Efficacy and Safety of Upadacitinib in Giant Cell Arteritis: 2-Year Results From the Re-Randomized, Double-Blind SELECT-GCA Phase 3 Trial

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OBJECTIVE

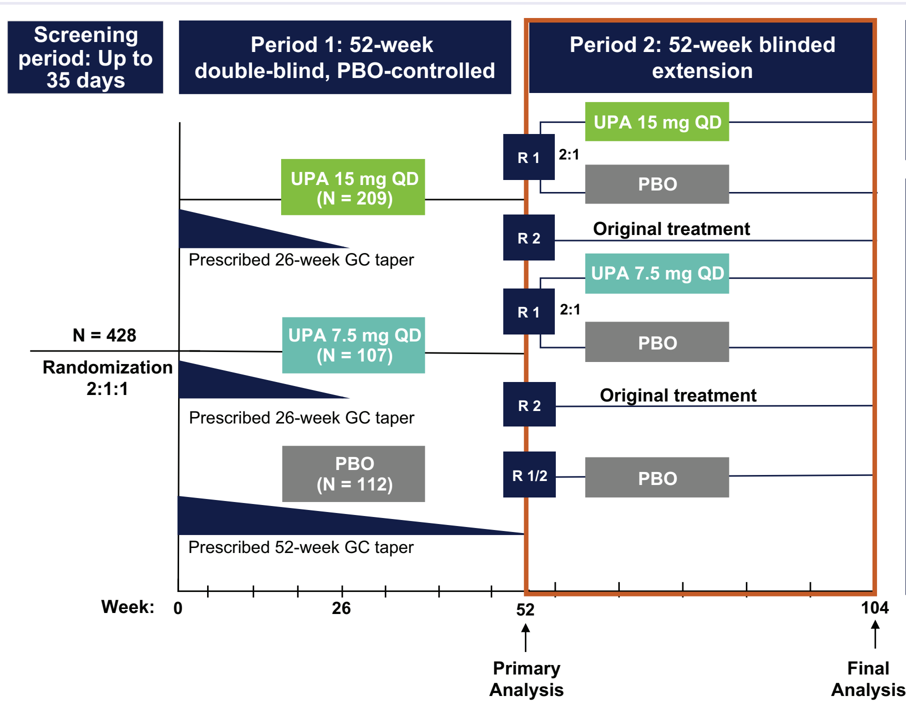
- To assess the efficacy and safety of UPA over 2 years in patients with GCA having ≥ 24 weeks of consecutive remission prior to the week-52 visit

BACKGROUND

- In the SELECT-GCA phase 3 trial, patients with GCA receiving upadacitinib (UPA) 15 mg had **higher rates of disease remission, fewer disease flares**, and **reduced use of glucocorticoids** compared with patients receiving placebo (PBO) through week 52[1]
  - **Sustained remission at week 52** (primary endpoint): **29.0%with PBO vs 46.4% with UPA 15 mg** (*P* = .002)
  - **Median cumulative glucocorticoid exposure** through week 52: **2882 mg with PBO vs 1615 mg with UPA 15 mg**
- **UPA 15 mg once daily is approved** for the treatment of adults with giant cell arteritis in many countries, including the United States and the European Union

METHODS

Figure 1. SELECT-GCA Study Design



Period 1

Purpose: To assess the efficacy and safety of UPA combined with a 26-week GC taper vs PBO with a 52-week GC taper through 52 weeks

Period 2: Eligible patients meeting R1 or R2 criteria

Purpose: To evaluate the long-term efficacy and safety of continuing vs withdrawing UPA in patients who achieved remission in period 1

R1: Sustained remission for ≥ 24 consecutive weeks prior to week 52
- Patients receiving UPA were re-randomized at a 2:1 ratio to either UPA at their original dose or switched to PBO at week 52
- Patients receiving PBO remained on PBO

R2: Remission at week 52 but < 24 consecutive weeks prior to week 52
- Patients continued period 1 treatment assignment

GC, glucocorticoid; PBO, placebo; QD, once daily; UPA, upadacitinib.

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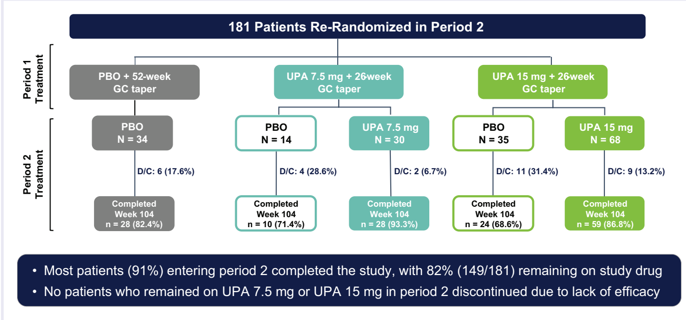
METHODS (CONTINUED)

Table 1. Definitions of Flare and Remission-Based Assessments in Period 2

Term	Definition
Disease flare	• Recurrence of signs or symptoms of GCA or ESR > 30 mm/hour (attributable to GCA) • Requiring reinitiation of GCs
Remission	• Absence of signs and symptoms of GCA • No GC use for GCA
Complete remission	• Remission • Normalization of ESR (≤ 30 mm/hour)[a] • Normalization of hsCRP (< 1 mg/dL)
Cumulative dose of GCs	• Total amount of GCs, in mg of prednisone equivalent, received from week 52 to week 104

GC, glucocorticoid.
[a]If ESR > 30 mm/hour and the elevation was not attributable to GCA, this criterion could still be met.

Figure 2. Disposition of Patients Entering Period 2[a]



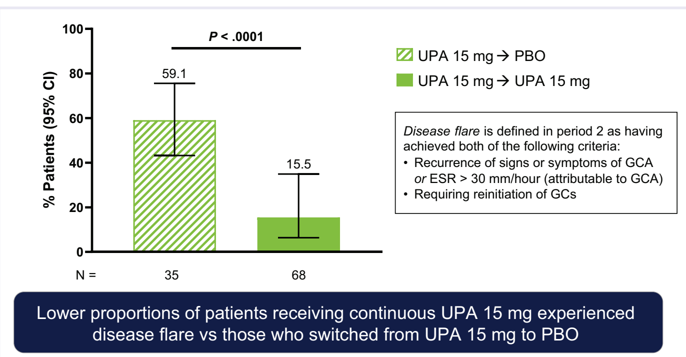
GC, glucocorticoid; PBO, placebo; UPA, upadacitinib.
[a]Includes patients who achieved ≥ 24 weeks of consecutive remission before the week 52 visit.

Table 2. Baseline Characteristics of Patients Entering Period 2

Baseline characteristics, n (%) unless specified		PBO + 52-week GC taper → PBO N = 34	UPA 7.5 mg + 26-week GC taper → PBO N = 14	UPA 7.5 mg + 26-week GC taper → UPA 7.5 N = 30	UPA 15 mg + 26-week GC taper → PBO N = 35	UPA 15 mg + 26-week GC taper → UPA 15 N = 68
Sex	Female	21 (61.8)	11 (78.6)	21 (70.0)	27 (77.1)	51 (75.0)
	Male	13 (38.2)	3 (21.4)	9 (30.0)	8 (22.9)	17 (25.0)
Age (years)	Mean (SD)	70.2 (7.8)	71.0 (7.5)	71.8 (7.2)	69.9 (6.7)	71.3 (8.2)
	Min, Max	54, 84	56, 84	55, 88	56, 82	51, 88
Race	Asian	2 (5.9)	0	0	4 (11.4)	4 (5.9)
	White	32 (94.1)	14 (100)	30 (100)	31 (88.6)	64 (94.1)
Disease status	New onset	26 (76.5)	9 (64.3)	19 (63.3)	26 (74.3)	49 (72.1)
	Relapsing	8 (23.5)	5 (35.7)	11 (36.7)	9 (25.7)	19 (27.9)
Disease duration since diagnosis (days)	New onset, mean (SD) Median	33.9 (7.5) 34.5	40.4 (13.3) 43	31.5 (8.8) 30	39.9 (13.7) 41	46.0 (45.5) 36
	Relapsing, mean (SD) Median	661.6 (968.5) 161	648.6 (254.2) 497	492.1 (616.8) 205	931.6 (769.7) 993	757.4 (770.6) 323
GC dose (mg)	Mean (SD)	33.5 (12.3)	32.9 (13.3)	32.7 (13.4)	32.3 (12.4)	33.1 (12.4)
	Median	30.0	35.0	30.0	30.0	30.0
ESR (mm/hour)	Mean (SD)	17.5 (19.2)	25.7 (32.2)a	17.3 (13.4)a	15.9 (12.8)	20.9 (17.9)
hsCRP (mg/dL)	Median	0.17	0.28	0.24	0.24	0.26
Prior use of IL-6 inhibitor	Yes	2 (5.9)	2 (14.3)	1 (3.3)	4 (11.4)	2 (2.9)

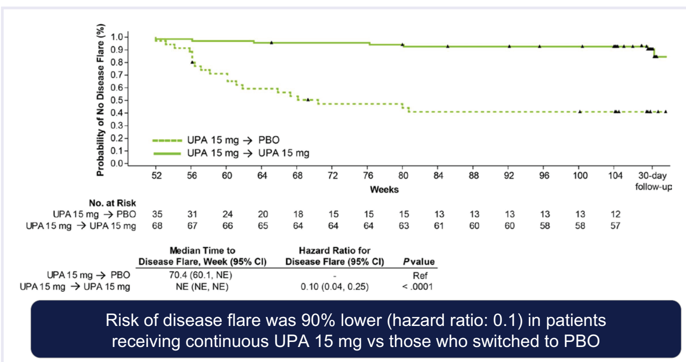
GC, glucocorticoid; PBO, placebo; UPA, upadacitinib.
[a]n = 13.

Figure 3. Proportion of Patients Experiencing ≥ 1 Disease Flare From Week 52 to Week 104 Plus 30 Days Follow-Up



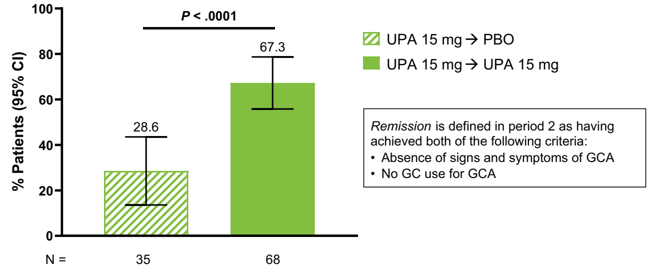
GC, glucocorticoid; PBO, placebo; UPA, upadacitinib.
All *P* values are nominal.

Figure 4. Time to First Disease Flare From Week 52 to Week 104 Plus 30 Days Follow-Up



NE, not estimable; PBO, placebo; Ref, reference; UPA, upadacitinib.Values marked as NE could not be estimated within the 104-week treatment period and are indicative of a timepoint > week 104.
All *P* values are nominal.

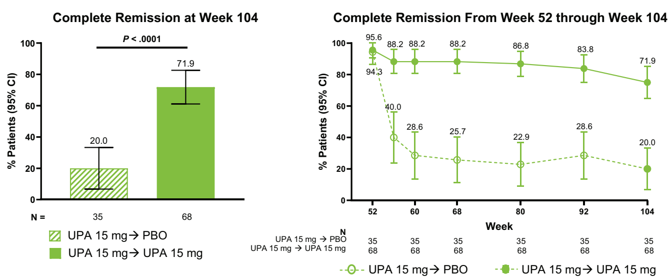
Figure 5. Proportion of Patients Maintaining Remission From Week 52 to Week 104



Higher proportions of patients receiving continuous UPA 15 mg maintained remission vs those who switched from UPA 15 mg to PBO

GC, glucocorticoid; PBO, placebo; UPA, upadacitinib.
All *P* values are nominal.

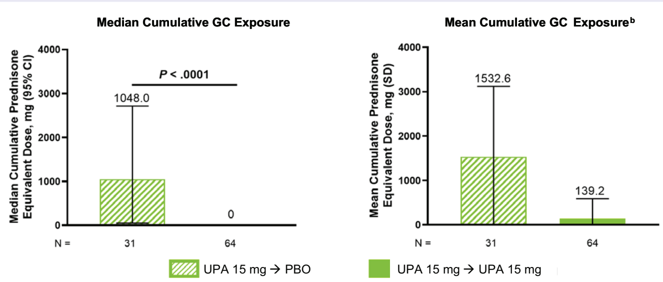
Figure 6. Proportion of Patients in Complete Remission From Week 52 to Week 104[a]



Higher proportions of patients receiving continuous UPA 15 mg achieved complete remission vs those who switched from UPA 15 mg to PBO

GC, glucocorticoid; PBO, placebo; UPA, upadacitinib.
[a]Complete remission is defined in period 2 as having achieved: (1) absence of the signs and symptoms of GCA, (2) no GC use for GCA, (3) normalization of ESR to ≤ 30 mm/hour (if ESR > 30 mm/hour and the elevation was not attributable to GCA; however, this criterion could still be met), and (4) normalization of hsCRP to < 1 mg/dL.
All *P* values are nominal.

Figure 7. Cumulative GC Exposure From Week 52 to Week 104



Cumulative GC exposure from week 52 to week 104 was lower in patients who remained on UPA 15 mg vs those who switched from UPA 15 mg to PBO[a]

GC, glucocorticoid; PBO, placebo; UPA, upadacitinib.
[a]In prednisone/prednisolone equivalence.
[b]Differences in mean cumulative GC exposure between groups were not tested for statistical significance.
All *P* values are nominal.

Table 3. Summary of Treatment-Emergent Adverse Event Rates Through 2 Years in SELECT-GCA[a,b]

Events/100 PY (95% CI) [No. of Events]	Through 1 Year (Period 1)		Through 2 Years	
	PBO + 52-week GC taper (N = 112) (PY = 94.3)	UPA 15 mg + 26-week GC taper (N = 209) (PY = 178.1)	PBO + 52-week GC taper (N = 112) (PY = 133.9)	UPA 15 mg + 26-week GC taper (N =209) (PY = 270.3)
Any TEAE	748.6 (694.4, 805.9) [706]	817.7 (776.2, 860.8) [1456]	651.9 (609.4, 696.6) [873]	681 (650.2, 712.8) [1841]
Serious TEAE	42.4 (30.3, 57.8) [40]	36.5 (28.2, 46.5) [65]	36.6 (27.1, 48.4) [49]	31.1 (24.8, 38.5) [84]
AE leading to study drug discontinuation	32.9 (22.3, 46.7) [31]	23.0 (16.5, 31.2) [41]	26.1 (18.2, 36.3) [35]	19.2 (14.4, 25.2) [52]
Deaths	2.1 (0.3, 7.7) [2]	1.1 (0.1, 4.1) [2]	1.5 (0.2, 5.4) [2]	0.7[c] (0.1, 2.7) [2]

AE, adverse event; PBO, placebo; PY, patient-years; TEAE, treatment-emergent adverse event; UPA, upadacitinib.
[a]All events are reported as TEAEs, which are defined as any adverse event with an onset date that is on or after the first dose of study drug, and no more than 30 days after the last dose of study drug. Safety analysis includes all patients enrolled in SELECT-GCA who received ≥ 1 dose of study drug.
[b]Safety outcomes were also evaluated and found to be similar in patients originally randomized to PBO, UPA 7.5 mg, or UPA 15 mg and who received continuous treatment with the same drug and dose thereafter in period 2 (data not shown).
[c]One non-treatment-emergent death also occurred 60 days after the last dose of study drug in the UPA 15 mg group.
Primary safety results through 1 year are further described in Blockmans D, et al. *NEJM.* 2025;392:2013–24.

Table 4. Rates of Treatment-Emergent Adverse Events of Special Interest Through 2 Years in SELECT-GCA[a,b] (1/2)

Events/100 PY (95% CI) [No. of Events]	Through 1 Year (Period 1)		Through 2 Years	
	PBO + 52-week GC taper (N = 112) (PY = 94.3)	UPA 15 mg + 26-week GC taper (N = 209) (PY = 178.1)	PBO + 52-week GC taper (N = 112) (PY = 133.9)	UPA 15 mg + 26-week GC taper (N =209) (PY = 270.3)
Serious infection	12.7 (6.6, 22.2) [12]	7.9 (4.3, 13.2) [14]	10.5 (5.7, 17.5) [14]	5.9 (3.4, 9.6) [16]
Opportunistic infection[c]	1.1 (0, 5.9) [1]	2.2 (0.6, 5.8) [4]	1.5 (0.2, 5.4) [2]	1.8 (0.6, 4.3) [5]
Herpes zoster	4.2 (1.2, 10.9) [4]	7.3 (3.9, 12.5) [13]	3.0 (0.8, 7.6) [4]	5.9 (3.4, 9.6) [16]
CPK elevation	0	3.4 (1.2, 7.3) [6]	0	3.3 (1.5, 6.3) [9]
Hepatic disorder	6.4 (2.3, 13.8) [6]	7.3 (3.9, 12.5) [13]	5.2 (2.1, 10.8) [7]	5.5 (3.1, 9.2) [15]
NMSC[d]	2.1 (0.3, 7.7) [2]	2.8 (0.9, 6.6) [5]	3.8 (1.2, 8.9) [5]	2.6 (1.1, 5.4) [7]
Malignancy excluding NMSC[d]	2.1 (0.3, 7.7) [2]	2.3 (0.6, 5.8) [4]	1.5 (0.2, 5.4) [2]	1.9 (0.6, 4.4) [5]
MACE (adjudicated)[d,e]	2.1 (0.3, 7.7) [2]	0	1.5 (0.2, 5.4) [2]	0
VTE (adjudicated)[d,f]	4.3 (1.2, 10.9) [4]	3.9 (1.6, 8.1) [7]	3.0 (0.8, 7.7) [4]	3.0 (1.3, 5.8) [8]
Anemia	3.2 (0.7, 9.3) [3]	8.4 (4.7, 13.9) [15]	4.5 (1.6, 9.8) [6]	8.1 (5.1, 12.3) [22]
Lymphopenia	0	2.2 (0.6, 5.8) [4]	0.7 (0, 4.2) [1]	1.8 (0.6, 4.3) [5]
Neutropenia	1.1 (0, 5.9) [1]	0	0.7 (0, 4.2) [1]	0
Retinal detachment	3.2 (0.7, 9.3) [3]	2.2 (0.6, 5.8) [4]	3.0 (0.8, 7.6) [4]	1.8 (0.6, 4.3) [5]
Bone fracture[d]	6.5 (2.4, 14.2) [6]	7.7 (4.1, 13.1) [13]	4.7 (1.7, 10.1) [6]	6.2 (3.6, 10.1) [16]

PBO, placebo; PY, patient-years; UPA, upadacitinib.
[a]Safety analysis includes all patients enrolled in SELECT-GCA who received ≥ 1 dose of study drug.
[b]Safety outcomes were also evaluated and found to be similar in patients originally randomized to PBO, UPA 7.5 mg, or UPA 15 mg and who received continuous treatment with the same drug and dose thereafter in period 2 (data not shown).
[c]Excludes herpes zoster.
[d]Reported as exposure-adjusted incidence (n/100 PY) [no. of patients].
[e]Defined as cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.
[f]Includes pulmonary embolism and deep vein thrombosis.
Primary safety results through 1 year are further described in Blockmans D, et al. *NEJM.* 2025;392:2013–24.

No events of TB, GI perforation, or lymphoma were reported in any of the treatment groups

CONCLUSIONS

- Continuing UPA 15 mg in patients with ≥ 24 weeks of remission prior to week 52 vs switching to PBO was associated with lower risk of flare and higher rates of remission through week 104 (end of trial)
- Patients receiving continuous UPA 15 mg showed an approximately 1-gram reduction in cumulative exposure of GCs from week 52 to week 104 compared with those who switched from UPA 15 mg to PBO at week 52
- In this population (mean age: 71 yrs), long-term use of UPA revealed no new clinically-significant safety signals, and safety remained consistent with initial 52-week results and the established profile of UPA[1,2]
- The 2-year data from SELECT-GCA further support a favorable benefit-risk profile for UPA 15 mg in GCA

REFERENCES

1. Blockmans D, et al. *NEJM*. 2025;392:2013–24.

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