Efficacy and Safety of Topical Nitric Oxide–Releasing Berdazimer Gel in Patients With Molluscum Contagiosum: Results from B-SIMPLE4, A Phase 3 Randomized Clinical Trial

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Synopsis

RCT: Efficacy and Safety of Topical Nitric Oxide-Releasing Berdazimer Gel in Patients With Molluscum Contagiosum

POPULATION
441 Males, 450 Females

Immunocompetent children and adults aged ≥6 mo with 3-70 raised molluscum contagiosum (MC) lesions

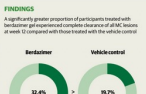
Mean age, 6.6 y (range, 0.9–49.0 y)

INTERVENTION
891 Participants randomized

444 Berdazimer: Topical, once-daily application of berdazimer gel, 10.3%, to all active MC lesions for up to 12 wk

447 Vehicle: Topical, once-daily application of vehicle control gel to all active MC lesions for up to 12 wk

FINDINGS
A significantly greater proportion of participants treated with berdazimer gel experienced complete clearance of all MC lesions at week 12 compared with those treated with the vehicle control



OR, 2.0 (95% CI, 1.5-2.8); P <.001

SETTINGS / LOCATIONS
55 Clinics in the US

PRIMARY OUTCOME
Proportion of participants who achieved complete clearance of all treatable MC lesions at week 12, with clearance defined as a lesion count of 0 as documented by a consistent assessor

Browning JC, Enloe C, Cartwright M, et al. Efficacy and safety of topical nitric oxide–releasing berdazimer gel in patients with molluscum contagiosum: a phase 3 randomized clinical trial. *JAMA Dermatol*. Published online July 13, 2022. doi:10.1001/jamadermatol.2022.2721

https://media.jamanetwork.com/news-item/visual-abstract-efficacy-safety-of-berdazimer-gel-for-molluscum-contagiosum/

Importance

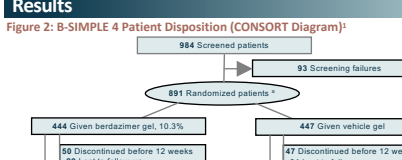
Molluscum Contagiosum (MC)

Molluscum contagiosum is caused by a pox virus and is characterized by small, round, firm, umbilicated, often painless bumps[1-4]

There are **4 known types** of MC virus (MCV1, 2, 3, and 4), with MCV1 and MCV2 being the most common[1,5]

MC can take a long time to resolve, ranging from **13 months to 5 years**[1,5,6,7]

Absence of an animal or cell culture model for MC poses a **research challenge**[8]



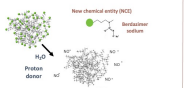
FDA, US Food and Drug Administration.
1. Silverberg NB. *Cutis*. 2019;104(5):301-305. 2. Mirza-Romero R, et al. *Clin Cosmet Investig Dermatol*. 2019;12:373-381. 3. Bhatia N. *Pract Derm*. 2021;34-35. 4. Hebert AJ, et al. *Pediatrics*. 2013;132(5):e1650-e1653. 5. Coyner T. *J Dermatol Nurs Assoc*. 2009;1(3):115-120. 6. Olsen JR, et al. *Lancet Infect Dis*. 2015;15(2):190-195. 7. Molluscum contagiosum: diagnosis and treatment. American Academy of Dermatology. Accessed July 12, 2022. https://www.aad.org/public/diseases/a-z/molluscum-contagiosum-treatment. 8. Brauer A, et al. *Pediatr Dermatol*. 2005;22(4):287-294. 9. About molluscum. Accessed December 3, 2021. https://aboutmolluscum.com/. 10. Global molluscum contagiosum epidemiology forecast to 2028. December 16, 2019. Accessed December 3, 2021. https://www.businesswire.com/news/home/20191216005278/en/Global-Molluscum-Contagiosum-Epidemiology-Forecast-to-2028--ResearchAndMarkets.com. 11. Basdag H, et al. *Pediatr Dermatol*. 2015;32(3):353-357. 12. Ong SK, et al. *Pediatr Dermatol*. 2021;38(5):1400-1403.

Berdazimer Gel, 10.3%

- A nitric oxide (NO)–releasing medication in phase 3 clinical development

If FDA approved, it could be the first potential prescription treatment for MC[1]

- **Berdazimer sodium is a new chemical entity (NCE)[2]**
- It is a macromolecule composed of a polysiloxane backbone with covalently bound *N*-diazeniumdiolate NO donors[3]
- Co-administration with a proton donor promotes NO release from the macromolecule[3]



Berdazimer gel, 10.3% is an investigational gel that consists of 2 components[3]

Gel containing berdazimer sodium

Hydrogel that promotes nitric oxide release

Berdazimer gel, 10.3% addresses many of the challenges of NO delivery[4]

Berdazimer gel 10.3% is not FDA approved. The safety and effectiveness of berdazimer gel, 10.3% has not been established. The mechanism of action of berdazimer gel, 10.3% is unknown.
1. Browning JC, et al. *JAMA Dermatol*. 2022;158(8):871-878. doi:10.1001/jamadermatol.2022.2721 2. Data on File. FDA communication. Novan Inc 2022. 3. Maeda-Chubachi T, et al. *Int Immunopharmacol*. 2021;1(3):100019. 4. Del Rosso JQ, Kircik LH. *J Drugs Dermatol*. 2017;16(1):s4-s10.

Objective

- To assess the efficacy and safety of berdazimer gel, 10.3%, a novel topical NO–releasing medication, for the treatment of MC

Methods

Figure 1: B-SIMPLE 4 Study Design

- Multicenter, randomized, double-blind, vehicle-controlled, parallel trial to evaluate the efficacy and safety of berdazimer gel, 10.3% once daily for the treatment of MC (NCT04535531)[1,2]

Key Inclusion Criteria
- Male and female patients
- ≥6 months of age
- 3-70 lesions at baseline

Randomization 1:1

Vehicle gel once daily

Berdazimer gel, 10.3% once daily

Additional 12-week safety follow-up (no treatment)

Patients or their caregivers applied for 12 weeks to all treatable lesions (baseline and new)

Primary Endpoint
- Proportion of patients with complete clearance of all treatable MC lesions at week 12

Representative Secondary Endpoints
- Proportion of patients achieving a lesion count of 0 or 1 of all treatable MC at week 12
- Proportion of patients achieving ≥90% reduction from baseline in the number of all treatable MC lesions at week 12

Safety Measures
- Treatment-emergent adverse events (TEAEs) and local skin reactions (LSRs) through week 24

Berdazimer gel 10.3% is not FDA approved. The safety and effectiveness of berdazimer gel, 10.3% has not been established. The mechanism of action of berdazimer gel, 10.3% is unknown. Vehicle gel does not contain berdazimer.
1. ClinicalTrials.gov. NCT04535531. Accessed November 9, 2021. https://clinicaltrials.gov/ct2/show/NCT04535531. 2. Browning JC, et al. *JAMA Dermatol*. 2022;158(8):871-878. doi:10.1001/jamadermatol.2022.2721

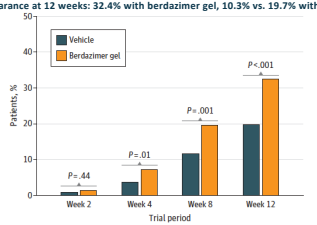
Results

Figure 2: B-SIMPLE 4 Patient Disposition (CONSORT Diagram)[1]

[a]After 200 patients were randomized, a data safety monitoring board reviewed all available unblinded safety data, including completed patch testing results for allergic dermatitis, and recommended that the study proceed without modification.

Primary Endpoint

Figure 3A: Berdazimer Gel, 10.3% Demonstrated Statistically Significant Efficacy in the Primary Endpoint of Complete Clearance of All Lesions By Week 12[1]



Secondary Endpoints

- Berdazimer gel, 10.3% demonstrated statistically significant efficacy in **secondary endpoints** of 0 or 1 remaining lesion and ≥90% clearance at week 12[1]

Figures 3B, 3C: A Higher Proportion of Patients Treated with Berdazimer Gel Compared with Vehicle Gel Had 0 Or 1 Lesion at Week 12 and ≥90% Complete Clearance at Week 12

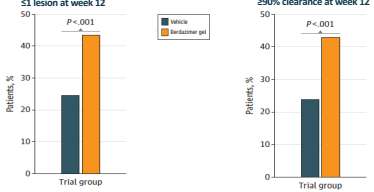
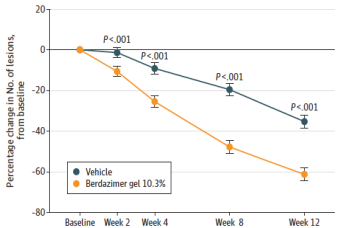


Figure 4: In B-SIMPLE 4 the Mean Percent Change from Baseline Lesion Count Was Statistically Significant for Berdazimer Gel vs. Vehicle Gel[1]



Safety and Tolerability

Table 1: Treatment-emergent Adverse Events (TEAEs)

- TEAEs were mostly mild if they occurred, with few TEAEs leading to study drug discontinuation[1]

TEAE	Berdazimer gel, 10.3% (n=444) n (%)	Vehicle gel (n=447) n (%)
Patients with ≥1 TEAE	191 (43.0)	103 (23.0)
Patients with ≥1 serious TEAE	0	1 (0.2)[a]
Patients with ≥1 TEAE leading to study drug discontinuation	18 (4.1)	3 (0.7)
Patients with a TEAE leading to death	0	0
Maximum severity		
Mild	108 (24.3)	75 (16.8)
Moderate	7 (17.6)	26 (5.8)
Severe	5 (1.1)	2 (0.4)
Patients with TEAE leading to study drug discontinuation	18 (4.1)	3 (0.7)
Application-site pain	10 (2.3)	3 (0.7)
Application-site dermatitis	4 (0.9)	0

[a]Humerus fracture deemed not treatment related.

Table 2: TEAEs At Application Site Affecting ≥5% of Patients in Either Group, By Severity

Application-site TEAE	Berdazimer gel, 10.3% (n=444) n (%)			Vehicle gel (n=447) n (%)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Patients with ≥1 TEAE	108 (24.3)	78 (17.6)	5 (1.1)	75 (16.8)	26 (5.8)	2 (0.4)
Application-site pain [a]	64 (14.4)	18 (4.1)	1 (0.2)	21 (4.7)	2 (0.4)	0
Application-site erythema	25 (5.6)	26 (5.9)	1 (0.2)	5 (1.1)	1 (0.2)	0
Application-site pruritus	25 (5.6)	8 (1.8)	0	4 (0.9)	1 (0.2)	0
Application-site exfoliation	11 (2.5)	16 (3.6)	0	0	0	0
Application-site dermatitis	8 (1.8)	16 (3.6)	2 (0.5)	1 (0.2)	2 (0.4)	0
Application-site scar [b]	20 (4.5)	1 (0.2)	0	28 (6.3)	0	0

[a]**Transient pain** is discussed in the text, not the table.
[b]**Application-site scar**: The US Food and Drug Administration required that temporary epidermal atrophy from the resolution of a space occupying lesion be captured as a scar. All scars, including pitted scars (indentations), were considered AEs.

Summary of Local Skin Reactions (LSRs)[1]

- LSRs were evaluated based on a 0, 1, 2, 3, 4 scoring system
- Flaking/scaling, crusting, and swelling were not present in >90% of patients at week 12
- Most patients (≥92%) in both groups had an absence of vesiculation/pustulation and erosion/ulceration at week 12

Table 3: Erythema Was Most Frequently Observed LSR Throughout Study[1]

LSR–Erythema (events) by week, n (n/N) [a]	Berdazimer gel, 10.3% (n=444)	Vehicle gel (n=447)
Week 2	206 (50)	100 (24)
Week 4	195 (47)	89 (21)
Week 8	166 (42)	81 (20)
Week 12	110 (28)	82 (21)
Erythema severity at week 12, %		
0 (not present)	71.8%	79.3%
1 (slightly pink)	16.9%	14.1%
2 (pink or light red)	7.9%	5.5%
3 (red, restricted to treatment area)	2.6%	0.5%
4 (red extending outside treatment area)	0.8%	0.5%

[a] Percentages for LSRs over time are based on observed data at each timepoint and represent the sum of all patients with a score of 1, 2, 3, or 4.

Table 4: Summary of LSRs by Composite Score and Other Local AEs[1]

Mean LSR composite score by week (LSR scores were summed, range, 0-24)[a]	Berdazimer gel, 10.3% (n=444)	Vehicle gel (n=447)
Week 2	2.3	0.6
Week 4	2.4	0.5
Week 8	1.8	0.6
Week 12	1.0	0.5
Other local AEs, n (%)		
Scar [b]		
Week 12	13 (2.9)	10 (2.2)
Week 24	12 (2.7)	18 (4.0)
Hypo- and hyperpigmentation		
Through week 12	6 (1.4)	0
Through week 24	3 (0.7)	0

[a]Sum of 6 LSR component scores (range, 0-4 for each component).
[b]Scar assessment was performed at each visit independent of AE assessment. Clinically significant scars were reported as AEs. No patients in either group had keloidal or hypertrophic scars during the 24-week study period.

Conclusion

- Once-daily application of berdazimer gel, 10.3%, a novel topical NO–releasing medication, appears to demonstrate efficacy and favorable safety in patients 6 months and older with molluscum[1]

Reference:
1. Browning JC, Enloe C, Cartwright M, et al. Efficacy and Safety of Topical Nitric Oxide–Releasing Berdazimer Gel in Patients With Molluscum Contagiosum: A Phase 3 Randomized Clinical Trial. *JAMA Dermatol*. 2022;158(8):871-878. doi:10.1001/jamadermatol.2022.2721 (OPEN ACCESS)

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