Benefit of Topical Combination Therapy for Acne Treatment: Analysis of Effect Size Using Number Needed to Treat

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NUMBER NEEDED TO TREAT (NNT)

WHAT IS NNT?

- NNT is a metric for quantifying effect sizes of clinically relevant study endpoints[1]
- NNT represents the number of patients needed to treat to achieve an additional cure in a given timeframe[1-3]
  - For example, NNT=3 means that 3 patients would need to be treated with active drug rather than vehicle before expecting an additional responder[2]

HOW IS NNT USED?

- In the absence of head-to-head studies, NNT may be used to indirectly assess comparative efficacy of treatments
  - Evaluation of NNT has been conducted in a variety of therapeutic areas, including psychiatry/neurology, cardiology, oncology, and dermatology
- While a clinically relevant NNT threshold has not been established for acne, lower values indicate more favorable treatment (larger effect size) versus vehicle

HOW IS NNT CALCULATED?

- NNT is the reciprocal of the absolute risk reduction (ARR), rounded up to the nearest whole number[1-3]

$$\frac{1}{(\%\ \text{Success With Active Treatment} - \%\ \text{Success With Vehicle})} * 100$$

WHAT ARE SOME LIMITATIONS OF NNT?

- Evaluates one binary outcome (eg, week 12 treatment success)[2,4]
- No consideration of drug tolerability or study design/ population differences[1-4]
- Clinical meaning subject to interpretation[5]
- Benefits of a well-designed vehicle subtracted from active treatment,[a] leading to higher NNT values

[a]Due to the potential of a well-designed vehicle to result in higher efficacy rates in the control group.

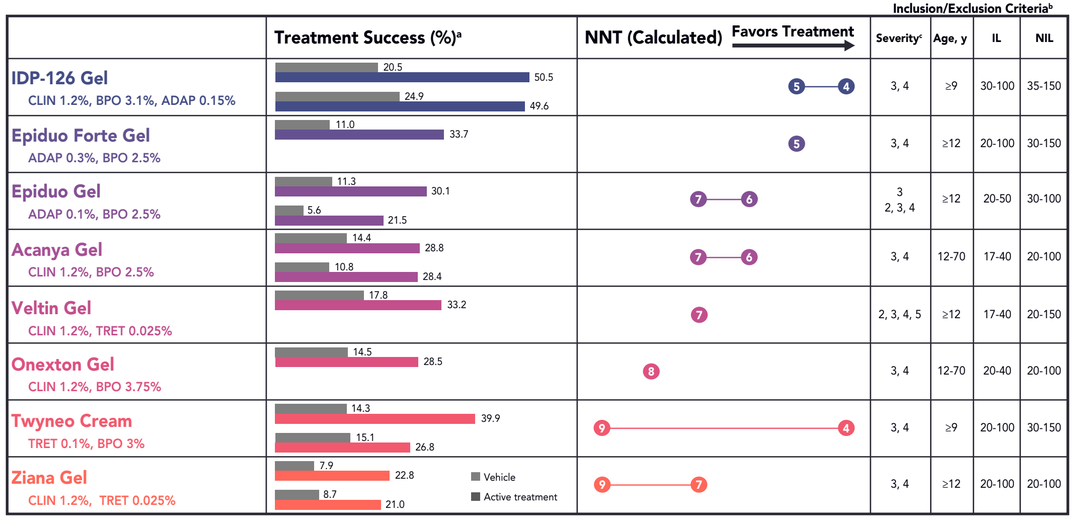
NNTs FOR COMBINATION TOPICAL ACNE TREATMENTS

Objectives and Methods

- The objective was to evaluate NNT values for combination topical acne treatments
- NNT to achieve treatment success was calculated for 8 combination treatments: 7 dual-combinations (FDA approved) and 1 triple-combination (in development)
- Treatment success was defined as ≥2-grade EGSS/IGA improvement and clear/almost clear skin at week 12

Results

- Treatment success rates and calculated NNT values from 13 studies are shown in the Figure
  - Eleven studies enrolled patients with moderate-to-severe acne and 2 studies included those with mild and/or very severe acne; additional inclusion/exclusion criteria are shown
- The lowest NNT values (most favorable) were achieved with IDP-126 gel—fixed-dose, triple combination clindamycin phosphate 1.2%, BPO 3.1%, adapalene 0.15%—which is in development for the treatment of acne



[a]Defined as percentage of patients achieving ≥2-grade reduction from baseline in EGSS/IGA and clear/almost clear skin at week 12. Data for approved treatments were from prescribing information and/or FDA medical reviews.[6] Data for IDP-126 were from two phase 3 studies.[7]
[b]Inclusion/exclusion criteria were for facial acne or were not specified.
[c]Studies evaluated severity via 5- or 6-point EGSS or IGA. Though there were slight differences in definition, generally: 0=clear, 1=almost clear/minimal, 2=mild, 3=moderate, 4=severe, 5=very severe.

CONCLUSIONS

- Given the paucity of head-to-head studies in acne, NNT may be used as a simple way to compare drug effects across clinical trials
- IDP-126 gel (clindamycin phosphate 1.2%, BPO 3.1%, adapalene 0.15%) had the most favorable NNT values (lowest), with treatment success rates of ~50%
- Due to the multifactorial pathogenesis of acne, a triple-combination topical treatment may result in clinical success more often than seen with two-ingredient combination products
  - These NNT values are supported by phase 2 study results, in which IDP-126 led to significantly greater treatment success rates at week 12 compared with its three component dyads in the same vehicle formulation[7,8]

ABBREVIATIONS

ADAP, adapalene; BPO, benzoyl peroxide; CLIN, clindamycin phosphate; EGSS, Evaluator's Global Severity Scale; IGA, Investigator's Global Assessment; IL, inflammatory lesions; NIL, noninflammatory lesions; NNT, number needed to treat; TRET, tretinoin.

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