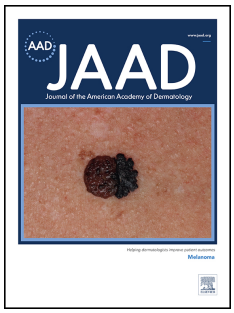
Journal Pre-proof



The efficacy and tolerability of tetracyclines and clindamycin plus rifampicin for the treatment of hidradenitis suppurativa; results of a prospective European cohort study

K.R. van Straalen, MD, PhD, T. Tzellos, MD, PhD, P. Guillem, MD, PhD, F. Benhadou, MD, PhD, C. Cuenca-Barrales, MD, M. Daxhelet, MD, M. Daoud, MD, O. Efthymiou, MD, E.J. Giamarellos-Bourboulis, MD, PhD, G.B.E. Jemec, MD, DMSci, A.C. Katoulis, MD, A. Koenig, MD, PhD, E. Lazaridou, MD, PhD, A.V. Marzano, MD, Ł. Matusiak, MD, PhD, A. Molina-Leyva, MD, PhD, C. Moltrasio, MRes, A. Pinter, MD, PhD, C. Potenza, MD, J. Romaní, MD, PhD, D.M. Saunte, MD, PhD, N. Skroza, MD, D. Stergianou, MD, J. Szepietowski, MD, PhD, FRCP, A. Trigoni, MD, PhD, E. Vilarrasa, MD, H.H. van der Zee, MD, PhD

PII: S0190-9622(21)00176-6

DOI: https://doi.org/10.1016/j.jaad.2020.12.089

Reference: YMJD 15592

To appear in: *Journal of the American Academy of Dermatology*

Received Date: 28 September 2020

Revised Date: 19 December 2020

Accepted Date: 29 December 2020

Please cite this article as: van Straalen KR, Tzellos T, Guillem P, Benhadou F, Cuenca-Barrales C, Daxhelet M, Daoud M, Efthymiou O, Giamarellos-Bourboulis EJ, Jemec GBE, Katoulis AC, Koenig A, Lazaridou E, Marzano AV, Matusiak Ł, Molina-Leyva A, Moltrasio C, Pinter A, Potenza C, Romaní J, Saunte DM, Skroza N, Stergianou D, Szepietowski J, Trigoni A, Vilarrasa E, van der Zee HH, The efficacy and tolerability of tetracyclines and clindamycin plus rifampicin for the treatment of hidradenitis suppurativa; results of a prospective European cohort study *Journal of the American Academy of Dermatology* (2021), doi: https://doi.org/10.1016/j.jaad.2020.12.089.

during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The efficacy and tolerability of tetracyclines and clindamycin plus rifampicin for the treatment of hidradenitis suppurativa; results of a prospective European cohort study

K.R. van Straalen[1]* (MD, PhD), T. Tzellos[2]* (MD, PhD), P. Guillem[3] (MD, PhD), F. Benhadou[4] (MD, PhD), C. Cuenca-Barrales[5,6] (MD), M. Daxhelet[4] (MD), M. Daoud[4] (MD), O. Efthymiou[7] (MD), E.J. Giamarellos-Bourboulis[8] (MD, PhD), G.B.E Jemec[9] (MD, DMSci), A.C. Katoulis[7] (MD), A. Koenig[10] (MD, PhD), E. Lazaridou[11] (MD, PhD), A.V. Marzano[12,13] (MD), Ł. Matusiak[14] (MD, PhD), A. Molina-Leyva[5,6] (MD, PhD), C. Moltrasio[12,15] (MRes), A. Pinter[10] (MD, PhD) , C. Potenza[16] (MD), J. Romaní[17] (MD, PhD), D.M. Saunte[9] (MD, PhD), N. Skroza[16] (MD), D. Stergianou[8] (MD), J. Szepietowski[14] (MD, PhD, FRCP), A. Trigoni[11] (MD, PhD), E. Vilarrasa (MD)[18], H.H. van der Zee[1] (MD, PhD)

**Authors contributed equally to this manuscript*

1. Erasmus MC, University Medical Center Rotterdam, Department of Dermatology, The Netherlands.
2. Department of Dermatology, Nordland Hospital Trust, Bodø, Norway.
3. Department of Surgery, Clinique du Val d'Ouest (Lyon), ResoVerneuil (Paris) and Groupe de Recherche en Proctologie de la Société Nationale Française de ColoProctologie, Paris, France.
4. Department of Dermatology, Université Libre de Bruxelles, Erasme Hospital, Brussels, Belgium.
5. Department of Dermatology, Hospital Universitario Virgen de las Nieves, Granada, Spain.
6. TECe19-Clinical and Translational Dermatology Investigation Group Ibs. Granada, Spain.
7. Second Department of Dermatology and Venereology, National and Kapodistrian University of Athens, Medical School, "Attikon" General University Hospital, Athens, Greece.
8. Fourth Department of Internal Medicine, National and Kapodistrian University of Athens, Medical School, Athens, Greece.
9. Department of Dermatology, Zealand University Hospital, Roskilde and Health Sciences Faculty, University of Copenhagen, Denmark.
10. Department of Dermatology, Venereology and Allergology, University Hospital Frankfurt am Main, Germany.
11. Second Department of Dermatology and Venereology, Aristotle University of Thessaloniki, General Hospital Papageorgiou, Thessaloniki, Greece.
12. Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.
13. Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy.
14. Department of Dermatology, Venereology and Allergology, Medical University, Wroclaw, Poland.
15. Department of Medical Surgical and Health Sciences, University of Trieste, Trieste, Italy.
16. Dermatology Unit 'Daniele Innocenzi', Department of Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Polo Pontino-Latina, Italy.
17. Department of Dermatology, Corporació Sanitaria Parc Taulí, Sabadell, Spain.
18. Department of Dermatology, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain

Corresponding author:
H.H. van der Zee
Department of Dermatology,
Erasmus University Medical Center,
dr. Molewaterplein 40,
3015 GD Rotterdam, The Netherlands
tel: +31 10 704 0110
email: h.vanderzee@erasmusmc.nl

Conflict of interest:
KRvS: None declared.
TT: Abbvie, UCB, Sanofi Genzyme
PG: honoraria from AbbVie and Novartis as a consultant and nonpaid lectures for AbbVie, Brothier, Cicaplus, Coloplast, Inresa and Novartis
FB: None declared.
CCB: None declared.
MDax: None declared.
MDao: None declared.
OE: None declared.
EJGB: honoraria from Abbott CH, Angelini Italy, bioMérieux Inc, InflaRx GmbH, MSD Greece, and XBiotech Inc.; independent educational grants from AbbVie, Abbott, Astellas Pharma Europe, AxisShield, bioMérieux Inc, InflaRx GmbH, ThermoFisher Brahms GmbH, and XBiotech Inc; and funding from the FrameWork 7 program HemoSpec (granted to the National and Kapodistrian University of Athens), the Horizon2020 Marie-Curie Project European Sepsis Academy (granted to the National and Kapodistrian University of Athens), and the Horizon 2020 European Grant ImmunoSep (granted to the Hellenic Institute for the Study of Sepsis).
GBEJ: GBE Jemec has received honoraria from AbbVie, Chemocentryx, Coloplast, Incyte, Inflarx, Kymera, Leo Pharma, Novartis, and UCB for participation on advisory boards, and grants from Abbvie, Astra-Zeneca, Inflarx, Janssen-Cilag, Leo Pharma, Novartis, Regeneron and Sanofi, for participation as an investigator, and received speaker honoraria from AbbVie, Boehringer-Ingelheim, Galderma, and Novartis. He has also received unrestricted departmental grants from Leo Pharma and Novartis.
ACK: Abbvie, Novartis, Genesis Pharma, Mylan, Jannsen, Leo Pharma, Lilly
AK: was an investigator, speaker or advisor for AbbVie, Braun-Stiftung and Celgene
EL: Speaker honoraria, and/or honoraria for participation in advisory boards, and/or grants from Abbvie, Novartis, Genesis Pharma, Mylan, Pfizer, Janssen, Leo Pharma, Roche, Lilly, UCB and Sanofi
AVM: None declared.
ŁM: reports personal fees from AbbVie, Amgen, Galapagos, InflaRx, Janssen-Cilag, LEO, Menlo, Novartis, Pfizer, Pierre Fabre, Regeneron, Trevi and UCB.
AML: None declared.
CM: None declared.
AP: was an investigator, speaker or advisor for AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Biontec, Boehringer-Ingelheim, Celgene, GSK, Eli Lilly, Galderma, Hexal, Janssen, LEO-Pharma, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi-Genzyme, Schering-Plough and UCB Pharma.
CP: None declared.
JR: Abbvie, Novartis, LeoPharma, Janssen, Almirall, Isdín
DMS: DM Saunte was paid as a consultant for advisory board meeting by AbbVie, Janssen, Sanofi, Leo Pharma and received speaker's honoraria and/or received grants from the following companies: Abbvie, Pfizer, Galderma, Novartis and Leo Pharma during the last 5 years.
JS: reports personal fees from AbbVie, Amgen, Galapagos, InflaRx, Janssen-Cilag, LEO, Menlo, Novartis, Pfizer, Pierre Fabre, Regeneron, Sandoz, Sanofi, Sienna, Trevi and UCB.
NS: None declared.
DS: None declared.
AT: Abbvie, UCB, Novartis, LEO
EV: None declared.
HHvdZ: honoraria from AbbVie

ORCID IDs
K.R. van Straalen: 0000-0003-3305-3814, T. Tzellos: 0000-0003-2356-0847, P. Guillem: 0000-0002-5449-3897, F. Benhadou: 0000-0002-4533-8297, C. Cuenca-Barrales: 0000-0001-7579-4931, M. Daxhelet: 0000-0003-4506-6989, M. Daoud: 0000-0003-4188-1986, O. Efthymiou: 0000-0002-0466-7553, E.J. Giamarellos-Bourboulis: 0000-0003-4713-3911, G.B.E Jemec: 0000-0002-0712-2540, A. Koenig: 0000-0001-9969-2315, E. Lazaridou: 0000-0002-4072-3591, A.V. Marzano: 0000-0002-8160-4169, Ł. Matusiak: 0000-0003-2067-4929, A. Molina-Leyva: 0000-0001-6882-2113, A. Pinter: 0000-0002-1330-1502, C. Potenza: 0000-0002-6300-8697, J. Romaní: 0000-0002-6134-5155, D.M. Saunte: 0000-0001-7953-1047, N. Skroza: 0000-0003-4478-5404, D. Stergianou: 0000-0002-3014-3155, J. Szepietowski: 0000-0003-0766-6342, A. Trigoni: 0000-0002-2202-2337, H.H. van der Zee: 0000-0002-2874-7726.

Funding sources: None.

IRB approval status: The study was performed within daily practice and in accordance with current guidelines, therefore this study was deemed exempt from IRB review.

Manuscript word count: 2238
Abstract word count: 200
Capsule summary word count: 50
References: 36
Figures: 1
Tables: 4
Supplemental tables: 2
Supplemental material available at https://data.mendeley.com/datasets/xkz8rfyvdp/1

Keywords: acne inversa, treatment, therapy, antibiotics, tetracycline, doxycycline, minocycline, clindamycin, rifampicin, efficacy, outcome, guideline

ABSTRACT

Background: Tetracyclines and clindamycin plus rifampicin combination therapy are both considered first-line therapy in current Hidradenitis Suppurativa (HS) guidelines. However, evidence for their efficacy is drawn from small studies, often without validated outcomes.

Objective: To assess the 12-week efficacy of oral tetracyclines and a combination of clindamycin and rifampicin.

Methods: A prospective, international cohort study performed between October 2018 and August 2019.

Results: In total, 63.6% of the included 283 patients received oral tetracyclines and 36.4% were treated with clindamycin and rifampicin. Both groups showed a significant decrease in IHS4 from baseline (both $p<0.001$). HiSCR was achieved in 40.1% and 48.2% of patients, respectively ($p=0.26$). Patient characteristics or disease severity were not associated with attainment of HiSCR or the minimal clinically important differences for the DLQI and pain.

Limitations: Cohort study. Respectively 23.9% and 19.4% of patients had to be excluded from the HiSCR analysis for the tetracycline and combination therapy group due to a low abscess and nodule count at baseline.

Conclusion: This study shows significant efficacy of both tetracycline treatment and clindamycin and rifampicin combination therapy after 12 weeks in patients with HS. No significant differences in efficacy were observed between the two treatments, regardless of disease severity.

INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic, auto-inflammatory skin disease characterized by painful, deep-seated, highly inflamed nodules and draining tunnels in the intertriginous areas of the body.[1-3] Traditionally HS has been treated with systemic antibiotics, which remain the first-line medical therapy to date. Current guidelines and consensus statements on the treatment of HS consistently recommend two types of antibiotic therapy as first-line treatment.[4-11] Oral tetracyclines, such as doxycycline and minocycline, are recommended as a first-line therapy for mild-to-moderate HS.[4-11] The combination of clindamycin and rifampicin is favored as a first-line therapy for moderate-to-severe HS but is also recommended as a second-line therapy for mild-to-moderate disease unresponsive to oral tetracyclines prior to biologic treatment.[4-11]

Even though these treatments are considered first-line therapy, the evidence to support their efficacy is weak. Oral tetracycline has been studied in an small randomized controlled trial, showing similar efficacy to topical clindamycin.[12] The efficacy of clindamycin and rifampicin combination therapy is derived from several small retrospective and prospective case series.[13-22] Therefore, the aim of this multicenter, international study was to assess the 12-week efficacy of oral tetracyclines and a combination of clindamycin and rifampicin using validated and clinically meaningful physician and patient reported outcomes in patients with HS. In addition, we aimed to identify factors associated with treatment response.

MATERIALS AND METHODS

Study design

A detailed protocol including study design, in- and exclusion criteria, HS treatment guidelines, assessment schedule, and timeline and was sent out in October 2018 to all centers who previously participated in an European Hidradenitis Suppurativa Foundation consortium study.[5,11]

Participants

Following this protocol, patients treated according to the current international guidelines with either oral tetracyclines (tetracycline 500mg b.i.d, doxycycline 100mg once daily, minocycline 100mg once daily) or clindamycin 300mg b.i.d in combination with rifampicin 600mg a day in daily practice were included from 15 European centers between October 2018 and August 2019. Patients were included in a real-life clinical practice setting without blinding or randomization. Exclusion criteria were concomitant systemic therapy, invasive treatment (deroofing, excision, laser therapy, incision and drainage procedure, or intralesional corticosteroids) during the 12 weeks, and missing lesion counts at either baseline of follow-up. Patient characteristics (age, gender, body mass index; BMI, disease duration, 1st or 2nd degree family history) were collected at baseline. Patient reported outcome measures (PROMs; numerical rating scale (NRS) pain, NRS pruritus, and Dermatological Life Quality Index; DLQI), and physician scores (inflammatory nodule count, abscess count, draining sinus tract count, International Hidradenitis Suppurativa Severity Score System; IHS4, modified Sartorius score, Hurley and Refined Hurley staging) were assessed at baseline and after 12 weeks of treatment.[23-25] Hidradenitis Suppurativa Clinical Response (HiSCR; ≥ 50% reduction in inflammatory lesion count (abscesses + inflammatory nodules) and no increase in abscesses or draining fistulas compared with baseline) was calculated at 12 weeks.[26]

Minimal clinical important difference (MCID) was calculated for the DLQI score (≥4 point reduction from baseline) and for NRS Pain (≥30% and ≥1 point reduction from baseline).[27,28] MCIDs were considered missing when patient did not meet baseline requirements for MCID calculations; i.e. DLQI score <4 and NRS pain score <3. HiSCR was calculated for patients with a baseline abscess and nodule count of ≥3.[26] Patients who discontinued treatment were deemed non-achievers of HiSCR, MCID DLQI, and MCID NRS Pain.

Statistical analyses

Patient characteristics are presented as number (percentage, %) for categorical variables and as mean ± standard deviation (SD) or median [interquartile range, IQR] where appropriate for continuous variables. Normality was assessed using the Kolmogorov-Smirnov test. Differences in patient characteristics, PROMs and physician scores between treatment groups were assessed using independent Student t-tests or Mann-Whitney U tests for continuous variables and Chi-square tests or Fisher's exact test for categorical variables, where appropriate. Change from baseline after 12 weeks of treatment was assessed using paired T-tests or Wilcoxon signed-rank test for continuous variables. Univariate logistic regression models were constructed to assess the association of antibiotic treatment and HiSCR, MCID DLQI, and MCID NRS Pain attainment as well as to identify factors associated with treatment response.

RESULTS

In total 283 patients were included; 63.6% (180/283) patients received tetracycline treatment (tetracycline n=42, doxycycline n=121, minocycline n=17) and 36.4% (103/283) patients received treatment with a combination of clindamycin plus rifampicin. There were no significant differences between these two treatment groups regarding gender, age, age of onset, disease duration, BMI, smoking status, family history of HS, or previous surgical treatment (Table 1). Patients treated with clindamycin and rifampicin had significantly more severe disease reflected in a significantly higher number of inflammatory nodules (p=0.029) and draining sinus tracts (p=0.003), higher IHS4 score (p=0.019), Hurley stage (p=0.004), modified Sartorius (p<0.001), and NRS pain score (p=0.005) compared with patients treated with tetracycline.

Both groups showed a significant decrease in IHS4 from baseline; from median of 9.0 [5.0-18.5] to 5.0 [2.0-12.0] (p<0.001) in the tetracycline group and from 13.0 [6.0-27.0] to 6.0 [1.0-17.0] (p<0.001) in the combination therapy(Table 2 and Figure 1). Reductions in all lesion counts were observed (inflammatory nodules, abscesses, and draining tunnels) There

was no significant difference in the percentage of patients achieving HiSCR between the tetracycline group (40.1%) and the clindamycin and rifampicin group (48.2%), p=0.263 (Table 2). HiSCR attainment was not related to Hurley stage or IHS4 category for either tetracyclines (p= 0.920 and p=0.495) and clindamycin and rifampicin (p=0.807 and p=0.796), see Table 3 and 4.

Patients in both groups reported a significant decrease in DLQI, NRS pain, and NRS pruritus after 12 weeks of treatment (Table 2 and Figure 1). There was no significant difference between the treatment groups regarding the percentage of patients that achieved either the MCID for NRS pain or the MCID for the DLQI, p= 0.643 and p=0.084 respectively. MCID pain was significantly more often achieved by patients in Hurley stage III or IHS4 severe category, respectively p=0.028 and p=0.001 in the tetracycline group. No significant difference for MCID pain attainment was found in the clindamycin and rifampicin group.

Univariate regression analysis revealed no significant difference between treatment with tetracycline or clindamycin and rifampicin regarding attainment of either HiSCR, MCID NRS Pain, or MCID DLQI; respectively OR 1.39 (95% CI 0.80-2.40, p=0.243), OR 1.58 (95% CI 0.94-2.65, p=0.085), and OR 1.18 (95% CI 0.64-2.18, p=0.590), see Table 3. HiSCR attainment was not associated with specific patient characteristics, baseline PROMs or physician scores for either tetracycline or clindamycin and rifampicin treatment (Supplemental Table 1 and 2 available through *[Mendeley link]*). Baseline inflammatory nodule count was significantly associated with MCID NRS Pain attainment in both the tetracycline and the combination treatment group, respectively OR 1.15 (95% CI 1.02-1.30, p=0.023) and OR 1.11 (95% CI 1.01-1.23, p=0.034), see Supplemental Table 1 and 2.

Gastrointestinal side effects, not leading to treatment discontinuation, were reported by 16.4% of patients in the tetracycline group compared with 11.8% of the patients in the combination treatment group, p=0.346. The percentage of participants discontinuing either tetracycline treatment (10.7%) or clindamycin and rifampicin treatment (15.8%) due to side effects did not differ significantly, p=0.260.

No significant associations were found for BMI, age, smoking status, discontinuation of treatment, or gastrointestinal side effects for either tetracycline or combination treatment, data not shown. Women more often reported gastrointestinal side effects compared with men when treated with tetracyclines, OR 2.81 (95% CI 1.04-7.56, p=0.041). No such association was found for treatment with clindamycin and rifampicin.

DISCUSSION

This multicenter, prospective study shows significant reduction in IHS4, pain and DLQI scores after 12 weeks of treatment with both tetracyclines treatment and clindamycin and rifampicin combination therapy. The use of tetracyclines in HS is derived from a small randomized controlled trial showing equal efficacy of oral tetracyclines and topical clindamycin in patients with mild-moderate HS using a non-validated outcome.[12] More recently, HiSCR response was assessed in a retrospective case series of patients treated with systemic doxycycline 100mg b.i.d, with 60% of patients achieving HiSCR after 12 weeks of treatment.[14] This is markedly higher than the 40.1% HiSCR attainment found in the tetracycline group in our study. However, no baseline AN-count was reported by Vural et al., which is known to influence HiSCR attainment, and the included population may not be comparable to our study.[14] Nonetheless, doxycycline has previously been shown to have a dose-response effect in reducing inflammatory lesions in patients with moderate to severe acne vulgaris.[29] As the same mechanisms of effect of tetracyclines (anti-bacterial and anti-inflammatory) are assumed in acne and HS, a similar dose-response effect in HS is conceivable.

Current guidelines advice the use of clindamycin 300mg bid and rifampicin 300mg twice daily or 600mg once daily for a duration of 10-12 weeks for moderate-to-severe HS.[30] Treatment with clindamycin and rifampicin has been previously assessed in one prospective and several smaller retrospective trials with differing types of administration (IV or oral), dosage (e.g. 4 times 125 mg of clindamycin or 300mg twice daily,) and timing of the primary

endpoint (ranging from 8 – 12 weeks).[13-22] Overall, HiSCR was achieved by 33.3%-56.7% of patients treated with clindamycin + rifampicin. Even though some of these studies report excluding patients lost to follow-up from the efficacy analysis, potentially inflating response rates, our study found HiSCR attainment in the higher end of this range (48.2%). Severe HS might represent a specific subtype.[31] Contradictory results regarding an association between disease severity and clinical response have been reported. Caposiena Caro et al. found that HiSCR attainment on clindamycin plus rifampicin therapy was significantly more common in patients with mild and moderate disease, measured with both the Hurley stage and IHS4 (respectively p<.001and p=0.02).[15] Our results show no association between disease severity and HiSCR attainment, similar to the results from Dessinioti et al..[18]

Current guidelines advice the use of a combination of clindamycin and rifampicin.[4-11] However, rifampicin has been shown to dramatically reduce plasma concentrations of clindamycin, making a meaningful contribution of clindamycin to either bacterial resistance or reduction of inflammation in this combination unlikely.[32] A retrospective study found similar rates of HiSCR attainment between treatment with clindamycin and rifampicin compared with clindamycin alone after eight weeks of treatment; 56.7% vs. 63.3% (p=0.598), excluding patients who were lost to follow-up from the efficacy analysis.[19]

Even though there are validated MCID values for both the NRS pain and the DLQI only one registry study has published MCID results to date, with them lacking in the large randomized controlled trials.[26-28,33] Achieving the MCID, defined as the smallest change that a patient would identify as clinically meaningful, could be more informative and clinically relevant than the mean reductions in DLQI or pain scores frequently reported in HS clinical trials. Overall, in our study approximately 60% of patients attained a clinically meaningful difference in NRS pain and between 36-47% a meaningful improvement in DLQI score, with no significant differences between treatment groups.

Gastro-intestinal side effects are a main concern as they often lead to discontinuation of treatment.[34,35] The frequency of gastro-intestinal side effects in our study (11.8%) was slightly lower than those previously reported in a large retrospective study and the only

prospective study on clindamycin and rifampicin to date, respectively 14% and 19.2%.[17,18] However, the discontinuation rate (15.8%) in our study was slightly higher than seen in these studies, 11.4% and 11.5% respectively. Interestingly, more gastrointestinal side effects, not leading to treatment discontinuation, were noted in the tetracycline group while more treatment discontinuation was seen in the clindamycin and rifampicin group.

In the current HS treatment guidelines and consensus statements, tetracyclines are considered first-line treatment for mild-to-moderate HS whereas the combination of clindamycin and rifampicin is favored for moderate-to-severe HS.[4-11] Interestingly our study revealed no significant differences between the two antibiotic strategies for the validated outcomes HiSCR, MCID Pain, or MCID DLQI even in patients with moderate-to-severe HS. These results suggest that tetracyclines could be considered as first-line treatment in patients with moderate-to-severe disease. This could prove especially valuable in countries with endemic tuberculosis where rifampicin is preferably reserved for the treatment of tuberculosis or in patients with relative contraindications due to potential drug interaction such as e.g. oral contraceptives.[36] Moreover, guidelines advice that biologics (adalimumab) can be initiated after failure of conventional treatment, often clindamycin and rifampicin combination therapy.[4-11] However, as our study suggests that this treatment is similar to treatment with tetracyclines, failure on tetracycline treatment could be a sufficient indication for biologic eligibility. Nonetheless, a head-to-head randomized, blinded controlled trial comparing tetracycline treatment with clindamycin and rifampicin combination therapy is needed to increase the evidence to a level where firmer conclusions can be drawn.

A limitation of this study is inherent to the calculation of the HiSCR. In accordance with its original publication, HiSCR can only be calculated in patients with three or more inflammatory lesions (abscesses and nodules) at baseline.[26] Overall, respectively 23.9% and 19.4% of patients had to be excluded from the HiSCR analysis for the tetracycline and combination therapy group based on the low abscess and nodule count at baseline. However, this is not representative of real life and hampers the extrapolation of HiSCR

results to routine clinical settings. This issue could potentially be overcome by a dichotomous version of the IHS4 score.

In conclusion, this study shows no significant difference between patients treated with tetracyclines or with a combination of clindamycin and rifampicin in the validated outcomes HiSCR, IHS4, MCID DLQI, and MCID Pain after 12 weeks, regardless of disease severity. These results might suggest that tetracyclines could be considered as first-line treatment in patients with moderate-to-severe disease, and failure to tetracyclines may be a sufficient indication for the initiation of biologic therapy.

REFERENCES

1 Tricarico PM, Boniotto M, Genovese G *et al.* An Integrated Approach to Unravel Hidradenitis Suppurativa Etiopathogenesis. *Front Immunol* 2019; **10**: 892.

2 Vossen ARJV, van der Zee HH, Prens EP. Hidradenitis suppurativa: a systematic review integrating inflammatory pathways into a cohesive pathogenic model. *Frontiers in Immunology* 2018; **9**: 2965.

3 Jemec GB. Clinical practice. Hidradenitis suppurativa. *N Engl J Med* 2012; **366**: 158-64.

4 Ingram JR, Collier F, Brown D *et al.* British Association of Dermatologists guidelines for the management of hidradenitis suppurativa (acne inversa) 2018. *British Journal of Dermatology* 2019; **180**: 1009-17.

5 Zouboulis CC, Desai N, Emtestam L *et al.* European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. *Journal of the European Academy of Dermatology and Venereology* 2015; **29**: 619-44.

6 Alikhan A, Sayed C, Alavi A *et al.* North American clinical management guidelines for hidradenitis suppurativa: A publication from the United States and Canadian Hidradenitis Suppurativa Foundations: Part II: Topical, intralesional, and systemic medical management. *J Am Acad Dermatol* 2019; **81**: 91-101.

7 Hunger RE, Laffitte E, Läuchli S *et al.* Swiss practice recommendations for the management of hidradenitis suppurativa/acne inversa. *Dermatology* 2017; **233**: 113-9.

8 Magalhães RF, Rivitti-Machado MC, Duarte GV *et al.* Consensus on the treatment of hidradenitis suppurativa-Brazilian Society of Dermatology. *Anais brasileiros de dermatologia* 2019; **94**: 7-19.

9 Alavi A, Lynde C, Alhusayen R *et al.* Approach to the management of patients with hidradenitis suppurativa: A consensus document. *Journal of cutaneous medicine and surgery* 2017; **21**: 513-24.

10 Gulliver W, Landells IDR, Morgan D *et al.* Hidradenitis Suppurativa: A Novel Model of Care and an Integrative Strategy to Adopt an Orphan Disease. *J Cutan Med Surg* 2018; **22**: 71-7.

11 Gulliver W, Zouboulis CC, Prens E *et al.* Evidence-based approach to the treatment of hidradenitis suppurativa/acne inversa, based on the European guidelines for hidradenitis suppurativa. *Reviews in Endocrine and Metabolic Disorders* 2016; **17**: 343-51.

12 Jemec GBE, Wendelboe P. Topical clindamycin versus systemic tetracycline in the treatment of hidradenitis suppurativa. *Journal of the American Academy of Dermatology* 1998; **39**: 971-4.

13 Van Straalen KR, Schneider-Burrus S, Prens EP. Current and future treatment of hidradenitis suppurativa. *British Journal of Dermatology* 2018.

14 Vural S, Gündoğdu M, Akay BN *et al.* Hidradenitis suppurativa: Clinical characteristics and determinants of treatment efficacy. *Dermatologic Therapy* 2019; **32**: e13003.

15 Caposiena Caro RD, Cannizzaro MV, Botti E *et al.* Clindamycin versus clindamycin plus rifampicin in hidradenitis suppurativa treatment: Clinical and ultrasound observations. *Journal of the American Academy of Dermatology* 2019; **80**: 1314-21.

16 Marasca C, Annunziata MC, Villani A *et al.* Adalimumab versus Rifampicin Plus Clindamycin for the Treatment of Moderate to Severe Hidradenitis Suppurativa: A Retrospective Study. *Journal of drugs in dermatology: JDD* 2019; **18**: 437-8.

17 Gener G, Canoui-Poitrine F, Revuz JE *et al.* Combination therapy with clindamycin and rifampicin for hidradenitis suppurativa: a series of 116 consecutive patients. *Dermatology* 2009; **219**: 148-54.

18 Dessinioti C, Zisimou C, Tzanetakou V *et al.* Oral clindamycin and rifampicin combination therapy for hidradenitis suppurativa: a prospective study and 1-year follow-up. *Clinical and experimental dermatology* 2016; **41**: 852-7.

19 Caro RDC, Cannizzaro MV, Botti E *et al.* Clindamycin versus clindamycin plus rifampicin in hidradenitis suppurativa treatment: clinical and ultrasound observations. *Journal of the American Academy of Dermatology* 2019; **80**: 1314-21.

20 Bettoli V, Zauli S, Borghi A *et al.* Oral clindamycin and rifampicin in the treatment of hidradenitis suppurativa-acne inversa: a prospective study on 23 patients. *J Eur Acad Dermatol Venereol* 2014; **28**: 125-6.

21 Mendonça CO, Griffiths CE. Clindamycin and rifampicin combination therapy for hidradenitis suppurativa. *Br J Dermatol* 2006; **154**: 977-8.

22 van der Zee HH, Boer J, Prens EP *et al.* The effect of combined treatment with oral clindamycin and oral rifampicin in patients with hidradenitis suppurativa. *Dermatology* 2009; **219**: 143-7.

23 Zouboulis CC, Tzellos T, Kyrgidis A *et al.* Development and validation of the International Hidradenitis Suppurativa Severity Score System (IHS4), a novel dynamic scoring system to assess HS severity. *Br J Dermatol* 2017; **177**: 1401-9.

24 Horváth B, Janse IC, Blok JL *et al.* Hurley staging refined: a proposal by the Dutch Hidradenitis Suppurativa Expert Group. *Acta dermato-venereologica* 2017; **97**: 412-3.

25 Sartorius K, Emtestam L, Jemec GB *et al.* Objective scoring of hidradenitis suppurativa reflecting the role of tobacco smoking and obesity. *Br J Dermatol* 2009; **161**: 831-9.

26 Kimball AB, Sobell JM, Zouboulis CC *et al.* HiSCR (Hidradenitis Suppurativa Clinical Response): a novel clinical endpoint to evaluate therapeutic outcomes in patients with hidradenitis suppurativa from the placebo-controlled portion of a phase 2 adalimumab study. *Journal of the European Academy of Dermatology and Venereology* 2016; **30**: 989-94.

27 Basra MKA, Salek MS, Camilleri L *et al.* Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. *Dermatology* 2015; **230**: 27-33.

28 Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. *The Journal of pain* 2003; **4**: 407-14.

29 Leyden JJ, Bruce S, Lee CS *et al.* A randomized, phase 2, dose-ranging study in the treatment of moderate to severe inflammatory facial acne vulgaris with doxycycline calcium. *J Drugs Dermatol* 2013; **12**: 658-63.

30 Orenstein LAV, Nguyen TV, Damiani G *et al.* Medical and Surgical Management of Hidradenitis Suppurativa: A Review of International Treatment Guidelines and Implementation in General Dermatology Practice. *Dermatology* 2020: 1-20.

31 Vanlaerhoven AMJD, Ardon CB, van Straalen KR *et al.* Hurley III Hidradenitis Suppurativa Has an Aggressive Disease Course. *Dermatology* 2018; **234**: 232-3.

32 Join-Lambert O, Ribadeau-Dumas F, Jullien V *et al.* Dramatic reduction of clindamycin plasma concentration in hidradenitis suppurativa patients treated with the rifampin-clindamycin combination. *European Journal of Dermatology* 2014; **24**: 94-5.

33 Grimstad Ø, Tzellos T, Dufour DN *et al.* Evaluation of medical and surgical treatments for hidradenitis suppurativa using real-life data from the Scandinavian registry (HISREG). *Journal of the European Academy of Dermatology and Venereology* 2019; **33**: 1164-71.

34 Schneller-Pavelescu L, Vergara-de Caso E, Martorell A *et al.* Interruption of oral clindamycin plus rifampicin therapy in patients with hidradenitis suppurativa: An observational study to assess prevalence and causes. *Journal of the American Academy of Dermatology* 2019; **80**: 1455-7.

35 Albrecht J, Baine PA, Ladizinski B *et al.* Long-term clinical safety of clindamycin and rifampicin combination for the treatment of hidradenitis suppurativa. A Critically Appraised Topic. *Br J Dermatol* 2019; **180**: 749-55.

36 Yazdanyar S, Jemec GB. KITTEN following CAT on the long-term use of rifampicin in hidradenitis suppurativa and effectiveness of oral contraceptives. *Br J Dermatol* 2019; **181**: 225-6.

TABLE LEGENDS

Table 1. Baseline characteristics

BMI; body mass index, HS; Hidradenitis Suppurativa, DLQI; Dermatology Quality of Life Index, NRS; Numerical rating scale, IHS4; International Hidradenitis Suppurativa Scoring System

Table 2. Response to treatment after 12 weeks

DLQI; Dermatology Quality of Life Index, MCID; minimal clinically important difference, NRS; Numerical rating scale, IHS4; International Hidradenitis Suppurativa Scoring System, HiSCR; Hidradenitis Suppurativa Clinical Response.* compared with baseline scores, ^ comparison of tetracycline and clindamycin + rifampicin groups

Table 3. Response to treatment per disease severity category

MCID; minimal clinically important difference, DLQI; Dermatology Quality of Life Index, HiSCR; Hidradenitis Suppurativa Clinical Response. * Hurley stage missing for 1 patient on tetracyclines.

Table 4. Regression analysis of validated outcomes

OR; Odds ratio, MCID; minimal clinically important difference, DLQI; Dermatology Quality of Life Index, NRS; Numerical rating scale, BMI; body mass index, IHS4; International Hidradenitis Suppurativa Scoring System. * reference categories; female, non-smokers, no family history, no previous surgical treatment

Supplemental Table 1. Identification of factors associated with response to tetracyclines

OR; Odds ratio, MCID; minimal clinically important difference, DLQI; Dermatology Quality of Life Index, NRS; Numerical rating scale, BMI; body mass index, IHS4; International Hidradenitis Suppurativa Scoring System. * reference categories; female, non-smokers, no family history, no previous surgical treatment

Supplemental Table 2. Identification of factors associated with response to clindamycin and rifampicin

OR; Odds ratio, MCID; minimal clinically important difference, DLQI; Dermatology Quality of Life Index, NRS; Numerical rating scale, BMI; body mass index, IHS4; International Hidradenitis Suppurativa Scoring System. * reference categories; female, non-smokers, no family history, no previous surgical treatment

FIGURE LEGENDS

Figure 1. Response after 12 weeks of treatment

A. DLQI, B. IHS4, C. NRS Pain, D. NRS Pruritus

DLQI; Dermatology Quality of Life Index, IHS4; International Hidradenitis Suppurativa Scoring System, NRS; Numerical rating scale. * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

488 **Table 1. Baseline characteristics**

	Tetracyclines n=180		Clindamycin and Rifampicin n=103		p-value
Patient characteristics					
Gender					
Females, *n (%)*	106	(58.9)	56	(54.4)	0.533
Age, *median [IQR]*	37	[26-46]	36	[27-45]	0.917
Missing, *n*	0		1		
Age of onset, *median [IQR]*	21	[15-30]	21	[16-28]	0.854
Missing, *n*	3		0		
Disease duration, *median [IQR]*	10	[6-19]	10	[5-17]	0.415
Missing, *n*	3		1		
BMI, *mean (SD)*	29.81	(6.1)	29.21	(6.2)	0.428
Missing, *n*	6		0		
Current smoker, *n (%)*	110	(61.8)	56	(56.6)	0.443
Missing, *n*	2		4		
Family history of HS, *n (%)*	58	(34.3)	34	(35.1)	1.000
Missing, *n*	11		6		
Previous surgical treatment, *n (%)*	69	(38.3)	39	(38.6)	1.000
Missing, *n*	0		2		
Patient reported outcomes					
DLQI, *mean (SD)*	13.3	(7.5)	15.1	(7.9)	0.071
Missing, *n*	8		7		
NRS Pain, *median [IQR]*	6	[4-8]	7	[5-8]	**0.005**
Missing, *n*	7		3		
NRS Pruritus, *median [IQR]*	3	[0-6]	4	[0-7]	0.204
Missing, *n*	13		8		
Physician scores					
Inflammatory nodules, *median [IQR]*	3.5	[1.0-6.0]	4	[2-9]	**0.029**
Abscesses, *median [IQR]*	0.0	[0.0-2.0]	0	[0-2]	0.975
Draining sinus tracts, *median [IQR]*	1.0	[0.0-2.0]	1	[0-4]	**0.003**
Hurley stage					
Stage I, *n (%)*	54	(30.2)	14	(13.6)	**0.004**
Stage II, *n (%)*	90	(50.3)	58	(56.3)	
Stage III, *n (%)*	35	(19.5)	31	(30.1)	
Missing, *n*	1		0		
Refined Hurley stage					
Stage Ia, *n (%)*	22	(12.3)	2	(1.9)	**0.004**
Stage Ib, *n (%)*	24	(13,4)	9	(8.7)	
Stage Ic, *n (%)*	17	(9.5)	11	(10.7)	
Stage IIa, *n (%)*	22	(12.3)	6	(5.8)	
Stage IIb, *n (%)*	42	(23.5)	25	(24.3)	
Stage IIc, *n (%)*	29	(16.2)	28	(27.2)	
Stage III, *n (%)*	23	(12.8)	22	(21.4)	
Missing , *n*	1		0		
IHS4, *median [IQR]*	9.0	[5.0-18.5]	13.0	[6.0-27.0]	**0.019**
Mild, *n (%)*	29	(16.1)	8	(7.8)	**0.032**
Moderate, *n (%)*	77	(42.8)	38	(36.9)	
Severe, *n (%)*	74	(41.1)	57	(55.3)	
Modified Sartorius, *median [IQR]*	25.5	[17.0-44.0]	40.0	[26.0-59.0]	**<0.001**
Missing, *n*	38		46		

489 BMI; body mass index, HS; Hidradenitis Suppurativa, DLQI; Dermatology Quality of Life Index, NRS; Numerical rating scale, IHS4; International Hidradenitis Suppurativa Scoring System.

490

491 **Table 2. Response to treatment after 12 weeks**

	Tetracyclines n= 180		p-value*	Clindamycin & Rifampicin n=103		p-value*	p-value^
Patient reported outcomes							
DLQI, *mean (SD)*	10.2	(8.2)	**<0.001**	9.8	(7.6)	**<0.001**	
Missing, *n*	7			3			
DLQI MCID achieved, *n (%)*	58	(36.3)		44	(47.3)		0.084
Missing, *n*	20			10			
NRS Pain, *median [IQR]*	4.0	[1.5-7.0]	**<0.001**	3	[0.0-5.5]	**<0.001**	
Missing, *n*	4			3			
NRS Pain MCID achieved	58	(59.8)		51	(63.8)		0.643
Missing, *n*	83			23			
NRS Pruritus, *median [IQR]*	1.0	[0.0-5.0]	**<0.001**	1.0	[0.0-5.0]	**<0.001**	
Missing, *n*	12			8			
Physician scores							
Inflammatory nodule count, *median [IQR]*	2.0	[0.0-4.0]	**<0.001**	2.0	[0.0-4.0]	**<0.001**	
Abscess count, *median [IQR]*	0.0	[0.0-1.0]	**<0.001**	0.0	[0.0-1.0]	**0.001**	
Draining sinus tract count, *median [IQR]*	0.0	[0.0-2.0]	**<0.001**	1.0	[0.0-2.0]	**<0.001**	
IHS4, *median [IQR]*	5.0	[2.0-12.0]	**<0.001**	6.0	[1.0-17.0]	**<0.001**	
Mild, *n (%)*	58	(32.2)		34	(33.0)		
Moderate, *n (%)*	70	(38.9)		29	(28.2)		
Severe, *n (%)*	52	(28.9)		40	(38.8)		
Modified Sartorius, *median [IQR]*	17.0	[10.0-35.0]	**<0.001**	25.0	[13.0-44.0]	**<0.001**	
Missing, *n*	41			45			
HiSCR achieved	55	(40.1)		40	(48.2)		0.263
Missing due to baseline count <3, *n*	43			20			
Discontinuation and side effects							
Discontinuation	19	(10.7)		16	(15.8)		0.260
Missing, *n*	3			2			
GI side effects not leading to discontinuation	24	(16.4)		10	(11.8)		0.346
Missing	34			18			

DLQI; Dermatology Quality of Life Index, MCID; minimal clinically important difference, NRS; Numerical rating scale, IHS4; International Hidradenitis Suppurativa Scoring System, HiSCR; Hidradenitis Suppurativa Clinical Response.* compared with baseline scores, ^ comparison of tetracycline and clindamycin + rifampicin groups

492

493

494

495

496

497

498

499 **Table 3. Response to treatment per disease severity category**

	Hurley stage I	Hurley stage II	Hurley stage III	p-value	IHS4 mild	IHS4 moderate	IHS4 severe	p-value
Tetracyclines	n=54*	n=90*	n=35*		n=29	n=77	n=74	
HiSCR achieved, *n (%)*	15 (39.5)	30 (41.7)	10 (37.0)	0.920	5 (41.7)	20 (34.5)	30 (44.8)	0.495
Missing, *n*	16	18	8		17	19	7	
MCID DLQI achieved, *n (%)*	20 (41.7)	28 (35.4)	10 (31.3)	0.629	9 (31.0)	25 (32.5)	24 (34.3)	0.901
Missing, *n*	6	11	3		6	10	4	
MCID Pain achieved, *n (%)*	13 (41.9)	29 (64.4)	16 (76.2)	**0.028**	3 (23.1)	19 (51.4)	36 (76.6)	**0.001**
Missing, *n*	23	45	14		16	40	27	
Clindamycin + Rifampicin	n=14	n=58	n=31		n=8	n=38	n=57	
HiSCR achieved, *n (%)*	3 (37.5)	24 (51.1)	13 (46.4)	0.807	1 (25.0)	12 (48.0)	27 (50.0)	0.796
Missing, *n*	6	11	3		4	13	3	
MCID DLQI achieved, *n (%)*	6 (54.5)	25 (49.0)	13 (41.9)	0.763	2 (33.3)	16 (47.1)	26 (49.1)	0.843
Missing, *n*	3	7	0		2	4	4	
MCID Pain achieved, *n (%)*	5 (62.5)	28 (62.2)	18 (66.7)	0.941	2 (40.0)	17 (58.6)	32 (69.6)	0.357
Missing, *n*	6	13	4		3	9	11	

MCID; minimal clinically important difference, DLQI; Dermatology Quality of Life Index, , HiSCR; Hidradenitis Suppurativa Clinical Response. * Hurley stage missing for 1 patient on tetracyclines.

500

501 **Table 4. Regression analysis of validated outcomes**

	HiSCR			MCID DLQI			MCID Pain		
	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value	n	OR (95% CI)	p-value
Antibiotic treatment	220	1.39 (0.80-2.40)	0.243	253	1.58 (0.94-2.65)	0.085	177	1.18 (0.64-2.18)	0.590
Patient characteristics									
Gender*	220	1.03 (0.60-1.77)	0.910	253	0.98 (0.59-1.62)	0.928	177	0.97 (0.52-1.79)	0.915
Age	219	1.02 (1.00-1.04)	0.051	252	1.00 (0.99-1.03)	0.395	177	1.03 (1.00-1.05)	**0.042**
Age of onset	218	1.02 (0.99-1.05)	0.126	250	1.00 (0.98-1.03)	0.855	176	1.03 (1.00-1.07)	0.051
Disease duration	217	1.02 (0.99-1.05)	0.291	249	1.01 (0.99-1.04)	0,257	176	1.00 (0.98-1.03)	0.782
BMI	215	0.99 (0.95-1.04)	0.786	247	0.96 (0.96-1.04)	0.799	173	1.00 (0.94-1.05)	0.858
Smoking status*	218	1.35 (0.78-2.36)	0.286	250	1.34 (0.80-2.27)	0.271	174	2.03 (1.09-3.80)	**0.026**
Family history of HS*	208	1.02 (0.57-1.81)	0.955	238	1.07 (0.62-1.83)	0.820	165	1.15 (0.60-2.22)	0.673
Previous surgical treatment*	219	1.14 (0.66-1.96)	0.644	251	1.21 (0.72-2.02)	0.468	175	1.63 (0.86-3.09)	0.138
Patient reported outcome measures at baseline									
DLQI	211	1.04 (1.00-1.07)	0.053	251	1.11 (1.07-1.16)	<0.001	170	1.02 (0.98-1.07)	0.305
NRS Pain	216	1.03 (0.93-1.14)	0.601	250	1.06 (0.97-1.17)	0.215	176	1.01 (0.88-1.16)	0.867
NRS Pruritus	208	1.07 (0.98-1.16)	0.131	240	1.11 (1.03-1.20)	0.009	169	1.07 (0.97-1.18)	0.154
Physician scores at baseline									
Inflammatory nodule count	220	1.06 (1.00-1.12)	**0.044**	253	1.03 (0.98-1.08)	0.299	177	1.13 (1.05-1.22)	**0.002**
Abscess count	220	0.96 (0.87-1.07)	0.473	253	1.06 (0.96-1.17)	0.271	177	1.18 (1.02-1.37)	**0.026**
Draining sinus tract count	220	0.96 (0.87-1.04)	0.340	253	0.92 (0.84-1.00)	0.054	177	1.06 (0.94-1.19)	0.328
Presence of sinus tracts	220	0.90 (0.52-1.54)	0.690	253	0.78 (0.47-1.31)	0.352	177	1.36 (0.73-2.54)	0.332
Hurley stage									
Hurley stage I		*reference*			*reference*			*reference*	
Hurley stage II	220	1.22 (0.71-2.08)	0.475	252	1.03 (0.62-1.70)	0.922	177	1.16 (0.63-2.13)	0.626
Hurley stage III	220	0.93 (0.50-1.72)	0.814	252	0.80 (0.44-1.44)	0.459	177	1.75 (0.86-3.57)	0.125
IHS4	220	1.00 (0.98-1.01)	0.677	253	0.99 (0.98-1.01)	0.331	177	1.03 (1.01-1.05)	**0.017**
Mild		*reference*			*reference*			*reference*	
Moderate	220	0.74 (0.42-1.28)	0.281	253	1.02 (0.61-1.70)	0.941	177	0.63 (0.34-1.17)	0.139
Severe	220	1.43 (0.83-2.45)	0.194	253	1.03 (0.62-1.70)	0.916	177	2.85 (1.52-5.34)	**0.001**
Modified Sartorius	161	0.99 (0.98-1.00)	0.100	183	0.99 (0.98-1.00)	0.054	122	1.00 (0.98-1.01)	0.603

OR; Odds ratio, MCID; minimal clinically important difference, DLQI; Dermatology Quality of Life Index, NRS; Numerical rating scale, BMI; body mass index, IHS4; International Hidradenitis Suppurativa Scoring System. * reference categories; female, non-smokers, no family history, no previous surgical treatment

502

503

504

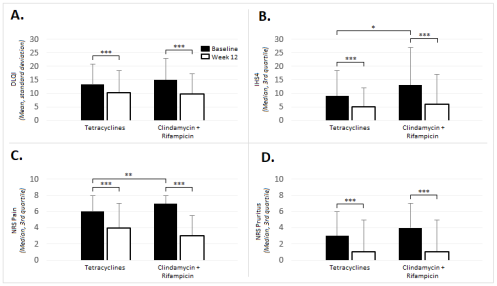
505

506

507

Supplemental Table 1. Identification of factors associated with response to tetracyclines

Supplemental Table 2. Identification of factors associated with response to clindamycin and rifampicin



CAPSULE SUMMARY

- Evidence for the efficacy of tetracyclines and clindamycin plus rifampicin in Hidradenitis Suppurativa (HS) is drawn from small studies, often without validated outcomes.
- Both treatments with tetracyclines and clindamycin combined with rifampicin show significant efficacy in patients with HS. No significant differences in efficacy were observed, regardless of disease severity.