Response rates of cutaneous melanoma metastases to diphencyprone: A meta-analysis

To the Editor: Cutaneous metastases of melanoma represent a heterogeneous group of clinical presentations, and several treatment options have been reported. In this context, diphencyprone (DPCP) has been used in some case series as a cost-effective strategy with acceptable toxicity and good response rates. (A full list of references is provided in the supplemental material; available via Mendeley at https://doi.org/10.17632/rmh9nzy8s8.2). DPCP is a potent contact sensitizer historically used as immunotherapy in alopecia areata and viral warts, with a sensitization rate reaching 99% in some studies. The earliest reports of DPCP used for cutaneous melanoma metastases included patients with satellite lesions who received a combination of DPCP with cimetidine, dacarbazine, and radiotherapy.

This study aims to evaluate DPCP response rates in previously reported case series as a meta-analysis. Briefly, 2 authors searched relevant databases for studies that reported the use of DPCP for the management of melanoma cutaneous metastases. Random or fixed effects models were fitted to obtain the summary measures. Heterogeneity was examined by using the Q statistic and by the I^2 statistics. The random effects model was preferred when I^2 was higher than 40%; otherwise, the fixed effect model was fitted. All statistical tests were 2 sided, and the significance level was fixed at 5% for all tests. (A full description of the methodology is available in the supplemental material).

From 233 studies retrieved from the databases, 6 studies were ultimately used in the meta-analysis (Supplemental Fig 1; available via Mendeley at https://doi.org/10.17632/rmh9nzy8s8.2). Out of 179 patients from the selected studies, 55 (30.7%) had complete response (CR), 60 (33.51%) presented partial response, 41 (22.9%) did not respond, and 24 (13.4%) developed progression of disease, according to each study's assessment of response (Supplemental Table I and Supplemental Fig 2; available via Mendeley at https://doi.org/10.17632/rmh9nzy8s8.2). From this analysis, 43 (47.7%) patients required lower doses to remain on the treatment. There were 15 patients who discontinued treatment because of progression of disease, and 5 other patients who discontinued because of toxicity. The most common reported adverse effects were blisters, local erythema, and pruritus with skin ulceration.

The CR rate with random effects model presented was 29.94% (95% confidence interval, 20.65-41.22), with I^2 = 48% (Fig 1). The evaluation of overall response rate (ORR, equal to CR + partial response) with the random effects model was 60.48% (95% confidence interval, 45.90-73.42), with I^2 = 66% (Fig 2).

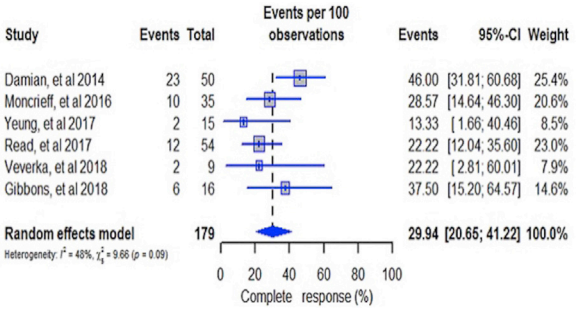

Fig 1. Forest plot of complete response. Studies included Damian et al[1]; Moncrieff M, Dadhill M, Garioch J, et al. Topical diphencyprone for the treatment of locoregional intralymphatic melanoma metastases of the skin; the 5-year Norwich experience. *Br J Dermatol* 2016; 174(5):1141-1142; Yeung et al[2]; Read et al[3]; Veverka et al[4]; and Gibbons et al.[5] *CI,* Confidence interval.

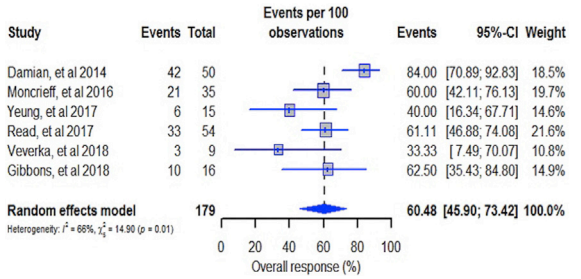

Fig 2. Forest plot of overall response. Studies included Damian et al[1]; Moncrieff M, Dadhill M, Garioch J, et al. Topical diphencyprone for the treatment of locoregional intralymphatic melanoma metastases of the skin; the 5-year Norwich experience. *Br J Dermatol* 2016;174(5):1141-1142; Yeung et al[2]; Read et al[3]; Veverka et al[4]; and Gibbons et al.[5] *CI,* Confidence interval.

The 60.48% ORR and 29.94% of CR rate shows encouraging data when compared to other approved therapies for the treatment of melanoma in transit metastases. These data, in addition to the high cost effectiveness of treatment (less than US$1/week), suggest that DPCP is a viable option as a single agent in patients who are not candidates for targeted therapies or immunotherapies but also in conjunction with these therapies, when feasible, because both scenarios happened in the reported studies.

Despite the few studies and the small number of patients involved, ORR and CR rate are consistent and balanced across studies, even with epidemiologic differences among them. This meta-analysis shows satisfactory response rates, which makes us believe

that larger studies should be considered to evaluate how DPCP might play a role in treatment algorithms for a subset of patients with cutaneous melanoma.

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Guselkumab dosing interval optimization in adult patients with psoriasis: A retrospective, multicenter case series

To the Editor: The currently approved dosing schedule for guselkumab in Canada is 100 mg subcutaneous injection at week 0 and week 4, followed by maintenance dosing every 8 weeks thereafter.[1] Three randomized controlled trials have shown that guselkumab has a favorable efficacy and safety profile.[2-4] Currently, to our knowledge, there are no published data on the off-label regimens for guselkumab. This case series aims to investigate the effectiveness and safety of guselkumab dosing interval optimization.

A retrospective chart review was conducted at 2 academic hospitals and 1 community dermatology clinic in Ontario, Canada. Responders were defined

Table I. Demographics, efficacy outcomes, and safety outcomes of patients using regimens with increased guselkumab frequency

Variable*	Value
Sex, n (%)	
Male	16 (59.3)
Female	11 (40.7)
Age, y, mean ± SD	54.7 ± 12.3
Number of previously failed treatments, mean ± SD	
Systemics	1.4 ± 1.1
Biologics	2.1 ± 1.9
Standard dosing	
Baseline PASI, mean ± SD (n)	11.9 ± 5.2 (16)
Treatment duration before shortening the dosing interval, wk, mean ± SD	32.2 ± 24.7
Off-label shortened dosing interval regiment	
PASI before frequency escalation, mean ± SD (n)	7.1 ± 6.4 (18)
PGA scores before frequency escalation, n	0
1	1
2	4
3	3
4	1
Dosing regimen, n (%)	
100 mg every 6 weeks	6 (22.2)
100 mg every 4 weeks	21 (77.8)
Follow-up time, wk, mean ± SD	19.0 ± 6.7
Patients achieving efficacy, n (%)	20 (74.1)
PGA 0	6.0 (22.2)
PGA 1	14.0 (51.9)
Nonresponders to shortened-interval regimen, n (%)	7.0 (25.9)
Concomitant systemic agents, n (%)	2.0 (7.4)
Methotrexate	1.0 (3.7)
Cyclosporine	1.0 (3.7)
Reported adverse events, n (%)	3.0 (11.1)
Common cold	1.0 (3.7)
Gastrointestinal symptoms	1.0 (3.7)
Headache and dizziness	1.0 (3.7)

PASI, Psoriasis Area and Severity Index; *PGA,* Physician Global Assessment.
*n indicates the number of individuals meeting criteria.