

Ribociclib induced vitiligo-like lesions

Dear Editor,

Ribociclib is a cyclin-dependent kinase (CDK 4/6) inhibitor that is used in metastatic breast cancer treatment. We herein report a rare case of ribociclib-induced vitiligo-like lesions and a comprehensive literature review of this uncommon adverse effect which summarises the features of 25 reported cases till date.¹⁻⁶ Considering the increasing use of this medication and the social stigma associated with vitiligo, it is crucial to be aware of this adverse effect and counsel the patients prior to starting the therapy.

A 51-year-old female with metastatic breast carcinoma was started on injection ribociclib 400 mg/day for 3-weeks/month with letrozole 2.5 mg/day, following which she developed depigmented macules over the face, neck and forearms, ten months after therapy initiation [Figure 1a]. There was no prior history of an autoimmune condition in the patient or family. Dermoscopy revealed ill-defined white structureless areas, reduced pigment-network, scaling, reticulated telangiectasias, coiled-hairs (likely secondary to

chemotherapy) and leukotrichia [Figure 1b]. A skin biopsy showed significant loss of melanocytes and focal melanin pigment incontinence favouring vitiligo [Figure 1c]. She was treated with 0.1% mometasone cream and 0.1% tacrolimus ointment. Follow-up at 6-months revealed a stable disease with minimal repigmentation.

CDK4/6 inhibitors are associated with a wide range of cutaneous adverse-effects, the most common of which is alopecia, followed by rash and pruritus, usually reported within 1–4 months of treatment initiation. Other rare side-effects include trichorrhexis, onychoclasia, erythema multiforme, bullous dermatitis and vitiligo.¹ Ribociclib-induced vitiligo-like lesions are reported more commonly in the 4th–7th decade, a common age-group for breast cancer. It predominantly involves the photo-exposed areas; however, it may also involve the trunk and extremities. The interval between ribociclib initiation and the development of vitiligo varies between 3 and 10 months and the lesions are commonly pruritic. There are no treatment guidelines;

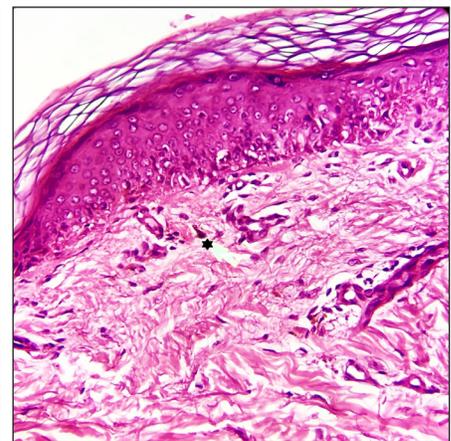
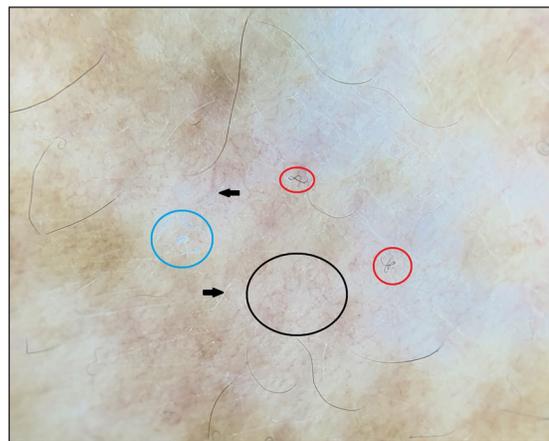


Figure 1a: Multiple depigmented macules over face, neck and forearms.

Figure 1b: Dermoscopy showing ill-defined white structureless areas due to pigment loss, reduced pigment network, reticulated telangiectasias (black circle), scaling (blue circle), coiled hairs (red circles) likely due to chemotherapy and leukotrichia (black arrows). (Illuco IDS-1100, Polarized 10x).

Figure 1c: Histopathology from the forearm showing significantly reduced melanocytes in the basal layer and focal melanin pigment incontinence (five-point star) favouring vitiligo (Haematoxylin and eosin, 400x).

How to cite this article: Kothari R, Darling HS, Bhatnagar A, Janney M, Mohan S, Kumar R. Ribociclib induced vitiligo-like lesions. *Indian J Dermatol Venereol Leprol*. doi: 10.25259/IJDVL_239_2024

Received: February, 2024 **Accepted:** July, 2024 **Epub Ahead of Print:** August, 2024

DOI: 10.25259/IJDVL_239_2024

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Table 1: Characteristics of ribociclib-induced vitiligo-like lesions in literature.

Study	No. of patients	Patient's age	Latency of vitiligo lesions	Distribution of lesions	Symptoms	Treatment	Outcome
Raschi E <i>et al.</i> ¹	6	-	-	-	-	-	-
Silvestre-Torner <i>et al.</i> ²	1	70 years	8 months	Face, neck, with affectation of hair follicle	Asymptomatic	-	-
Anjaneyan <i>et al.</i> ³	1	78 years	7 months	Face, hands, forearms, arms, thighs, legs, feet, chest, abdomen	Pruritus	Betamethasone (5 mg two consecutive days/week), levocetirizine (5 mg at night) & moisturisers	Lesions didn't progress & mild improvement.
Chan <i>et al.</i> ⁴	2	71 years; & 54 years	7 months; & 3 months	Legs, arms, V of neck, cheeks, posterior neck, back; & Face, arms, and trunk	-	-	No repigmentation at the 12-month follow-up; & depigmentation lessened over several months but some remain over her arms and upper chest.
Sharaf <i>et al.</i> ⁵	1	78 years	5 months	Face, hands, feet	-	Topical steroids	Little improvement
Sollena <i>et al.</i> ⁶	14	40–79 years	-	Face, hands, and chest, trunk, extremities	Pruritus	Topical calcineurin inhibitors ± topical/systemic steroids ± UVB	Partial response
Present case	1	51 years	10 months	Face, neck, & forearms	Asymptomatic	Topical calcineurin inhibitors + topical steroids	Lesions did not progress & showed little improvement

however, topical steroids/calcineurin inhibitors, emollients, and antihistamines may be used. In extensive cases, oral steroids and phototherapy may be tried. The response to therapy is discouraging in almost all the cases and the aim should be to halt the disease progression rather than aiming for repigmentation.¹⁻⁶ The depigmentation may lessen over several months after stopping the drug; however, a few areas may remain depigmented.⁴ None of the reported cases, except one, had a history of vitiligo.⁶ The characteristics of all the reported cases are summarised in Table 1. The exact cause of these lesions is not known. It is hypothesised that apoptosis of the melanocytes secondary to CDK4/6 inhibitors and keratinocyte precursors with altered proliferation may be responsible. We also hypothesise that there may be a role of ultraviolet radiation (UVB) due to the characteristic distribution of the lesions. UVB radiation induces DNA damage, which may be more pronounced in the background of CDK 4/6 inhibition. There is scanty data to assign any prognostic significance to these lesions and it may be considered a class-specific adverse-effect.

The increasing use of ribociclib and the possibility of underreporting vitiligo due to social stigma associated with the condition, emphasise the importance of awareness of this adverse-effect and counselling the patients prior to initiation of chemotherapy, as it is usually resistant to treatment.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

Rohit Kothari, HS Darling¹, Anuj Bhatnagar, Manasa Janney, Shilpa Mohan, Rahul Kumar

Departments of Dermatology, ¹Medical Oncology & Haemato-Oncology, Command Hospital Air Force, Bangalore, India.

Corresponding author:

Dr. Rohit Kothari,
Department of Dermatology, Command Hospital Air Force,
Bangalore, India.
rohitkothari3422@gmail.com

References

- Raschi E, Fusaroli M, La Placa M, Ardizzoni A, Zamagni C, Poluzzi E, *et al.* Skin toxicities with cyclin-dependent kinase 4/6 inhibitors in breast cancer: Signals from disproportionality analysis of the FDA adverse event reporting system. *Am J Clin Dermatol* 2022;23: 247–55
- Silvestre-Torner N, Aguilar-Martínez A, Echarri-González MJ, Tabbara-Carrascosa S, Román-Sainz J, Gruber-Velasco F. Ribociclib-induced vitiligo: A case report. *Dermatol Pract Concept* 2022;12: e2022045.
- Anjaneyan G, Keechilat P, Duraisamy P, Eapen M. Ribociclib-induced extensive vitiligo-like lesions: Possible pathomechanisms with clinical, dermoscopic and histological correlation. *BMJ Case Rep* 2022;15:e248782.
- Chan OB, Su JC, Yazdabadi A, Chan A. Drug induced vitiligo-like depigmentation from a CDK 4/6 inhibitor. *Asia Pac J Clin Oncol* 2022;18:e154–e156.
- Sharaf B, AlMasri R, Abdel-Razeq N, Salama O, Hamad I, Abunasser M, *et al.* Vitiligo-like lesions in a patient with metastatic breast cancer treated with cyclin-dependent kinase (CDK) 4/6 inhibitor: A case report and literature review. *Clin Cosmet Investig Dermatol* 2022;15: 5–10.
- Sollena P, Nikolaou V, Soupos N, Kotteas E, Voudouri D, Stratigos AJ, *et al.* European Network for cutaneous adverse event of oncologic drugs (ENCADO) group. Vitiligo-like lesions in patients with advanced breast cancer treated with cyclin-dependent kinases 4 and 6 inhibitors. *Breast Cancer Res Treat* 2021;185:247–53.