SUPPLEMENTARY MATERIALS

Safety and Efficacy of Upadacitinib for Atopic Dermatitis in Japan: Analysis of the 3-Year Phase 3 Rising Up Study

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Supplementary Table 1 Patient demographics and baseline characteristics among adolescents

Characteristic	Upadacitinib 15 mg (*N* = 10)	Upadacitinib 30 mg (*N* = 10)	Placebo (*N* = 9)
Age, years, mean (SD)	15.4 (1.9)	16.3 (1.5)	14.9 (1.6)
Sex, *n* (%)			
Female	3 (30.0)	2 (20.0)	2 (22.2)
Male	7 (70.0)	8 (80.0)	7 (77.8)
Weight, kg, mean (SD)	51.3 (7.2)	60.7 (12.9)	58.8 (10.8)
Affected BSA, %, mean (SD)	64.7 (21.5)	65.4 (25.2)	57.5 (26.3)
Disease duration since diagnosis, years, mean (SD)	10.4 (5.1)	12.0 (4.6)	9.5 (5.1)
vIGA-AD, *n* (%)			
Moderate (score of < 4)	6 (60.0)	6 (60.0)	5 (55.6)
Severe (score of 4)	4 (40.0)	4 (40.0)	4 (44.4)
EASI, mean (SD)	34.6 (13.4)	37.0 (14.7)	32.3 (16.0)
WP-NRS, mean (SD)	6.7 (1.4)	5.9 (1.1)	6.4 (1.6)
hsCRP, mg/L, mean (SD)	1.7 (2.9)	0.9 (0.9)	5.1 (13.1)

BSA body surface area, *EASI* Eczema Area and Severity Index, *hsCRP* high-sensitivity C-reactive protein, *vIGA-AD* validated Investigator Global Assessment for Atopic Dermatitis, *WP-NRS* Worst Pruritus Numerical Rating Scale

Percentages were calculated using nonmissing values

Supplementary Table 2 Exposure-adjusted event rates through 112 weeks and 160 weeks in the Rising Up study

	Week 112[a]		Week 160	
Events (E/100 PY)	**Upadacitinib 15 mg (*N* = 133; PY = 289.4)**	**Upadacitinib 30 mg (*N* = 136; PY = 287.7)**	**Upadacitinib 15 mg (*N* = 133; PY = 363.8)**	**Upadacitinib 30 mg (*N* = 136; PY = 362.9)**
Overview				
Any AE	563 (194.5)	594 (206.4)	699 (192.1)	778 (214.4)
AE with reasonable possibility of being drug-related	146 (50.4)	155 (53.9)	170 (46.7)	195 (53.7)
Severe AE	20 (6.9)	19 (6.6)	22 (6.0)	23 (6.3)
Serious AE	17 (5.9)	11 (3.8)	18 (4.9)	16 (4.4)
AE leading to discontinuation of study drug	7 (2.4)	5 (1.7)	9 (2.5)	7 (1.9)
Deaths	0	0	0	0
Most common AEs[b]				
Nasopharyngitis	51 (17.6)	65 (22.6)	55 (15.1)	68 (18.7)
Acne	39 (13.5)	58 (20.2)	43 (11.8)	64 (17.6)
Herpes zoster	18 (6.2)	33 (11.5)	27 (7.4)	40 (11.0)
Pyrexia	14 (4.8)	17 (5.9)	25 (6.9)	33 (9.1)
Injection site pain[c]	1 (0.3)	5 (1.7)	4 (1.1)	19 (5.2)
Dermatitis atopic	17 (5.9)	10 (3.5)	20 (5.5)	18 (5.0)
Headache	10 (3.5)	9 (3.1)	11 (3.0)	16 (4.4)
Blood CPK increased	6 (2.1)	13 (4.5)	8 (2.2)	16 (4.4)
Arthralgia	1 (0.3)	13 (4.5)	2 (0.5)	15 (4.1)
Herpes simplex	23 (7.9)	11 (3.8)	32 (8.8)	14 (3.9)
Oral herpes	16 (5.5)	11 (3.8)	19 (5.2)	14 (3.9)

Supplementary Table 2 Exposure-adjusted event rates through 112 weeks and 160 weeks in the Rising Up study

	Week 112[a]		Week 160	
Events (E/100 PY)	**Upadacitinib 15 mg (*N* = 133; PY = 289.4)**	**Upadacitinib 30 mg (*N* = 136; PY = 287.7)**	**Upadacitinib 15 mg (*N* = 133; PY = 363.8)**	**Upadacitinib 30 mg (*N* = 136; PY = 362.9)**
ALT increased	8 (2.8)	10 (3.5)	13 (3.6)	13 (3.6)
Tinea pedis	2 (0.7)	11 (3.8)	3 (0.8)	13 (3.6)
Paronychia	0	4 (1.4)	1 (0.3)	12 (3.3)
Influenza	7 (2.4)	11 (3.8)	7 (1.9)	11 (3.0)
Neutropenia	0	9 (3.1)	1 (0.3)	11 (3.0)
Asthma	1 (0.3)	9 (3.1)	1 (0.3)	10 (2.8)
Eczema herpeticum	15 (5.2)	6 (2.1)	18 (4.9)	9 (2.5)
Folliculitis	17 (5.9)	7 (2.4)	18 (4.9)	8 (2.2)
Skin papilloma	16 (5.5)	7 (2.4)	17 (4.7)	8 (2.2)
Pharyngitis	6 (2.1)	6 (2.1)	6 (1.6)	8 (2.2)
Anemia	3 (1.0)	6 (2.1)	3 (0.8)	8 (2.2)
COVID-19	2 (0.7)	3 (1.0)	8 (2.2)	7 (1.9)
Conjunctivitis allergic	5 (1.7)	4 (1.4)	10 (2.7)	6 (1.7)
Gastroenteritis	8 (2.8)	5 (1.7)	9 (2.5)	5 (1.4)
Dental caries	7 (2.4)	4 (1.4)	8 (2.2)	4 (1.1)
Furuncle	8 (2.8)	4 (1.4)	9 (2.5)	4 (1.1)
Tonsillitis	7 (2.4)	2 (0.7)	9 (2.5)	2 (0.6)

AE adverse event, *ALT* alanine aminotransferase, *CPK* creatine phosphokinase, *E/100 PY* events per 100 patient-years, *PY* patient-years

[a]Data through week 112 were previously reported [17]

[b]Most common AEs are defined as those occurring at a rate of ≥ 2 E/100 PY in either treatment group at week 160

[c]All AEs of injection site pain were considered to be possibly related to COVID-19 vaccination

Supplementary Table 3 Treatment-emergent serious adverse events with reasonable possibility of being related to study drug

	Week 160	
Events (E/100 PY)	**Upadacitinib 15 mg (*N* = 133; PY = 363.8)**	**Upadacitinib 30 mg (*N* = 136; PY = 362.9)**
Any AE	7 (1.9)	8 (2.2)
Herpes zoster	1 (0.3)	2 (0.6)
Herpes zoster cutaneous disseminated	0	1 (0.3)
Herpes zoster disseminated	0	1 (0.3)
Herpes simplex	0	1 (0.3)
Appendicitis	1 (0.3)	1 (0.3)
Pneumothorax	0	1 (0.3)
Large intestine polyp	0	1 (0.3)
Inguinal hernia	1 (0.3)	0
Enteritis infectious	1 (0.3)	0
Pneumocystis jirovecii pneumonia	1 (0.3)	0
Cerebellar hemorrhage	1 (0.3)	0
Somatic symptom disorder	1 (0.3)	0

AE adverse event, *E/100 PY* events per 100 patient-years, *PY* patient-years

Supplementary Table 4 Treatment-emergent adverse events leading to study drug discontinuation

	Week 160	
Events (E/100 PY)	**Upadacitinib 15 mg (*N* = 133; PY = 363.8)**	**Upadacitinib 30 mg (*N* = 136; PY = 362.9)**
Any AE	9 (2.5)	7 (1.9)
ALT increased	1 (0.3)[a]	1 (0.3)[a]
Herpes zoster disseminated	0	1 (0.3)[a]
Acne	0	1 (0.3)[a]
Lymphopenia	0	1 (0.3)[a]
Neutropenia	0	1 (0.3)[a]
Oedema peripheral	0	1 (0.3)[a]
Dermatitis atopic	1 (0.3)[a]	0
Lymphocyte morphology abnormal	0	1 (0.3)[a]
Rectal cancer	1 (0.3)	0
COVID-19	1 (0.3)	0
Eczema herpeticum	1 (0.3)	0
Pneumocystis jirovecii pneumonia	1 (0.3)[a]	0
Cerebellar hemorrhage	1 (0.3)[a]	0
Septic shock	1 (0.3)	0
AST increased	1 (0.3)[a]	0

AE adverse event, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *E/100 PY* events per 100 patient-years, *PY* patient-years

[a]Considered by the investigator as having a reasonable possibility of being related to study drug

Supplementary Table 5 Long-term safety of upadacitinib among adolescents in the Rising Up study

Parameter	Week 112; *n*/PY (*n*/100 PY)[a]		Week 160; *n*/PY (*n*/100 PY)	
	Upadacitinib 15 mg (*N* = 14)	Upadacitinib 30 mg (*N* = 14)	Upadacitinib 15 mg (*N* = 14)	Upadacitinib 30 mg (*N* = 14)
Overview				
Any AE	13/8.3 (155.8)	12/4.6 (260.9)	13/8.3 (155.8)	13/4.7 (274.0)
AE with reasonable possibility of being drug-related	8/19.9 (40.2)	6/21.4 (28.1)	8/22.5 (35.6)	7/24.6 (28.4)
Severe AE	2/28.3 (7.1)	1/24.9 (4.0)	2/33.6 (6.0)	1/30.5 (3.3)
Serious AE	3/28.0 (10.7)[b]	0/27.2	3/32.9 (9.1)[b]	1/32.7 (3.1)[c]
AE leading to discontinuation of upadacitinib	1/30.8 (3.2)[d]	1/27.1 (3.7)[e]	1/37.4 (2.7)[d]	1/33.4 (3.0)[e]
Deaths	0/31.1	0/27.2	0/37.7	0/33.5
Most common AEs[d]				
Acne	6/20.6 (29.2)	7/13.7 (51.2)	6/23.7 (25.3)	7/16.2 (43.1)
Nasopharyngitis	4/24.5 (16.4)	7/18.3 (38.2)	4/29.0 (13.8)	7/22.3 (31.4)
Influenza	2/27.0 (7.4)	2/23.2 (8.6)	2/32.5 (6.1)	2/29.1 (6.9)
Upper RTI	3/24.1 (12.4)	1/24.7 (4.0)	3/29.0 (10.3)	1/30.5 (3.3)
Anemia	3/28.0 (10.7)	0/27.2	3/33.0 (9.1)	0/33.5
Asthma	1/29.2 (3.4)	2/23.5 (8.5)	1/35.1 (2.8)	2/28.6 (7.0)
Blood CPK increased	2/27.2 (7.4)	1/26.8 (3.7)	2/32.9 (6.1)	1/33.0 (3.0)
Headache	1/30.2 (3.3)	2/25.6 (7.8)	1/36.1 (2.8)	4/30.2 (13.2)
Otitis externa	2/28.5 (7.0)	1/26.2 (3.8)	2/34.0 (5.9)	1/32.0 (3.1)
Pharyngitis	1/29.7 (3.4)	2/23.8 (8.4)	1/35.9 (2.8)	2/28.9 (6.9)

Supplementary Table 5 Long-term safety of upadacitinib among adolescents in the Rising Up study

Parameter	Week 112; *n*/PY (*n*/100 PY)[a]		Week 160; *n*/PY (*n*/100 PY)	
	Upadacitinib 15 mg (*N* = 14)	Upadacitinib 30 mg (*N* = 14)	Upadacitinib 15 mg (*N* = 14)	Upadacitinib 30 mg (*N* = 14)
Pyrexia	2/27.5 (7.3)	1/24.9 (4.0)	2/33.1 (6.0)	3/29.6 (10.1)
Skin papilloma	1/30.8 (3.2)	2/25.9 (7.7)	2/36.6 (5.5)	2/30.9 (6.5)
Enterocolitis	0/31.1	2/25.3 (7.9)	0/37.7	2/31.0 (6.5)
Gastroenteritis	2/30.2 (6.6)	0/27.2	2/35.8 (5.6)	0/33.5
Hepatic function abnormal	2/30.2 (6.6)	0/27.2	2/36.2 (5.5)	0/33.5
Herpes zoster	0/31.1	2/26.3 (7.6)	0/37.7	3/31.3 (9.6)
Impetigo	2/30.0 (6.7)	0/27.2	2/35.9 (5.6)	0/33.5
Dermatitis atopic	1/30.8 (3.2)	1/25.5 (3.9)	1/37.4 (2.7)	3/31.3 (9.6)
Malaise	1/28.8 (3.5)	0/27.2	2/34.2 (5.8)	2/32.5 (6.2)
Alanine aminotransferase increased	1/30.4 (3.3)	0/27.2	2/35.7 (5.6)	0/33.5
Vaccination site pain	0/31.1	0/27.2	0/37.7	2/32.6 (6.1)

AE adverse event, *CPK* creatine phosphokinase, *n/100 PY* number of patients with at least one event per 100 patient-years, *n/PY* number of patients with at least one event/patient-years for patients at risk of an event, *RTI* respiratory tract infection

[a]Data through week 112 were previously reported [17]

[b]Serious AEs included appendicitis (considered possibly related to study drug), concussion due to accident (unrelated to study drug), and irritable bowel syndrome (unrelated to study drug)

[c]Meniscus injury (unrelated to study drug)

[d]Worsening of atopic dermatitis (considered possibly related to study drug).

[e]Atypical lymphocytes seen in peripheral blood smear that resolved; event was not considered a malignancy

[f]Most common AEs are defined as those occurring in ≥ 2 patients in either adolescent treatment group at week 160

Supplementary Table 6 Exposure-adjusted event rates for AESIs through 112 weeks and 160 weeks in the Rising Up study

	Week 112, events (E/100 PY)[a]		Week 160, events (E/100 PY)	
AESI	**Upadacitinib 15 mg (*N* = 133; PY = 289.4)**	**Upadacitinib 30 mg (*N* = 136; PY = 287.7)**	**Upadacitinib 15 mg (*N* = 133; PY = 363.8)**	**Upadacitinib 30 mg (*N* = 136; PY = 362.9)**
Serious infections	6 (2.1)	4 (1.4)	7 (1.9)	9 (2.5)
Opportunistic infection excluding TB and herpes zoster	16 (5.5)	7 (2.4)	19 (5.2)	10 (2.8)
Malignancy	1 (0.3)	0	1 (0.3)	0
NMSC	0	0	0	0
Malignancy excluding NMSC	1 (0.3)	0	1 (0.3)	0
Lymphoma	0	1 (0.3)	0	1 (0.3)
Hepatic disorder	18 (6.2)	19 (6.6)	25 (6.9)	26 (7.2)
Gastrointestinal perforation	0	0	0	0
Anemia	5 (1.7)	9 (3.1)	5 (1.4)	11 (3.0)
Neutropenia	2 (0.7)	12 (4.2)	3 (0.8)	14 (3.9)
Lymphopenia	0	2 (0.7)	0	5 (1.4)
Herpes zoster	21 (7.3)	37 (12.9)	31 (8.5)	48 (13.2)
CPK elevation	6 (2.1)	13 (4.5)	8 (2.2)	16 (4.4)
Renal dysfunction	0	0	0	0
Active TB	0	0	0	0
Adjudicated MACE[b]	1 (0.3)	0	1 (0.3)	0
Adjudicated VTE[c]	0	0	0	0

AESI adverse event of special interest, *MACE* major adverse cardiovascular event, *E/100 PY* events per 100 patient-years, *NMSC* nonmelanoma skin cancer, *PY* patient-years, *TB* tuberculosis, *VTE* venous thromboembolic events

[a]Data through week 112 were previously reported [17]

[b]MACE is defined as cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke

[c]VTE is defined as deep vein thrombosis and pulmonary embolism (fatal and nonfatal)

Supplementary Table 7 Long-term exposure-adjusted incidence rates for AESIs among adolescents in the Rising Up study

AESI	Week 112; *n*/PY (*n*/100 PY)[a]		Week 160; *n*/PY (*n*/100 PY)	
	Upadacitinib 15 mg (*N* = 14)	**Upadacitinib 30 mg (*N* = 14)**	**Upadacitinib 15 mg (*N* = 14)**	**Upadacitinib 30 mg (*N* = 14)**
Serious infection	1/29.6 (3.4)[b]	0/27.2	1/35.5 (2.8)[b]	0/33.5
Opportunistic infection excluding TB and herpes zoster	1/30.8 (3.2)[c]	0/27.2	1/37.4 (2.7)[c]	0/33.5
Malignancy	0/31.1	0/27.2	0/37.7	0/33.5
NMSC	0/31.1	0/27.2	0/37.7	0/33.5
Malignancy excluding NMSC	0/31.1	0/27.2	0/37.7	0/33.5
Lymphoma	0/31.1	1/27.1 (3.7)[d]	0/37.7	1/33.4 (3.0)[d]
Hepatic disorder	3/29.5 (10.2)	1/26.1 (3.8)	4/34.1 (11.7)	1/31.9 (3.1)
Gastrointestinal perforation	0/31.1	0/27.2	0/37.7	0/33.5
Anemia	3/28.0 (10.7)	0/27.2	3/33.0 (9.1)	0/33.5
Neutropenia	0/31.1	1/26.1 (3.8)	0/37.7	1/31.9 (3.1)
Lymphopenia	0/31.1	0/27.2	0/37.7	0/33.5
Herpes zoster	0/31.1	2/26.3 (7.6)	0/37.7	3/31.3 (9.6)
CPK elevation	2/27.2 (7.4)	1/26.8 (3.7)	2/32.9 (6.1)	1/33.0 (3.0)
Renal dysfunction	0/31.1	0/27.2	0/37.7	0/33.5
Active tuberculosis	0/31.1	0/27.2	0/37.7	0/33.5
Adjudicated MACE	0/31.1	0/27.2	0/37.7	0/33.5
Adjudicated VTE	0/31.1	0/27.2	0/37.7	0/33.5

AESI adverse event of special interest, *MACE* major adverse cardiovascular event, *n/100 PY* number of patients with at least one event per 100 patient-years, *NMSC* nonmelanoma skin cancer, *n/PY* number of patients with at least one event/patient-years for patients at risk of an event, *TB* tuberculosis, *VTE* venous thromboembolic events

[a]Data through week 112 were previously reported [17]

[b]Appendicitis (considered possibly related to study drug)

[c]Eczema herpeticum (considered possibly related to study drug)

[d]Atypical lymphocytes seen in peripheral blood smear that resolved; event was not considered a malignancy

Supplementary Table 8 Institutional review boards and ethics committees for the Rising Up study

IRB/IEC Name	City	Prefecture	Country
Asahikawa Medical University Hospital Institutional Review Board	Asahikawa-shi	Hokkaido	Japan
Central Japan International Medical Center Institutional Review Board	Minokamo-shi	Gifu	Japan
Fukuyama City Hospital Institutional Review Board	Fukuyama-shi	Hiroshima	Japan
Gunma University Hospital Institutional Review Board	Maebashi-shi	Gunma	Japan
Hokkaido P.W.F.A.C Sapporo-Kosei General Hospital Institutional Review Board	Sapporo-shi	Hokkaido	Japan
Hyogo Prefectural Amagasaki General Medical Center Institutional Review Board	Amagasaki-shi	Hyogo	Japan
Ichinomiya Municipal Hospital Institutional Review Board	Ichinomiya-shi	Aichi	Japan
Japan Conference of Clinical Research	Toshima-ku	Tokyo	Japan
Joint Institutional Review Board	Kochi-shi	Kochi	Japan
Kansai Rosai Hospital Institutional Review Board	Amagasaki-shi	Hyogo	Japan
Kiryu Kosei General Hospital Institutional Review Board	Kiryu-shi	Gunma	Japan
Kobe University Hospital Institutional Review Board	Kobe-shi	Hyogo	Japan
Nagaoka Red Cross Hospital Institutional Review Board	Nagaoka-shi	Niigata	Japan
Nagasaki University Hospital Institutional Review Board	Nagasaki-shi	Nagasaki	Japan
Nagoya City University Institutional Review Board	Nagoya-shi	Aichi	Japan

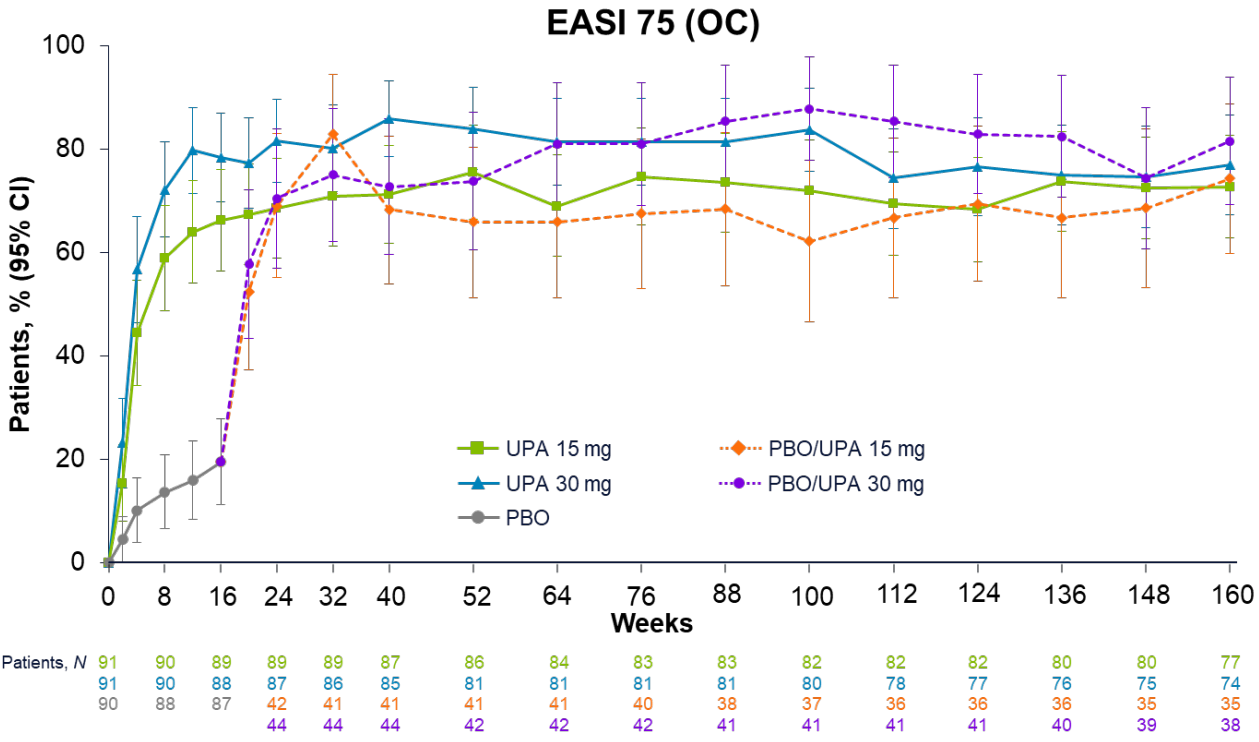
Supplementary Table 8 Institutional review boards and ethics committees for the Rising Up study

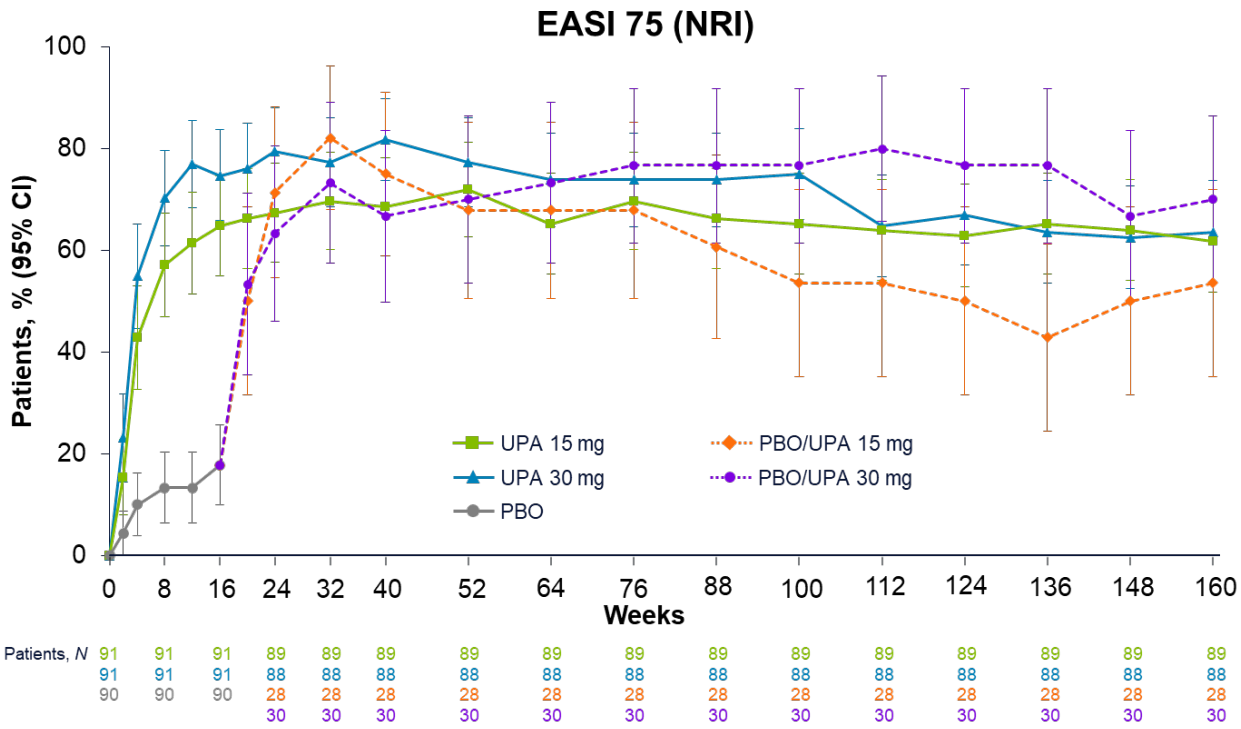
IRB/IEC Name	City	Prefecture	Country
Nakameguro Atlas Clinic Institutional Review Board	Meguro-ku	Tokyo	Japan
Nihon University Hospitals' Joint Institutional Review Board	Itabashi-Ku	Tokyo	Japan
Nihonbashi Sakura Clinic Institutional Review Board	Chuo-ku	Tokyo	Japan
Nippon Medical School Musashi Kosugi Hospital Institutional Review Board	Kawasaki-shi	Kanagawa	Japan
Shizuoka General Hospital Institutional Review Board	Shizuoka shi	Shizuoka	Japan
Tokai University Hospital-Isehara Campus	Isehara-Shi	Kanagawa	Japan
Tokyo Allergy and Respiratory Disease Research Institute Institutional Review Board	Taito-ku	Tokyo	Japan
Tokyo Eki Center Building Clinic Institutional Review Board	Chuo-ku	Tokyo	Japan
Tokyo Rosai Hospital Institutional Review Board	Ohta-ku	Tokyo	Japan
Toyama Prefectural Central Hospital Institutional Review Board	Toyama-shi	Toyama	Japan
Yokohama Rosai Hospital Institutional Review Board	Yokhama-shi	Kanagawa	Japan

Supplementary Fig. 1 Patients achieving EASI 75 from baseline to week 160 among all study cohorts, including patients who switched from placebo to upadacitinib

EASI 75 ≥ 75% improvement in Eczema Area and Severity Index, *NRI* nonresponder imputation, *OC* observed cases, *PBO* placebo, *UPA* upadacitinib

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit. The NRI analysis categorizes any patient without an evaluation during a specific visit window as a nonresponder for that visit; the exception is if the patient is a responder both before and after a specific visit window, then the patient will be categorized as a responder for that visit




EASI 75 (NRI)
Patients, % (95% CI)
100
80
60
40
20
0
UPA 15 mg
UPA 30 mg
PBO
PBO/UPA 15 mg
PBO/UPA 30 mg
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
91 91 91 89 89 89 89 89 89 89 89 89 89 89 89 89
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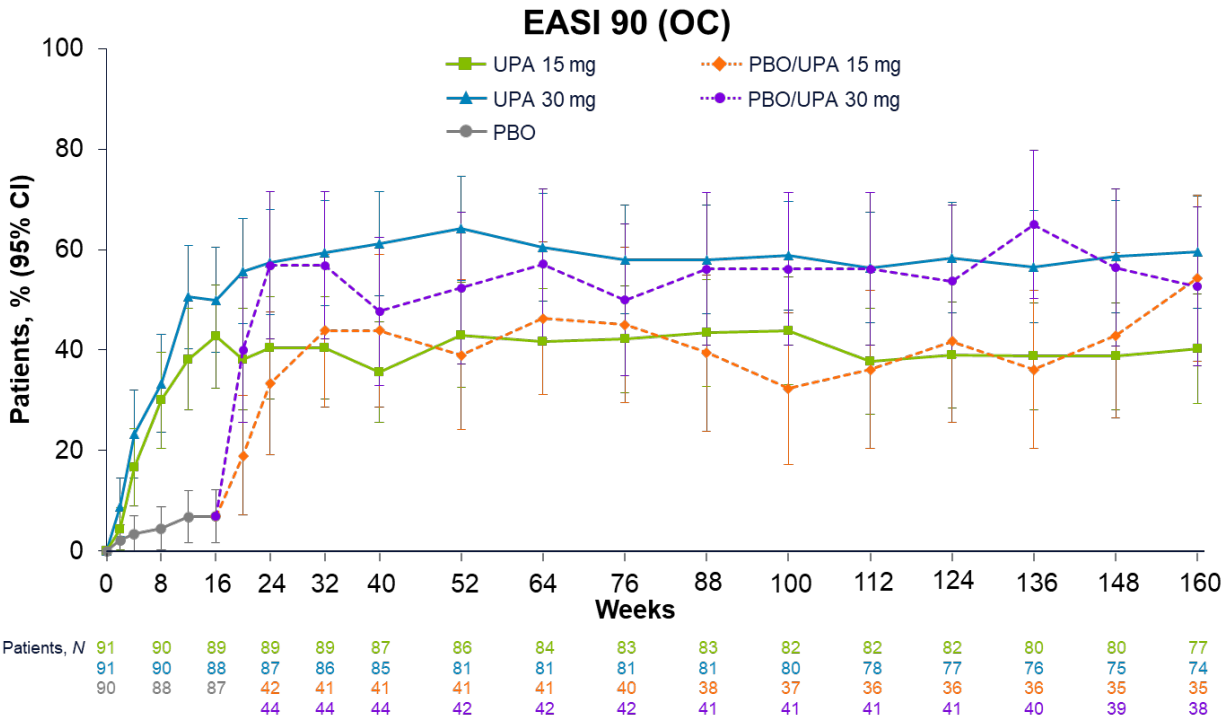
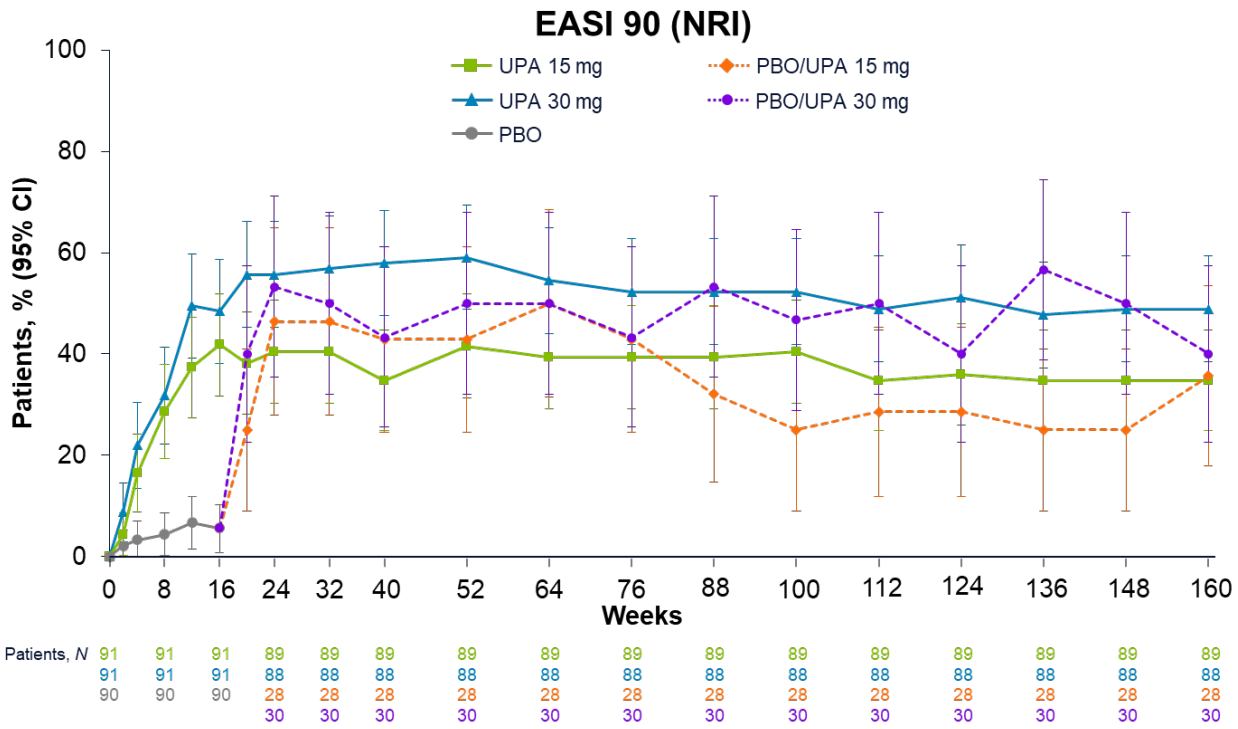
30 30 30 30 30 30 30 30 30 30 30 30 30 30

Supplementary Fig. 2 Patients achieving EASI 90 from baseline to week 160 among all study cohorts, including patients who switched from placebo to upadacitinib

EASI 90 ≥ 90% improvement in Eczema Area and Severity Index, *NRI* nonresponder imputation, *OC* observed cases, *PBO* placebo, *UPA* upadacitinib

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit. The NRI analysis categorizes any patient without an evaluation during a specific visit window as a nonresponder for that visit; the exception is if the patient is a responder both before and after a specific visit window, then the patient will be categorized as a responder for that visit



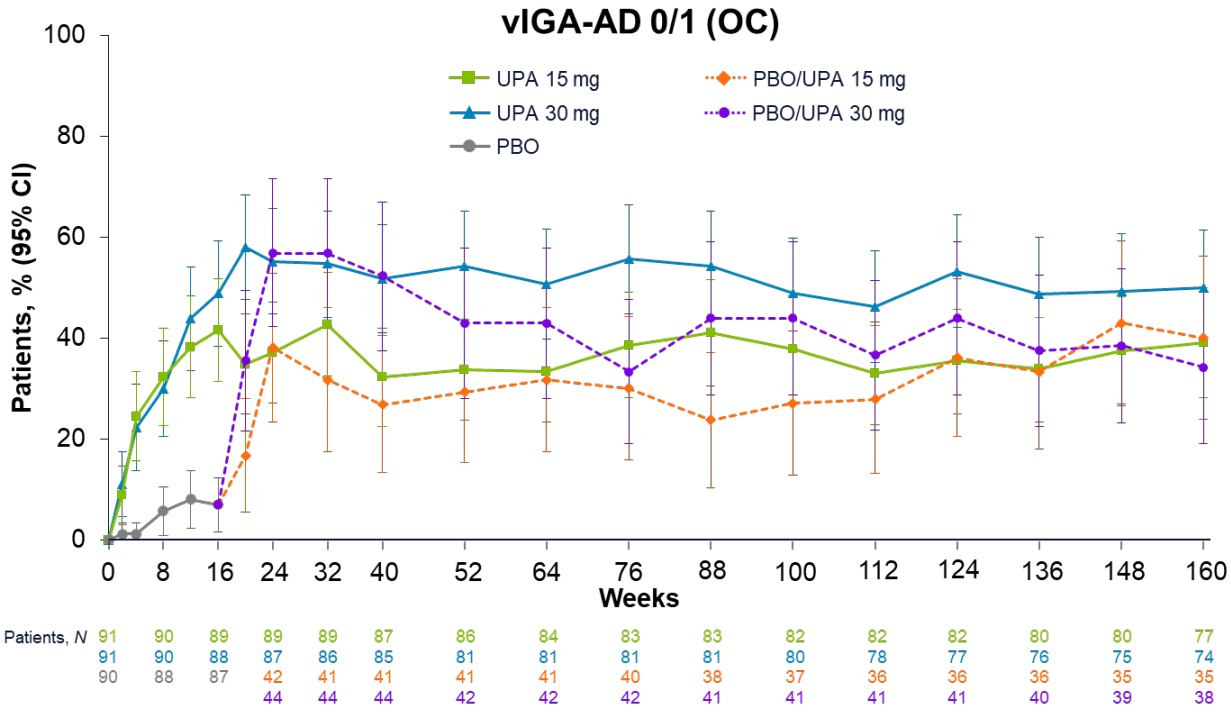

EASI 90 (NRI)
UPA 15 mg
UPA 30 mg
PBO
PBO/UPA 15 mg
PBO/UPA 30 mg
Patients, % (95% CI)
100
80
60
40
20
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
91 91 91 89 89 89 89 89 89 89 89 89 89 89 89 89
91 91 91 88 88 88 88 88 88 88 88 88 88 88 88 88
90 90 90 28 28 28 28 28 28 28 28 28 28 28 28 28
30 30 30 30 30 30 30 30 30 30 30 30

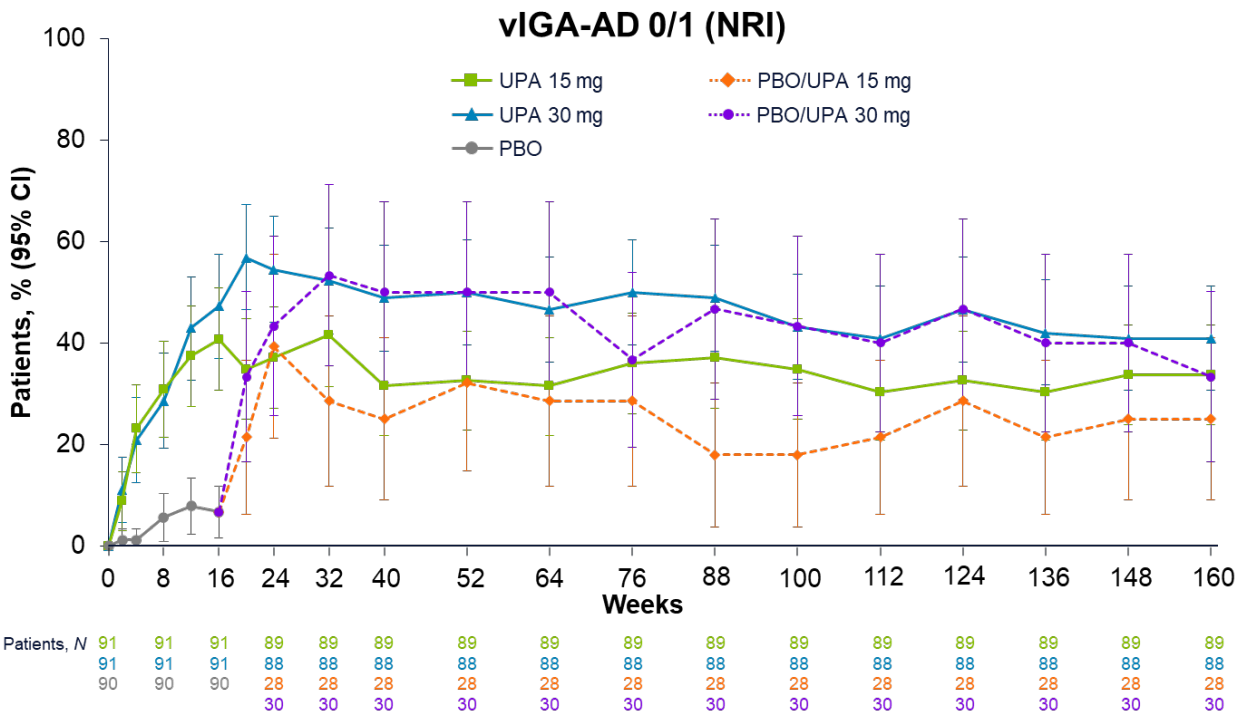
Supplementary Fig. 3 Patients achieving vIGA-AD 0/1[a] from baseline to week 160 among all study cohorts, including patients who switched from placebo to upadacitinib

NRI nonresponder imputation, *OC* observed cases, *PBO* placebo, *UPA* upadacitinib, *vIGA-AD 0/1* validated Investigator Global Assessment for Atopic Dermatitis score of clear or almost clear

[a]Patients achieving vIGA-AD 0/1 with at least two grades of reduction from baseline

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit. The NRI analysis categorizes any patient without an evaluation during a specific visit window as a nonresponder for that visit; the exception is if the patient is a responder both before and after a specific visit window, then the patient will be categorized as a responder for that visit



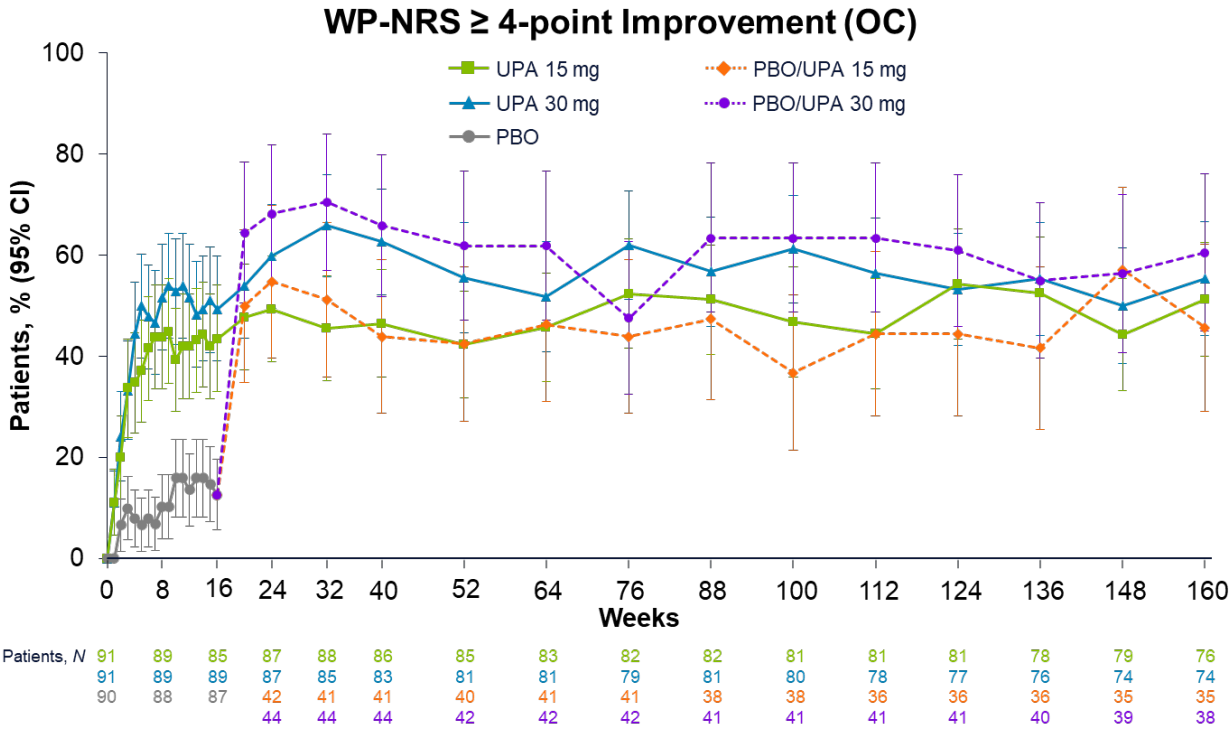

vIGA-AD 0/1 (NRI)
UPA 15 mg
UPA 30 mg
PBO
PBO/UPA 15 mg
PBO/UPA 30 mg
Patients, % (95% CI)
100
80
60
40
20
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
91 91 91 89 89 89 89 89 89 89 89 89 89 89 89 89
91 91 91 88 88 88 88 88 88 88 88 88 88 88 88 88
90 90 90 28 28 28 28 28 28 28 28 28 28 28 28 28
30 30 30 30 30 30 30 30 30 30 30 30

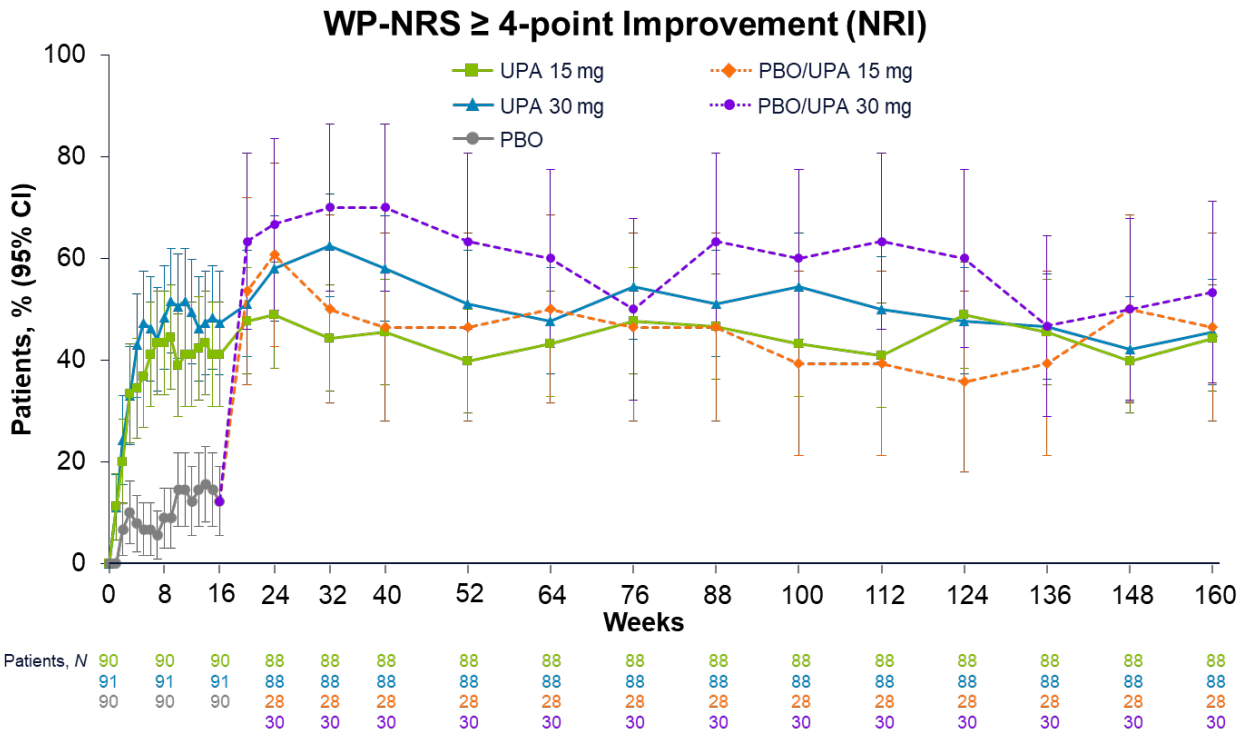
Supplementary Fig. 4 Patients achieving WP-NRS ≥ 4-point improvement[a] from baseline to week 160 among all study cohorts, including patients who switched from placebo to upadacitinib

NRI nonresponder imputation, *OC* observed cases, *PBO* placebo, *UPA* upadacitinib, *WP-NRS* Worst Pruritus Numerical Rating Scale

[a]Among patients with WP-NRS scores ≥ 4 at baseline

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit. The NRI analysis categorizes any patient without an evaluation during a specific visit window as a nonresponder for that visit; the exception is if the patient is a responder both before and after a specific visit window, then the patient will be categorized as a responder for that visit

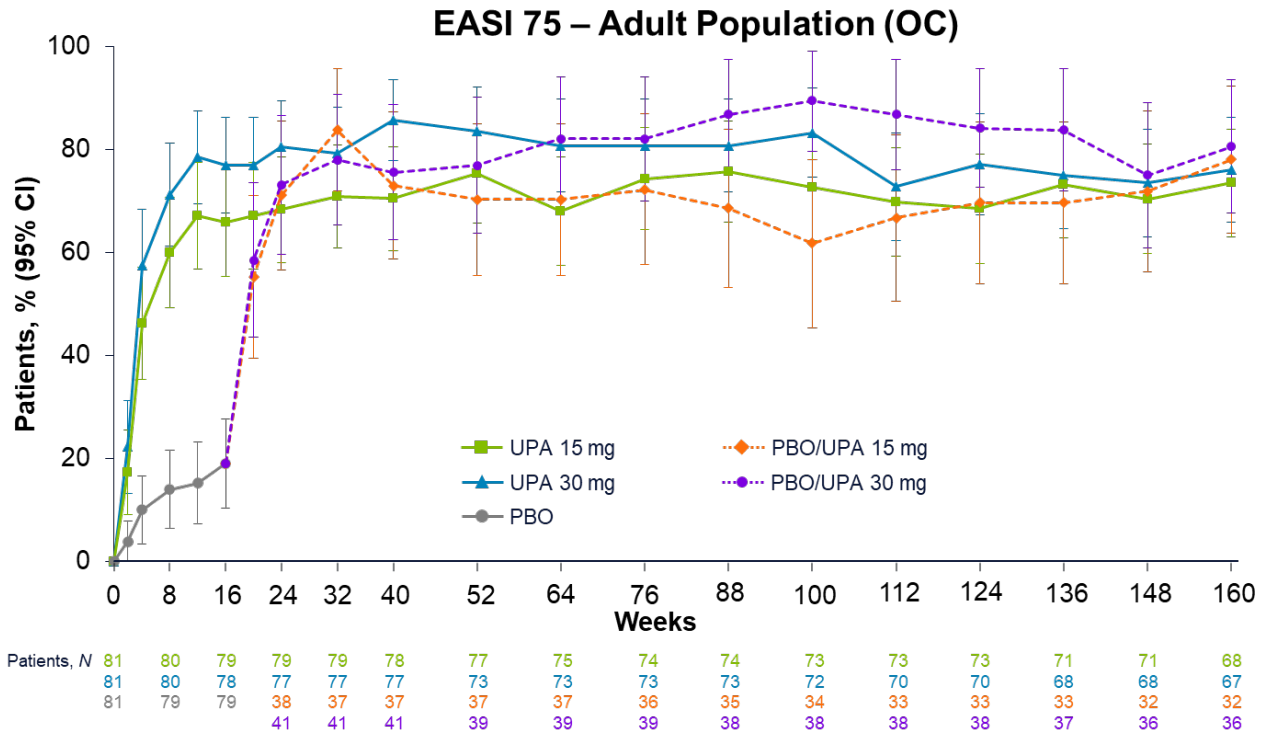


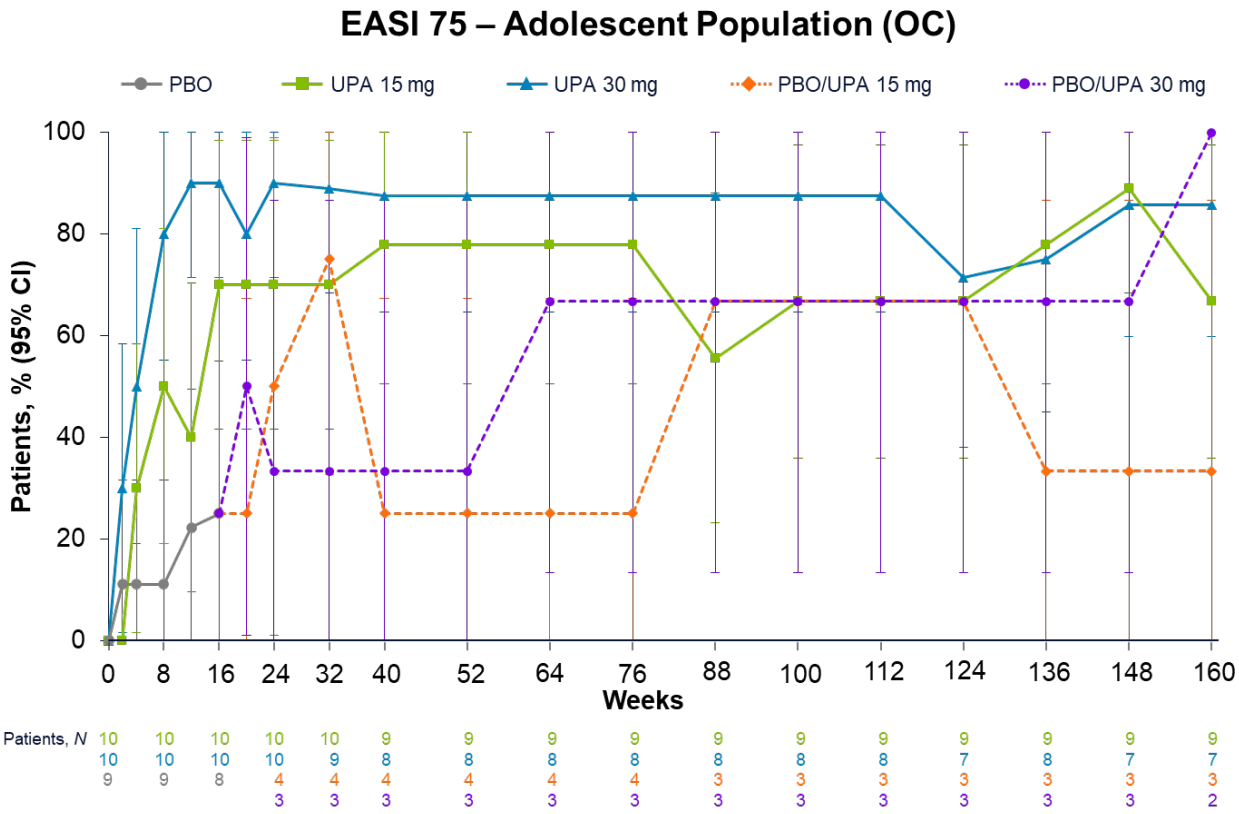

WP-NRS ≥ 4-point Improvement (NRI)
UPA 15 mg
UPA 30 mg
PBO
PBO/UPA 15 mg
PBO/UPA 30 mg
Patients, % (95% CI)
100
80
60
40
20
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
90 90 90 88 88 88 88 88 88 88 88 88 88 88 88 88
91 91 91 88 88 88 88 88 88 88 88 88 88 88 88 88
90 90 90 28 28 28 28 28 28 28 28 28 28 28 28 28
30 30 30 30 30 30 30 30 30 30 30 30 30 30

Supplementary Fig. 5 Adults and adolescents achieving EASI 75 from baseline to week 160 among all study cohorts, including adults and adolescents who switched from placebo to upadacitinib

EASI 75 ≥ 75% improvement in Eczema Area and Severity Index, *OC* observed cases, *PBO* placebo, *UPA* upadacitinib

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit

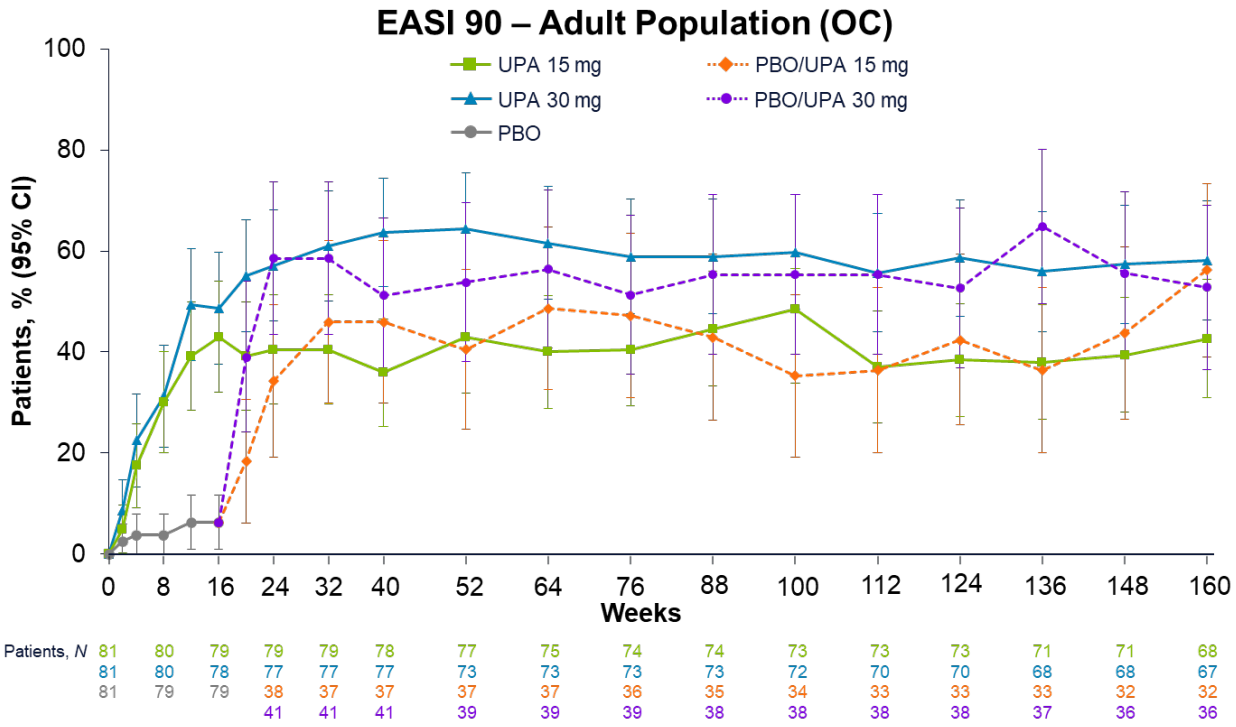



EASI 75 – Adolescent Population (OC)
PBO
UPA 15 mg
UPA 30 mg
PBO/UPA 15 mg
PBO/UPA 30 mg
Patients, % (95% CI)
100
80
60
40
20
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
10 10 10 10 10 9 9 9 9 9 9 9 9 9 9
10 10 10 10 9 8 8 8 8 8 8 8 7 8 7 7
9 9 8 4 4 4 4 4 4 3 3 3 3 3 3 3
3 3 3 3 3 3 3 3 3 3 3 3 3 3 2

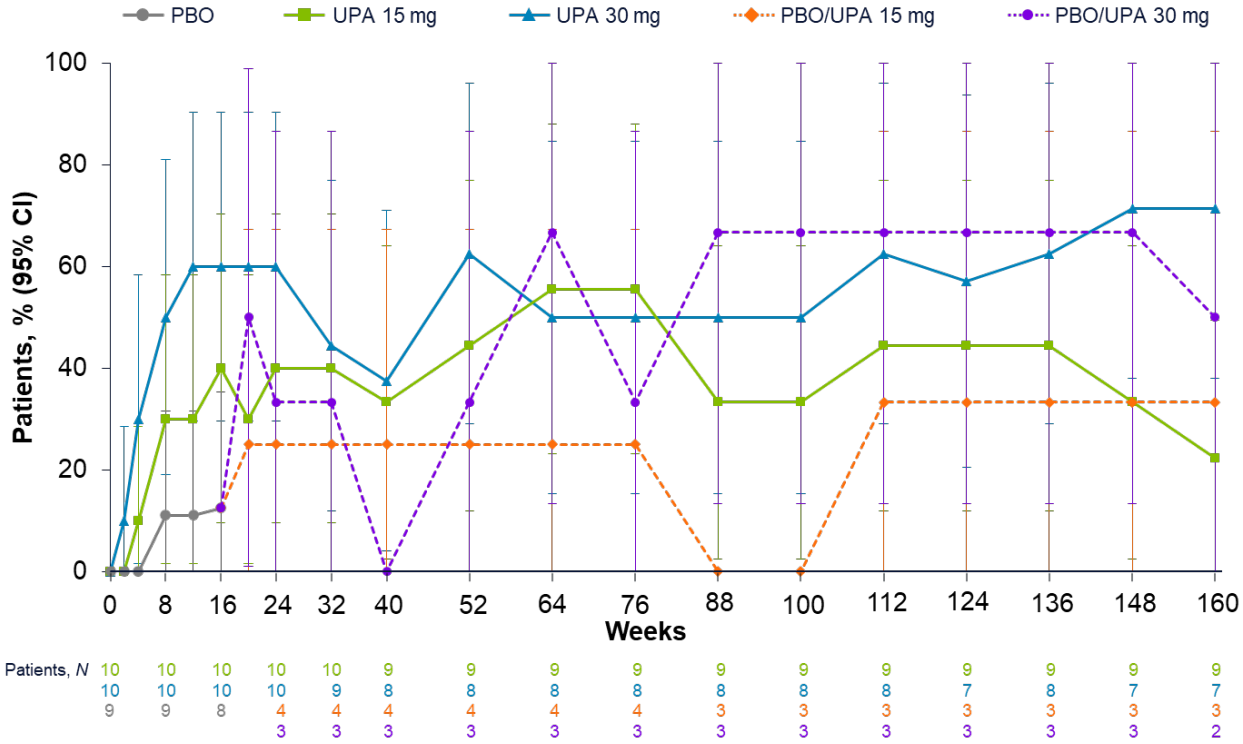
Supplementary Fig. 6 Adults and adolescents achieving EASI 90 from baseline to week 160 among all study cohorts, including adults and adolescents who switched from placebo to upadacitinib

EASI 90 ≥ 90% improvement in Eczema Area and Severity Index, *OC* observed cases, *PBO* placebo, *UPA* upadacitinib

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit



EASI 90 – Adolescent Population (OC)



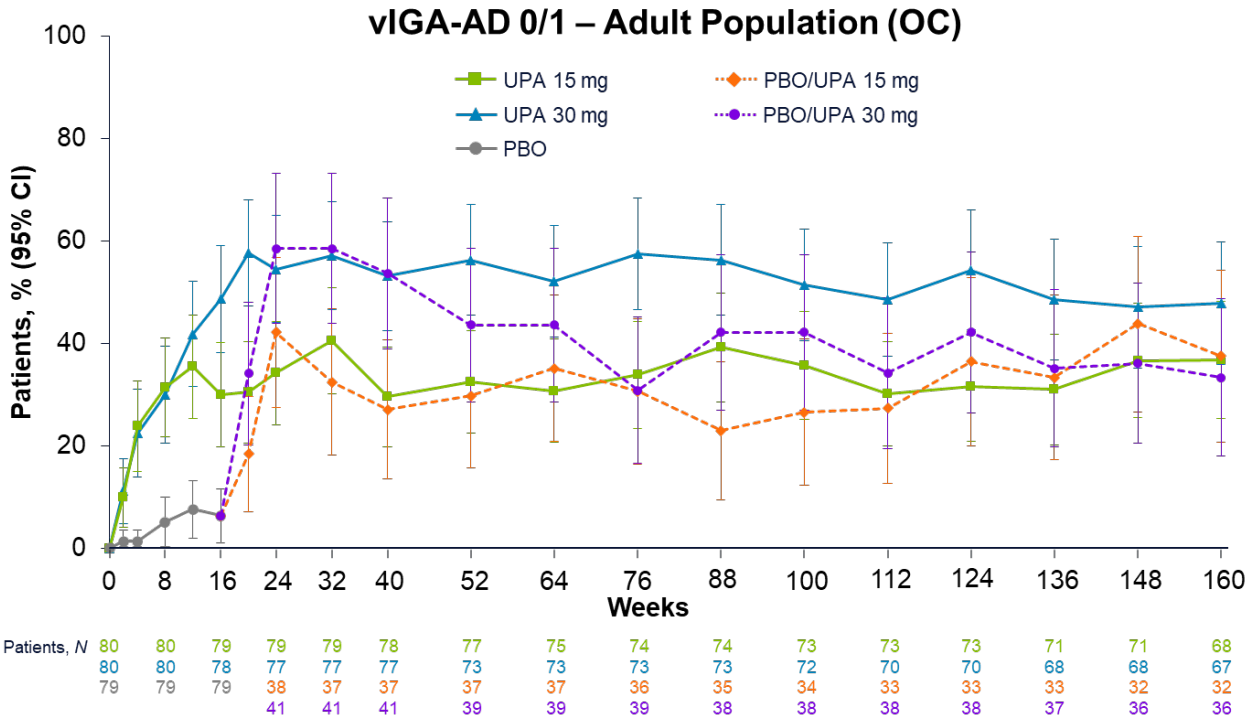
Patients, *N*																
	10	10	10	10	10	9	9	9	9	9	9	9	9	9	9	9
	10	10	10	10	9	8	8	8	8	8	8	8	7	8	7	7
	9	9	8	4	4	4	4	4	4	3	3	3	3	3	3	3
				3	3	3	3	3	3	3	3	3	3	3	3	2

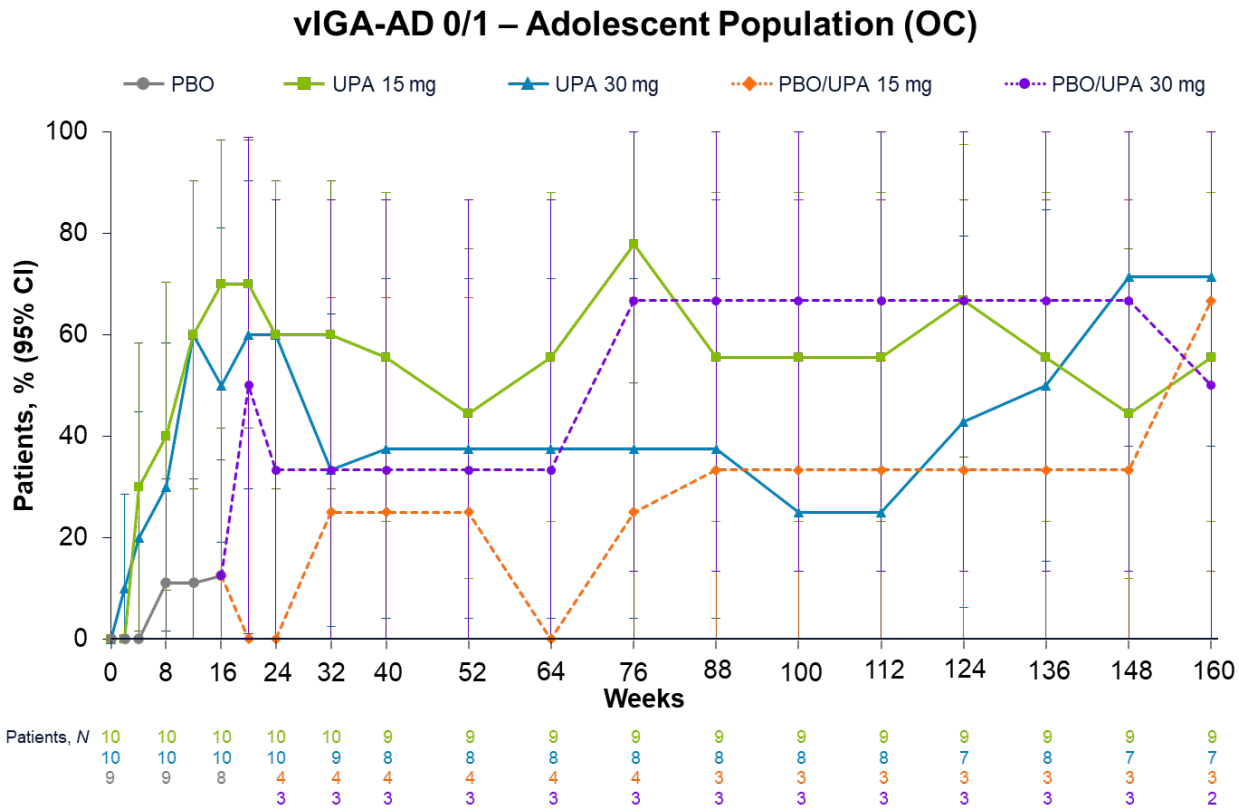
Supplementary Fig. 7 Adults and adolescents achieving vIGA-AD 0/1[a] from baseline to week 160 among all study cohorts, including adults and adolescents who switched from placebo to upadacitinib

OC observed cases, *PBO* placebo, *UPA* upadacitinib, *vIGA-AD 0/1* validated Investigator Global Assessment for Atopic Dermatitis score of clear or almost clear

[a]Patients achieving vIGA-AD 0/1 with at least two grades of reduction from baseline

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit



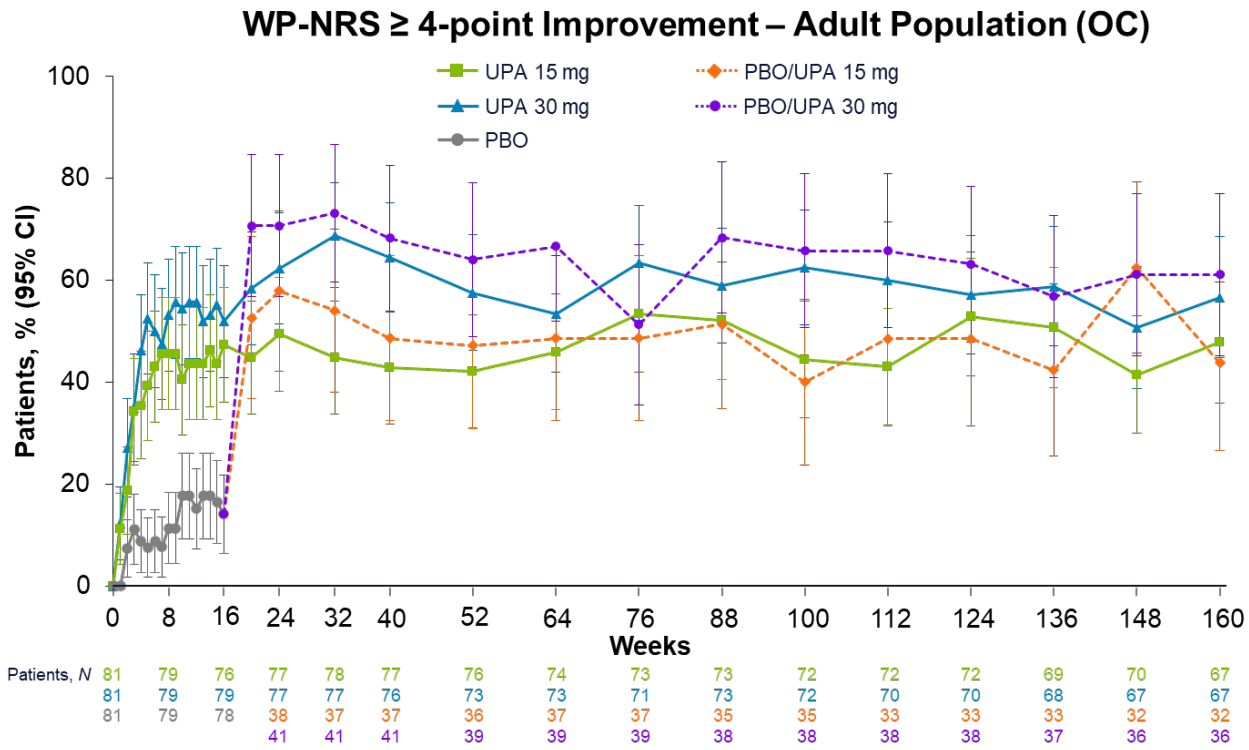

vIGA-AD 0/1 – Adolescent Population (OC)
PBO
UPA 15 mg
UPA 30 mg
PBO/UPA 15 mg
PBO/UPA 30 mg
Patients, % (95% CI)
100
80
60
40
20
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
10 10 10 10 10 9 9 9 9 9 9 9 9 9 9 9
10 10 10 10 9 8 8 8 8 8 8 8 7 8 7 7
9 9 8 4 4 4 4 4 4 3 3 3 3 3 3 3
3 3 3 3 3 3 3 3 3 3 3 2

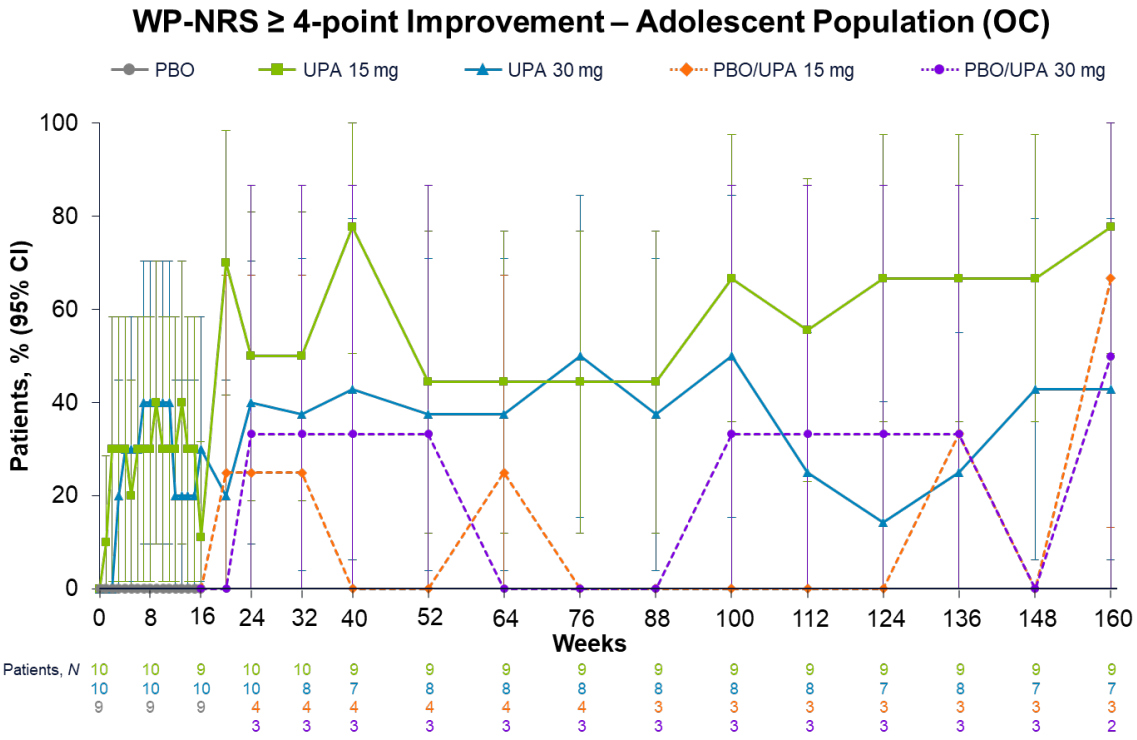
Supplementary Fig. 8 Adults and adolescents achieving WP-NRS ≥ 4-point improvement[a] from baseline to week 160 among all study cohorts, including adults and adolescents who switched from placebo to upadacitinib

OC observed cases, *PBO* placebo, *UPA* upadacitinib, *WP-NRS* Worst Pruritus Numerical Rating Scale

[a]Among patients with WP-NRS scores ≥ 4 at baseline

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit




WP-NRS ≥ 4-point Improvement – Adolescent Population (OC)
PBO
UPA 15 mg
UPA 30 mg
PBO/UPA 15 mg
PBO/UPA 30 mg
Patients, % (95% CI)
100
80
60
40
20
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
10 10 9 10 10 9 9 9 9 9 9 9 9 9 9 9
10 10 10 10 8 7 8 8 8 8 8 8 7 8 7 7
9 9 9 4 4 4 4 4 4 3 3 3 3 3 3 3
3 3 3 3 3 3 3 3 3 3 3 3 3 3 2

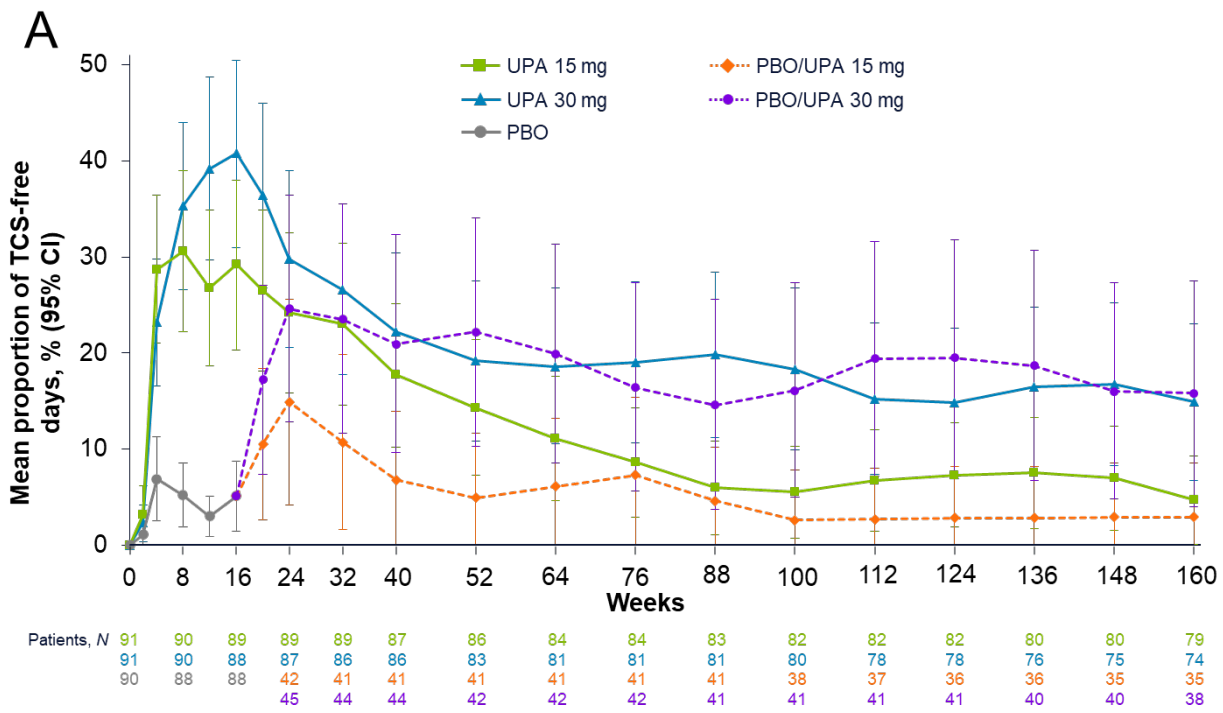
Supplementary Fig. 9 Mean proportion of days in which patients were not receiving concomitant TCS therapy from baseline to week 160 among all study cohorts, including patients who switched from placebo to upadacitinib (OC)

EASI 75 ≥ 75% improvement in Eczema Area and Severity Index, *OC* observed cases, *PBO* placebo, *TCS* topical corticosteroids, *UPA* upadacitinib

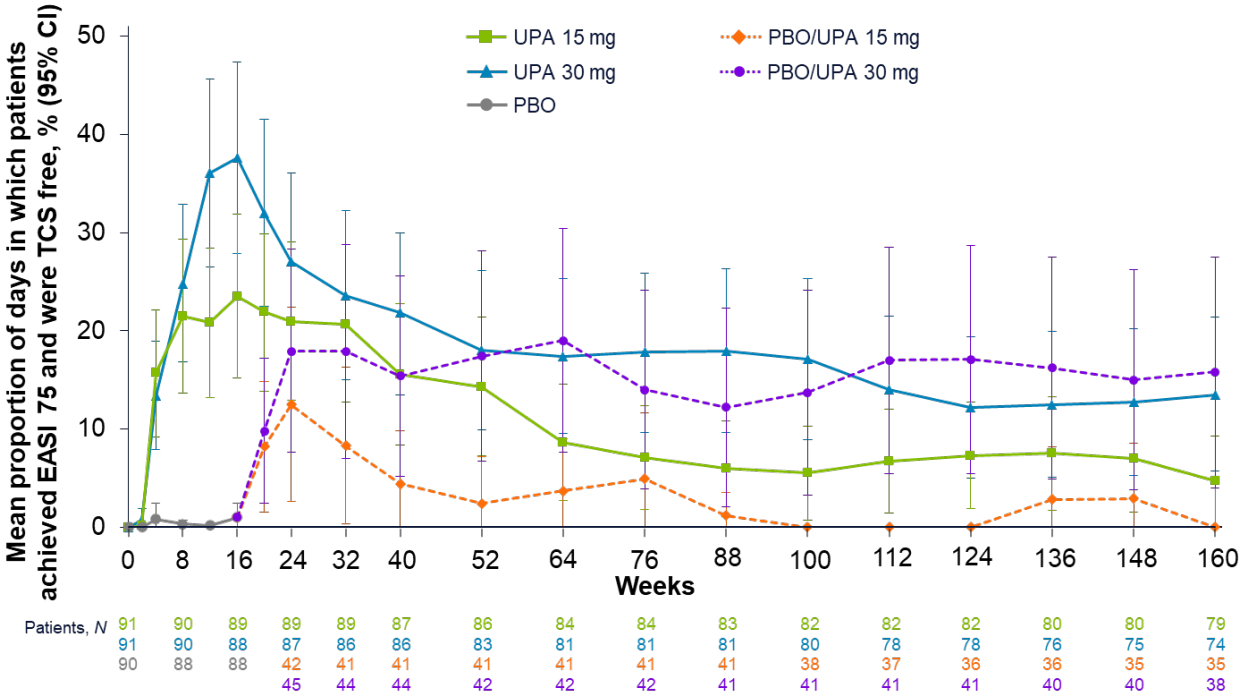
A Visit window average of proportion of days in which patients were not receiving concomitant TCS therapy from baseline to week 160

B Visit window average of proportion of days in which patients achieved EASI 75 and were not receiving concomitant TCS therapy from baseline to week 160

The OC analysis does not impute values for missing evaluations; patients without an evaluation at a scheduled visit will be excluded from the OC analysis for that visit



B


UPA 15 mg
UPA 30 mg
PBO
PBO/UPA 15 mg
PBO/UPA 30 mg
Mean proportion of days in which patients achieved EASI 75 and were TCS free, % (95% CI)
50
40
30
20
10
0
0 8 16 24 32 40 52 64 76 88 100 112 124 136 148 160
Weeks
Patients, N
91 90 89 89 89 87 86 84 84 83 82 82 82 80 80 79
91 90 88 87 86 86 83 81 81 81 80 78 78 76 75 74
90 88 88 42 41 41 41 41 41 41 38 37 36 36 35 35
45 44 44 42 42 42 41 41 41 40 40 38