Immunogenicity of an Adjuvant Recombinant Zoster Vaccine in Patients With Rheumatoid Arthritis Treated With Upadacitinib: 60-Week Results From a Randomized Sub-Study

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Presented at the European Congress of Rheumatology (EULAR), June 12–15, 2024, Vienna, Austria

OBJECTIVE

- To assess the immunogenicity of open-label adjuvant recombinant zoster vaccine (RZV) through week 60 in patients with RA receiving upadacitinib (UPA) 15 mg once daily (QD) with background MTX

INTRODUCTION

- Patients with RA have an increased burden of infections[1]
- UPA, an approved treatment for moderately to severely active RA, has been associated with a low but elevated risk of herpes zoster (HZ)[2]
- RZV is effective in preventing HZ in adults aged ≥ 50 years,[3] but its biological and clinical effects and cell-mediated immunogenicity are not well studied in patients with RA receiving JAK inhibitors, particularly those on UPA with background MTX
- In a sub-study of the SELECT-COMPARE trial, most patients with RA receiving UPA 15 mg QD and background MTX achieved humoral and cell-mediated immune responses to RZV at week 16 (4 weeks after RZV dose 2)[4]

METHODS

- This optional sub-study of the phase 3 SELECT-COMPARE trial (NCT02629159) included patients aged ≥ 50 years with RA who were on UPA 15 mg QD + stable doses of background MTX for ≥ 8 weeks before the first vaccination through ≥ 4 weeks after the second vaccination

SUB-STUDY ASSESSMENTS

Primary Endpoint

- Achievement of humoral response to RZV (≥ 4-fold increase in pre-vaccination concentration of anti-gE antibody titers)[a] at week 16 (4 weeks after dose 2 vaccination)

Secondary Endpoints

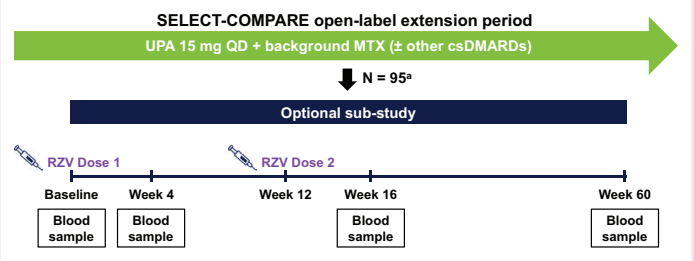
- Achievement of humoral response to RZV at weeks 4 and 60
- Geometric mean fold rise (GMFR) in pre-vaccination anti-glycoprotein E (gE) antibody levels at weeks 4, 16, and 60

Exploratory Endpoints (assessed in a subcohort of 40 patients)

- Achievement of cell-mediated immune response at weeks 4, 16, and 60
  - Defined as a gE-specific CD4+ [2+] T cell (CD4+ T cells expressing ≥ 2 of 4 activation markers: interferon-gamma (IFN-γ), IL-2, TNF-α, and CD40 ligand) frequency of ≥ 2-fold the baseline frequency[b]
- GMFR in pre-vaccination gE-specific CD4+ [2+] T cell levels at weeks 4, 16, and 60

ELISA, enzyme-linked immunosorbent assay.
[a]Measured by ELISA. [b]Measured using intracellular cytokine staining and flow cytometry.

SELECT-COMPARE Sub-Study Design



sDMARDs, conventional synthetic DMARDS; QD, once daily; RZV, adjuvant recombinant zoster vaccine; UPA, upadacitinib.
[a]Number of patients who received ≥ 1 RZV dose.

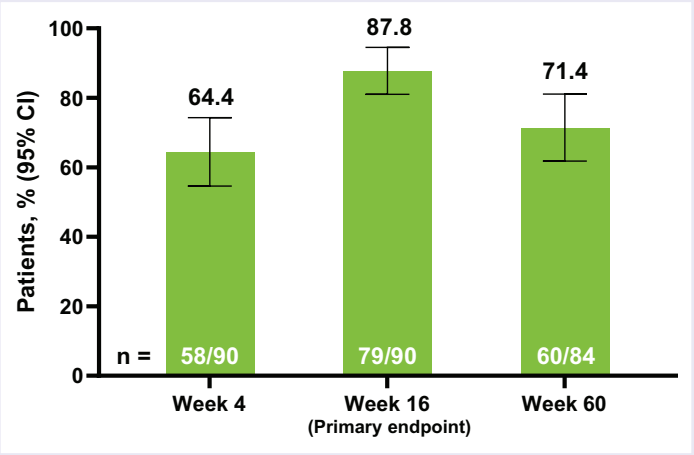
RESULTS

Baseline Demographic and Clinical Characteristics

Characteristic[a]	UPA 15 mg QD (n = 93)[b]
Female, n (%)	73 (78.5)
Age, years, mean (SD)	62.4 (7.5)
White, n (%)	74 (79.6)
Region, n (%)	
North America	35 (37.6)
South or Central America	37 (39.8)
Other	21 (22.6)
Duration of RA since initial symptoms, years, median (range)	11.7 (4.9–41.6)
Duration of UPA treatment, years, median (range)	3.9 (2.9–5.8)
Concomitant MTX use, n (%)	91 (97.8)
MTX dose, mg, median (range)	15.0 (7.5–25.0)
Oral CS use at sub-study baseline, n (%)	46 (49.5)
Oral CS dose, mg, median (range)	5.0 (2.5–10.0)

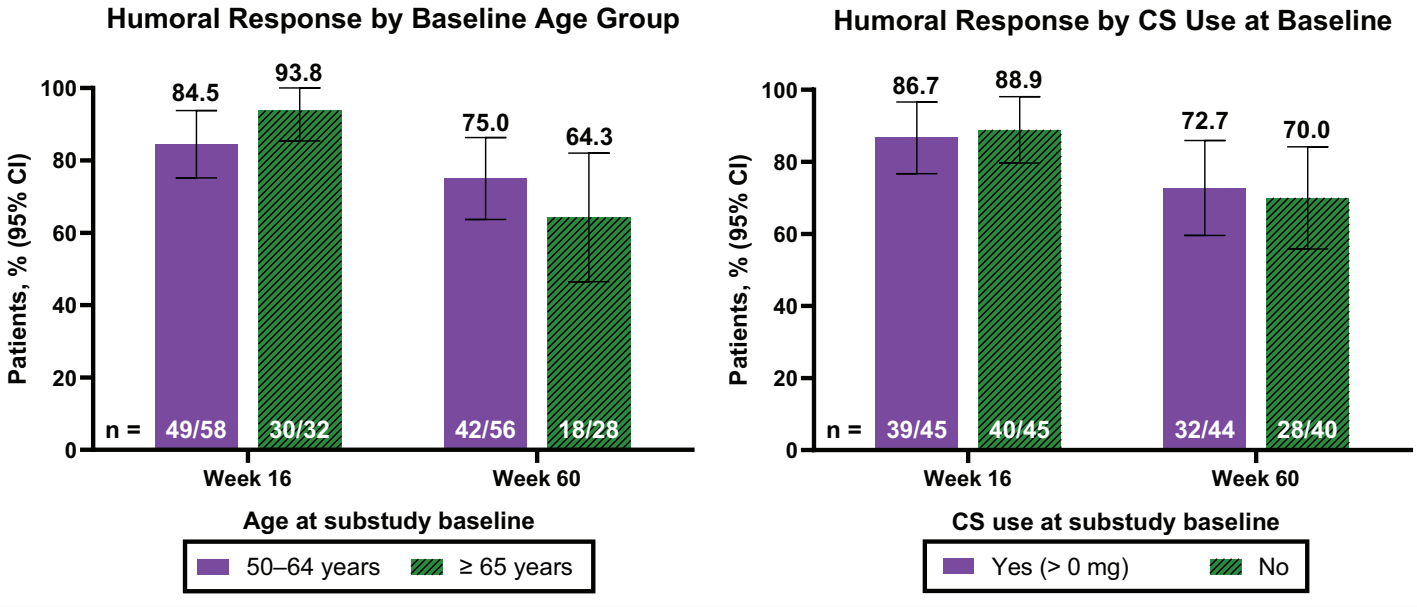
CS, corticosteroid; QD, once daily; RZV, adjuvant recombinant zoster vaccine; UPA, upadacitinib.
[a]Baseline demographic and clinical characteristics were based on the sub-study baseline visit.
[b]Number of patients who received both RZV doses.

Proportion of Patients Treated With UPA 15 mg QD and Background MTX Achieving Humoral Response to RZV



gE, glycoprotein E; QD, once daily; RZV, adjuvant recombinant zoster vaccine; UPA, upadacitinib.
The number of patients was based on the availability of blood samples collected at baseline and the study visits.
Humoral response was defined as a ≥ 4-fold increase in pre-vaccination concentration of anti-gE titers.

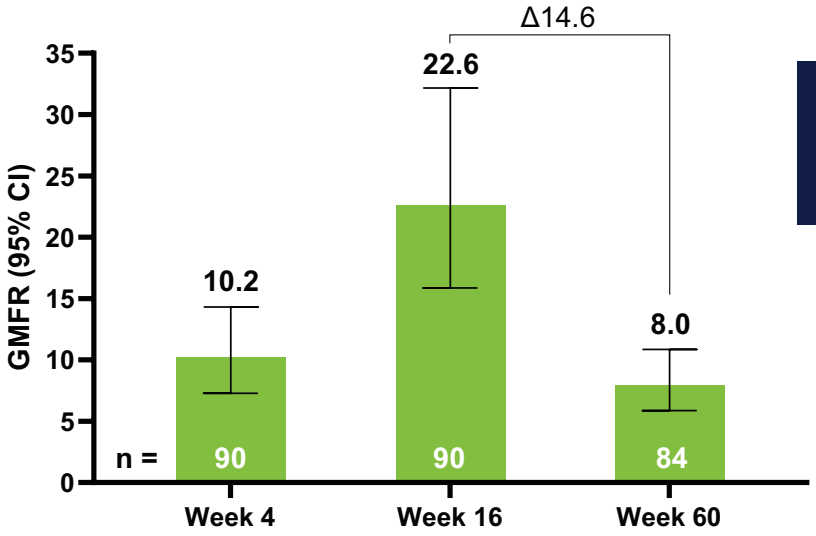
Achievement of Humoral Response to RZV Was Not Affected by Age and Concomitant Corticosteroid Use



CS, corticosteroid; gE, glycoprotein E; RZV, adjuvant recombinant zoster vaccine.
The number of patients was based on the availability of blood samples collected at baseline and the study visits. Humoral response was defined as a ≥ 4-fold increase in pre-vaccination concentration of anti-gE titers.

RESULTS (CONTINUED)

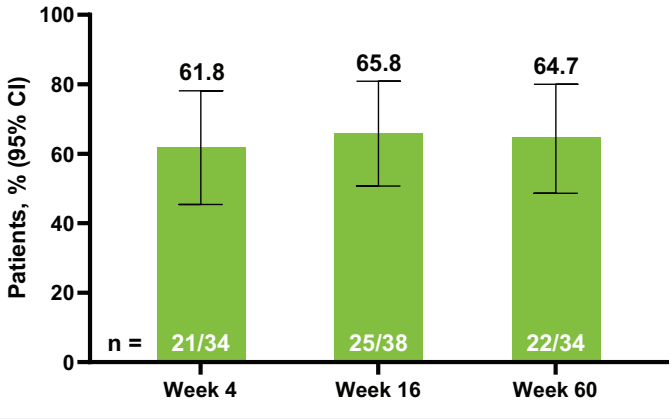
GMFR in Pre-Vaccination Anti-gE Antibody Levels in Patients Treated With UPA 15 mg QD and Background MTX



A notable decrease in GMFR was observed from week 16 to week 60[a]

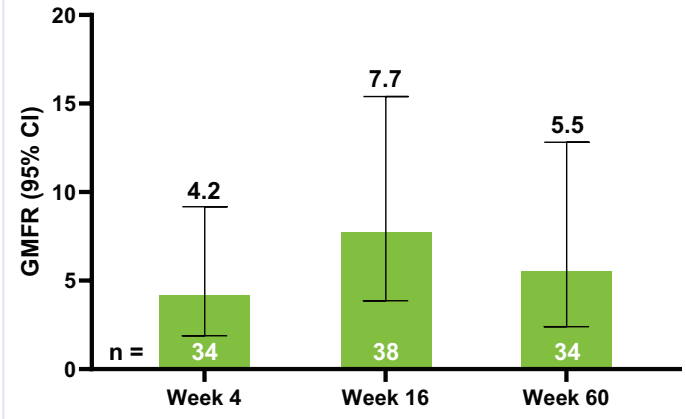
gE, glycoprotein E; GMFR, geometric mean fold rise; QD, once daily; UPA, upadacitinib.
The number of patients was based on the availability of blood samples collected at baseline and the study visits.
[a]Results are presented descriptively as formal tests for statistical significance were not conducted.

Proportion of Patients Treated With UPA 15 mg QD and Background MTX Achieving Cell-Mediated Immune Response to RZV



gE, glycoprotein E; QD, once daily; RZV, adjuvant recombinant zoster vaccine; UPA, upadacitinib.
The number of patients was based on the availability of blood samples collected at baseline and the study visits.
Cell-mediated immune response was defined as a gE-specific CD4+ [2+] T cell frequency of ≥ 2-fold the baseline frequency; a technical cutoff was assigned to non-positive frequency values to calculate the fold rise.

GMFR in Pre-Vaccination gE-specific CD4+ [2+] T Cell Levels in Patients Treated With UPA 15 mg QD and Background MTX



gE, glycoprotein E; GMFR, geometric mean fold rise; QD, once daily; UPA, upadacitinib.
The number of patients was based on the availability of blood samples collected at baseline and the study visits.

RESULTS (CONTINUED)

Rates of AEs Through 30 Days Post-RZV Vaccination

Event, n (%)	UPA 15 mg QD (N = 95)
Any AE[a]	37 (38.9)
Most common AEs (reported in ≥ 3 patients)	
Injection site pain	4 (4.2)
Hypertension	3 (3.2)
Increased blood creatine phosphokinase	3 (3.2)
COVID-19	3 (3.2)
Headache	3 (3.2)
Urinary Tract Infection	3 (3.2)
Severe AE[b]	1 (1.1)
Serious AE	0
AE with reasonable possibility of being related to UPA[c]	11 (11.6)
AE with reasonable possibility of being related to RZV[c]	16 (16.8)
AE leading to discontinuation of UPA	0
Death[d]	0

- Through week 60 of the sub-study, 1 event (0.9 events/100 PY) of HZ was observed 4 months after the second RZV dose
- Among patients in the main study treated with UPA 15 mg who did not receive RZV, 110 events (2.3 events/100 PY) of HZ were observed[e]

AE, adverse event; HZ, herpes zoster; PY, patient-years; QD, once daily; RZV, adjuvant recombinant zoster vaccine; UPA, upadacitinib.
[a]One patient with a first RZV dose date of 24 November 2020 was originally reported to experience an AE starting on 3 December 2020; the AE start date was changed by the clinical trial site to 30 December 2020 and was no longer considered treatment-emergent due to the AE starting > 30 days after the first RZV dose.
[b]Hypersensitivity.
[c]As assessed by the investigator.
[d]One death due to COVID-19 pneumonia was observed in a 68-year-old male patient 239 days after receiving the second RZV dose.
[e]Includes any HZ observed starting from the first UPA dose date until 30 days after the last UPA dose if UPA was discontinued or until the final patient visit date of the sub-study.

CONCLUSIONS

- Most patients receiving long-term treatment with UPA 15 mg QD and background MTX achieved humoral and cell-mediated immune responses to RZV at weeks 4, 16, and 60, supporting the potential of RZV to protect against HZ in a patient population with elevated risk
- Achievement of humoral response to RZV was not affected by age and concomitant CS use
- RZV was well tolerated with no serious AEs reported within 30 days post-RZV vaccination

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2. Burmester GR, et al. *RMD Open*. 2023;9:e002735.
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ACKNOWLEDGMENTS

AbbVie Inc. funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the presentation. All authors had access to relevant data and participated in the drafting, review, and approval of this presentation. No honoraria or payments were made for authorship.

AbbVie and authors thank all the trial investigators and the patients who participated in the study. Medical writing support was provided by Jay Parekh, PharmD, ISMPP CMPP, of JB Ashtin, and funded by AbbVie.

DISCLOSURES

K.L. Winthrop has received consulting fees and/or research grants from AbbVie, BMS, Galapagos, Gilead, Lilly, Pfizer, Roche, and UCB. C. García has received medical fees to serve as principal investigator in AbbVie clinical trials. E. Mysler has received or has pending grants from BMS, Novartis, Pfizer, and Roche. He has received honorarium from AbbVie, Amgen, AZ, GSK, Lilly, Pfizer, Roche, Sandoz, Sanofi; has provided writing assistance, medicines, equipment, or administrative support to AbbVie, Pfizer, and Roche; and has received payment for lectures including service on speakers bureaus from AbbVie, Alpine Immunology, Amgen, AZ, GSK, Hi Bio, Janssen, Lilly, Pfizer, Roche, Sandoz, and Sanofi. A. Wells has received honoraria from AbbVie, Amgen, BMS, Lilly, Novartis, Pfizer, and Sanofi. A.L. Cunningham has received honoraria paid to his institution from BioCSL/Sequirus, GSK, Moderna, and MSD. S.K. Penn, J. Klaff, Y. Liu, X. Bu, I. Lagunes, and M. Chen are full-time employees of AbbVie, and may hold AbbVie stock or stock options.