

Clinical Drug Investigation

Safety of Janus Kinase inhibitors in patients with alopecia areata: A systematic review.

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Supplementary Table 1. Adverse effects of systemic JAK inhibitors in adults with alopecia areata

Tofacitinib (JAK 1/3)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
Crispin et al. (2016) [22]	clinical trial	31/35	37	3	URI (11), headache (5), abdominal pain (5), acne (5), diarrhea (4), fatigue (4), hot flashes (3), pruritus (2), folliculitis (2), numbness (2), UTI (2), H.zoster (1), conjunctivitis (1), bronchitis (1), mononucleosis (1), paronychia (1), cough (1), nausea (1), amenorrhea (1), dry eyes (1), weight gain (1), elevated liver enzymes (1)
Benton et al. (2022) [36]	retrospective observational study	8/27	43,5	20,6	anemia (4), elevated urea (4), hypercholesterolemia (4), H.zoster (1), elevated liver enzymes (2), neutropenia (1), peripheral edema (1), hyperaldosteronism (1)
AlMarzoug et al. (2021) [37]	prospective cohort study	37/28	27,8	6	elevated liver enzymes (1)
Dincer Rota et al. (2021) [32]	retrospective observational study	5/8	30	3-15 (median 12)	acne (8), elevated liver enzymes (3)
Lai et al. (2021) [51]	clinical trial	4/14	45,11	3	no significant adverse effects were observed
Term et al. (2019) [21]	retrospective observational study	2/18	54,5	0,5-28 (median 13)	hypercholesterolemia (4), URI (2), elevated liver enzymes (2), AKI (1), H. zoster (1), skin rash (1), palpitations (1), leukopenia (1)
Akdogan et al. (2019) [19]	retrospective observational study	8/1	26	6	UTI (2), proteinuria (1)
Almutairi et al. (2019) [18]	comparative study	22/15	47,4	6	UTI (4), bacterial skin infection (4), warts (3), URI (3), hypercholesterolemia (3), leukopenia (2), elevated liver enzymes (2), headache (2), weight gain (2), H. zoster (1), bronchitis (1)
Cheng et al. (2018) [35]	case series	3/8	41	4,5-27 (median 14,4)	joint aches (2), weight gain (1), hypercholesterolemia (1), multiple sclerosis (1)
Chen et al. (2019) [52]	case series	2/4	24,5	6	no serious adverse effects were observed
Serdaroğlu et al. (2019) [17]	retrospective observational study	33/30	27	6-30 (median 12)	hyperseborrhea (21), URI (10), acne (9)
Shivanna et al. (2018) [31]	case series	3/3	27	3-6	acne (2)
Park et al. (2017) [53]	case series	16/16	30	4-17 (median 7,5)	no serious adverse effects were observed
Liu et al. (2017) [24]	retrospective observational study	33/32	32	4-18 (median 12)	URI (26), headache (13), acne (7), fatigue (6), weight gain (6), night sweats (4), UTI (3), folliculitis (3), tonsillitis (2), H. zoster (2), nausea (2), conjunctivitis (1), bronchitis (1), abdominal pain (1), diarrhea (1), verruca vulgaris (1), tinnitus (1), numbness (1), palpitations (1), bruising (1), leukopenia (1), elevated liver enzymes (1), hypercholesterolemia (1)
Shin et al. (2019) [16]	retrospective observational study	7/11	28	6	UTI (1), abdominal pain (1), palmoplantar desquamation (1), skin rash (1), urticaria (1), warts (1), anemia (1)
Ibrahim et al. (2017) [20]	retrospective observational study	1/12	50	0,5-13 (median 6)	skin rash (1), peripheral edema (1), elevated liver enzymes (1), hypercholesterolemia (1)

Jabbari et al. (2018) [12]	clinical trial	4/8	36,5	6-18	URI (11), blood in urine (4), abdominal pain (4), acne (3), diarrhea (3), weight gain (2)asymptomatic bacteriuria (2), urinary retention (1), conjunctivitis (1), dizziness (1), headache (1), neuropathic pain (1), bloating (1), vaginal spotting (1), hypertensive urgency (1), elevated liver enzymes (1)
Zhang et al. (2022) [56]	retrospective study	7/13	26,1	7.0-16.5 (median 12.1)	acne (4), H. zoster (1), fatigue (1), join aches (1), hypertriglyceridemia (2), hypercholesterolemia (2)
Ruxolitinib (JAK 1/2)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
Almutairi et al. (2019) [18]	clinical trial	21/17	35,5	6	UTI (5), elevated liver enzymes (3), H. zoster (2), headache (2), leukopenia (2), fatigue (2), abdominal pain (1), URI (1), bacterial skin infection (1), diarrhea (1), weight gain (1)
Liu et al. (2019) [29]	case series	4/4	20	5-31 (mean 13,9)	URI, acne, fatigue, bruising, weight gain, leukopenia (1)
Mackay-Wiggan et al. (2016) [28]	clinical trial	5/7	43,67	3-6	URI (9), allergy symptoms (7), bacterial skin infection (3), UTI (1), conjunctival hemorrhage (1), pneumonia (1), anemia (1)
Baricitinib (JAK 1/2)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
King et al. (2021) [30]	randomized clinical trial	4/23	42,5	9	URI (3), H. simplex (3), elevated CPK (3), acne (2), nausea (2), H. zoster (1)
		2/25	42,4	9	URI (3), acne (3), nausea (2), H. simplex (1), H. zoster (1), neutropenia (1),
King et al. (2022) [15]	randomized clinical trial	74/109	38	9	hypercholesterolemia (27), nasopharyngitis (12), acne (10), URI (9), headache (8), UTI (2), H. zoster (1), elevated CPK (3), hypertriglyceridemia (1), myocardial infarction (1)
		115/165	36,3	9	hypercholesterolemia (57), URI (21), nasopharyngitis (21), acne (16), elevated CPK (16), headache (14), UTI (7), H. simplex (5), hypertriglyceridemia (4), H. zoster (2)
		52/103	39	9	hypercholesterolemia (27), URI (12), UTI (12), headache (12), acne (9), H. simplex (6), H. zoster (3), nasopharyngitis (2), elevated CPK (0), hypertriglyceridemia (0),
		89/144	38	9	hypercholesterolemia (54), headache (21), URI (15), nasopharyngitis (15), UTI (11), acne (11), elevated CPK (7), H. zoster (3), H. simplex (2), new malignancy (1), hypertriglyceridemia (0)
Ritlecitinib (JAK 3)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
King et al. (2021) [14]	randomized clinical trial	11/37	37	6	headache (6), nasopharyngitis (6),acne (5), URI (4), diarrhea (4), allergy symptoms (3), folliculitis (3), nausea (3), lymphopenia (1)

Brepocitinib (JAK1/TYK2)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
King et al. (2021) [14]	randomized clinical trial	15/32	34	6	URI (11),elevated creatinine level (13), acne (5), nasopharyngitis (4), headache (4), oropharyngeal pain (3), sinusitis (3),nausea (3), abdominal pain (3), rhabdomyolysis (2), neutropenia (2), elevated liver enzymes (2), allergy symptoms (1), diarrhea (1), folliculitis (1), elevated CPK (1), hypercholesterolemia (1)
Deuruxolitinib (JAK1/2)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
King et al. (2021) [13]	randomized clinical trial	22/8	35,7	6	headache (5), acne (4), cough (4), nausea (4), URI (2), oropharyngeal pain (3), nasopharyngitis (3), diarrhea (3), folliculitis (3), elevated CPK (3), hyperkalemia (1), hyperglycemia (1), neutropenia (1), elevated lipase (1), elevated liver enzymes (1)
		26/12	37,3	6	headache (10), acne (4), nausea (4), hypercholesterolemia (4), nasopharyngitis (3), URI (2), folliculitis (2), elevated CPK (2), oropharyngeal pain (1), diarrhea (1), cough (1), elevated phosphate (1), neutropenia (1), elevated lipase (1), elevated amylase (1)
		28/9	35,8	6	nasopharyngitis (9), URI (7), headache (7), acne (6), elevated lipase (3), cough (2), elevated phosphate (2), elevated urea (2), folliculitis (1), nausea (1), elevated CPK (1), hyperkalemia (1), elevated amylase (1), hypertriglyceridemia (1)

JAK – Janus Kinase, TYK – tyrosine kinase, URI – upper respiratory infection, UTI – urinary tract infection, CPK – creatine phosphokinase, H. zoster – Herpes zoster, H. simplex – Herpes simplex

Supplementary Table 2. Adverse effects of topical JAK inhibitors in adults with alopecia areata

Tofacitinib (JAK 1/3)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
Cheng et al. (2018) [35]	case series	3/1	42	3-11 (median7)	no serious adverse effects were observed
Liu et al. (2018) [33]	clinical trial	6/4	36,9	6	scalp skin irritation (4), hypercholesterolemia (4), folliculitis (1)
Ruxolitinib (JAK 1/2)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
Bokhari et al. (2018) [54]	randomized clinical trial	not reported	not reported	3	no serious adverse effects were observed
Olsen et al. (2020) [34]	randomized clinical trial	3/9	47,6	6	scalp skin irritation (2)
		15/24	44,3	6	scalp skin irritation (5)

JAK – Janus Kinase, TYK – tyrosine kinase, URI – upper respiratory infection, UTI – urinary tract infection, CPK – creatine phosphokinase, H. zoster – Herpes zoster, H. simplex – Herpes simplex

Supplementary Table 3. Adverse effects of systemic JAK inhibitors in children with alopecia areata

Tofacitinib (JAK 1/3)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
McKenzie et al. (2022) [27]	retrospective observational study	10/1	15,5	12-58 (mean 31)	URI (4), abdominal pain (3),
Kibbie et al. (2022) [39]	case series	4/7	17	5-39 (median 32)	lymphopenia (1), elevated alkaline phosphatase (1), elevated liver enzymes (1), hipertriglicerydemia (1)
Jerjen et al. (2021) [26]	retrospective observational study	7/7	6	7-38 (median 9)	elevated liver enzymes (5), eosynophilia (5), hiperkaliemia (3), elevated urea (3), URI (3), hypercholesterolemia (3), hyperbilirubinemia (1), low total protein (1), hipertriglicerydemia (1)
Dai et al. (2019) [25]	case series	2/1	4,5	6-21 (median 12)	URI (1), diarrhea (1),
Craiglow et al. (2017) [23]	retrospective observational study	10/3	15	2-16 (median 5)	URI (4), elevated liver enzymes (4), headache (3),
Craiglow et al. (2019) [38]	case series	1/3	9	6-15 (median 6,5)	no serious adverse effects were observed
Youssef et al. (2022) [57]	case series	5/5	13	1-6 (median 2)	acne (1)

JAK – Janus Kinase, TYK – tyrosine kinase, URI – upper respiratory infection, UTI – urinary tract infection, CPK – creatine phosphokinase, H. zoster – Herpes zoster, H. simplex – Herpes simplex

Supplementary Table 4. Adverse effects of topical JAK inhibitors in children with alopecia areata

Tofacitinib (JAK 1/3)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
Bayart et al. (2017) [40]	clinical trial	1/3	4,5	3-12	leukopenia (1), elevated liver enzymes (1)
Putterman et al. (2018) [55]	clinical trial	2/9	12	2-19	no serious adverse effects were observed
Ruxolitinib (JAK 1/2)					
Study	Type of study	Sex (m/f)	Age (median)	Therapy duration (months)	Adverse effects
Bayart et al. (2017) [40]	clinical trial	1/1	10,5	3-12	no serious adverse effects were observed

JAK – Janus Kinase, TYK – tyrosine kinase, URI – upper respiratory infection, UTI – urinary tract infection, CPK – creatine phosphokinase, H. zoster – Herpes zoster, H. simplex – Herpes simplex