Impact of Glucocorticoid Tapering in Giant Cell Arteritis: Analysis From the SELECT-GCA Trial

OP0057

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OBJECTIVE

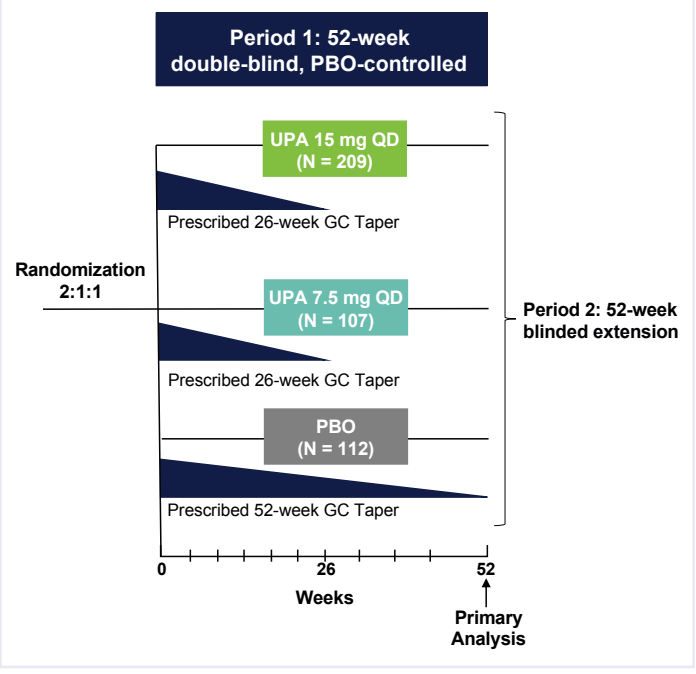
- To assess the occurrence of adverse events of serious infection, herpes zoster, and opportunistic infection during concomitant treatment with glucocorticoids (GCs) and after GC tapering in patients with GCA receiving upadacitinib (UPA) or placebo (PBO)

BACKGROUND

- GCA is a chronic systemic vasculitis that affects people ≥ 50 years of age, with a mean age > 70 years[1,2]
- Management typically involves the use of GCs to control inflammation and alleviate symptoms[3]
- However, prolonged GC use, even at low doses, can lead to adverse effects, including an increased risk of infections[4]
- In the SELECT-GCA phase 3 trial, UPA once daily in combination with a protocolized 26-week GC taper demonstrated a favorable benefit-risk profile compared with PBO with a protocolized 52-week GC taper, providing an alternative option to reduce GC dependency while maintaining disease control in patients with GCA[5]

METHODS

Figure 1. SELECT-GCA Study Design and Key Eligibility Criteria

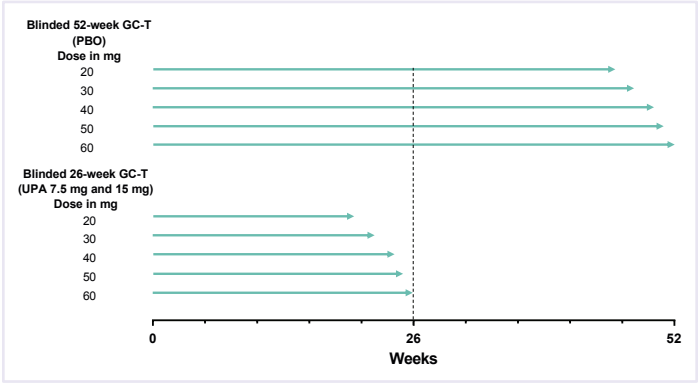


GC, glucocorticoid; PBO, placebo; QD, once daily; UPA, upadacitinib.

ELIGIBILITY CRITERIA

- ≥ 50 years old
- New-onset or relapsing GCA
- Received ≥ 40 mg prednisone/day before baseline and were taking prednisone ≥ 20 mg/day at baseline
- Baseline GC dose (ranging from 20 to 60 mg daily) was determined by the investigator
- Exclusions included:
  - Prior exposure to JAK inhibitors
  - Inadequate response to IL-6 or exposure within 4 weeks before baseline
  - Prior chronic use of systemic GCs for non-GCA reasons

Figure 2. Glucocorticoid Tapering Schedule in the SELECT-GCA Trial



GC, glucocorticoid; GC-T, glucocorticoid tapering; PBO, placebo; UPA, upadacitinib.

METHODS (CONTINUED)

ASSESSMENTS

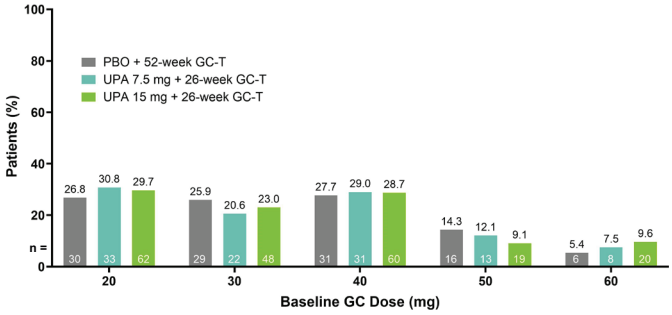
- Safety outcomes are from the first 52 weeks (period 1) of the SELECT-GCA trial
- Serious infections, herpes zoster, and opportunistic infections were assessed through week 26 (ie, the duration of the GC taper regimen for patients randomized to UPA 7.5 mg or 15 mg) and week 26 through week 52 (ie, after the protocol-defined GC taper regimen for UPA groups)
- Serious infections were also evaluated based on initial GC dose and time period, including during the GC taper (≤ week 26) and post-taper (> week 26 through week 52) for patients treated with UPA; for patients receiving PBO, infections were assessed during their ongoing GC taper phase through week 52

STATISTICAL ANALYSIS

- Treatment-emergent event rate calculations included data from patients with ≥ 1 event of the same type (with each event contributing to the calculation) and are reported as exposure-adjusted adverse event rates (EAERs); 95% CI results were calculated based on the exact method for the Poisson mean
- Infectious events through week 52 were also analyzed using the Kaplan-Meier method and presented as time to first event
- The Kaplan-Meier analysis models time to first event for each patient, with data from patients without events censored at the end of the study period

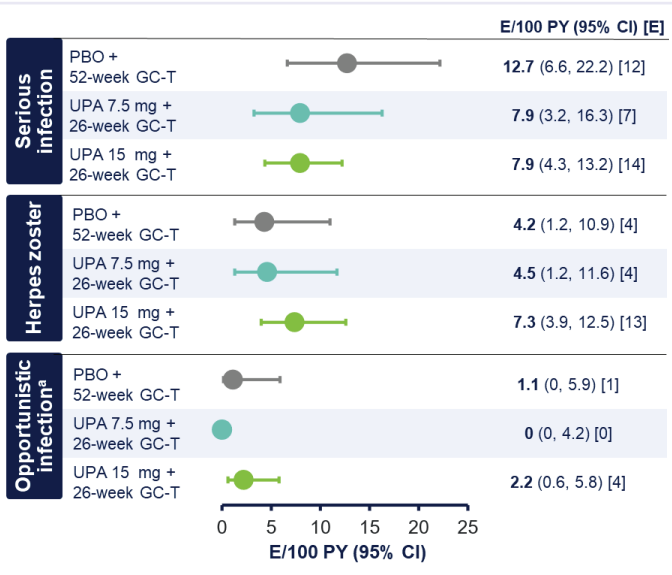
RESULTS

Figure 3. Distribution of Glucocorticoid Doses at Baseline



GC, glucocorticoid; GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.
The numbers of patients in each GC dose group at baseline are shown in white text at the bottom of each column.

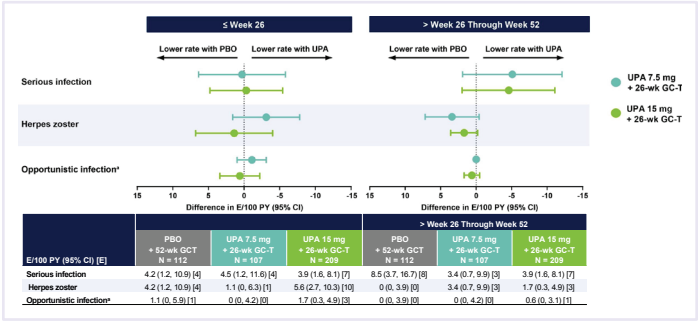
Figure 4. Overall EAERs of Serious Infections, Herpes Zoster, and Opportunistic Infections Through Week 52



E, event; EAER, exposure-adjusted event rate; E/100 PY, events per 100 patient-years; GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.
[a]Excludes herpes zoster and tuberculosis. There was 1 event of esophageal candidiasis in the PBO group. In the UPA 15 mg group, there was 1 event of esophageal candidiasis, 2 oral fungal infections, and 1 *Pneumocystis jirovecii* pneumonia.

- Serious infection rates were numerically lower with UPA 7.5 mg or 15 mg than PBO through week 52
- Rates of herpes zoster, a known risk for JAK inhibitors including UPA, were higher with UPA 15 mg vs PBO
- Opportunistic infection rates were low across all groups and numerically higher with UPA 15 mg than PBO; none occurred with UPA 7.5 mg

Figure 5. EAERs of Serious Infections, Herpes Zoster, and Opportunistic Infections Through Week 52 by Time Period During Glucocorticoid Taper



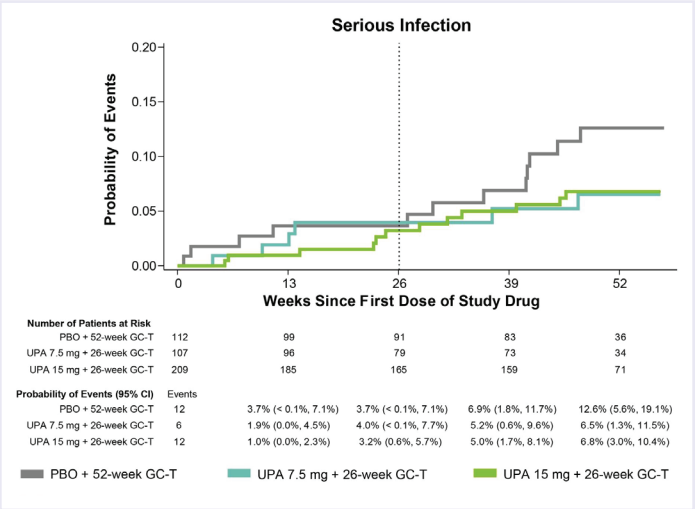
E/100 PY (95% CI) [E]	≤ Week 26			> Week 26 Through Week 52		
	PBO + 52-wk GCT N = 112	UPA 7.5 mg + 26-wk GC-T N = 107	UPA 15 mg + 26-wk GC-T N = 209	PBO + 52-wk GCT N = 112	UPA 7.5 mg + 26-wk GC-T N = 107	UPA 15 mg + 26-wk GC-T N = 209
Serious infection	4.2 (1.2, 10.9) [4]	4.5 (1.2, 11.6) [4]	3.9 (1.6, 8.1) [7]	8.5 (3.7, 16.7) [8]	3.4 (0.7, 9.9) [3]	3.9 (1.6, 8.1) [7]
Herpes zoster	4.2 (1.2, 10.9) [4]	1.1 (0, 6.3) [1]	5.6 (2.7, 10.3) [10]	0 (0, 3.9) [0]	3.4 (0.7, 9.9) [3]	1.7 (0.3, 4.9) [3]
Opportunistic infection[a]	1.1 (0, 5.9) [1]	0 (0, 4.2) [0]	1.7 (0.3, 4.9) [3]	0 (0, 3.9) [0]	0 (0, 4.2) [0]	0.6 (0, 3.1) [1]

E, event; EAER, exposure-adjusted event rate; E/100 PY, events per 100 patient-years; GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.
[a]Excludes herpes zoster and tuberculosis.

- Serious infection rates were numerically lower in the post-taper period with UPA 7.5 mg or 15 mg relative to PBO
- Herpes zoster rates were similar with UPA 15 mg relative to PBO during and after the prespecified GC taper
- Of the 4 opportunistic infections with UPA 15 mg, 3 occurred during the prespecified GC taper and 1 after in a patient receiving GC escape therapy

RESULTS (CONTINUED)

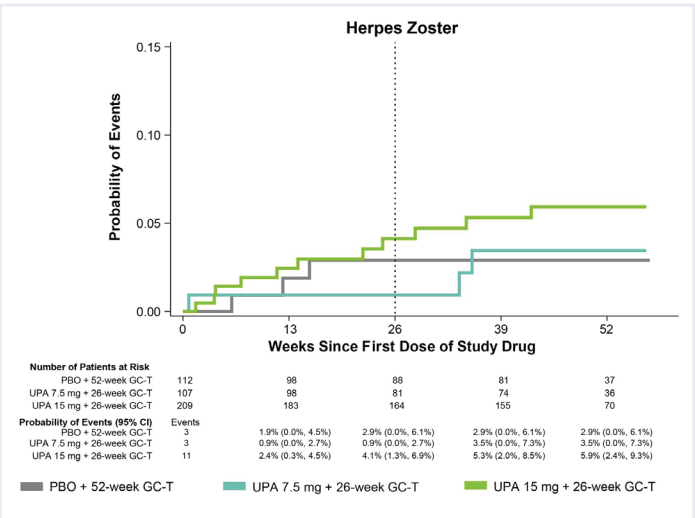
Figure 6. Time to First Event of Serious Infection During Glucocorticoid Taper



GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.

- Fewer serious infections occurred post-taper with UPA compared with during the prespecified GC taper, while serious infections increased in the PBO group throughout

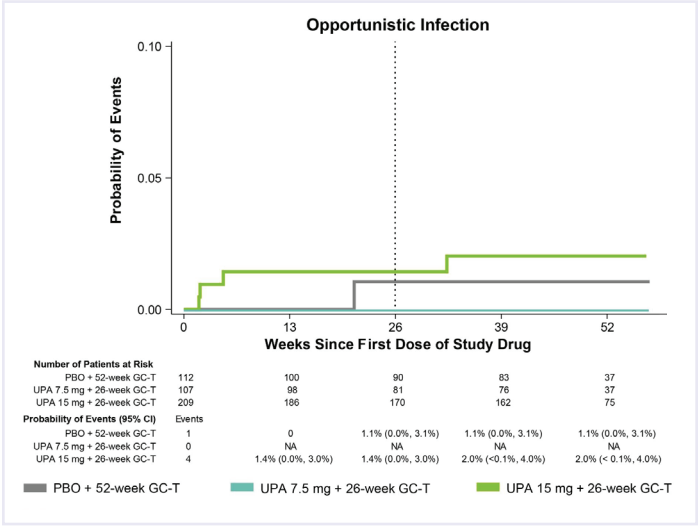
Figure 7. Time to First Event of Herpes Zoster During Glucocorticoid Taper



GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.

- Herpes zoster incidence was higher with UPA 15 mg than PBO; GC tapering did not notably affect herpes zoster occurrence with UPA

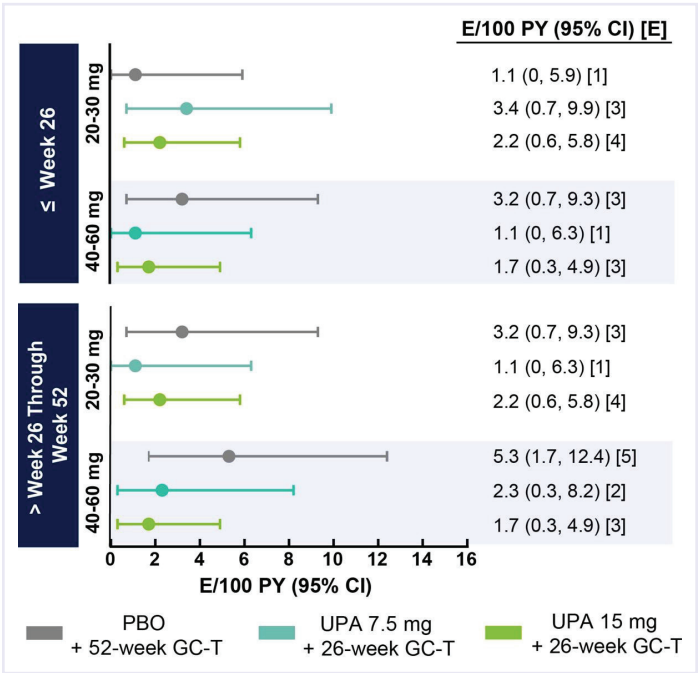
Figure 8. Time to First Event of Opportunistic Infection[a] During Glucocorticoid Taper



GC-T, glucocorticoid taper; NA, not available; PBO, placebo; UPA, upadacitinib.
[a]Excludes herpes zoster and tuberculosis.

- Opportunistic infections were uncommon but numerically higher with UPA 15 mg vs PBO; none occurred with UPA 7.5 mg

Figure 9. EAERs of Serious Infections Through Week 52 by Time Period and Starting Dose of Glucocorticoid Taper



E, event; EAER, exposure-adjusted event rate; E/100 PY, events per 100 patient-years; GC-T, glucocorticoid taper; PBO, placebo; UPA, upadacitinib.

- Baseline GC dose did not notably impact the occurrence of serious infections

CONCLUSIONS

- Rates of serious infections through 52 weeks were numerically lower in patients treated with UPA 7.5 mg or 15 mg combined with a 26-week GC taper vs PBO with a 52-week GC taper, with rates lower with UPA relative to PBO after tapering GCs at 6 months in the UPA groups
- The decrease in serious infection rates during the GC-free phase suggests concomitant use of GCs may contribute to the risk of serious infections
- GC tapering did not appear to affect the occurrence of herpes zoster in either UPA group
- Of the 4 opportunistic infections occurring in patients receiving UPA 15 mg, 3 events occurred during the prespecified GC taper and 1 occurred after the prespecified GC taper in a patient receiving GC escape therapy
- Overall, these results, together with the superior efficacy of UPA 15 mg with a 26-week GC taper compared to PBO with a 52-week GC taper,[5] support the potential benefits of a shorter GC taper period

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