menses or other clinical signs of hyperandrogenism. Notably, serum hormone values were not required in our patient population to meet PCOS diagnostic criteria. This is of particular clinical importance, because many women are taking hormonal contraception at the time of presentation, precluding accurate testing of these laboratory values. Identification of PCOS is critical, given that these women have a higher risk for metabolic syndrome, some malignancies, and infertility.[2] Dermatologists treating patients with FPHL are uniquely poised to aid in early diagnosis and enable pharmacologic interventions and lifestyle management.

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Integrated safety analysis: Frequency of urinary tract infections in patients with psoriasis treated with ixekizumab

To the Editor: Urinary tract infections (UTIs) occur very frequently, affecting approximately 150 million people globally each year, and are associated with significant societal and personal burden.[1] Lower UTIs, limited to the urethra and bladder, are generally uncomplicated and afebrile, whereas upper UTIs involving the kidneys and ureters are usually complicated and febrile. To date, clinical studies into interleukin 17 (IL-17) inhibitors have not identified UTI adverse events (AEs) as safety signals.[2,3] One recent real-world evidence study identified 3 cases (incidence rate per 100 person-years [IR], 0.64; 95% confidence interval [CI], 0.2-2.0) of upper UTI in patients with psoriasis exposed to IL-17 inhibitors, suggesting that these may be class-specific AEs.[4] We performed an integrated safety analysis of the frequency of UTIs in clinical trial patients with psoriasis treated with the IL-17A antagonist ixekizumab.

Integrated analysis of 6091 patients with psoriasis (17,499 person-years) treated with ixekizumab in 14 clinical trials showed treatment-emergent AEs for upper UTI (n = 23; IR, 0.1; 95% CI, 0.1-0.2), lower UTI (n = 424; IR, 2.4; 95% CI, 2.2-2.7), and prostatitis (n = 12; IR, 0.1; 95% CI, 0.0-0.1). Analyses comparing UTI rates for ixekizumab, placebo, etanercept, and ustekinumab showed no statistical significance in IR between ixekizumab and other treatment groups (Table I).

Of 14 upper UTIs deemed serious AEs (SAEs), a review of patient histories showed 12 patients (85.7%) had a history of UTI or predisposing factors, or both, 9 (64.3%) were categorized with obesity (body mass index ≥30.0 kg/m^2), and 9 (64.3%) were aged >50 years (Table II). None of the patients received additional immunosuppressive treatment (eg, methotrexate) or were otherwise immunocompromised (eg, HIV, diabetes).

This integrated safety analysis found that the reported UTI IR with ixekizumab is low, and so contrasts with the Spanish registry data that showed increased febrile UTI with anti−IL-17 use.[4] However, comparing both outcomes is difficult because the registry data used grouped analysis of multiple unspecified anti−IL-17 agents and short sampling

Table I. Urinary tract infection (*UTI*) incidence rate per 100 person-years (*IR*) in patients with psoriasis in clinical trials who received placebo (*PBO*), ixekizumab (*IXE*), etanercept (*ETN*), or ustekinumab (*UST*)

	Double-blind 0-12 weeks: UNCOVER-2 (NCT01597245), UNCOVER-3 (NCT01646177)			Double-blind 0-52 weeks: IXORA-S (NCT02561806)		All IXE exposure up to 5 years* (14 psoriasis studies)†
Variable	**PBO**	**IXE**	**ETN**	**IXE**	**UST**	**IXE**
Total patients, No.	360	1463	739	166	135	6091
Total person-years‡	83.2	336.5	169.2	159.5	131.4	17,499
Patients with ≥1 upper UTI						
No.	0	1	0	0	0	23
IR (95% CI)	0.0 (NA)	0.3 (0.04-2.11)	0.0 (NA)	0.0 (NA)	0.0 (NA)	0.1 (0.1-0.2)
Patients with ≥1 lower UTI						
No.	3	26	7	4	5	424
IR (95% CI)	3.6 (1.16-11.2)	7.7 (5.26-11.4)	4.1 (1.97-8.68)	2.5 (0.94-6.68)	3.8 (1.58-9.15)	2.4 (2.2-2.7)
Patients with ≥1 prostatitis						
No.	0	1	0	1	0	12
IR (95% CI)	0.0 (NA)	0.3 (0.04-2.11)	0.0 (NA)	0.6 (0.09-4.45)	0.0 (NA)	0.1 (0.0-0.1)

CI, Confidence interval; *NA*, not available.
*Naïve pooling: Total of numerators divided by total of denominators.
†Psoriasis studies: I1F-EW-RHBZ, I1F-JE-RHAT, I1F-MC-RHAG, I1F-MC-RHAJ, I1F-MC-RHAZ, I1F-MC-RHBA, I1F-MC-RHBC, I1F-MC-RHBL, I1F-MC-RHBP, I1F-MC-RHBQ, I1F-MC-RHBS, I1F-MC-RHBU, I1F-MC-RHCD, I1F-US-RHBO.
‡Total person-years: Total time at risk in years.

Table II. Individual patient profiles for upper urinary tract infection (*UTI*) serious adverse events in patients with psoriasis treated with ixekizumab*

Age (y)	Sex	Baseline BMI (kg/m^2)	Infective agent	UTI history	Predisposing factors
54	M	24.2	*E coli*		Kidney stones
74	F	34.0	*E coli*	UTIs in medical history	
38	F	22.1	*E coli*		
38	M	44.1	*E coli*		
21	F	29.2	*E coli*		Chalices neck stenosis
58	F	39.6	*E coli*		Kidney stones
54	F	49.6	*E coli*		Atrophic left kidney, chronic renal failure
73	M	37.2	*E faecalis*	UTIs in medical history	Benign prostatic hyperplasia
66	F	33.8	*K pneumoniae*		Bladder neck polyps
72	M	29.2	*K pneumoniae*		TURP
71	M	30.1	MRSA		Benign prostatic hyperplasia
50	F	47.3	Unknown	UTIs in medical history	Kidney stones
26	M	33.2	Unknown		Kidney stones
32	F	27.4	Unknown	UTIs in medical history	

BMI, Body mass index; *E coli*, *Escherichia coli*; *E faecalis*, *Enterococcus faecalis*; *K pneumoniae*, *Klebsiella pneumoniae*; *MRSA*, methicillin-resistant *Staphylococcus aureus; TURP*, transurethral resection of the prostate.
*Data shown are upper UTI serious adverse events data arising from 6091 patients across 14 psoriasis studies: I1F-EW-RHBZ, I1F-JE-RHAT, I1F-MC-RHAG, I1F-MC-RHAJ, I1F-MC-RHAZ, I1F-MC-RHBA, I1F-MC-RHBC, I1F-MC-RHBL, I1F-MC-RHBP, I1F-MC-RHBQ, I1F-MC-RHBS, I1F-MC-RHBU, I1F-MC-RHCD, and I1F-US-RHBO.

duration (466 person-years), and clinical trials may not adequately represent all patient groups.[5] Review of the medical histories of ixekizumab-treated patients who developed upper UTI SAEs in our clinical studies (Table II) showed most patients had known risk factors to UTI development (increased age, high body mass index, UTI history, predisposing factors, or a combination of these).

UTI SAEs were caused by *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterococcus faecalis*, which is expected given their dominance as drivers of UTI.[1]

Although clinical trial populations may not represent typical real-world patient populations, trial data comprising 17,499 person-years shows that ixekizumab treatment carries a low overall UTI rate and does not show ixekizumab is related to an increased UTI rate vs placebo, etanercept, or ustekinumab. In UTI SAEs that occurred in the ixekizumab-treated trial population, an in-depth analysis of patient histories revealed most patients were predisposed to UTIs based on known risk factors. Considering predisposing factors is important when evaluating infection rates in patients with psoriasis and when judging the suitability of anti–IL-17 agents or any other biologic for patients with psoriasis.

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Cyclosporine for treatment of acute generalized exanthematous pustulosis: A retrospective analysis

To the Editor: Acute generalized exanthematous pustulosis (AGEP) is a severe cutaneous adverse reaction, typically to a medication, that is characterized by fever, neutrophilia, and a disseminated