

# Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 Inhibitor, Compared With Placebo and Apremilast in Moderate to Severe Plaque Psoriasis: Efficacy and Safety Results From the POETKY PSO-1 and POETKY PSO-2 Trials

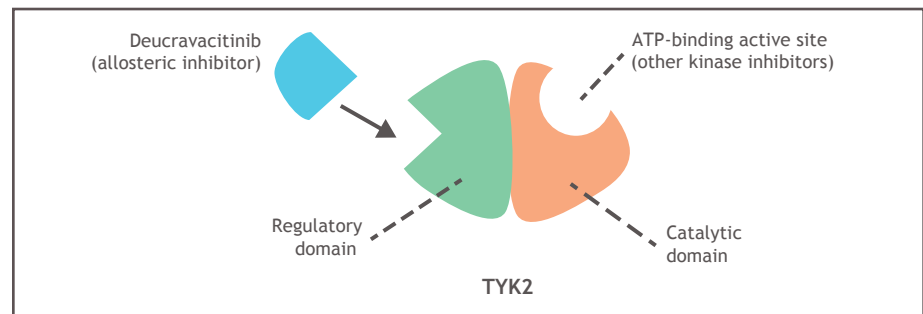
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## Introduction

- Deucravacitinib
  - Novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor with a unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors<sup>1</sup> (Figure 1)
  - Achieves a high degree of selectivity by uniquely binding to the regulatory, rather than to the active, domain of TYK2, which is structurally distinct from the regulatory domains of JAK 1/2/3<sup>1</sup>
    - ≥100-fold greater selectivity for TYK2 vs JAK1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK2 in cellular assays<sup>1,2</sup>
  - Inhibits TYK2-mediated signaling by key cytokines involved in psoriasis pathogenesis (eg, interleukin [IL]-23, IL-12, and Type 1 interferons)
- Previously demonstrated efficacy and tolerability in Phase 2 trials in moderate to severe plaque psoriasis<sup>3</sup> and active psoriatic arthritis<sup>4</sup>

Figure 1. Mechanism of action of deucravacitinib



TYK2, tyrosine kinase 2.

## Objective

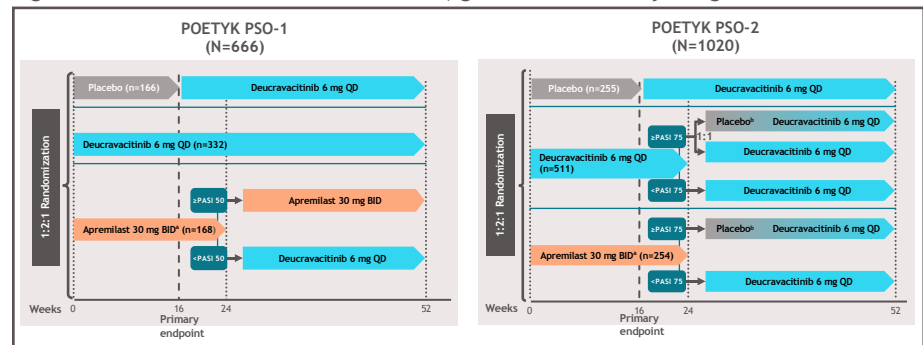
- To compare the efficacy and safety of deucravacitinib vs placebo and apremilast in patients with plaque psoriasis

## Methods

### Study design

- The POETKY PSO-1 and PSO-2 study designs are shown in Figure 2
- Key eligibility criteria
  - Adults with moderate to severe plaque psoriasis
  - Psoriasis Area and Severity Index (PASI) ≥12, static Physician's Global Assessment (sPGA) ≥3, body surface area ≥10%
- Patients were stratified by geographic region, body weight, and prior biologic use
- Patients receiving placebo switched to deucravacitinib at Week 16 and patients receiving apremilast failing to meet study-specific efficacy thresholds (≥50% reduction from baseline PASI [PASI 50] in PSO-1, ≥75% reduction from baseline PASI [PASI 75] in PSO-2) switched to deucravacitinib at Week 24
- PSO-2 included a randomized withdrawal phase starting at Week 24; those results will be presented at a future date
  - All patients were eligible for a long-term extension study after 52 weeks of treatment

Figure 2. POETKY PSO-1 and POETKY PSO-2, global Phase 3 study designs



Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.  
 \*Upon release (±50% loss of Week 24 PASI percent improvement from baseline), patients were switched to deucravacitinib 6 mg QD.  
 BID, twice daily; PASI, Psoriasis Area and Severity Index; PSO, PSO-1, ≥50% reduction from baseline PASI; PSO-2, ≥75% reduction from baseline PASI; QD, once daily; sPGA, static Physician's Global Assessment.

### Study endpoints

- Coprimary endpoints, deucravacitinib vs placebo (Week 16)
  - PASI 75
  - sPGA score of 0/1
- Secondary endpoints included PASI 90, scalp-specific PGA (ss-PGA) 0/1 for those with baseline score ≥3, sPGA 0, 100% reduction from baseline PASI (PASI 100), Psoriasis Symptoms and Signs Diary (PSSD) symptom score 0 for those with baseline score ≥1, Dermatology Life Quality Index (DLQI) 0/1 for those with baseline score ≥2, time to relapse until Week 52 for Week 24 PASI 75 responders (PSO-2 only), PGA-fingernail (PGA-F) 0/1 for those with baseline score ≥1, and change from baseline in PSSD symptom score (which includes itching, pain, stinging, burning, and skin tightness)
- Safety (adverse events [AEs] and laboratory parameters) for the 2 trials are presented in integrated fashion
  - Safety analyses included all patients who received ≥1 dose of study treatment
  - Safety results are expressed as exposure-adjusted incidence rates (EAIRs) to account for variable periods of exposure to each treatment

## Results

### Patient disposition

- 92.5% of patients in PSO-1 and 89.4% in PSO-2 completed 16 weeks of deucravacitinib treatment vs 87.9% and 83.5%, respectively, for placebo, and 86.3% and 85.4%, respectively, for apremilast

### Baseline demographics and clinical characteristics

- Baseline demographics and disease characteristics were largely similar across studies and treatment groups, and typical for studies in moderate to severe plaque psoriasis (Table 1)
- PSO-1 included sites in Asia, whereas PSO-2 did not
  - Mean patient weight was slightly higher in PSO-2 vs PSO-1, likely reflecting differences in geographic distribution

Table 1. Baseline demographics and disease characteristics

Rank	POETKY PSO-1			POETKY PSO-2		
	Placebo n=166	Deucravacitinib n=332	Apremilast n=168	Placebo n=255	Deucravacitinib n=511	Apremilast n=254
Age, y, mean (SD)	47.9 (14.0)	45.9 (13.7)	44.7 (12.1)	47.3 (13.6)	46.9 (13.4)	46.4 (13.3)
Weight, kg, mean (SD)	89.1 (22.3)	87.9 (21.8)	87.5 (21.1)	91.5 (20.2)	92.3 (21.9)	93.5 (22.2)
Female, n (%)	53 (31.9)	102 (30.7)	58 (34.5)	74 (29.0)	175 (34.2)	97 (38.2)
Race, n (%)						
White	128 (77.1)	267 (80.4)	139 (82.7)	232 (91.0)	474 (92.8)	229 (90.2)
Asian	34 (20.5)	59 (17.8)	28 (16.7)	8 (3.1)	24 (4.7)	12 (4.7)
Other	4 (2.4)	6 (1.8)	1 (0.6)	15 (5.9)	13 (2.6)	13 (5.1)
Disease duration, y, mean (SD)	17.3 (12.8)	17.1 (12.4)	17.7 (11.8)	19.9 (12.8)	19.6 (12.9)	18.9 (12.4)
sPGA, n (%)						
3 = moderate	128 (77.1)	257 (77.4)	139 (82.7)	217 (85.1)	408 (79.8)	196 (77.2)
4 = severe	37 (22.3)	75 (22.6)	29 (17.3)	38 (14.9)	103 (20.2)	58 (22.8)
PASI, mean (SD)	20.7 (8.0)	21.8 (8.6)	21.4 (9.0)	21.1 (9.0)	20.7 (7.5)	21.6 (8.4)
PSSD symptom score, mean (SD)*	51.4 (26.8)	51.7 (25.2)	56.2 (25.2)	50.1 (24.8)	52.3 (26.3)	51.9 (25.4)
DLQI, mean (SD)	11.4 (6.6)	12.0 (6.7)	12.4 (6.8)	11.8 (6.8)	11.8 (6.5)	12.5 (6.7)
Prior systemic treatment use, n (%)						
Biologic	63 (38.0)	130 (39.2)	66 (39.3)	83 (32.5)	165 (32.3)	79 (31.1)
No prior systemic therapy	57 (34.3)	132 (39.8)	59 (35.1)	116 (45.5)	237 (46.4)	114 (44.9)

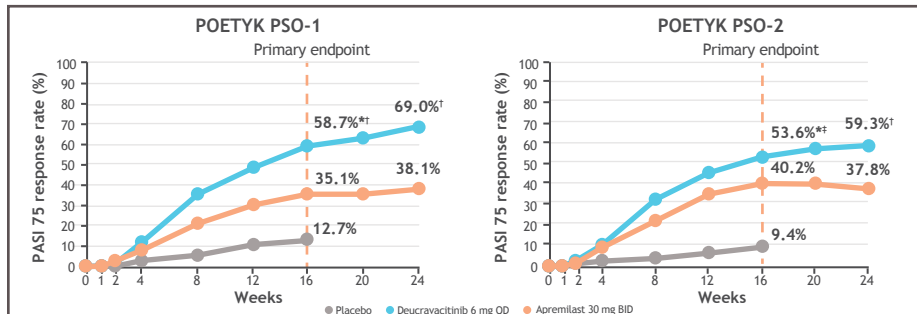
\*PSSD symptom score is the average severity of 5 symptoms (itch, pain, burning, stinging, and skin tightness) over the previous 24 hours scored on a numerical scale ranging from 0 (absent) to 100 (worst).  
 DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment.

### Efficacy

#### Coprimary endpoints

- The coprimary endpoints were met in both studies (PASI 75 and sPGA 0/1 vs placebo at Week 16)
  - Significantly greater proportions of patients in the deucravacitinib arm compared with the placebo and apremilast arms achieved PASI 75 response at Week 16 in both trials (Figure 3)
  - Deucravacitinib was also superior to apremilast at Week 24
- 82.6% (PSO-1) and 82.5% (PSO-2) of deucravacitinib patients who achieved PASI 75 at Week 24 and continued treatment maintained PASI 75 response at Week 52

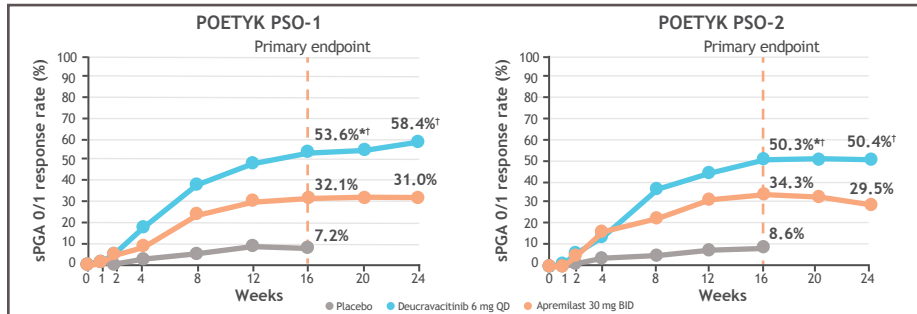
Figure 3. PASI 75 response at Week 16 (coprimary endpoint) and through Week 24



Missing data were imputed with nonresponder imputation.  
 \*P<0.0001 vs placebo; \*P<0.0001 vs apremilast; \*P<0.0003 vs apremilast.  
 BID, twice daily; PASI 75, ≥75% reduction from baseline Psoriasis Area and Severity Index; QD, once daily.

- Significantly greater proportions of patients in the deucravacitinib arm compared with the placebo and apremilast arms achieved sPGA 0/1 at Week 16 in both trials (Figure 4)
- Deucravacitinib was also superior to apremilast at Week 24 in both trials

Figure 4. sPGA 0/1 response\* at Week 16 (coprimary endpoint) and through Week 24



Missing data were imputed with nonresponder imputation.  
 \*Response defined as sPGA score of 0 or 1 with ≥2-point improvement from baseline.  
 \*P<0.0001 vs placebo; \*P<0.0001 vs apremilast.  
 BID, twice daily; QD, once daily; sPGA, static Physician's Global Assessment.

### Key secondary endpoints

- Statistical significance was achieved for deucravacitinib vs placebo and apremilast for multiple ranked secondary endpoints in both trials (Tables 2 and 3)

Table 2. Comparisons vs placebo; 2-sided α=0.025

Rank	Endpoint vs placebo	POETKY PSO-1	POETKY PSO-2
		P value	P value
1	PASI 90 at W16	<0.0001	<0.0001
2	ss-PGA 0/1 (BL ≥3) at W16	<0.0001	<0.0001
3	sPGA 0 at W16	<0.0001	<0.0001
4	PASI 100 at W16	<0.0001	<0.0001
5	PSSD symptom score 0 (BL ≥1) at W16	0.0013	0.0005
6*	DLQI 0/1 (BL ≥2) at W16	<0.0001	<0.0001
7*	Time to relapse until W52 for W24 PASI 75 responders	Not applicable	<0.0001
8*	PGA-F 0/1 (BL ≥3) at W16	NS (0.10)	NS (0.062)

\*US hierarchy only.  
 \*145-15% study population had PGA-F scores ≥3 at baseline.  
 BL, baseline; DLQI, Dermatology Life Quality Index; NS, not significant; PASI, Psoriasis Area and Severity Index; PASI 90, ≥90% reduction from BL PASI; PASI 100, 100% reduction from BL PASI; PGA-F, Physician's Global Assessment-Fingernail; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment; ss-PGA, scalp-specific Physician's Global Assessment; W, week.

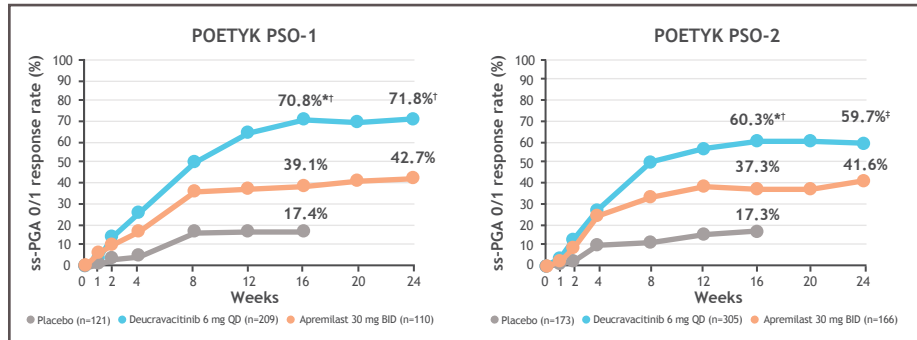
Table 3. Comparisons vs apremilast; 2-sided α=0.025

Rank	Endpoint vs apremilast	POETKY PSO-1	POETKY PSO-2
		P value	P value
1	sPGA 0/1 at W16	<0.0001	<0.0001
2	PASI 75 at W16	<0.0001	0.0003
3	PASI 90 at W16	0.0001	0.0056
4	sPGA 0/1 at W24	<0.0001	<0.0001
5	PASI 75 at W24	<0.0001	<0.0001
6*	PASI 90 at W24	<0.0001	<0.0001
7	CFB PSSD symptom score at W16	<0.0001	<0.0001
8	ss-PGA 0/1 at W16 (BL ≥3)	<0.0001	<0.0001
9	sPGA 0/1 at W52 and W24	<0.0001	Not applicable
10	PASI 75 at W52 and W24	<0.0001	Not applicable
11	PASI 90 at W52 and W24	0.0002	Not applicable
12	sPGA 0 at W16	<0.0001	0.0002
13	PSSD symptom score 0 at W16 (BL ≥1)	NS (0.17)	NS (0.093)

BL, baseline; CFB, change from baseline; NS, not significant; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from BL PASI; PASI 90, ≥90% reduction from BL PASI; PSSD, Psoriasis Symptoms and Signs Diary; sPGA, static Physician's Global Assessment; ss-PGA, scalp-specific Physician's Global Assessment; W, week.

- Significantly greater proportions of patients in the deucravacitinib vs placebo and apremilast arms achieved an ss-PGA score of 0/1 response at Week 16 in both trials (Figure 5)
  - Deucravacitinib was also superior to apremilast at Week 24 in both trials
  - ≥60% of patients in both trials had moderate to severe scalp psoriasis at baseline

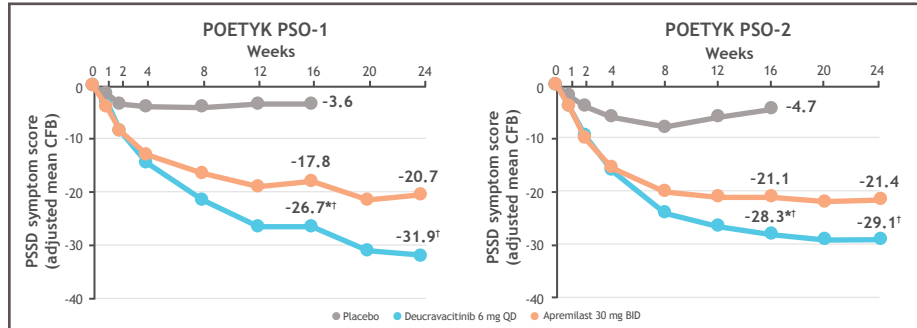
Figure 5. Scalp psoriasis: ss-PGA 0/1\* responses through Week 24



Missing data were imputed with nonresponder imputation.  
 \*Included patients with a baseline ss-PGA score of ≥3.  
 \*P<0.0001 vs placebo; \*P<0.0001 vs apremilast; \*P<0.0002 vs apremilast.  
 BID, twice daily; QD, once daily; ss-PGA, scalp-specific Physician's Global Assessment.

- Significantly greater improvement from baseline in PSSD symptom scores was observed for deucravacitinib vs apremilast at Week 16 in both trials (Figure 6)
- Significantly greater improvement from baseline for deucravacitinib vs apremilast was also seen at Week 24 in both trials

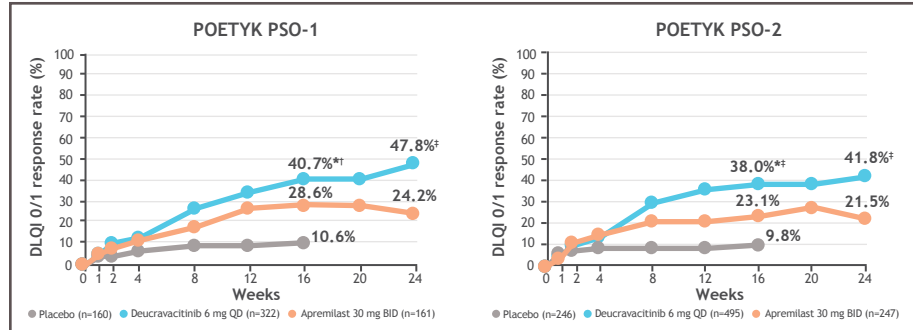
Figure 6. Change from baseline in PSSD symptom score through Week 24



Modified baseline observation carried forward method was used to impute missing data.  
 \*P<0.0001 vs placebo; \*P<0.0001 vs apremilast.  
 BID, twice daily; CFB, change from baseline; PSSD, Psoriasis Symptoms and Signs Diary; QD, once daily.

- Significantly greater proportions of patients in the deucravacitinib vs placebo and apremilast arms achieved DLQI 0/1 (no effect on quality of life) at Week 16 in both trials (Figure 7)
  - Deucravacitinib was also superior to apremilast at Week 24 in both trials
  - >95% of patients in both trials had a DLQI score of ≥2 at baseline

Figure 7. DLQI 0/1 responses\* through Week 24



Missing data were imputed with nonresponder imputation.  
 \*Among patients with a baseline DLQI score of ≥2.  
 \*P<0.0001 vs placebo; \*P<0.0106 vs apremilast; \*P<0.0001 vs apremilast.  
 BID, twice daily; DLQI, Dermatology Life Quality Index; QD, once daily.

### Safety

- The integrated safety data from both studies up to the primary endpoint at Week 16 are shown in Table 4
- The total number of AEs and serious AEs (SAEs) was similar across treatment groups, and AEs leading to discontinuation were numerically lower with deucravacitinib vs placebo and apremilast
- Nasopharyngitis and upper respiratory tract infection were the most common (≥5%) AEs in the deucravacitinib group
  - Diarrhea, headache, and nausea were the most common AEs in the apremilast group

Table 4. Safety summary, Weeks 0-16

AE category, n (%)	POETKY Integrated safety (PSO-1 and PSO-2)		
	Placebo n=419	Deucravacitinib n=842	Apremilast n=422
Any AEs	208 (49.6)	469 (55.7)	243 (57.6)
SAEs	12 (2.9)	15 (1.8)	5 (1.2)
AEs leading to discontinuation	16 (3.8)	20 (2.4)	22 (5.2)
Deaths	1* (0.2)	1* (0.1)	1* (0.2)
Most common AEs (≥5%) in any active treatment group			
Nasopharyngitis	36 (8.6)	76 (9.0)	37 (8.8)
Upper respiratory tract infection	17 (4.1)	46 (5.5)	17 (4.0)
Headache	19 (4.5)	38 (4.5)	45 (10.7)
Diarrhea	25 (6.0)	37 (4.4)	50 (11.8)
Nausea	7 (1.7)	14 (1.7)	42 (10.0)

\*One 57-year-old female patient receiving placebo experienced sudden cardiac death due to hypertensive cardiovascular disease.  
 \*One patient discontinued deucravacitinib after 4 days of treatment due to prohibited medication (levonorgestrel) and died 9 days later due to heart failure and sepsis.  
 \*One patient discontinued apremilast due to lung cancer after 3 months and died 1 month later due to lung cancer and gastrointestinal bleed.  
 AE, adverse event; SAE, serious adverse event.

- Integrated safety results from Weeks 0 to 52 are shown in Table 5
- Due to rerandomizations at Week 16 and Week 24, total exposure for deucravacitinib was 969.0 person-years (PY), compared with 240.9 PY for placebo and 221.1 PY for apremilast

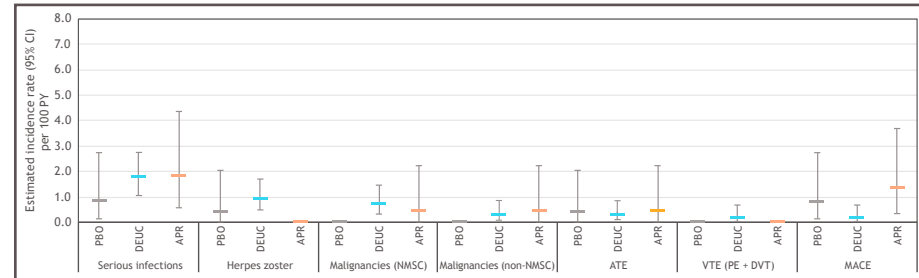
Table 5. Safety summary, Weeks 0-52

AE category	POETKY Integrated safety (PSO-1 and PSO-2)					
	Placebo n=666 (total PY, 240.9)		Deucravacitinib n=1364 (total PY, 969.0)		Apremilast n=422 (total PY, 221.1)	
	n*	EAIR*	n*	EAIR*	n*	EAIR*
Any AEs	347	217.9	995	229.2	299	281.1
SAEs	14	5.7	55	5.7	9	4.0
AEs leading to discontinuation	23	9.4	43	4.4	26	11.6
Deaths	1		2 <sup>c</sup>		1	
Most common AEs (≥5%) in any active treatment group						
Nasopharyngitis	54	22.9	229	26.1	54	25.9
Upper respiratory tract infection	33	13.6	124	13.4	27	12.4
Headache	21	8.6	80	8.5	53	26.0
Diarrhea	28	11.6	69	7.3	54	26.5
Nausea	10	4.1	20	2.1	47	22.9

\*Includes AEs between first dose and 30 days following last dose or rollover to long-term extension.  
 \*Incidence rate per 100 PY of exposure (IR/100 PY): 100/365.25 (total number of patients with AEs/total exposure time for the selected AE under each treatment).  
<sup>c</sup>1 additional death between Weeks 16 and 52 due to hepatocellular carcinoma in a patient with a history of hepatitis C virus infection and liver cirrhosis.  
 AE, adverse event; EAIR, exposure-adjusted incidence rate; IR, incidence rate; PY, person-years; SAE, serious adverse event.

- Skin events of interest noted in earlier studies: acneiform lesions
  - Folliculitis: placebo = 0, deucravacitinib = 2.0% (EAIR, 2.8), apremilast = 0.5% (EAIR, 0.9); acne: placebo = 0.2% (EAIR, 0.4), deucravacitinib = 2.1% (EAIR, 2.9), apremilast = 0
  - All cases were mild to moderate; 1 patient with folliculitis discontinued deucravacitinib treatment
- No new safety signals were observed during Weeks 16-52

- AEs of interest (EAIRs) are shown in Figure 8
- Figure 8. AEs of interest (integrated), Weeks 0-52



Total exposure: deucravacitinib, 969.0 PY; placebo, 240.9 PY; apremilast, 221.1 PY. Most placebo-related data were obtained during Weeks 0-16.  
 AE, adverse event; ARS, apremilast-related serious adverse events; DLQI, deucravacitinib; DVT, deep vein thrombosis; WACE, major adverse cardiovascular events; NMCC, nonmelanoma skin cancers; PBO, placebo; PE, pulmonary embolic events; PY, person-years; VTE (PE + DVT), venous thromboembolic events.

- None of the serious infections with deucravacitinib led to study discontinuation
- No cases of herpes zoster with deucravacitinib were serious, disseminated, systemic, or led to discontinuation
- No tuberculosis events and no opportunistic infections were reported with deucravacitinib
- 1 SAE adjudicated as a venous thromboembolic event occurred in a patient receiving deucravacitinib who had an aortic dissection complicated by a pulmonary embolic event; the patient recovered after aortic repair, resected treatment with deucravacitinib, and is continuing in the long-term extension study (NCT0436435) without occurrence of venous thromboembolic events
- No clinically significant trends were observed for laboratory parameters (Figure 9)
- Similar results were observed between Weeks 16 and 52 in these and additional laboratory parameters (data not shown)

Figure 9. Selected laboratory parameters of interest (integrated), Weeks 0-16

