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Meclozine, a new anti-inflammatory molecule to treat acne: from *in vitro* to proof-of-concept pilot clinical trial

Communication n° CO062

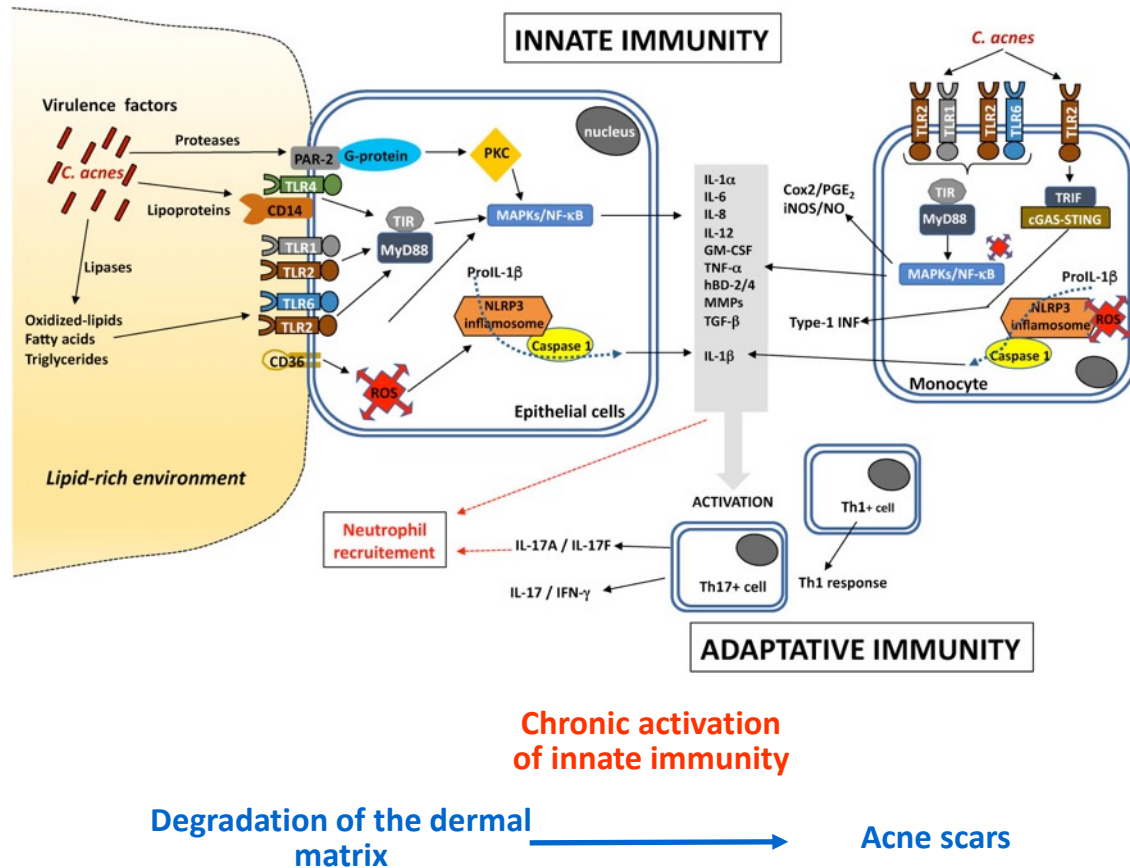
Philippe Alain GRANGE, Guillaume OLLAGNIER, Carole NICCO, Laurianne BEAUVAIS-REMIGEREAU, Philippe MORAND, Anne-Geneviève MARCELIN, Vincent CALVEZ et Nicolas DUPIN

**Philippe Alain GRANGE, Anne-Geneviève MARCELIN, Vincent CALVEZ
et Nicolas DUPIN sont co-fondateurs de la société SkinDermic**



C. acnes induces strong inflammation

Both innate and immune immunities are involved

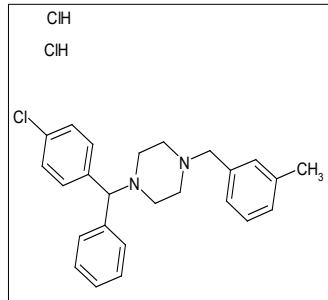


- C. acnes* trigger the production of pro-inflammatory molecules

Main proinflammatory molecules produced

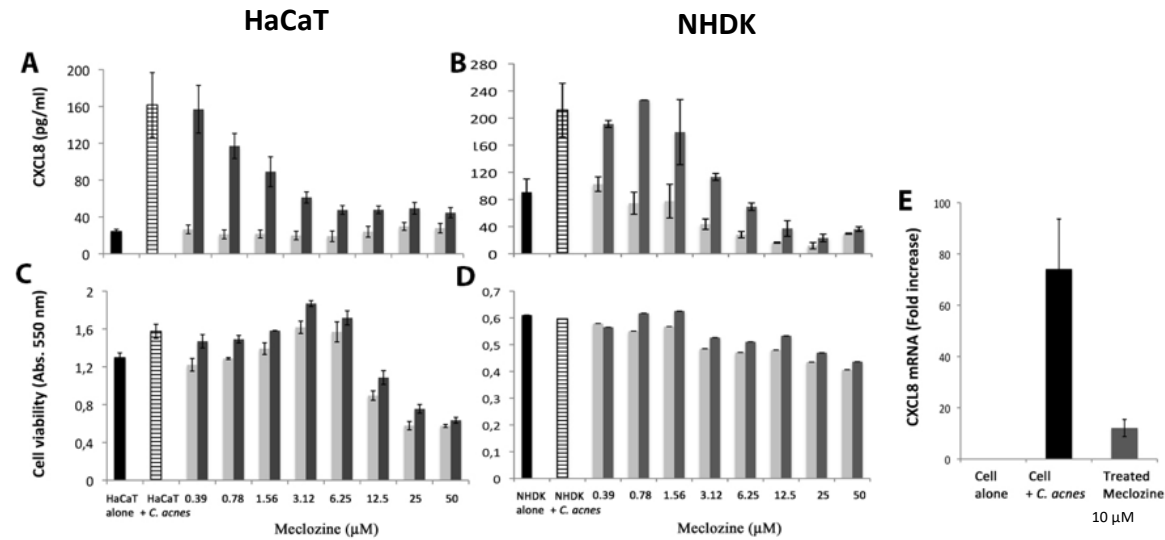
- From keratinocytes : CXCL8/IL-8
- From monocytes : IL-1

Meclozine inhibits the production of CXCL8/IL-8 and IL-1 β *in vitro*

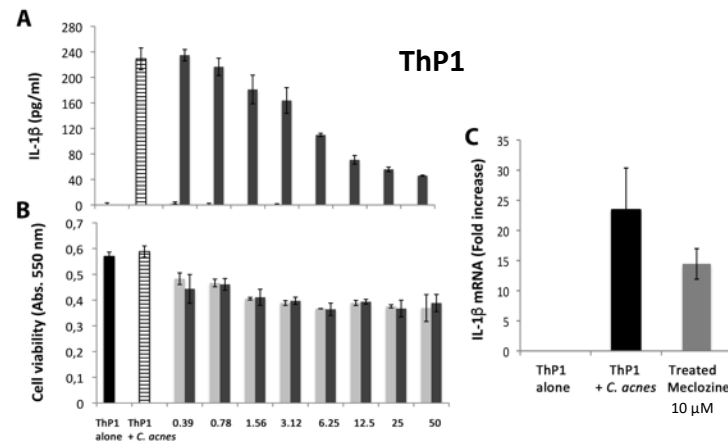


**Meclozine
dihydrochloride**

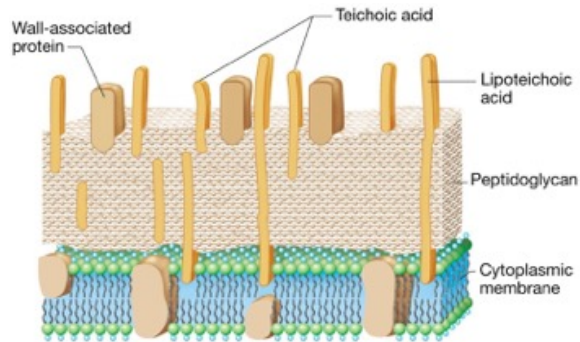
Keratinocyte



Monocyte



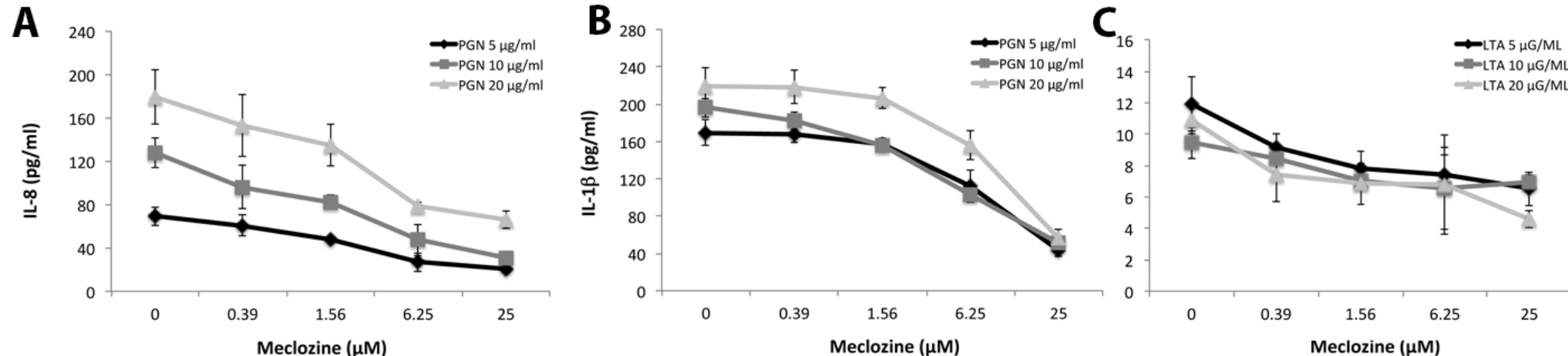
Meclozine inhibits the production of CXCL8/IL-8 and IL-1 β after stimulation by PGN and LTA *in vitro*



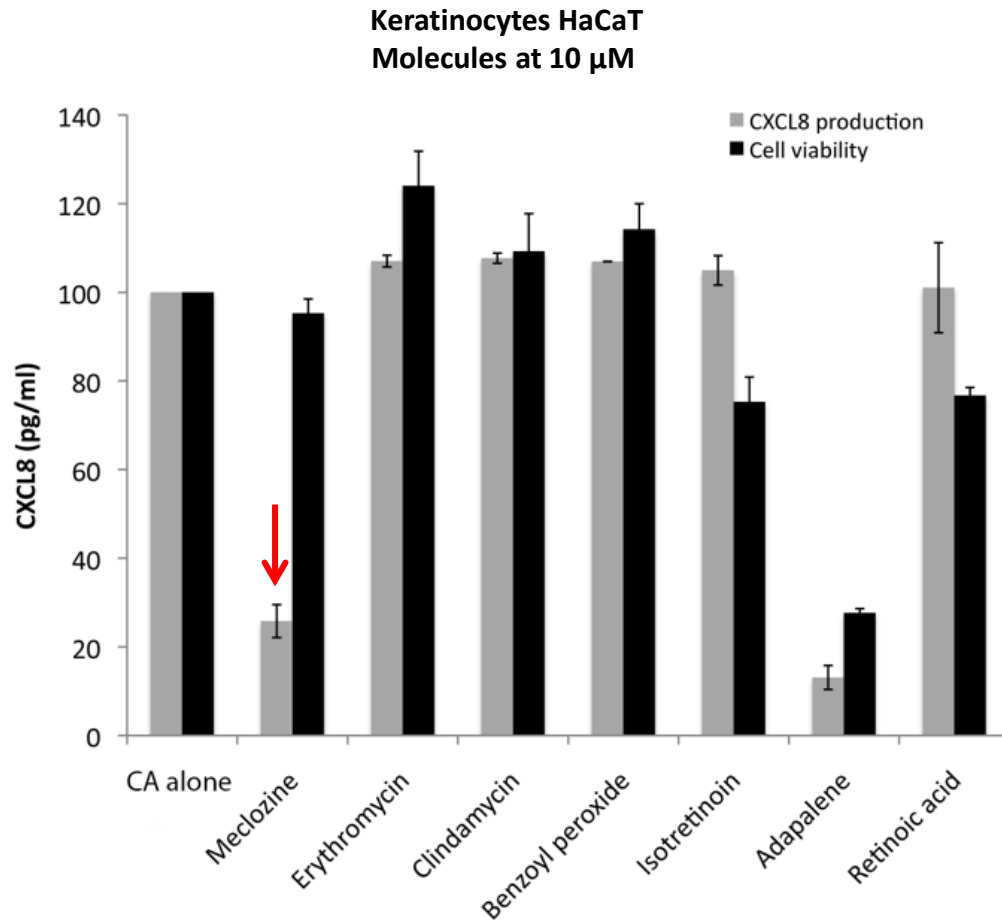
PGN : peptidoglycan

LTA : lipoteichoic acid

Major constituents of the cell wall
of gram-positive bacteria

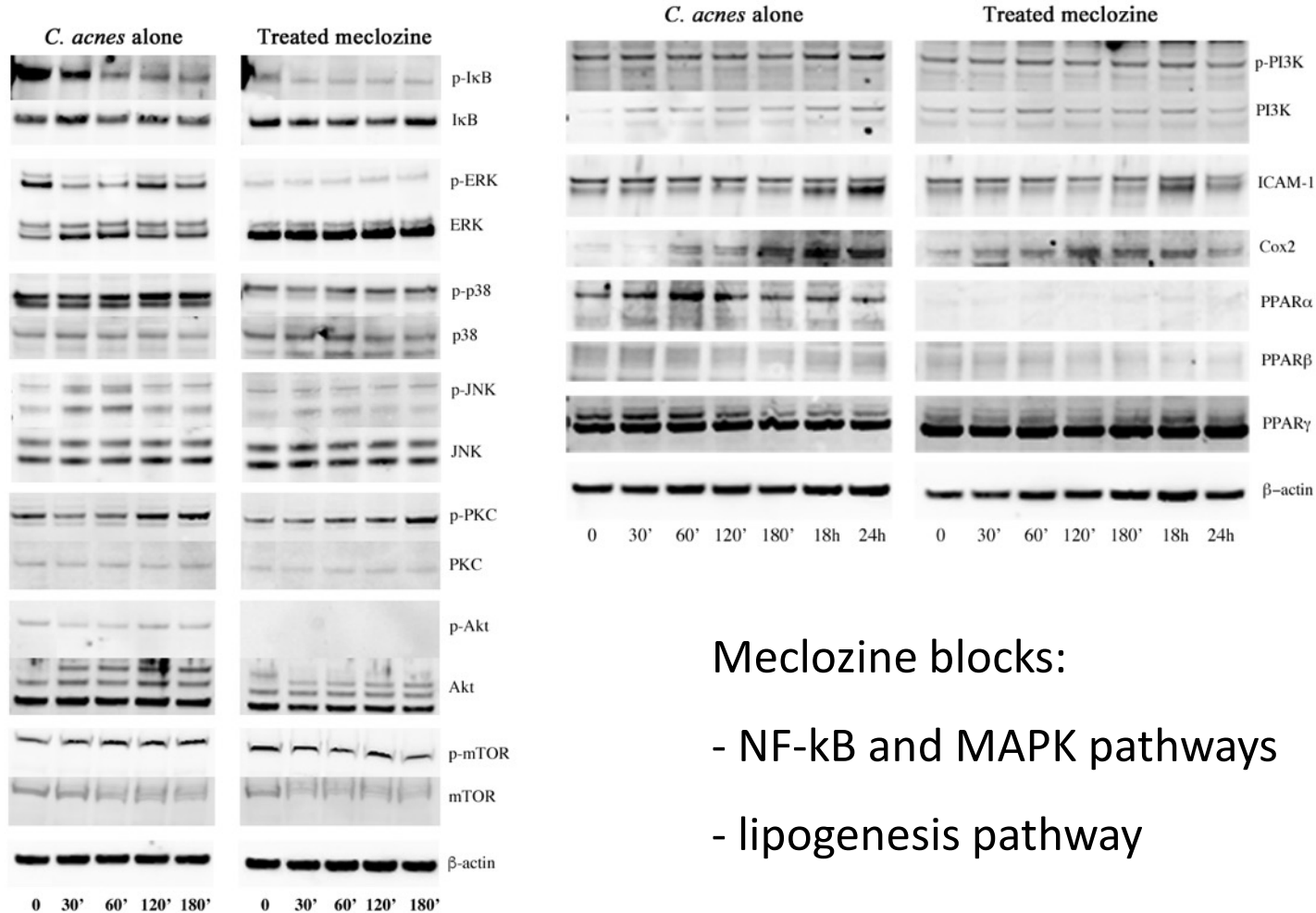


Comparison of meclozine anti-inflammatory property with molecules commonly used in acne treatment



- Much more active than the molecules commonly used in acne treatments
- No cellular toxicity

Mechanisms of action of meclozine



Meclozine blocks:

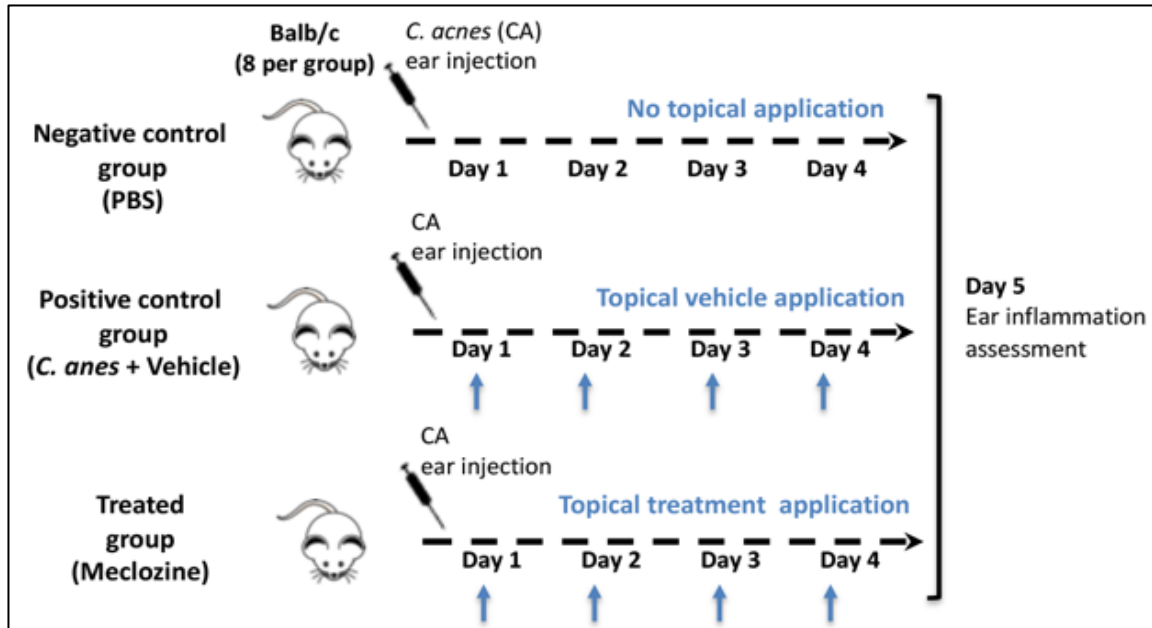
- NF-κB and MAPK pathways
- lipogenesis pathway

Signalling pathway	<i>P. acnes</i> alone	Meclozine
NF-κB	↗	↘
MAPK ERK	↗	↘
MAPK p38	↗	↘
MAPK JNK	↗	↘
PKC	↗	↘
Akt	↗	↘
PI3K	↗	→
mTORC	↗	→
PPARα	↗	↘
PPARβ	↗	↘
PPARγ	→	↘
Cox2	↗	↘
ICAM-1	↗	↘

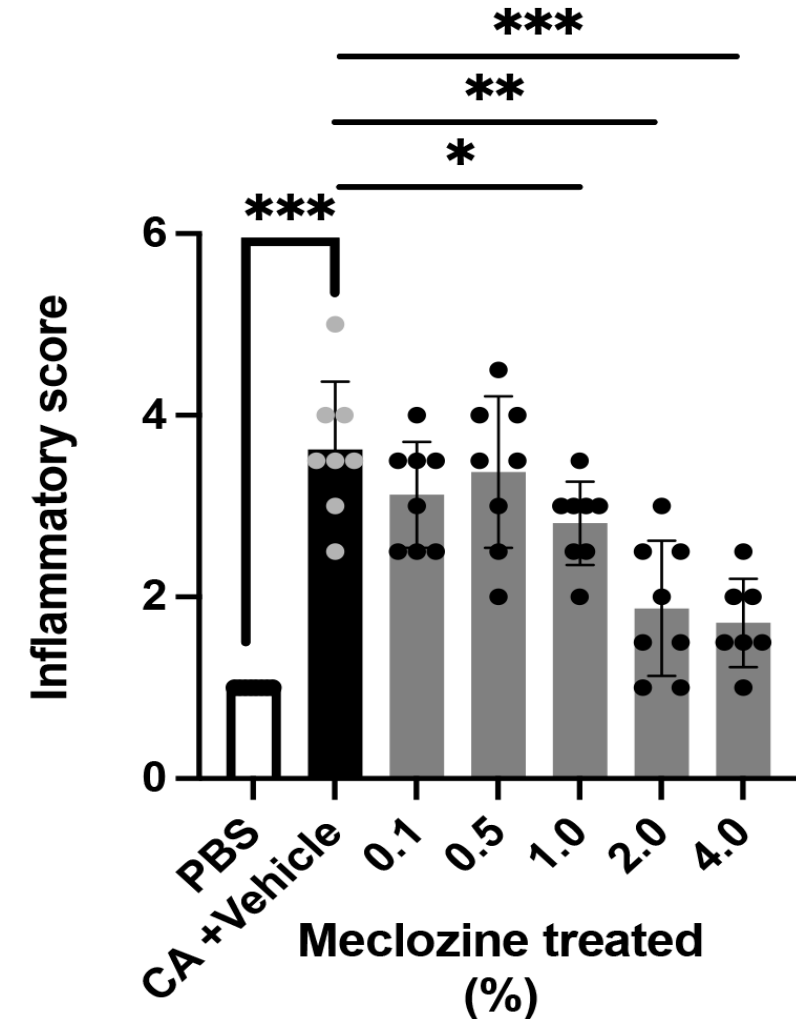
Legend	
↗	Activation
↘	Inhibition
→	Steady

Meclozine is active in vivo (1/2)

- 8 mice per group, 56 mice
- 7 groups :
 - untreated (PBS)
 - Stimulated *C. acnes* – treated vehicle
 - Stimulated *C. acnes* – treated with meclozine (5 groups, 0.1 to 4% méclozine)

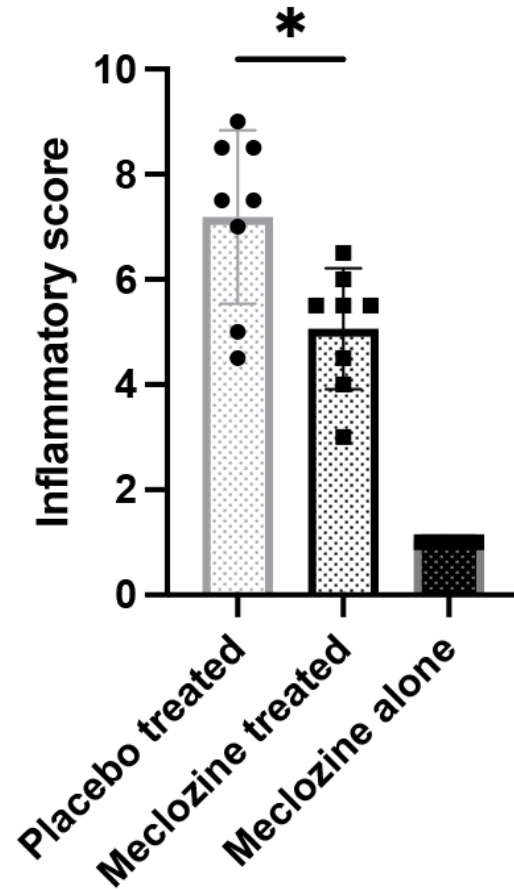


In house gel preparation
(vaseline / HS153070)

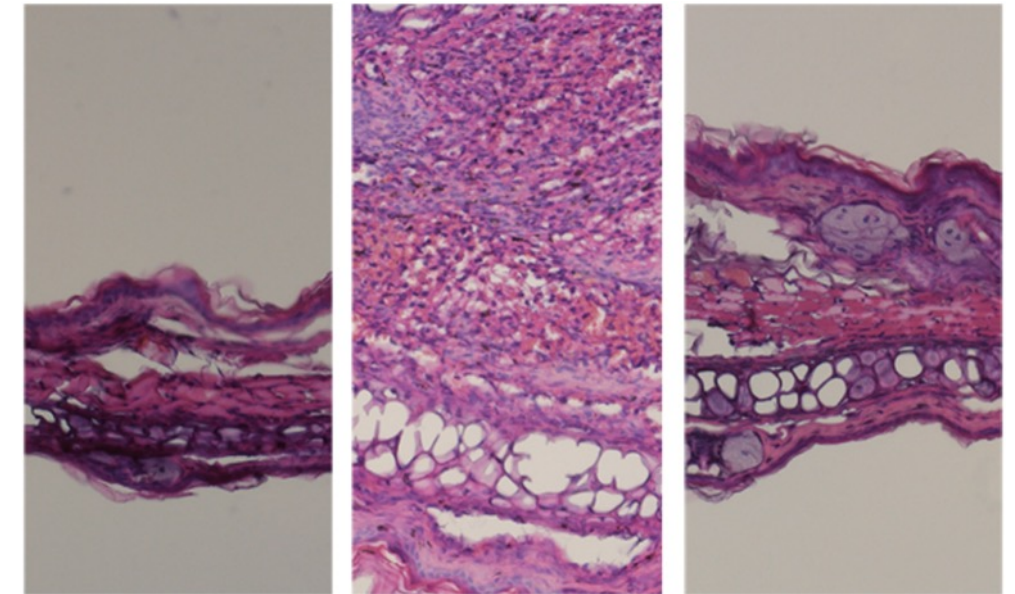
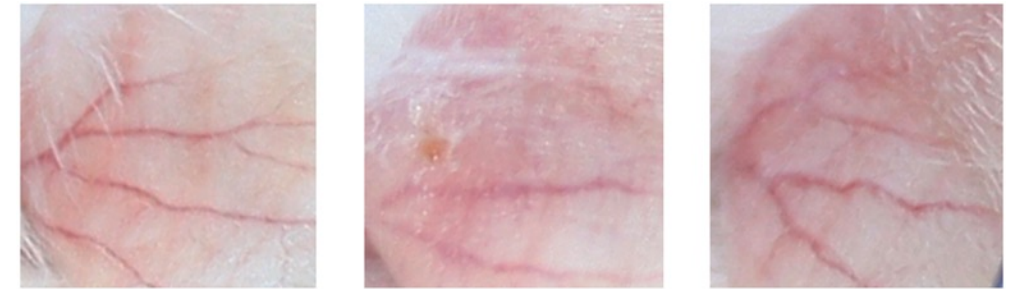


Meclozine-dependent dose activity

Meclozine is active in vivo (2/2)



1% meclozine gel
prototype
(Amatsi)



PBS

C. acnes + vehicle

1% meclozine treated

Meclozine treatment decreases inflammation induced by *C. acnes*

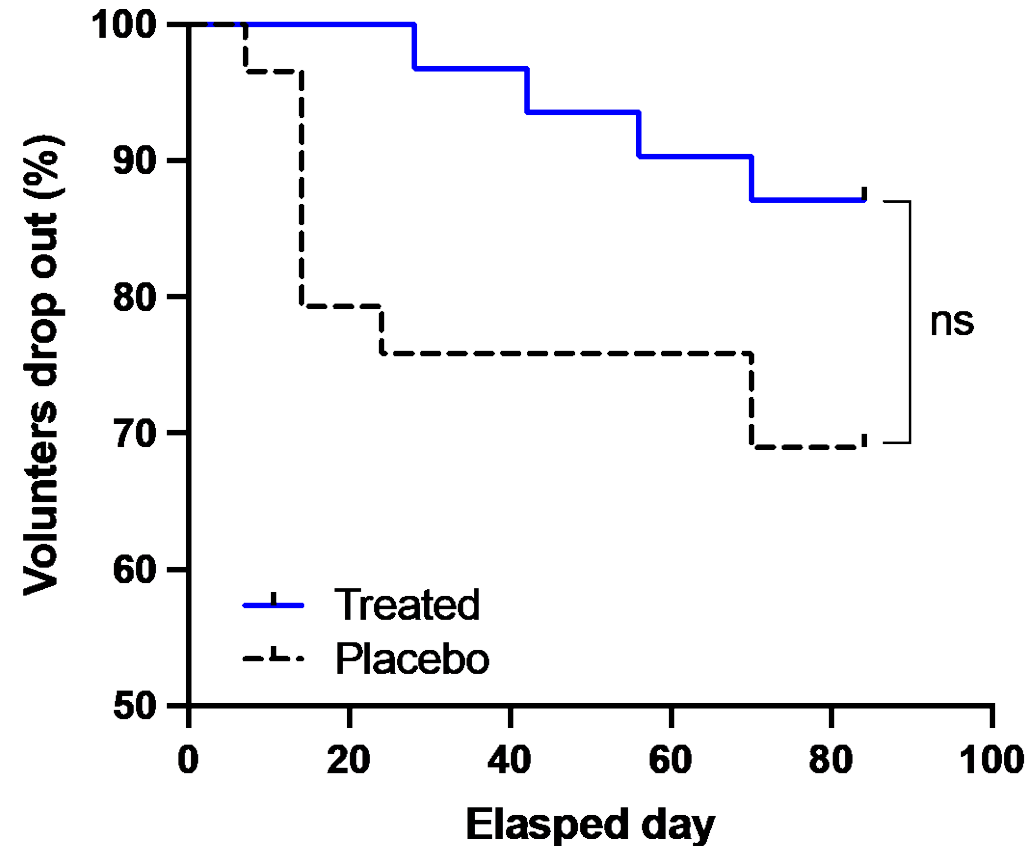
Clinical evaluation in humans of the efficacy and safety of meclozine after 12 weeks of treatment

- Prospective double-blind controlled study over 12 weeks
- Meclozine 2%
- Placebo

	Groupe A (treated)	Groupe B (placebo)
Number of patients included	30	30
Age (D.S.)	26,52 (5,44)	27,86 (6,33)
Sex	F (16), H (14)	F (24), H (6)

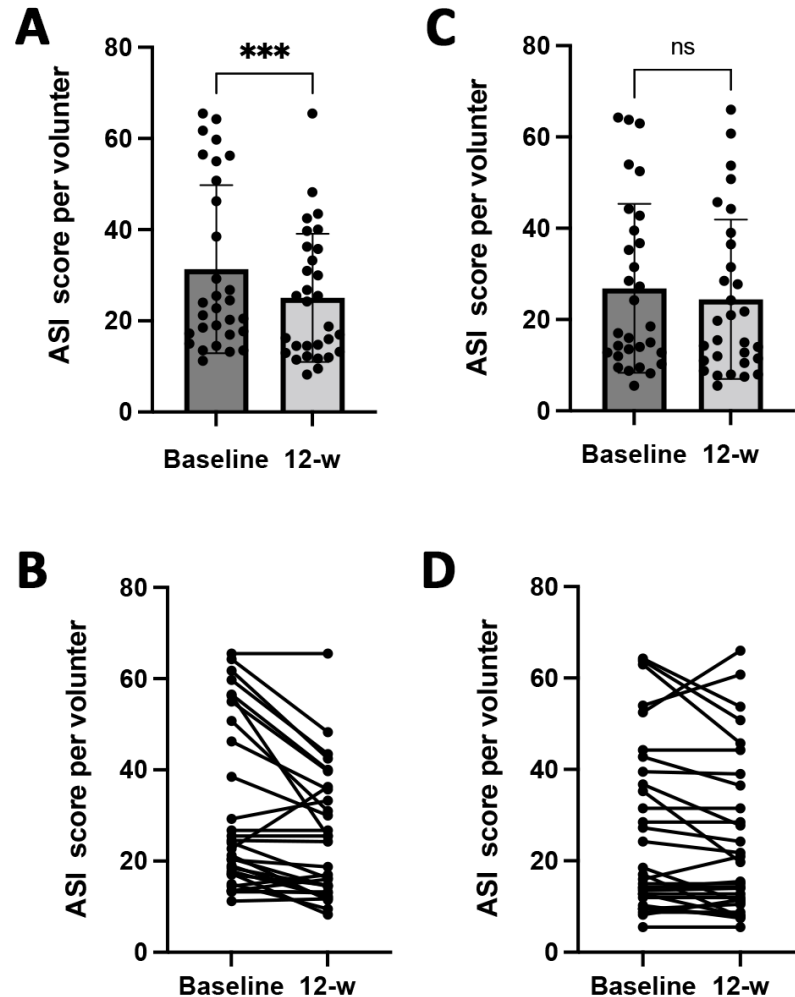
This study was conducted in accordance with Ellead's standard operating procedures.
To ensure compliance with the study protocol, the quality assurance unit conducted an audit of the study results and the final report.

Clinical evaluation in humans of the efficacy and safety of meclozine after 12 weeks of treatment (ITT)



Earlier and more treatment discontinues in the placebo arm

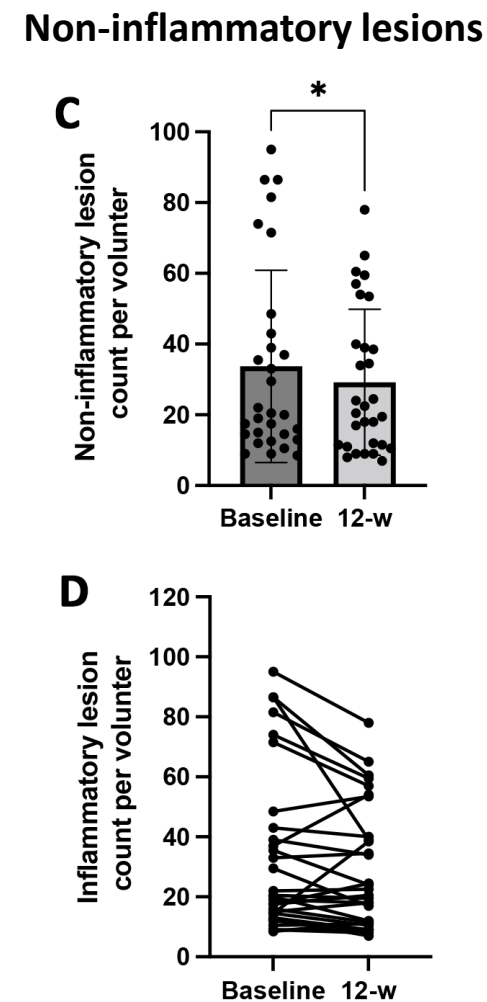
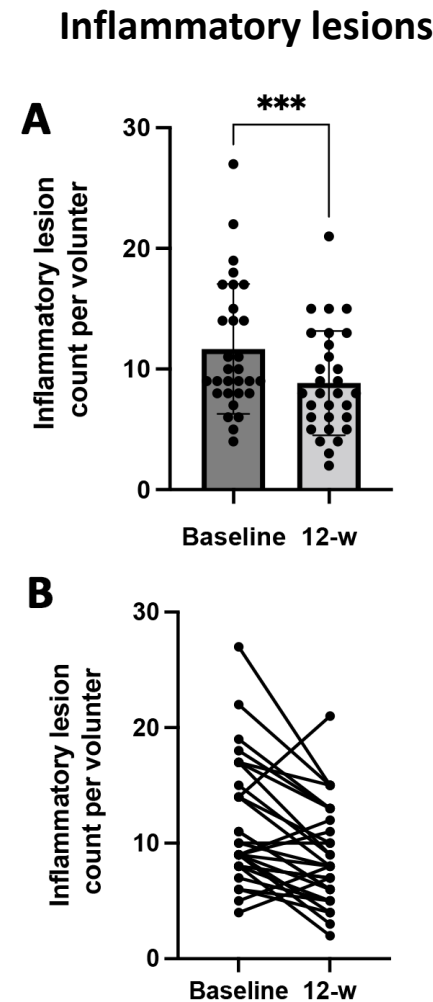
Michaelson Acne Severity Index (ASI) Assessment (ITT)



- Meclozine treatment arm:
 - Significant reduction in ASI
 - 20.09 %, ($p=0.0004$; Wilcoxon signed-rank test)
 - 73% of patients have an improvement in ASI
- Placebo arm:
 - Non-significant reduction in ASI
 - 43% of patients have an improvement in ASI
- Percentage of patients with improvement in ASI is significantly greater in the meclozine arm (73%) than in the placebo arm (43%): $p=0.03$ (Fisher exact test)
- Self assessment: "I feel my acne is reduced by using the test product »
 - YES: meclozine arm 58% vs placebo 29%

La méclozine est active sur les lésions inflammatoires et rétentionnelles (ITT)

Meclozine: decrease of 24.3%
inflammatory lesions
($p = 0.0008$, Wilcoxon signed-rank test)



Meclozine: decrease of 13.4%
non-inflammatory lesions
($p = 0.0379$, Wilcoxon signed-rank test)

Clinical response measured by VISIA-CR



J0 Inclusion
ASI: 50,7



Week 12
ASI: 31

Decrease : 39%



J0 inclusion
ASI: 21.2



Wek 12
ASI: 11.5

Decrease : 46%

After 12 weeks of application, meclozine significantly decreases the Acne Severity Index (ASI)

CONCLUSIONS

- Topical meclozine exhibits anti-inflammatory activity *in vitro* and *in vivo* against *C. acnes*
- Meclozine inhibits NF-kB and MAPK pathways as well as lipogenesis
- Topical meclozine appears as a new topical anti-acne in a randomized trial vs. placebo
- Meclozine mainly has an anti-inflammatory effect but also an activity on the retentional part of acne
- The safety of topical meclozine appears to be excellent: none of the patients treated in the two trials (open-label and randomised) experienced any side effects