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Symposium
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OF PREMIER MEDICAL & AESTHETIC
DERMATOLOGY EDUCATION

REIMAGINING
MEDICAL AND
AESTHETIC
DERMATOLOGY



Novel Approaches to Treating Actinic Keratosis

LIWDERM
REVOLUTIONIZING DERMATOLOGY EDUCATION

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Actinic Keratoses – What are they?

- Rough, scaly, erythematous, hyperkeratotic
- “Pre-cancers”
- May progress to SCC



AK's – Current “Gold Standard” Treatments

Cryosurgery

5-FU

Imiquimod

UW Derm
REVOLUTIONIZING DERMATOLOGY EDUCATION

AK's – Current “Gold Standard” Treatments

Cryosurgery

Painful
Incomplete removal
Hypopigmentation

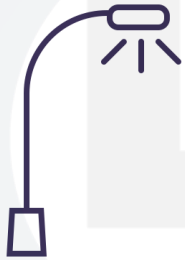
5-FU

Skin reactions/burning
Patient Non-Compliance

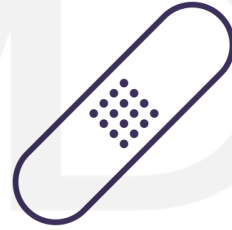
Imiquimod

Incomplete removal

New Approaches



MAL-PDT



ChemoWraps



Combination
Therapy



Methyl Aminolevulinate Photodynamic Therapy (MAL-PDT)

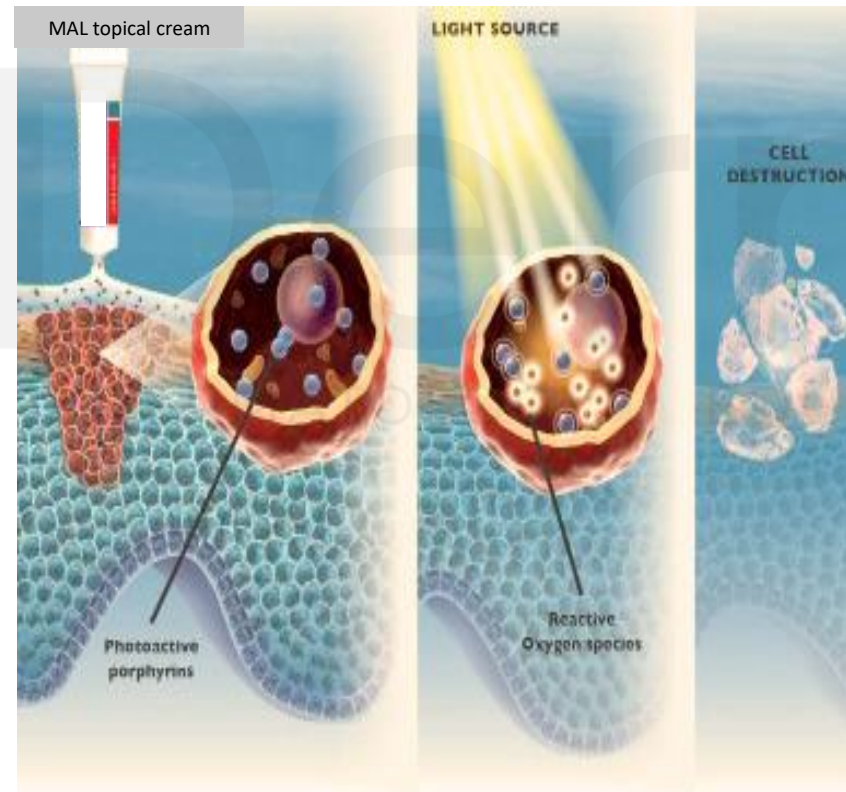


Efficacy

- Complete clearance rate: 92.8%

Safety

- Local skin reactions: 59.6%



Efficacy

- Complete clearance rate: 89.2%

Safety

- Local skin reactions: 45%

5-Fluorouracil “Chemowraps”



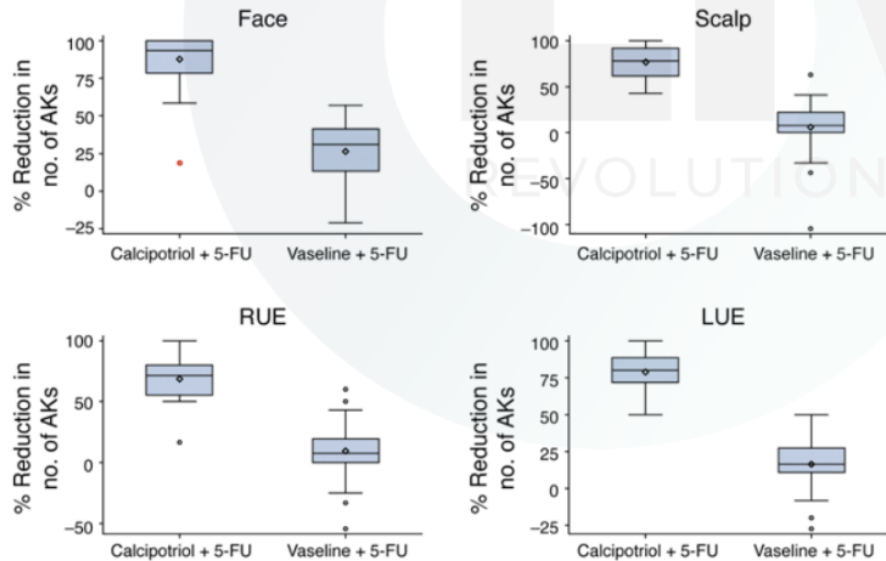
Before

After

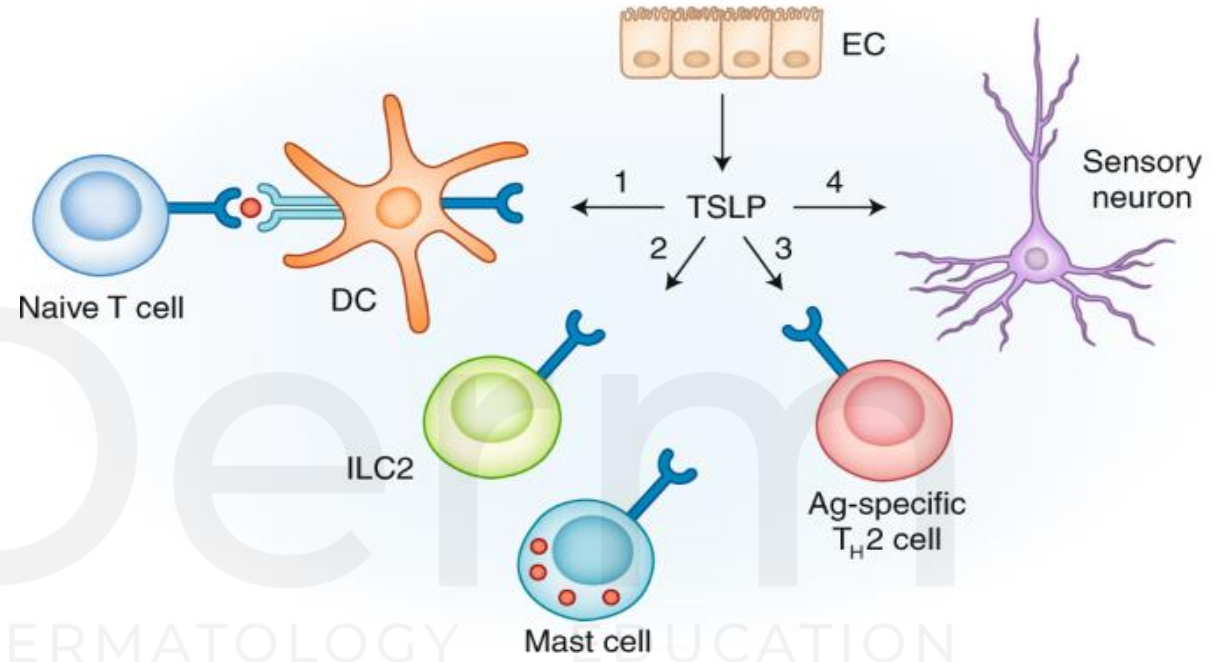
5-FU + Calcipotriol

What is calcipotriol?

- Thymic stromal lymphopoietin (TSLP) inducer
→ antitumor immunity in barrier-defective skin



RUE = right upper extremity; LUE = left upper extremity.



Before

During

After

Combination Therapy

Tx Combination	5-Fluorouracil + Cryosurgery vs Cryosurgery	3.75% Imiquimod + Cryosurgery vs Cryosurgery	3% Diclofenac Sodium + Cryosurgery vs Cryosurgery	5% Imiquimod + ALA-PDT vs ALA-PDT
Efficacy	↑	↑↑	↑	↑
Safety	--	↓	↓↓	--

Key: ↑↑ or ↓↓ = large increase or decrease; ↑ or ↓ = small increase or decrease; -- = no difference.

Eisen DB...Schlesinger T, et al. *J Am Acad Dermatol.* 2021 [Epub ahead of print].

Novel Treatments



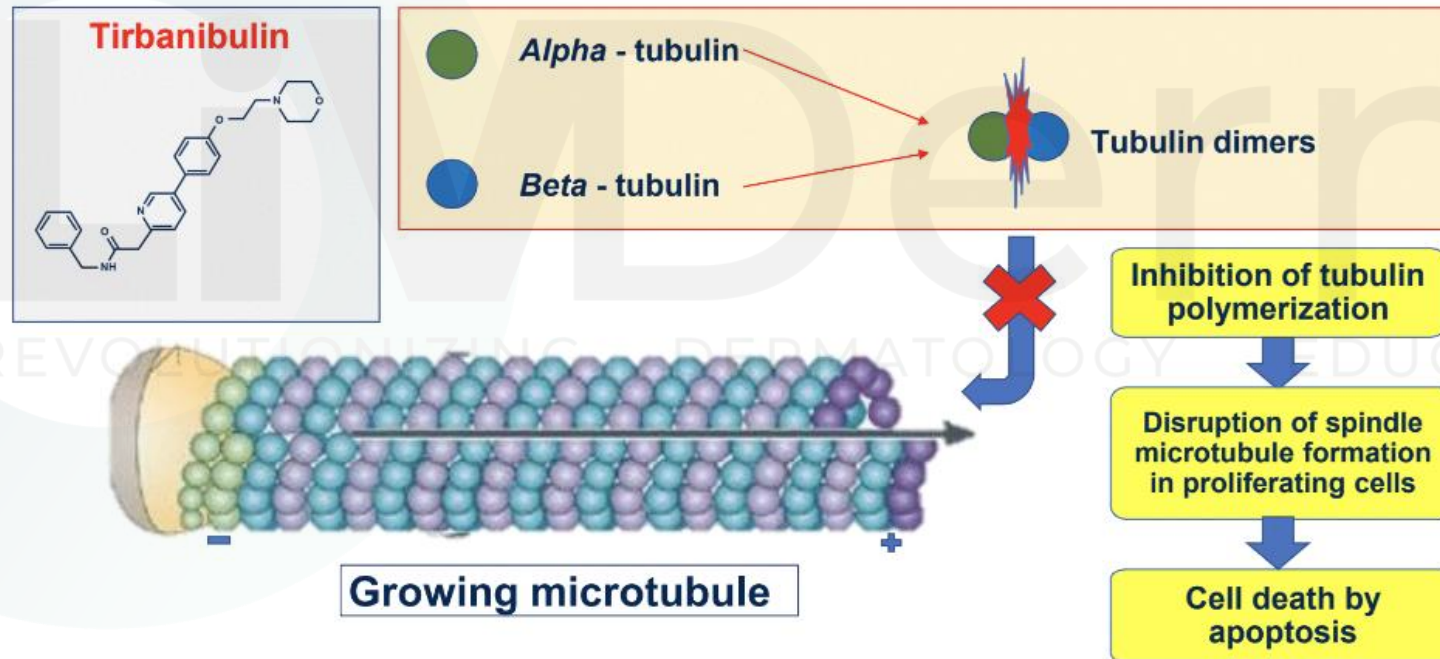
Tirbanibulin ointment



ALA-PDT

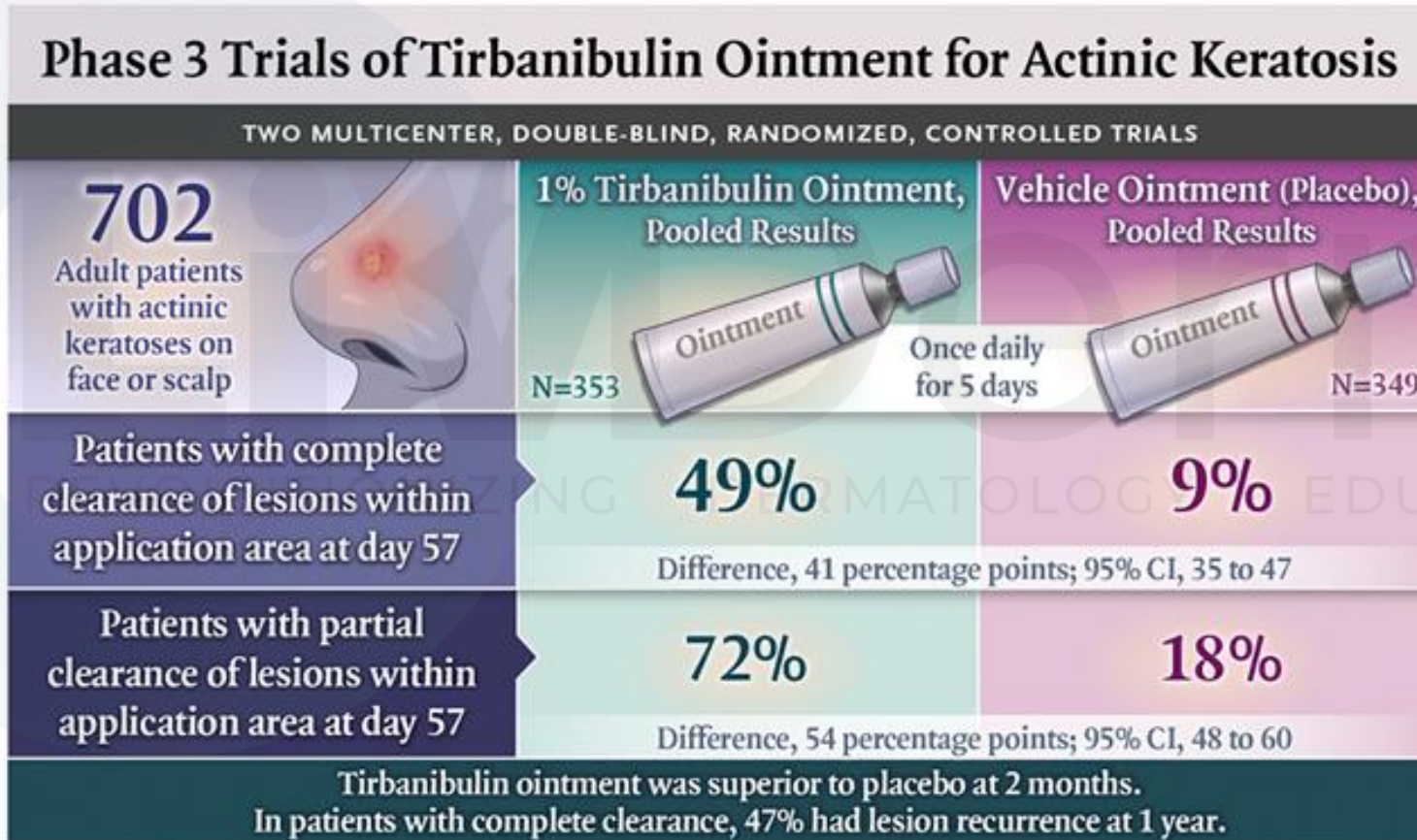
1% Tirbanibulin Ointment

Tirbanibulin: Inhibition of Tubulin Polymerization



1% Tirbanibulin Ointment: Phase III Trial

The NEW ENGLAND JOURNAL of MEDICINE



A. Blauvelt et al. 10.1056/NEJMoa2024040

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Aminolevulinic Acid Photodynamic Therapy (ALA-PDT)



Efficacy

- Complete clearance rate: 71.6% at 12 months post-treatment

Safety

- Local skin reactions: 99%



Efficacy

- Complete clearance rate: 86.3% at 12 months post-treatment

Safety

- Local skin reactions: 99.5%



Before

After

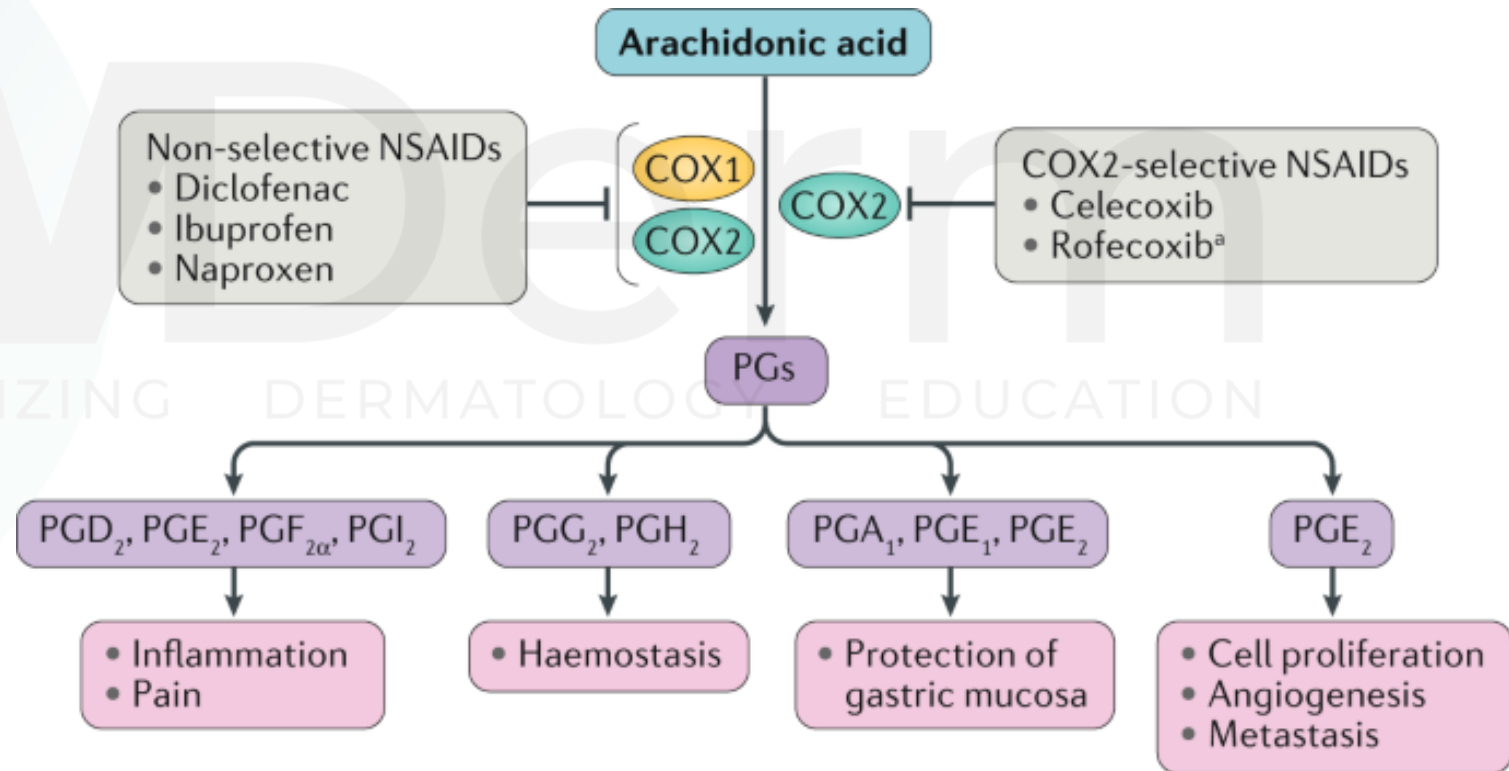
Diclofenac – Topical

Efficacy

- 29% complete clearance

Common adverse events

- Local skin reactions:
29%



NSAIDs = non-steroidal anti-inflammatory drugs.

Thomas GJ, et al. *Dermatol Ther.* 2019;32(3):e12800. Schjerning AM, et al. *Nat Rev Cardiol.* 2020;17(9):574-584. McEwan LE, et al.

Australas J Dermatol. 1997;38(4):187-189.

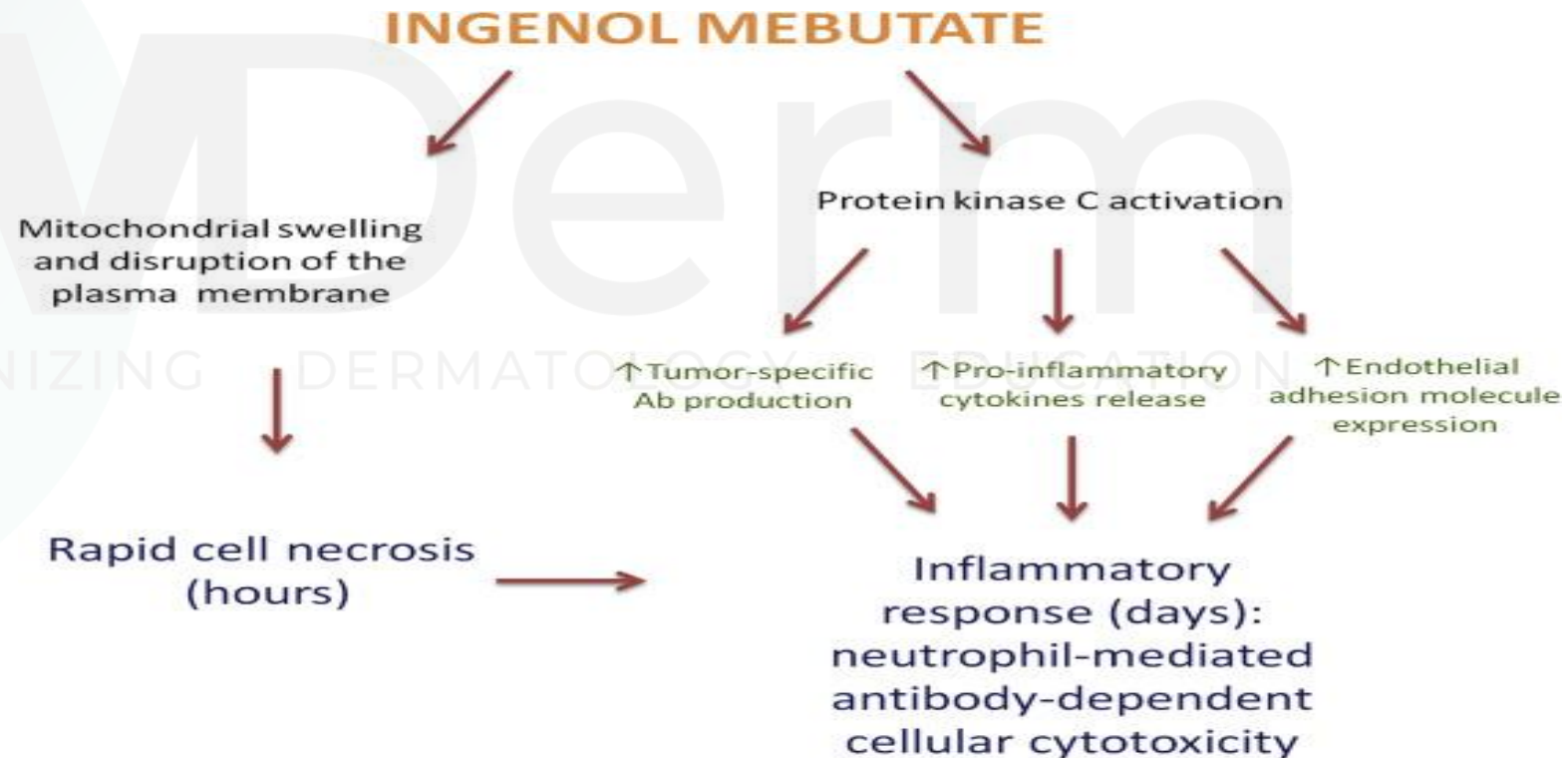
Ingenol Mebutate – Topical

Efficacy

- 78.7% complete clearance
- 95.7% no recurrence at 12 months

Safety: *Withdrawn from market in 2020

- 3x risk of skin cancer



Randomized Trial Assessing 4 Treatment Approaches

ORIGINAL ARTICLE

Randomized Trial of Four Treatment Approaches for Actinic Keratosis

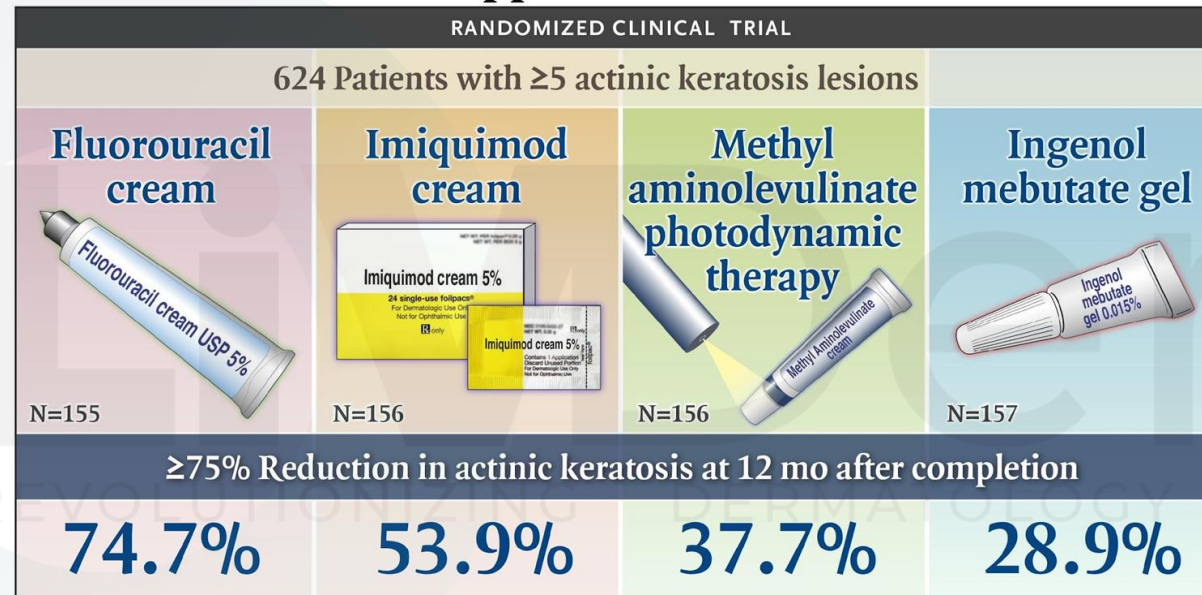
Maud H.E. Jansen, M.D., Janneke P.H.M. Kessels, M.D., Ph.D.,
Patty J. Nelemans, M.D., Ph.D., Nina Kouloubis, M.D.,
Aimée H.M.M. Arits, M.D., Ph.D., Han P.A. van Pelt, M.D., Ph.D.,
Patricia J.F. Quaedyliëg, M.D., Ph.D., Brigitte A.B. Essers, Ph.D.,
Peter M. Steijlen, M.D., Ph.D., Nicole W.J. Kelleners-Smeets, M.D., Ph.D.,
and Klara Mosterd, M.D., Ph.D.

- Inclusion criteria (N=624): 5+ AKs in 1 continuous area on head or neck
- Primary measure: Partial clearance rate at 3 and 12 months post-treatment
- Treatment groups
 1. 5% fluorouracil cream
 2. 5% imiquimod
 3. MAL-PDT
 4. 0.0015% ingenol mebutate

*Partial Clearance: $\geq 75\%$
reduction of AK lesion

Randomized Trial Assessing 4 Treatment Approaches

Four Treatment Approaches for Actinic Keratosis



The NEW ENGLAND JOURNAL of MEDICINE

Jansen et al. 2019

Adverse Event Incidence	5-FU	5% Imiquimod	MAL-PDT	0.0015% Ingenol Mebutate
	92.6%	85.1%	96.6%	95.7%

Current Guidelines: United States vs Europe

	Cryo-surgery	5-FU	IMQ	DHA	PDT
US Guidelines	Strong	Strong	Strong	Conditional	Conditional*
European Guidelines	Strong	Strong	Strong	Conditional	Strong*
Indication	Single lesion	Field therapy	Field therapy	Field therapy	Field therapy

5-FU = 5-fluorouracil; IMQ = imiquimod; DHA = diclofenac; PDT = ALA and MAL.

Eisen DB...Schlesinger T, et al. *J Am Acad Dermatol*. 2021 [Epub ahead of print]. Werner RN, et al. *J Eur Acad Dermatol Venereol*. 2015;29(11):2069-2079.

In Development

- Resiquimod
 - 0.01%, 0.03%, 0.06% and 0.1% tested – similar outcomes but 0.01% and 0.03% better tolerated
 - 3X/week for 4 weeks, possibly repeat treatment
- KOH 5% Solution
 - Comparison trial against 5-FU showed superiority at 1 month and similarity at 3 months

Conclusions

- **The abundance of AK's requires an effective but easily maintained treatment**
- **Cryosurgery is good clinical practice for singular or few lesions**
- **5-FU and Imiquimod are gold standard for field treatment**
- **Tirbanibulin has a novel MOA, a favorable safety profile and a shorter treatment interval**
- **More research needed and forthcoming for novel treatments and light therapies**

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