**SUPPLEMENTARY MATERIALS**

# Safety of Baricitinib in Adults with Severe Alopecia Areata from 2 Phase 3 Trials over a Median of 2.3 Years and up to 4 Years of Treatment

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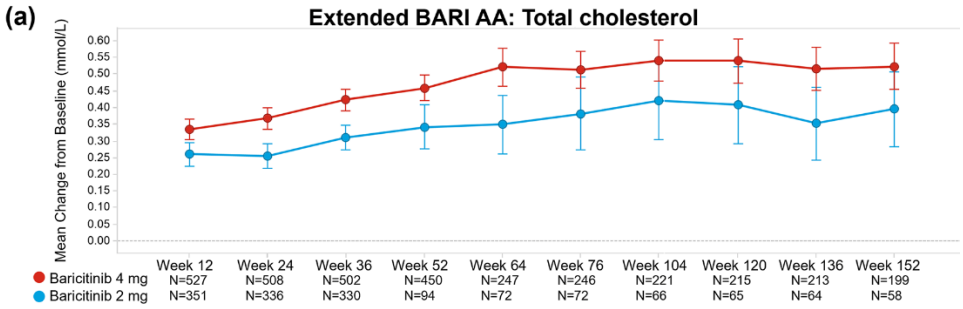
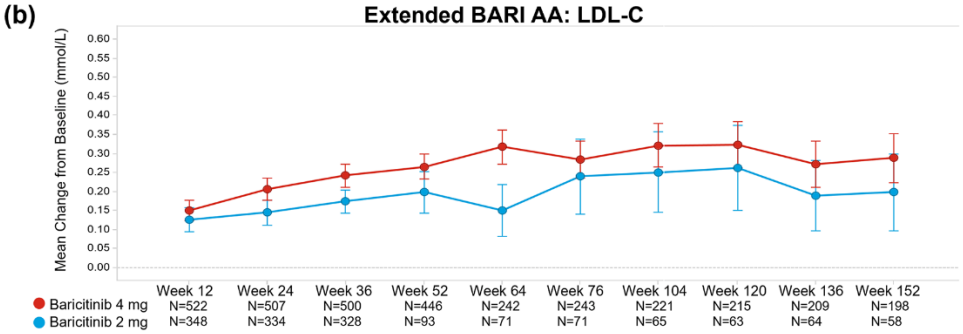
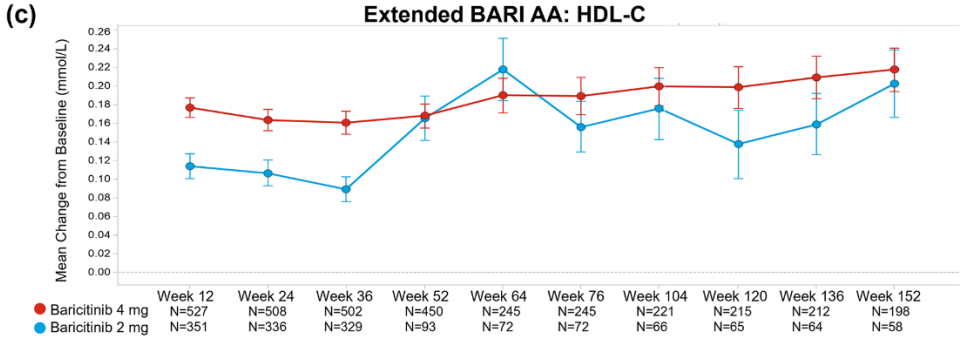
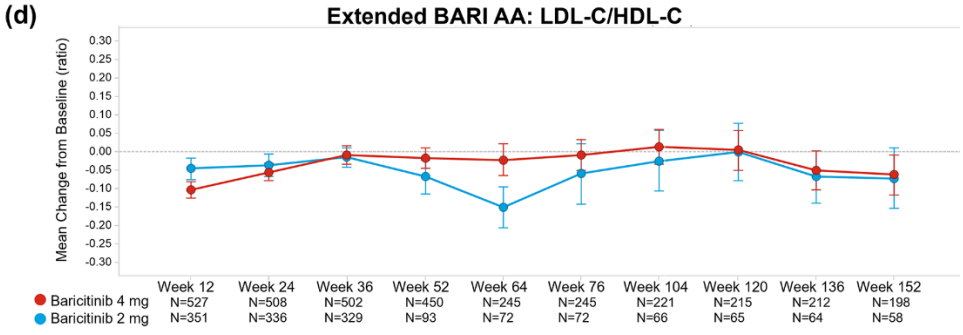

(a)
Extended BARI AA: Total cholesterol
Mean Change from Baseline (mmol/L)
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Week 12 Week 24 Week 36 Week 52 Week 64 Week 76 Week 104 Week 120 Week 136 Week 152
Baricitinib 4 mg N=527 N=508 N=502 N=450 N=247 N=246 N=221 N=215 N=213 N=199
Baricitinib 2 mg N=351 N=336 N=330 N=94 N=72 N=72 N=66 N=65 N=64 N=58


(b)
Extended BARI AA: LDL-C
Mean Change from Baseline (mmol/L)
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Week 12 Week 24 Week 36 Week 52 Week 64 Week 76 Week 104 Week 120 Week 136 Week 152
Baricitinib 4 mg N=522 N=507 N=500 N=446 N=242 N=243 N=221 N=215 N=209 N=198
Baricitinib 2 mg N=348 N=334 N=328 N=93 N=71 N=71 N=65 N=63 N=64 N=58


(c)
Extended BARI AA: HDL-C
Mean Change from Baseline (mmol/L)
0.26
0.24
0.22
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Week 12 Week 24 Week 36 Week 52 Week 64 Week 76 Week 104 Week 120 Week 136 Week 152
Baricitinib 4 mg N=527 N=508 N=502 N=450 N=245 N=245 N=221 N=215 N=212 N=198
Baricitinib 2 mg N=351 N=336 N=329 N=93 N=72 N=72 N=66 N=65 N=64 N=58


(d)
Extended BARI AA: LDL-C/HDL-C
Mean Change from Baseline (ratio)
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
Week 12 Week 24 Week 36 Week 52 Week 64 Week 76 Week 104 Week 120 Week 136 Week 152
Baricitinib 4 mg N=527 N=508 N=502 N=450 N=245 N=245 N=221 N=215 N=212 N=198
Baricitinib 2 mg N=351 N=336 N=329 N=93 N=72 N=72 N=66 N=65 N=64 N=58

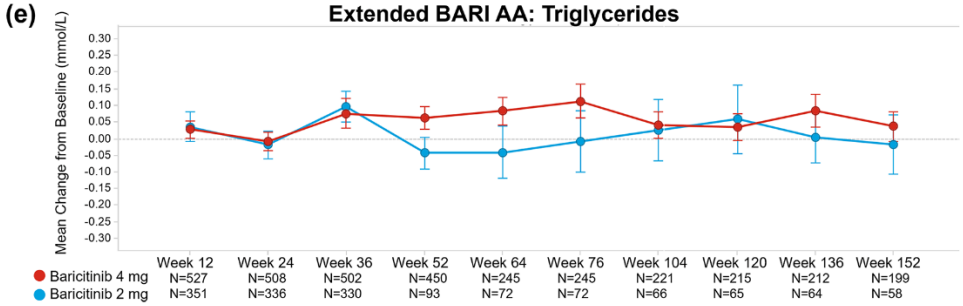

(e)
Extended BARI AA: Triglycerides
Mean Change from Baseline (mmol/L)
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
Week 12 Week 24 Week 36 Week 52 Week 64 Week 76 Week 104 Week 120 Week 136 Week 152
Baricitinib 4 mg N=527 N=508 N=502 N=450 N=245 N=245 N=221 N=215 N=212 N=199
Baricitinib 2 mg N=351 N=336 N=330 N=93 N=72 N=72 N=66 N=65 N=64 N=58

**Fig. S1** Change from baseline over time for (a) total cholesterol, (b) LDL-C, (c) HDL-C, (d) LDL-C/HDL-C ratio, and (e) triglycerides

Data points are mean change for baricitinib 4 mg (red) and 2 mg (blue) in Extended BARI AA, with whiskers showing standard error. The number of patients in each analysis set are shown below each time point. *AA, alopecia areata; BARI, baricitinib; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; N, number of patients.*

**Table S1.** Reasons for permanent discontinuation from treatment

| Reason, n (%) | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | Baricitinib 2 mg (N=383) | Baricitinib 4 mg (N=565) | All baricitinib doses (N=1303) |
| Completed treatment | 48 (12.5) | 60 (10.6) | 151 (11.6) |
| Adverse event | 15 (3.9) | 28 (5.0) | 53 (4.1) |
| Physician decision | 2 (0.5) | 2 (0.4) | 8 (0.6) |
| Pregnancy | 0 | 2 (0.4) | 5 (0.4) |
| Protocol deviation | 2 (0.5) | 3 (0.5) | 6 (0.5) |
| Study terminated in region[a] | 3 (0.8) | 6 (1.1) | 11 (0.8) |
| Withdrawal by patient[b] | 56 (14.6) | 75 (13.3) | 163 (12.5) |
| Lost to follow-up | 20 (5.2) | 24 (4.2) | 56 (4.3) |
| Lack of efficacy | 17 (4.4) | 43 (7.6) | 98 (7.5) |
| Other | 86 (22.5) | 114 (20.2) | 293 (22.5) |
| Automatically discontinued by IWRS for nonresponse[c] | 77 (20.1) | 101 (17.9) | 258 (19.8) |
| Other reason | 9 (2.3) | 13 (2.3) | 35 (2.7) |

[a]All patients were from closed sites in Japan. [b]Includes patients who transitioned to commercial material in geographies where baricitinib was approved for AA. [c]Patients who were nonresponders (Severity of Alopecia Tool score >20) at Weeks 52 and 76 were automatically discontinued from the study at Week 76 unless they had a ≥2-point improvement from baseline in the clinician-reported outcome measure for eyebrow or eyelash hair loss.

*AA, alopecia areata; BARI, baricitinib; IWRS, Interactive Web Response System; N, number of patients in the analysis population; n, number of patients in the specified category.*

**Table S2.** Summary of serious adverse events by Preferred Term within System Organ Class

| Event, n [IR] | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | Baricitinib 2 mg (N=383) | Baricitinib 4 mg (N=565) | All baricitinib doses (N=1303) |
| Patients with ≥1 SAE | 11 [2.0] | 33 [3.0] | 73 [2.6] |
| Infections and infestations | 2 [0.4] | 6 [0.5] | 16 [0.6] |
| COVID-19 pneumonia | 1 [0.2] | 0 | 4 [0.1] |
| COVID-19 | 0 | 1 [0.1] | 3 [0.1] |
| Appendicitis | 0 | 1 [0.1] | 2 [0.1] |
| Pyelonephritis | 1 [0.2] | 1 [0.1] | 2 [0.1] |
| Appendicitis perforated | 0 | 0 | 1 [<0.1] |
| Diverticulitis | 0 | 1 [0.1] | 1 [<0.1] |
| Herpes zoster | 0 | 1 [0.1] | 1 [<0.1] |
| Lyme disease | 0 | 1 [0.1] | 1 [<0.1] |
| Pneumonia | 0 | 1 [0.1] | 1 [<0.1] |
| Varicella | 0 | 0 | 1 [<0.1] |
| Injury, poisoning and procedural complications | 4 [0.7] | 7 [0.6] | 16 [0.6] |
| Ankle fracture | 2 [0.4] | 1 [0.1] | 4 [0.1] |
| Facial bone fracture | 0 | 2 [0.2] | 2 [0.1] |
| Foot fracture | 1 [0.2] | 0 | 2 [0.1] |
| Hand fracture | 1 [0.2] | 1 [0.1] | 2 [0.1] |
| Ligament sprain | 0 | 0 | 2 [0.1] |
| Anastomotic ulcer | 0 | 0 | 1 [<0.1] |
| Clavicle fracture | 0 | 1 [0.1] | 1 [<0.1] |
| Lumbar vertebral fracture | 0 | 1 [0.1] | 1 [<0.1] |
| Radius fracture | 1 [0.2] | 0 | 1 [<0.1] |
| Thermal burn | 0 | 1 [0.1] | 1 [<0.1] |
| Cardiac disorders | 2 [0.4] | 3 [0.3] | 6 [0.2] |
| Cardiac failure congestive | 1 [0.2] | 0 | 2 [0.1] |
| Acute myocardial infarction | 1 [0.2] | 0 | 1 [<0.1] |
| Aortic valve incompetence | 0 | 1 [0.1] | 1 [<0.1] |
| Atrial fibrillation | 0 | 1 [0.1] | 1 [<0.1] |
| Ventricular tachycardia | 0 | 1 [0.1] | 1 [<0.1] |
| Gastrointestinal disorders | 0 | 3 [0.3] | 6 [0.2] |
| Colitis | 0 | 1 [0.1] | 1 [<0.1] |

| Event, n [IR] | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | Baricitinib 2 mg (N=383) | Baricitinib 4 mg (N=565) | All baricitinib doses (N=1303) |
| Flatulence | 0 | 0 | 1 [<0.1] |
| Food poisoning | 0 | 1 [0.1] | 1 [<0.1] |
| Gastric stenosis | 0 | 0 | 1 [<0.1] |
| Inguinal hernia | 0 | 1 [0.1] | 1 [<0.1] |
| Obstruction gastric | 0 | 0 | 1 [<0.1] |
| Peptic ulcer hemorrhage | 0 | 0 | 1 [<0.1] |
| Reproductive system and breast disorders | 1 [0.2] | 1 [0.1] | 6 [0.2] |
| Adenomyosis[a] | 1 [0.3] | 0 | 1 [0.1] |
| Benign prostatic hyperplasia[b] | 0 | 0 | 1 [0.1] |
| Endometrial hyperplasia[a] | 0 | 0 | 1 [0.1] |
| Heavy menstrual bleeding[a] | 0 | 0 | 1 [0.1] |
| Vaginal dysplasia[a] | 0 | 0 | 1 [0.1] |
| Varicocele | 0 | 1 [0.1] | 1 [<0.1] |
| General disorders and administration site conditions | 1 [0.2] | 3 [0.3] | 5 [0.2] |
| Drug withdrawal syndrome[c] | 0 | 1 [0.1] | 2 [0.1] |
| Asthenia | 1 [0.2] | 0 | 1 [<0.1] |
| Chest pain | 0 | 1 [0.1] | 1 [<0.1] |
| Cyst | 0 | 1 [0.1] | 1 [<0.1] |
| Hepatobiliary disorders | 1 [0.2] | 4 [0.4] | 5 [0.2] |
| Cholecystitis acute | 1 [0.2] | 2 [0.2] | 3 [0.1] |
| Hepatitis acute | 0 | 2 [0.2] | 2 [0.1] |
| Neoplasms benign, malignant and unspecified | 0 | 2 [0.2] | 5 [0.2] |
| B-cell lymphoma | 0 | 1 [0.1] | 1 [<0.1] |
| Benign breast neoplasm | 0 | 0 | 1 [<0.1] |
| Chronic lymphocytic leukemia | 0 | 0 | 1 [<0.1] |
| Endometrial cancer stage I[a] | 0 | 0 | 1 [0.1] |
| Uterine leiomyoma[a] | 0 | 1 [0.1] | 1 [0.1] |
| Nervous system disorders | 0 | 3 [0.3] | 5 [0.2] |
| Sciatica | 0 | 1 [0.1] | 2 [0.1] |
| Guillain-Barre syndrome | 0 | 1 [0.1] | 1 [<0.1] |
| Intracranial aneurysm | 0 | 1 [0.1] | 1 [<0.1] |

| Event, n [IR] | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | Baricitinib 2 mg (N=383) | Baricitinib 4 mg (N=565) | All baricitinib doses (N=1303) |
| Stiff person syndrome | 0 | 0 | 1 [<0.1] |
| Eye disorders | 0 | 1 [0.1] | 2 [0.1] |
| Glaucoma | 0 | 1 [0.1] | 1 [<0.1] |
| Keratitis | 0 | 0 | 1 [<0.1] |
| Pregnancy, puerperium and perinatal conditions | 0 | 1 [0.1] | 2 [0.1] |
| Abortion missed[a] | 0 | 1 [0.1] | 1 [0.1] |
| Abortion spontaneous[a] | 0 | 0 | 1 [0.1] |
| Respiratory, thoracic and mediastinal disorders | 1 [0.2] | 0 | 2 [0.1] |
| Pulmonary embolism | 1 [0.2] | 0 | 2 [0.1] |
| Acute respiratory failure | 0 | 0 | 1 [<0.1] |
| Blood and lymphatic system disorders | 0 | 0 | 1 [<0.1] |
| Anemia | 0 | 0 | 1 [<0.1] |
| Endocrine disorders | 0 | 1 [0.1] | 1 [<0.1] |
| Inappropriate antidiuretic hormone secretion | 0 | 1 [0.1] | 1 [<0.1] |
| Investigations | 0 | 0 | 1 [<0.1] |
| Intraocular pressure increased | 0 | 0 | 1 [<0.1] |
| Metabolism and nutrition disorders | 0 | 0 | 1 [<0.1] |
| Hypokalemia | 0 | 0 | 1 [<0.1] |
| Product issues | 0 | 1 [0.1] | 1 [<0.1] |
| Device dislocation | 0 | 1 [0.1] | 1 [<0.1] |
| Psychiatric disorders | 0 | 0 | 1 [<0.1] |
| Depression | 0 | 0 | 1 [<0.1] |
| Surgical and medical procedures | 0 | 0 | 1 [<0.1] |
| Sleeve gastrectomy | 0 | 0 | 1 [<0.1] |
| Vascular disorders | 0 | 1 [0.1] | 1 [<0.1] |
| Hypertension | 0 | 1 [0.1] | 1 [<0.1] |

[a]Denominator and patient-years adjusted because event was specific to females: N=241 (Extended BARI AA 2 mg), N=350 (Extended BARI AA 4 mg), and N=804 (All BARI AA). [b]Denominator and patient-years adjusted because event was specific to males: N=142 (Extended BARI AA 2 mg), N=215 (Extended BARI AA 4 mg), and N=499 (All BARI AA). [c]Cases were not related to baricitinib treatment.

IRs were calculated per 100 patient-years.

*AA, alopecia areata; BARI, baricitinib; IR, incidence rate; N, number of patients in the analysis population; n, number of patients in the specified category; SAE, serious adverse event.*

**Table S3.** Adverse events leading to permanent discontinuation of study drug by Preferred Term within System Organ Class[a]

| Event, n [IR] | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | Baricitinib 2 mg (N=383) | Baricitinib 4 mg (N=565) | All baricitinib doses (N=1303) |
| Patients with ≥1 AE | 12 [2.2] | 23 [2.0] | 48 [1.7] |
| Investigations | 3 [0.5] | 4 [0.4] | 10 [0.3] |
| Hepatic enzyme increased | 1 [0.2] | 1 [0.1] | 3 [0.1] |
| Weight increased[b] | 1 [0.2] | 1 [0.1] | 3 [0.1] |
| Alanine aminotransferase increased | 0 | 1 [0.1] | 1 [<0.1] |
| Hepatitis B virus test positive | 0 | 0 | 1 [<0.1] |
| Lymphocyte count decreased | 0 | 1 [0.1] | 1 [<0.1] |
| Transaminases increased | 1 [0.2] | 0 | 1 [<0.1] |
| Neoplasms benign, malignant and unspecified (including cysts and polyps) | 0 | 3 [0.3] | 7 [0.2] |
| Breast cancer | 0 | 1 [0.1] | 2 [0.1] |
| B-cell lymphoma | 0 | 1 [0.1] | 1 [<0.1] |
| Chronic lymphocytic leukemia | 0 | 0 | 1 [<0.1] |
| Endometrial cancer stage I[c] | 0 | 0 | 1 [0.1] |
| Malignant melanoma | 0 | 1 [0.1] | 1 [<0.1] |
| Malignant melanoma in situ | 0 | 0 | 1 [<0.1] |
| Blood and lymphatic system disorders | 0 | 3 [0.3] | 5 [0.2] |
| Anemia | 0 | 1 [0.1] | 1 [<0.1] |
| Leukopenia | 0 | 1 [0.1] | 1 [<0.1] |
| Lymphocytosis | 0 | 0 | 1 [<0.1] |
| Lymphopenia | 0 | 1 [0.1] | 1 [<0.1] |
| Neutropenia | 0 | 0 | 1 [<0.1] |
| Psychiatric disorders | 3 [0.5] | 1 [0.1] | 4 [0.1] |
| Anxiety | 1 [0.2] | 0 | 1 [<0.1] |
| Depressed mood | 1 [0.2] | 0 | 1 [<0.1] |
| Depression | 1 [0.2] | 0 | 1 [<0.1] |
| Suicidal ideation | 0 | 1 [0.1] | 1 [<0.1] |
| Cardiac disorders | 1 [0.2] | 2 [0.2] | 3 [0.1] |
| Cardiac failure congestive | 1 [0.2] | 0 | 1 [<0.1] |
| Palpitations | 0 | 1 [0.1] | 1 [<0.1] |

| Event, n [IR] | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | Baricitinib 2 mg (N=383) | Baricitinib 4 mg (N=565) | All baricitinib doses (N=1303) |
| Ventricular tachycardia | 0 | 1 [0.1] | 1 [<0.1] |
| Hepatobiliary disorders | 0 | 2 [0.2] | 3 [0.1] |
| Cholecystitis acute | 0 | 1 [0.1] | 1 [<0.1] |
| Hepatitis acute | 0 | 1 [0.1] | 1 [<0.1] |
| Hypertransaminasemia | 0 | 0 | 1 [<0.1] |
| Infections and infestations | 1 [0.2] | 1 [0.1] | 3 [0.1] |
| COVID-19 | 0 | 1 [0.1] | 1 [<0.1] |
| Herpes zoster | 0 | 0 | 1 [<0.1] |
| Lower respiratory tract infection | 1 [0.2] | 0 | 1 [<0.1] |
| General disorders and administration site conditions | 1 [0.2] | 1 [0.1] | 2 [0.1] |
| Asthenia | 1 [0.2] | 0 | 1 [<0.1] |
| Non-cardiac chest pain | 0 | 1 [0.1] | 1 [<0.1] |
| Musculoskeletal and connective tissue disorders | 1 [0.2] | 1 [0.1] | 2 [0.1] |
| Back pain | 1 [0.2] | 0 | 1 [<0.1] |
| Bursitis | 0 | 1 [0.1] | 1 [<0.1] |
| Nervous system disorders | 0 | 2 [0.2] | 2 [0.1] |
| Guillain-Barre syndrome | 0 | 1 [0.1] | 1 [<0.1] |
| Intracranial aneurysm | 0 | 1 [0.1] | 1 [<0.1] |
| Respiratory, thoracic and mediastinal disorders | 1 [0.2] | 0 | 2 [0.1] |
| Pulmonary embolism | 1 [0.2] | 0 | 2 [0.1] |
| Skin and subcutaneous tissue disorders | 1 [0.2] | 1 [0.1] | 2 [0.1] |
| Acne | 1 [0.2] | 0 | 1 [<0.1] |
| Dermatitis atopic | 0 | 1 [0.1] | 1 [<0.1] |
| Congenital, familial and genetic disorders | 0 | 0 | 1 [<0.1] |
| Factor V Leiden mutation | 0 | 0 | 1 [<0.1] |
| Endocrine disorders | 0 | 1 [0.1] | 1 [<0.1] |
| Thyroid mass | 0 | 1 [0.1] | 1 [<0.1] |
| Vascular disorders | 0 | 1 [0.1] | 1 [<0.1] |

| Event, n [IR] | Extended BARI AA | | All BARI AA |
|---|---|---|---|
| | **Baricitinib 2 mg (N=383)** | **Baricitinib 4 mg (N=565)** | **All baricitinib doses (N=1303)** |
| Superficial vein thrombosis | 0 | 1 [0.1] | 1 [<0.1] |

[a]This table shows AEs reported by ≥1 patient in the All BARI AA group. [b]Increase (gain) ≥7%. [c]Denominator and patient-years adjusted as the event was specific to women.

IRs were calculated per 100 patient-years.

*AA, alopecia areata; AE, adverse event; BARI, baricitinib; IR, incidence rate; N, number of patients in the analysis population; n, number of patients in the specified category.*

**Patient Details for Newly Reported Adverse Events of Special Interest**

***Breast Cancer***

The patient was a 65-year-old female who was initially treated with placebo and then switched to baricitinib 2 mg on day 268. The event occurred on day 1009. Patient risk factors included obesity (body mass index of 31.9 $kg/m^2$ at baseline, which increased to 33.1 $kg/m^2$). The patient discontinued baricitinib and the study.

***Stage 1 Endometrial Cancer***

The patient was a 70-year-old female who was treated with baricitinib 2 mg for the first 373 days and then switched to 4 mg. The event occurred on study day 833. The patient was a nonsmoker and did not consume alcohol. The patient discontinued baricitinib and the study.

***Malignant Melanoma***

The patient was a 62-year-old female. The event occurred 811 days after starting baricitinib 4 mg. The patient was a nonsmoker with Fitzpatrick type III skin. The patient discontinued baricitinib and the study.

***Basal Cell Carcinoma***

The patient was a 70-year-old female who was treated with baricitinib 2 mg for the first 356 days, switched to placebo for 112 days in the withdrawal substudy, and was rescued to baricitinib 2 mg on day 477. The event occurred on day 1135. The patient had lifelong sun exposure and had experienced prior basal cell carcinoma on the left scapula on study day 410 while receiving placebo. The patient had a shave biopsy with clear margins and continued baricitinib treatment.