those sequenced from distant metastasis (73% vs 27%, $P = .027$). The remaining cases showed unremarkable smaller epithelioid and/or fusiform cells with no consistent architecture.

Inactivation of *PRKAR1A* is known to increase cyclic adenosine monophosphate–stimulated protein kinase A activity and has been shown to promote tumorigenesis and modulate the tumor microenvironment.[4] Preclinical data have shown possible targeted treatment strategies.[5] Although the current study is limited by its retrospective nature, enrichment for clinically advanced tumors, and the lack of follow-up data and patient-paired primary/metastatic tumor analysis, our findings suggest the need for further investigational studies to assess the outcomes of *PRKAR1A*-inactivated melanomas, including possible stratification of patients for personalized therapeutic options.

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Drugs associated with development of pityriasis rubra pilaris: A systematic review

To the Editor: Pityriasis rubra pilaris (PRP) is an idiopathic chronic disorder of keratinization characterized by follicular hyperkeratosis, orange-red plaques, islands of sparing, and waxy keratoderma. PRP-like eruptions have been reported with the use of various therapeutics and are important for health care providers to recognize and treat. This systematic review summarizes reports of PRP-like eruptions in association with various drugs.

An Embase and MEDLINE search was conducted on June 15, 2020, in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Supplemental Files 1 and 2, available via Mendeley at https://doi.org/10.17632/ndkcrb86k3.1). The 19 studies identified (Fig 1, Table I) included 25 patients (19 men) with a mean age of 59.4 years. The time period between initiation of drugs and PRP onset ranged from 3 days to 5 months, with a mean of 31.3 days. Reported drugs included tyrosine kinase inhibitors (n = 10), topical Toll-like receptor 7 agonists (n = 4), phosphoinositide 3-kinase inhibitors (n = 3), antiviral medications (n = 2), biologic (n = 1), programmed cell death protein 1 inhibitor (n = 1), vascular endothelial growth factor inhibitor (n = 1), statin (n = 1), insulin (n = 1), and an angiotensin-converting enzyme inhibitor (n = 1).

The location of PRP eruptions was generalized, with no predilection for anatomic sites. The suspect drug was discontinued in 10 patients, 8 continued on the drug, and continuation of

treatment was not reported in the remainder of the patients. Combinations of topical treatments involving corticosteroids, retinoids, and keratolytic agents, as well as oral corticosteroids and retinoids, led to complete resolution in 16 patients within 4.3 months of treatment. Of the 8 patients who continued the drug and received treatment for PRP lesions, 5 reported complete resolution in 35 days; whereas, of the 10 patients who discontinued the drug and received treatment for PRP lesions, complete resolution was noted in 7 patients in 67.2 days.

Although PRP has an unknown etiology, pharmacologic treatments and traumatic and infectious events have occasionally been reported as triggers.[1] Our review suggests that most drug-related PRP cases are associated with oral tyrosine kinase inhibitors. These agents modify inflammatory pathways, leading to alterations in regulatory immune surveillance and abnormal epidermal growth.[2] Topical imiquimod use has also been associated with the onset of PRP, suggesting its systemic effects on increasing proinflammatory cytokines, such as tumor necrosis factor-α, affect intercellular adhesions and result in acantholysis.[3] The mechanisms of PRP pathogenesis with other drug classes reported are even less clear and may be a consequence of drug initiation in the context of underlying immunologic conditions,[4,5] such as type 1 diabetes, hepatitis C virus infection, or malignancies. Fortunately, PRP-like drug eruptions may be responsive to treatment with combinations of oral and topical corticosteroids, retinoids, and keratolytic agents, without requiring offending drug discontinuation.

Limitations of our review include a small sample size and the observational nature of the included studies, making it difficult to generalize our findings. Because the mean Naranjo score (4.32) indicated a possible adverse drug reaction, concluding causality between medication use and PRP eruptions may be difficult. Further clinical

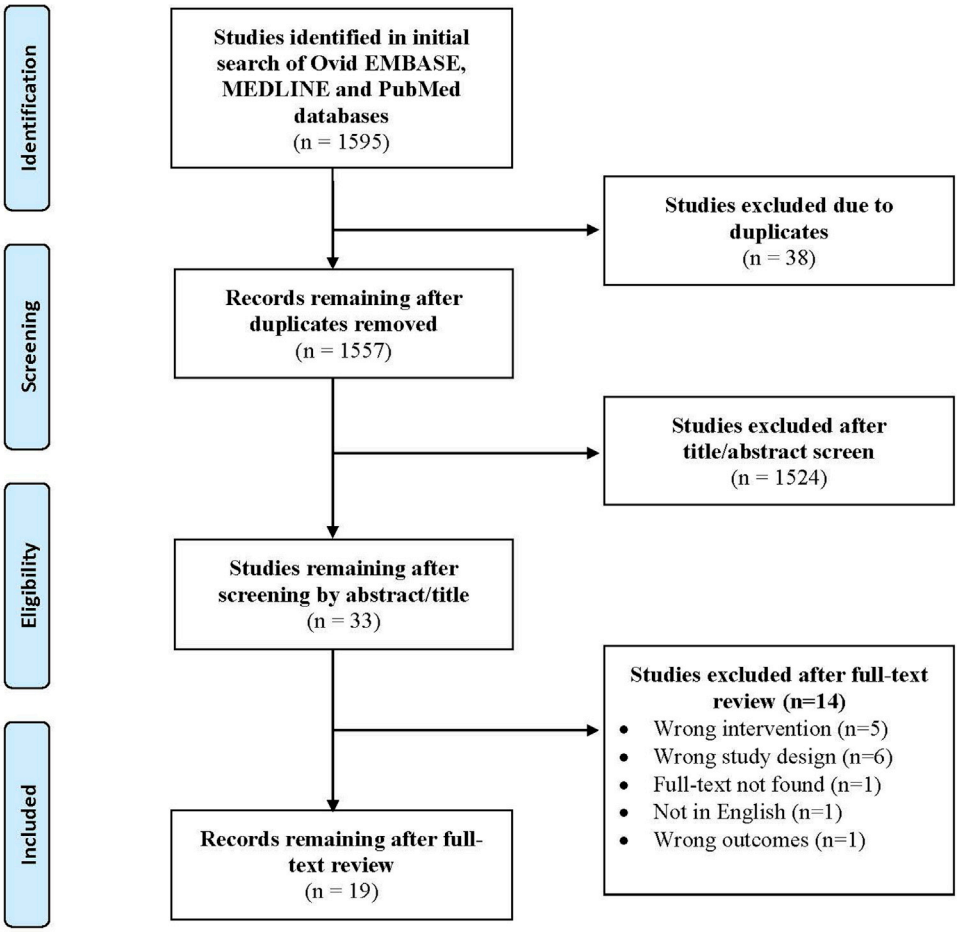

Fig 1. Flow diagram of literature screening using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRSMA) guidelines (adapted from http://prisma-statement.org).

Table I. Summary of reported pityriasis rubra pilaris (*PRP*) reactions to pharmacologic therapy

Study characteristics			Patient demo-graphics		Drug information			PRP Lesions				PRP outcomes[†]					
First author	Study design (level of evidence[*])	Sample size (n/N)	Age (y)/ sex	Comor-bidities	Drug (dose, frequency, duration)	Indication	Concomitant medications (dose, frequency, duration)	Family history of PRP	Morphologic features	Type and location	Biopsy findings	Latency period	Drug discontinua-tion timeline and duration	Treatment (dose, frequency, duration)	Resolution	Resolution period	Naranjo score[‡,1]
Alloo[2]	Case series (4)	n = 1/5	59/M	NR	Ponatinib (45 mg, daily)	Metastatic gastrointestinal stromal tumor	NR	NR	Red-orange, follicular-based papules, plaques with bran-like, powdery white scale	Thighs and axillae	NR	2 wk	NR	Triamcinolone cream	Complete resolution	NR	4
Alloo[2]	Case series (4)	n = 1/5	79/F	NR	Ponatinib (45 mg, daily)	Chronic myeloid leukemia	NR	NR	Pink-orange, thin plaquesDry skin with xerosis Plate-like patches	Proximal arms, axillae, lateral breasts, scalp Trunk Lower extremities	Subacute spongiotic dermatitis with orthokeratosis and parakeratosis	4 wk	NR	Period 1: Hydrocor-tisone 2.5% cream Period 2: Liberal emollients, keto-conazole shampoo, topical steroids Period 3: Topical tazarotene	Period 1: Partial resolution Period 2: Symptoms improved, but recurred upon steroid disconti-nuation Period 3: Complete resolution	Period 1: NR Period 2: NR Period 3: NR	4
Alloo[2]	Case series (4)	n = 1/5	65/M	NR	Ponatinib (45 mg, daily)	Metastatic gastrointestinal stromal tumor	NR	NR	Pruritic, pink, follicular-based papules Follicular prominence with hyper-keratotic spicules Alopecia Diffuse erythema, scale, hair thinning Ichthyosis vulgaris-like scale	Proximal thighs Beard area and eyebrows Lateral eyebrow Scalp Both legs	Superficial perifollicular fibrosis with focal zones of mild acanthosis and follicular dyskeratosis	10 d	NR	Ketoconazole shampoo and clobetasol solution for the scalp Topical tretinoin 0.1% cream and emollients for the face and trunk	Partial resolution	NR	4
Alloo[2]	Case series (4)	n = 1/5	72/M	NR	Ponatinib (45 mg, daily)	Metastatic gastrointestinal stromal tumor	NR	NR	Asymp-tomatic perifollicular erythema with prominent follicular hyperke-ratotic spicules	Chest, abdomen	Folliculocentric lymphocytic infiltrate with perifollicular fibrosis and follicular dyskeratosis	1 week	NR	Ammonium lactate 12% cream	Partial resolution	NR	4

Continued

Table I. Cont'd

Study characteristics			Patient demo-graphics		Drug information			PRP Lesions				PRP outcomes[†]					
First author	Study design (level of evidence[*])	Sample size (n/N)	Age (y)/ sex	Comor-bidities	Drug (dose, frequency, duration)	Indication	Concomitant medications (dose, frequency, duration)	Family history of PRP	Morphologic features	Type and location	Biopsy findings	Latency period	Drug discontinua-tion timeline and duration	Treatment (dose, frequency, duration)	Resolution	Resolution period	Naranjo score[‡,1]
Alloo[2]	Case series (4)	n = 1/5	62/M	NR	Period 1: Ponatinib (45 mg, daily) Period 2: Ponatinib (30 mg, daily; then return to 45 mg, daily)	Metastatic gastrointestinal stromal tumor	NR	NR	Minimally pruritic, orange-red, plate-like, annular plaques with islands of sparing Erythema, Scale, plate-like, xerotic patches	Bilateral cheeks, submental and posterior neck, upper back and bilateral upper arms Scalp Lateral thighs	NR	Period 1: 2 wk Period 2: NR	Period 1: After 3 mo of therapy due to elevated lipase levels Period 2: NR	Period 1: NR Period 2: Ketocona-zole shampoo for scalp, topical steroids, emollients, and topical tazarotene cream for trunk and extremities	Period 1: Complete resolution Period 2: Complete resolution	Period 1: Less than 7 d Period 2: NR	8
Eber[3]	Case report (5)	n = 1	50/F	NR	Ponatinib (45 mg, daily)	Chronic myelogenous leukemia	No	NR	Xerotic, atrophic, ichthyosiform pink plaques Red patches	Bilateral axillae, proximal thighs and abdomen Malar cheeks and forehead	Perifollicular fibrosis, alternating compact orthokeratosis and parakeratosis, sparse perivascular lymphocytic infiltrate	5 mo	No	Tretinoin 0.025% cream	Complete resolution	3 weeks	6
Jack[4]	Case report (5)	n = 1	53/M	NR	Ponatinib (45 mg, daily)	Chronic myeloid leukemia	NR	NR	Well-demarcated pink-yellow thin papules coalescent into plaques with scale and islands of sparing	Trunk, buttocks, arms, proximal legs and axillae	Thickened cornified layer characterized by alternating orthokeratosis and parakeratosis and a sparse superficial lymphocytic infiltrate	2-3 mo	No	Period 1: Topical mid- and high-potency corticos-teroids and acitretin (25 mg daily) Period 2: Acitretin (10 mg daily) and narrowband ultraviolet B phototherapy and keratolytics	Period 1: Complete resolution, but returned with temporary disconti-nuation of retinoid due to transaminitis Period 2: Complete resolution	Period 1: NR Period 2: NR	6

Krygier[5]	Case report (5)	n = 1	60/F	Type 2 diabetes mellitus, hypertension, hypercho -lesterolemia	Ponatinib (45 mg, daily)	Acute lymphoblastic leukemia	Metformin, olmesartan, simvastatin	NR	Pruritic, papules grouped in erythematous -squamous plaques in orange-red tones with islands of sparing	Back, abdomen, breasts, axillae	Orthokeratosis, perivascular inflammatory infiltrate of the superficial dermis	6 wk	No	Emollient and mometasone furoate 0.1%, 1 application/ d, 1 mo	Complete resolution	1 mo	3
Plana[6]	Case report (5)	n = 1	56/M	Mild psoriasis	Imatinib (400 mg/d)	Gastrointestinal stromal tumor	Topical drugs	NR	Large orange-red plaques with areas of uninvolved skin, and evidence follicular hyperke -ratosis Orange-red waxy keratoderma, with fissures Diffuse desquamation	Entire body surface Palms and soles Scalp	Irregular hyperkeratosis with alternating vertical and orthopara -keratosis and dilated hair follicles with keratinous plugs were also a distinctive feature	1 mo	No	Period 1: Narrow-band ultraviolet B therapy and topical corticosteroids Period 2: Acitretin (35 mg/d)	Period 1: No resolution Period 2: Complete resolution	Period 1: NR Period 2: 2 mo	3
Paz[7]	Case report (5)	n = 1	40/M	NR	Sorafenib (400 mg, twice daily)	Nonseminomatous germ cell carcinoma	Zolpidem, loratadine, hydrocodone, enoxaparin	No	Erythematous, scaly plaques and follicular papules	Lower back and bilateral buttocks	Alternating orthokeratosis and parakeratosis overlying a slightly acanthotic epidermis with infundibular keratinization	2 wk	No	Topical fluocinonide ointment	No resolution	3 mo	4
Atanaskova Mesinkovska[8]	Case report (5)	n = 1	65/M	Hypertension, hyper -lipidemia	Imiquimod cream (3.75%, once daily, for 6 wk: 2 wk on, 2 wk off, 2 wk on)	Actinic keratosis over left temple	NR	No	Painful, pruritic, salmon-colored erythematous plaques with superficial thin scales Sharply demarcated islands of normal unaffected skin Hyperkeratotic and erythematous, with mild ridging of nails	Entire face, scalp, neck, trunk, extremities Chest Both palms	Alternating parakeratosis and orthokeratosis in both vertical and horizontal directions, mildly acanthotic epidermis with confluent hypergranulosis. Epidermis had multiple small foci of acantholysis, located at suprabasilar or subcorneal levels. Very sparse superficial perivascular and interstitial lymphocytic infiltrate in the dermis	5 wk	No	Period 1: Oral prednisone, antihistamines Period 2: Triamcinolone 0.1% cream for body, desonide 0.5% cream for face (3 mo) Period 3: Whole-body narrowband ultraviolet B therapy (twice weekly)	Period 1: No resolution Period 2: Partial resolution Period 3: Partial resolution	Period 1: None Period 2: 3 mo Period 3: 1 wk	4

Continued

Table I. Cont'd

Study characteristics			Patient demo-graphics		Drug information			PRP Lesions				PRP outcomes[†]					
First author	Study design (level of evidence[*])	Sample size (n/N)	Age (y)/ sex	Comor-bidities	Drug (dose, frequency, duration)	Indication	Concomitant medications (dose, frequency, duration)	Family history of PRP	Morphologic features	Type and location	Biopsy findings	Latency period	Drug discontinua-tion timeline and duration	Treatment (dose, frequency, duration)	Resolution	Resolution period	Naranjo score[‡,1]
Gómez-Moyano[9]	Case report (5)	n = 1	56/M	NR	Imiquimod 5% cream	Superficial basal cell carcinoma on the back	NR	NR	Erythroderma with small islets of healthy skin Incipient peau d'orange Mild ectropion Small keratotic follicular papules	Diffuse Face Eyelid Chest	Alternating areas of parakeratosis and focal dyskeratosis with acantholysis, discreet spongiosis, and a band-like lymphocytic infiltrate in the superficial dermis	2 wk	Yes, discontinued (timeline NR)	Acitretin (35 mg/ day)	Complete resolution	2 mo	4
Leite[10]	Case report (5)	n = 1	60/F	NR	Imiquimod 5% cream (5 times/wk)	Actinic keratosis of the right chest	NR	NR	Ulceration of the initial lesion Erythematous Papulos-quamous lesions Erythroderma Ectropion Keratoderma	Right chest Scalp, face, trunk Diffusely Eyelid Palmoplantar	Psoriasiform hyperplasia of the epidermis, hyperpara-keratosis alternated with orthoke-ratosis, areas of hypogranu-losis, moderate superficial perivascular lympho-histiocytic infiltrate, and foci of acantholytic dyskeratosis	2 wk	Yes, discontinued (timeline NR)	Period 1: Topical corticos-teroids and oral antihista-mines Period 2: Prednisone, 40 mg/d Period 3: Methot-rexate (15 mg/ wk) and oral prednisone was withdrawn gradually	Period 1: Worsening of symptoms Period 2: Worsening of symptoms Period 3: Complete resolution	Period 1: NR Period 2: NR Period 3: Resolution began 3 mo after starting methotrexate	4

Yang[11]	Case report (5)	n = 1	67/M	Hypertension, hypercho -lesterolemia	Imiquimod 5% cream (3 times/wk)	Actinic keratoses on scalp and cheek	NR	NR	Rapidly spreading erythematous orange, follicularly based, papulos -quamous plaques Superficial desquamation	Scalp, trunk, upper extremities Fingertips	Acanthotic epidermis with psoriasiform hyperplasia, parakeratosis and focal spongiosis with superficial perivascular lymphocytic infiltrate and scattered eosinophils	2 wk	NR	Period 1: Prednisone, 60 mg taper over 4 wk Period 2: Oral acitretin	Period 1: None Period 2: Complete resolution	Period 1: 4 wk Period 2: 26 mo	3
Dewan[12]	Case series (4)	n = 1/3	49/F	NR	P13K/mTOR inhibitor	Grade III anaplastic oligodend -roglioma	NR	NR	Diffuse erythroderma with fine desquamative scale and madarosis Orange/pink erythroderma with islands of sparing Erythema and keratoderma Diffuse nonscarring alopecia, erythema, and perifollicular scale	Face Trunk and extremities Palms and soles Scalp	Pityriasiform changes with alternating orthokeratosis and parakeratosis, spongiotic dermatitis, numerous eosinophils	NR	Yes, discontinued, after 3 treatment periods	Period 1: High-potency topical steroids and oral antihista -mines Period 2: Short course of systemic prednisone Period 3: Acitretin (25 mg, daily)	Period 1: Partial resolution Period 2: Partial resolution Period 3: Partial resolution	Period 1: NR Period 2: NR Period 3: NR	5
Dewan[12]	Case series (4)	n = 1/3	67/M	NR	Ofatumumab and idelalisib	Chronic lymphocytic lymphoma/ small lymphocytic lymphoma	Trimethoprim/ sulfame -thoxazole (began 4 mo before symptom onset and was discontinued), duration NR	NR	Orange-red erythroderma with small islands of sparing, and overlying Pityriasiform scale Diffuse fine scaling and exfoliation, along with nonscarring alopecia Keratoderma Ectropion	Diffuse Scalp and eyebrows Palms and soles Eyelid	Pityriasiform and spongiotic dermatitis with eosinophils	5 mo	Yes, discontinued due to multiple life-threatening infections, timeline NR	Period 1: Systemic corticos -teroids Period 2: Prednisone taper and acitretin (10 mg, every other day), mid-potency topical corticos -teroids to the body, tazarotene cream to soles	Period 1: Partial resolution Period 2: Partial resolution	Period 1: NR Period 2: NR	5

Continued

Table I. Cont'd

Study characteristics			Patient demo -graphics		Drug information			PRP Lesions				PRP outcomes[†]					
First author	Study design (level of evidence[*])	Sample size (n/N)	Age (y)/ sex	Comor -bidities	Drug (dose, frequency, duration)	Indication	Concomitant medications (dose, frequency, duration)	Family history of PRP	Morphologic features	Type and location	Biopsy findings	Latency period	Drug discontinua -tion timeline and duration	Treatment (dose, frequency, duration)	Resolution	Resolution period	Naranjo score[‡,1]
Dewan[12]	Case series (4)	n = 1/3	68/M	NR	Idelalisib	Small lymphocytic leukemia	NR	NR	Diffuse, orange-red patches with follicular prominence and islands of sparing Exfoliative scale	Trunk and extremities Palms and soles	Subacute spongiotic dermatitis with Pityriasiform scale and superficial perivascular lymphocytic infiltrate	6 wk	Yes, discontinued 6 wk after symptom onset	Oral prednisone taper (2 wk) and mid-potency topical steroids	Complete resolution	2 mo	4
Stalling[13]	Case report (5)	n = 1	55/M	NR	Telaprevir (1650 mg every 8 h)	Hepatitis C virus	Ribavirin (1200 mg/d) and PEGylated interferon-α-2a (180 μg/wk subcutaneously)	NR	Generalized, salmon-red erythema with coarse desquamation and islands of sparing	Trunk, extremities, head, neck, soles of feet	Parakeratosis with basilar vacuolization, dyskeratotic keratinocytes, and a predo -minance of superficial perivascular lymphocytes with few eosinophils	6 wk	NR	Triamcinolone, 0.1% ointment and 1 mg/ kg/d prednisone taper over 3 wk	Complete resolution	3 wk	4
Cheung[14]	Case report (5)	n = 1	53/M	NR	Sofosbuvir	Hepatitis C virus	Peginterferon -α-2a, ribavirin	NR	Erythrodermic, diffuse salmon-to-orange colored finely scaly confluent patches and plaques Hyperkeratotic follicular papules coalescing into scaly orange plaques Islands of sparing Focal areas of yellowish waxy keratoderma	Scalp, face, trunk, upper extremities Lower extremities Face, abdomen, lower extremities Palms and soles	Follicular plugging, hyperkeratosis, alternating orthokeratosis, parakeratosis with peri-infundibular accentuation and irregular acanthosis with hypergranulosis overlying a mildly dense superficial perivascular and perifollicular lympho -histiocytic infiltrate	2 wk	No	Prednisone 40 mg daily taper, triamcinolone 0.1% cream, hydroxyzine	Partial resolution	4 mo	5

Badri[15]	Case report (5)	n = 1	29/M	N	Neutral protamine Hagedorn insulin (12 IU morning, 8 IU evening) and soluble regular insulin (4 IU BID)	Type 1 diabetes mellitus	No	No	Large areas of erythematous orange scaly plaques with small islands of uninvolved skin, and follicular keratotic papules Orange-red waxy keratoderma with fissures	Trunk and limbs Palms and soles	Irregular hyperkeratosis with orthokeratosis and parake -ratosis, dilated hair follicles, and keratinous plugs	3 d	Yes, discontinued 1week after initiation	Betamethasone ointment (30 g daily) and petrolatum	Complete resolution	2 mo	3
Bell[16]	Case report (5)	n = 1	72/M	Melanoma	Angiotensin-converting enzyme inhibitor ramipril	NR	NR	NR	Largely eczematous eruption Psoriasiform changes Marked hyperkeratosis, mild pitting of nails	Diffusely Knees Palmoplantar	Follicular hyperkeratosis, perifollicular parakeratosis and hyperke -ratosis with focal hyperke -ratosis alternating horizontally and vertically	1 mo	Discontinued 18 d after rash onset	Period 1: Emollients, topical mometasone furoate, tapering course of oral prednisone Period 2: Betametha -sone with salicylic acid for acral sites	Period 1: Partial resolution Period 2: Complete resolution	Period 1: 4 wk Period 2: NR	8
Coleman[17]	Case report (5)	n = 1	64/M	NR	Pembrolizumab	Stage IV squamous cell carcinoma	NR	N	Erythroderma with confluent red-orange patches with dry, desquamative scale Keratoderma with waxy scale	Began on scalp and distal extremities, then abruptly spread to remainder of body Palmoplantar	Acanthosis of the epidermis with orthoke -ratosis and parakeratosis, mild spongiosis, and intact granular layer. Superficial perivascular inflammatory infiltrate in the dermis	2 wk	Yes discontinued. Timeline NR	Period 1: Prednisone (40 mg/d, tapered over 4 wk) Period 2: Acitretin (50 mg/d) and Triamcino -lone ointment (both over 4 wk)	Period 1: No resolution Period 2: Partial resolution	Period 1: 4 wk Period 2: 8 wk	3
Brown[18]	Case report (5)	n = 1	70/M	Hypertension, hypercho -lesterolemia	Intravitreal injection of bevacizumab	Age-related macular degeneration	Valsartan, simvastatin	NR	Erythematous, edematous, scaly, intensely pruritic, exfoliative erythroderma with islands of sparing	Face, scalp, trunk, hands, feet	Foci of parake -ratosis and follicular plugging, superficial perivascular infiltrate of lymphocytes and eosinophils	4 d	NR	Period 1: Prednisone Period 2: Prednisone taper, desonide 0.05% cream for the face, triamcino -lone 0.1% topical cream for the body Period 3: Higher prednisone taper, clobetasol 0.05% ointment	Period 1: Partial resolution Period 2: worsening symptoms Period 3: Partial resolution	Period 1: 10 d Period 2: 1 wk Period 3: 2 wk	2

Continued

Table I. Cont'd

Study characteristics			Patient demo-graphics		Drug information			PRP Lesions				PRP outcomes[†]					
First author	Study design (level of evidence*)	Sample size (n/N)	Age (y)/ sex	Comor-bidities	Drug (dose, frequency, duration)	Indication	Concomitant medications (dose, frequency, duration)	Family history of PRP	Morphologic features	Type and location	Biopsy findings	Latency period	Drug discontinua-tion timeline and duration	Treatment (dose, frequency, duration)	Resolution	Resolution period	Naranjo score[‡1]
Gajinov[19]	Case report (5)	n = 1	61/M	NR	Simvastatin 10 mg daily	Moderate hyperlipidemia	No	NR	Erythroderma, with sharply demarcated islands of sparing Keratoderma Ectropion	Diffuse Palmoplantar Eyelid	Suprabasilar acantholysis, alternating hyper- and parakeratosis, dyskeratosis, follicular plugs, perivascular inflammation in upper dermis	1 wk	Yes, discontinued 5 d after symptom onset	Period 1: Methylpred-nisolone (80 mg daily, tapering down) Period 2: Acitretin (35 mg daily)	Period 1: No response Period 2: Complete resolution	Period 1: 4 wk Period 2: 3 mo	4
Salman[20]	Case report (5)	n = 1	53/F	NR	Infliximab (6 weeks)	Takayasu's arteritis	Methylpredni-solone, acetylsali-cylic acid, panto-prazole, calcium, vitamin D	No	Orange-to-salmon-colored, scaly patches with islands of sparing and follicular, erythematous papules Erythema with fine scales	Trunk, extremities Scalp and face	Hyperkeratosis and focal parakeratosis, necrotic keratinocytes, vacuolar degeneration, and mild acanthosis in the epidermis and extravasated erythrocytes and superficial perivascular mononuclear infiltration in dermis	2 wk	Yes (timeline NR)	None	Complete resolution	NR	4

BID, Twice daily; *CR*, complete resolution; *F*, female; *M*, male; *mTOR*, mammalian target of rapamycin; *NR*, not reported; *PEG*, polyethylene glycol; *P13K*, phosphoinositide 3-kinase inhibitors; *PR*, partial resolution.

*Level of evidence for all included articles was assessed using the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence.

[†]Latency period: time between drug initiation and onset of PRP lesions; Resolution: time between PRP treatment initiation and measurement of resolution.

[‡]Naranjo criteria[1] were used to assess the probability that each case with PRP was related to drug therapy. Naranjo score of 0 = doubtful association of PRP with drug, score of 1-4 = possible association, score of 5-8 probable association, score of ≥9 = definite association.

studies are needed to understand the pathogenesis for PRP eruptions associated with pharmacologic agents.

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Reprints not available from the authors.

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Development of morphea in patients receiving biologic therapies: A systematic review

To the Editor: An infrequently reported cutaneous complication of biologic treatment is the onset of localized scleroderma or morphea. Given the increasing use of biologic therapy worldwide, it is essential for health care providers to anticipate and manage potential adverse effects. This review aims to summarize reports of morphea development in patients receiving biologic therapies targeting inflammatory pathways implicated in psoriasis.

An EMBASE and MEDLINE search was conducted on May 8, 2020, in accordance with PRISMA