%)
Inflammatory	58/138 (42%)	46/118 (39%)	12/20 (60%)
Medical attendance (all respondents)[i]	9/2013 (0·4%)	7/1739 (0·4%)	2/274 (0·7%)
Impact on daily activities (all respondents)[j]	85/2013 (4·2%)	65/1739 (3·7%)	20/274 (7·3%)
Number of days impacted[k]			
1 day or less	56/85 (66%)	41/65 (63%)	15/20 (75%)
2 or more days	28/85 (33%)	23/65 (35%)	5/20 (25%)
Unknown	1/85 (1·2%)	1/65 (1·5%)	0/20 (0%)

[a]Denominator is the number of respondents. [b]Fever is a self-reported symptom and might not reflect the clinical definition of fever. [c]Gastrointestinal symptoms include nausea, vomiting, diarrhoea and abdominal pain. [d]Other symptoms include any symptoms not listed above. [e]Only chronic medical conditions with more than 100 responses are presented. [f]Sum of denominators of medical condition groups do not equal the total denominator of chronic medical condition as only chronic medical conditions with more than 100 responses are presented and respondents may select more than one condition. [g]Coronary heart disease, heart failure, hypertension. [h]Any tumour/malignancy diagnosed in the last 12 months, haematological malignancy diagnosed within the last 5 years, or currently receiving chemotherapy or radiotherapy. [i]All respondents who reported having medical attendance sought care at a primary healthcare practice. [j]Impact on daily activities defined as missing work, study, or unable to perform normal/routine duties following a vaccination event. [k]Denominator is the number of respondents who reported impact on daily activities.

Table 1: **Proportions of people aged ≥60 years with adverse events, medical review and impact on daily activities following administration of Arexvy reported by demographic, underlying medical conditions and concomitant vaccination status.**

individuals with chronic medical conditions (50% vs. 30%) compared to adults aged ≥60 years receiving high-dose or adjuvanted influenza vaccines covered by the NIP.[6] Proportions of people reporting AEFI were lower in our Australian cohort compared with US V-safe data, potentially because V-safe monitors participants for a

longer period (up to day 7 compared to first 3 days in our system),[2] and had a higher proportion of participants receiving concomitant vaccines (31·1%) compared to our cohort (13·6%). The slightly higher proportion of AEFI reported in people receiving concomitant vaccines may reflect the reactogenicity of the co-administered vaccines such as mRNA COVID-19 vaccine (Spikevax),[7] recombinant zoster vaccine (Shingrix),[8] or adjuvanted influenza vaccines[9] given together with Arexvy. Reassuringly, the reported medical attendance rate following Arexvy vaccination was similar in those who received Arexvy alone or with another vaccine.

In addition to AusVaxSafety surveillance, Australia's national regulatory agency, the Therapeutic Goods Administration (TGA), expanded its spontaneous reporting-based safety surveillance for Arexvy's introduction, including the more frequent monitoring of AEFI reports submitted to the TGA by consumers, health care professionals, and health departments. From March to September 2024, 24 AEFI reports associated with Arexvy were reported to the TGA in adults aged ≥60 years (equating to 7 reports per 10,000 Arexvy doses). The most frequently reported AEFI were fatigue and headache, followed by myalgia, nausea, pain in extremity, and diarrhoea. No safety signals associated with Arexvy have been identified by the TGA to date.

Australia's active safety surveillance and spontaneous AEFI reporting systems provides further evidence of the short-term safety profile of Arexvy in adults aged ≥60 years. These findings are important to understand safety in populations not included in clinical trials, to inform risk-benefit considerations for potential inclusion in the National Immunisation Program, and for guidance on co-administration with other vaccines. However, longer-term monitoring is essential to address potential concerns such as Guillain-Barré Syndrome, and additional studies are needed to evaluate safety in broader, more representative populations.

Contributors

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Data sharing statement

De-identified individual participant data underpinning the findings of this study may be made available upon request, pending approval from the data owner. Requests for data, accompanied by a methodologically sound proposal, can be submitted to AusVaxSafety. The study group will review all applications for data access. Upon approval, the data will be shared exclusively for the purposes outlined in the approved proposal. Data requesters must sign a data access agreement before gaining access.

Declaration of interests

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2025.101506.

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