Supplementary Materials

Pregnancy Outcomes in Patients Treated With Upadacitinib: Analysis of Data From Clinical Trials and Postmarketing Reports

Uma Mahadevan[1], Gweneth Levy[2], Lianne Gensler[3], Mira Ali[2], Ana P. Lacerda[2], Lani Wegrzyn[2], Hannah Palac[2], Tina Bhutani-Jacques[3], Millie Long[4], Megan E. B. Clowse[5], Alexa B. Kimball[6], Christina Chambers[7], Anthony R. Scialli[8]

[1]Division of Gastroenterology and Hepatology, University of California San Francisco, San Francisco, CA, USA; [2]AbbVie, Inc., Chicago, IL, USA; [3]Division of Rheumatology, University of California San Francisco, San Francisco, California, USA; [4]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA; [5]Division of Rheumatology & Immunology, Duke University, Durham, NC, USA; [6]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [7]Department of Pediatrics, University of California, San Diego, La Jolla, CA, USA; [8]Scialli Consulting LLC, Washington, DC, USA.

Corresponding Author:
Uma Mahadevan MD
University of California, San Francisco
1701 Divisadero Street #120
San Francisco, CA 94010
Email: Uma.mahadevan@ucsf.edu
Phone: 415-502-4444

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Online Resource Table S1 Preferred terms assessed in CMQ MedDRA queries

Preferred terms
1. Maternal exposure during pregnancy
2. Term baby
3. Paternal exposure before pregnancy
4. Fetal exposure during delivery
5. Multiple pregnancy
6. Premature baby
7. Fetal exposure during pregnancy
8. Decreased embryo viability
9. Paternal exposure timing unspecified
10. Maternal death
11. Normal newborn
12. Fetal death
13. Paternal exposure during pregnancy
14. Maternal exposure before pregnancy
15. Paternal drugs affecting fetus
16. Twin pregnancy
17. Exposure during pregnancy
18. Exposure via father
19. Drug exposure before pregnancy
20. Maternal drugs affecting fetus
21. Maternal exposure via partner during pregnancy
22. Fetal exposure timing unspecified

CMQ MeDRA, Customized MedDRA Query Medical Dictionary for Regulatory Activities

Online Resource Table S2 Relevant IRB/IEC Approval Information[a]

Rheumatoid Arthritis	Advarra Institutional Review Board (United States of America) Quorum Review IRB (United States of America)[b] Ethics Committee of Pekin Union Medical College Hospital (China) Commission Cantonale d'Ethique de la Recherche Vaud (CER-VD) (Switzerland)
Psoriatic Arthritis	Western Institutional Review Board (United States of America) London – London Bridge London REC Centre (United Kingdom)
Axial Spondyloarthritis	Oregon Health and Science University Institutional Review Board (United States of America)
Atopic Dermatitis	Quorum Review, INC (United States of America)[b] Advarra (United States of America) Health Research Ethics Board of Alberta – Clinical Trials Committee (Canada) Fukuyama City Hospital IRB (Japan) Clinical Research Ethics Committee of Cork Teaching Hospitals (Ireland) Research Review Board Inc (Canada)
Ulcerative Colitis	Conjoint Health Research Ethics Board of the University of Calgary (Canada)
Crohn's disease	Mayo Clinic IRB (United States of America) CEIC Hospital Universitario La Paz (Spain) Advarra IRB (United States of America)

[a]IRB approval information is provided for the coordinating investigator of studies where a pregnancy with a known outcome was reported.
[b]Quorum was acquired by Advarra effective February 28, 2019.

Online Resource Table S3 Demographic and clinical characteristics at the start of all pregnancies (N=97) observed in clinical trials

	Rheumatoid arthritis (n=39)	Psoriatic arthritis (n=6)	nr-axial spondyloarthritis (n=1)	Atopic dermatitis (n=30)	Ulcerative colitis (n=13)	Crohn's disease (n=8)	Total (N=97)
Patient characteristics							
Age [years], mean ± SD	32.4 ± 5.8	33.3 ± 4.6	27.0 ± 0.0	27.8 ± 7.1	31.9 ± 4.2	32.1 ± 5.7	30.9 ± 6.2
Age group [years], n (%)							
<20	0	0	0	5 (16.7)	0	0	5 (5.2)
20–24	2 (5.1)	0	0	6 (20.0)	0	0	8 (8.2)
25–29	12 (30.8)	2 (33.3)	1 (100)	6 (20.0)	5 (38.5)	2 (25.0)	28 (28.9)
30–34	11 (28.2)	2 (33.3)	0	8 (26.7)	5 (38.5)	5 (62.5)	31 (32.0)
35–39	10 (25.6)	1 (16.7)	0	2 (6.7)	2 (15.4)	0	15 (15.5)
40–44	4 (10.3)	1 (16.7)	0	3 (10.0)	1 (7.7)	0	9 (9.3)
≥45	0	0	0	0	0	1 (12.5)	1 (1.0)
BMI [kg/m^2], mean ± SD	28.2 ± 6.9	25.8 ± 4.9	18.4 ± 0.0	26.3 ± 6.6	24.9 ± 3.9	28.5 ± 10.6	27.0 ± 6.8
BMI category [kg/m^2], n (%)							
<30	26 (66.7)	4 (66.7)	1 (100)	22 (73.3)	9 (69.2)	6 (75.0)	68 (70.1)
≥30	13 (33.3)	2 (33.3)	0	6 (20.0)	3 (23.1)	2 (25.0)	26 (26.8)
Unknown	0	0	0	2 (6.7)	1 (7.7)	0	3 (3.1)
Time since diagnosis [years]							
Mean ± SD	6.7 ± 5.0	7.0 ±3.4	5.1 ± 0.0	19.8 ± 10.3	8.7 ± 4.7	7.9 ± 5.5	11.1 ± 9.0
<5 years, n (%)	19 (48.7)	3 (50.0)	0	4 (13.3)	3 (23.1)	3 (37.5)	32 (33.0)
≥5 years, n (%)	20 (51.3)	3 (50.0)	1 (100)	26 (86.7)	10 (76.9)	5 (62.5)	65 (67.0)
Treatment history							
Concomitant corticosteroids (all routes), n (%)	25 (64.1)	0 (0.0)	0 (0.0)	9 (30.0)	2 (15.4)	0 (0.0)	36 (37.1)
Concomitant corticosteroid prednisone equivalent dose [mg] (all routes), mean ± SD	5.3 ± 2.0	—	—	0.6 ± 0.5	16.3 ± 5.3	—	7.8 ± 4.0
Concomitant topical glucocorticoids, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	9 (30.0)	0 (0.0)	0 (0.0)	9 (9.3)
Concomitant topical glucocorticoids dose [mg], mean ± SD	—	—	—	0.6 ± 0.5	—	—	0.6 ± 0.5
Concomitant oral glucocorticoids, n (%)	25 (64.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (15.4)	0 (0.0)	27 (27.8)
Concomitant oral glucocorticoids dose [mg], mean ± SD	5.3 ± 2.0	—	—	—	16.3 ± 5.3	—	6.1 ± 3.6

Concomitant MTX, n (%)	21 (53.8)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	23 (23.7)
Concomitant MTX dose [mg/week], mean ± SD	16.8 ± 4.3	15.0 ± 7.1	—	—	—	—	16.6 ± 4.4
Concomitant NSAIDs, n (%)	21 (53.8)	0 (0.0)	0 (0.0)	2 (6.7)	1 (7.7)	0 (0.0)	24 (24.7)
Concomitant narcotic analgesics, n (%)	3 (7.7)	0 (0.0)	0 (0.0)	1 (3.3)	1 (7.7)	1 (12.5)	6 (6.2)
Disease Activity, n (%)							
CDAI remission (≤2.8)	24 (61.5)	—	—	—	—	—	—
DAS28 (CRP) remission (<2.6)	27 (69.2)	—	—	—	—	—	—
DAPSA remission (≤4)	—	3 (50.0)	—	—	—	—	—
MDA[a]	—	4 (66.7)	—	—	—	—	—
Achievement of EASI 75	—	—	—	29 (96.7)	—	—	—
vIGA-AD 0/1 achievement	—	—	—	26 (86.7)	—	—	—
ASDAS LDA (<2.1)	—	—	1 (100)	—	—	—	—
ASDAS ID (<1.3)	—	—	1 (100)	—	—	—	—
Clinical remission per adapted Mayo score[b]	—	—	—	—	5 (38.5)	—	—
Clinical remission per CDAI (CDAI<150)	—	—	—	—	—	8 (100)	—

Baseline is defined as the last nonmissing observation on or before the patient's reported last menstrual period. One patient had two pregnancies which are counted separately in this table

[a]MDA is defined as achieving 5 of the 7 following criteria: tender joint count = 1; swollen joint count = 1; Psoriasis Area and Severity Index = 1 or body surface area = 3%; patient pain visual analog score (VAS) = 15; patient global disease activity VAS = 20; Health Assessment Questionnaire (HAQ) Disability Index = 0.5; tender entheseal points = 1

[b]Clinical remission per Adapted Mayo score is defined as an Adapted Mayo score ≤2, with stool frequency subscore ≤1 and not greater than baseline, rectal bleeding subscore of 0, and endoscopic subscore ≤1

ASDAS, Ankylosing Spondylitis Disease Activity Score; BMI, body mass index; CDAI, Crohn's Disease Activity Index; CRP, c-reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28, disease activity score 28; EASI 75, 75% reduction from baseline in the Eczema Area and Severity Index; ID, inactive disease; LDA, low disease activity; MDA, minimal disease activity; MTX, methotrexate; nr, non-radiographic; NSAIDs, nonsteroidal anti-inflammatory drugs; SD, standard deviation; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis

Online Resource Table S4 Summary of pregnancy outcomes with maternal exposure in upadacitinib clinical trials stratified by dose

	6 mg BID[a] (n=1)	**12mg BID[a] (n=2)**	**15 mg QD (n=45)**	**24 mg QD (n=1)**	**30 mg QD (n=31)**
Live birth (without congenital anomaly)	1 (100%)	1 (50%)	25 (56%)	1 (100%)	14 (45%)
Live birth (with congenital anomaly)[b]	0	0	0	0	1 (3%)
Spontaneous abortion	0	0	14 (31%)	0	5 (16%)
Still birth (fetal defects)	0	0	0	0	0
Still birth (no fetal defects or unknown)	0	0	0	0	0
Ectopic pregnancy	0	0	0	0	1 (3%)
Elective termination (no fetal defects or unknown)	0	1 (50%)	6 (13%)	0	10 (32%)
Elective termination (fetal defects)	0	0	0	0	0

[a]Immediate-release formulation of upadacitinib (dosed twice daily) was evaluated in phase 2 clinical trials. Upadacitinib 15 mg and 30 mg once daily regimens of the extended-release formulation provide equivalent daily AUC and comparable C_{max} and C_{min} to 6 mg BID and 12 mg BID, respectively

[b]One pregnancy resulted in a live birth with congenital anomaly (atrial septal defect). AUC, area under the curve; BID, twice daily; C_{max}, maximum concentration; C_{min}, minimum concentration; QD, once daily

Online Resource Table S5 Summary of pregnant patients who delivered an infant preterm or with complications from postmarketing reports

	Maternal age	Disease state	Upadacitinib dose	Gestational exposure to upadacitinib	Additional case details
Premature infant born at 36 weeks gestation	31	Rheumatoid arthritis	Unknown	First trimester	No complications reported; birth weight of 2190 grams
Premature infant born at 34 weeks gestation	34	Ulcerative colitis	Unknown	First trimester	Patient had a history of premature delivery in 2 prior pregnancies No complications reported with this delivery
Premature infant born at 28 weeks	Unknown	Rheumatoid arthritis	Unknown	Unknown	Infant required intubation, neonatal resuscitation, and was in the neonatal intensive care unit for 34 days Birth weight of 1780 grams Reason for prematurity not provided Upon follow-up, normal growth and development were reported
Infant delivered of large gestational age	45	Unknown	Unknown	First trimester	Infant was considered large for gestational age (birth weight of 3960 grams); unknown gestational age at birth No gestational diabetes or other maternal complications were reported