Author/s:
Kok, Y;Nicolopoulos, J;Braue, A;Kern, JS;Varigos, G;Dolianitis, C

Title:
Measuring treatment response to adalimumab in hidradenitis suppurativa patients: An observational study

Date:
2020-08-01

Citation:
Kok, Y., Nicolopoulos, J., Braue, A., Kern, J. S., Varigos, G. & Dolianitis, C. (2020). Measuring treatment response to adalimumab in hidradenitis suppurativa patients: An observational study. Australasian Journal of Dermatology, 61 (3), pp.292-294. https://doi.org/10.1111/ajd.13245.

Title: Measuring treatment response to adalimumab in Hidradenitis Suppurativa patients: An observational study

Short running title: Measuring treatment response to adalimumab in Hidradenitis Suppurativa

Yonatan Kok[1], Jenny Nicolopoulos[1], Anna Braue[1,2], Johannes S. Kern[1,2,3], George Varigos[1,2], Con Dolianitis[1,2]

[1]The Royal Melbourne Hospital, Department of Dermatology, Parkville, Victoria, Australia

[2]The University of Melbourne, Department of Medicine, Parkville, Victoria, Australia

[3]University of Freiburg, Department of Dermatology, Faculty of Medicine, Medical Center, Freiburg, Germany

Corresponding author: Yonatan Kok

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/AJD.13245

Postal address: The Royal Melbourne Hospital, Level 8 Dermatology Office, 300 Grattan Street, Parkville, Victoria, Australia, 3050

Email address: yonatan.kok@mh.org.au

Telephone number: +61 434644543 (primary number) (03) 93424531

Acknowledgements

We would like to acknowledge the team of the Dermatology Department at the Royal Melbourne Hospital for their ongoing support in this study.

Conflict of interest

Yonatan Kok: Sub-Investigator in clinical trials for atopic dermatitis sponsored by AbbVie

Johannes S. Kern: Investigator in clinical trials for atopic dermatitis sponsored by AbbVie

Con Dolianitis: Past advisory board member for AbbVie

All other authors: No conflict of interest that would influence the author's objectivity.

2019

DR. YONATAN KOK (Orcid ID : 0000-0002-0604-1183)

Article type : Research Letter

Measuring treatment response to adalimumab in Hidradenitis Suppurativa patients: An observational study

Hidradenitis Suppurativa (HS) is a chronic, recurrent inflammatory dermatosis characterised by deep seated painful "boils," nodules, sinus tracts and scarring on the apocrine bearing glands of the skin[1,2]. HS is estimated to affect 1-4% of the global population and 0.67% of the Australian population[3,4].

Three primary outcome scores are used in our HS clinic to measure clinical response in HS including the Hidradenitis Suppurative Clinical Response (HiSCR), Dermatology Life Quality Index (DLQI) and Visual

Analogue Scale (VAS) pain score. The PIONEER I and II studies have previously shown that adalimumab improves disease severity in patients with moderate-to-severe HS at 12 weeks[5]. However, Australian data regarding its sustained clinical efficacy is lacking.

The aim of this study was to longitudinally measure treatment response in moderate-to-severe HS patients by using HiSCR, DLQI and pain scores from treatment onset to 12 months.

This retrospective longitudinal study was conducted at the Royal Melbourne Hospital dermatology outpatient's clinic, a tertiary referral centre, in Australia. Fifteen consecutive patients with Hurley stage 2 or 3 HS were treated with adalimumab. The total abscess and nodule count, DLQI and VAS pain score were measured at baseline and at three-, six-, nine- and twelve-months post commencement. Differences in mean scores were calculated using the two sample T-test.

Overall, apart from a higher prevalence of depression and hyperlipidaemia and a lower prevalence of obesity, our study cohort showed similar patient characteristics to the PIONEER I and II studies (see table 1).

The mean total abscess and nodule count was 25.5 at baseline and this was reduced to 6.7 at 3 months, 4.4 at 6 months, 5.3 at 9 months and 1.5 at 12 months (see table 2). The difference in mean total abscess and nodule count at each time point compared to baseline were all statistically significant. 87% of patients achieved HiSCR at 3-months whilst at 6-months, 100% achieved HiSCR. At the 9- and 12-months, 93% of patients achieved HiSCR.

The predominant lesions observed at baseline were inflammatory nodules with a mean count of 18.73 (see table 3). All lesional types had a statistically significant mean reduction in their mean count at 3- and 6- months ($p < 0.05$). There was a further decline in inflammatory nodule count seen at 9 months but an increase in abscess and fistula count. At the end of the study, all lesion types had a statistically significant mean reduction in their count compared to baseline.

The mean DLQI score at baseline was 14.5 (see table 2). There was a mean DLQI score reduction of 3.6 and 6.0 at 3- and 6-months respectively but this was not statistically significant. A statistically significant reduction in mean DLQI score was measured at 9-months (mean difference = 7.1, $p = 0.05$) and 12-months (mean difference = 9.3, $p = 0.01$).

The mean VAS pain score at baseline was 5.9 (see table 2). There was a statistically significant reduction in VAS pain score at all measured time points after starting adalimumab. The mean difference in VAS pain score were 4.8 at 3 months ($p < 0.01$), 3.6 at 6 months ($p = 0.03$), 4.6 at 9 months ($p = 0.01$) and 4.4 at 12 months ($p = 0.01$).

The main adverse event reported in this study was lower respiratory tract infections (40%). One patient developed deranged liver function tests (data not shown). No serious adverse events occurred.

The limitations of this study include the lack of a control group, small sample size and potential confounders such as the use of concomitant medications. There were high rates of antibiotic usage at baseline (80%) and 3 months (47%) with some patients reporting ongoing usage at the end of the study. There was also a reduction in the prevalence of smoking and use of tight clothing at twelve months compared to baseline (see table 1). Taken together, these factors may overestimate the improvement in disease severity scores attributed to adalimumab.

This study highlights that adalimumab is effective in improving HS disease severity and VAS pain score as early as three months in our Australian moderate-to-severe HS patient cohort. Adalimumab appears to control disease severity and pain level for at least one year. Improvements in DLQI scores, however, took up to 9 months to be significantly improved perhaps owing to multiple factors that contribute to quality of life. There is a scope for future studies in this field including a larger controlled study to validate the results of this study and an Australian study which assesses drug survival over a longer course.

References

1. Zouboulis CC, del Marmol V, Mrowietz U, Prens EP, Tzellos T, Jemec GBE. Hidradenitis Suppurativa/Acne Inversa: Criteria for Diagnosis, Severity Assessment, Classification and Disease Evaluation. Dermatology. 2015;231(2):184-90.

2. Maximilian vL, Peter H, Johannes W, Eckhard F, Volker S, Wolfgang Christian M. Hidradenitis suppurativa (acne inversa): early inflammatory events at terminal follicles and at interfollicular epidermis*. Experimental Dermatology. 2010(6):533.

3. Calao M, Wilson JL, Spelman L, Billot L, Rubel D, Watts AD, et al. Hidradenitis Suppurativa (HS) prevalence, demographics and management pathways in Australia: A population-based cross-sectional study. PLoS ONE. 2018(7).

4. Deirdre Nathalie D, Lennart E, Gregor B J. Hidradenitis suppurativa: a common and burdensome, yet under-recognised, inflammatory skin disease. Postgraduate Medical Journal. 2014(1062):216.

5. Kimball AB, Okun MM, Williams DA, Gottlieb AB, Papp KA, Zouboulis CC, et al. Two Phase 3 Trials of Adalimumab for Hidradenitis Suppurativa. 2016;375(5):422-34.

Tables

Table 1.

The basic demographic data of all adult HS patients in this study at baseline compared to PIONEER I and II studies on adalimumab.

	Our study (n = 15)	**PIONEER I and II**[5] (n = 316)

Age of onset (%)		
0 – 10 years	0 (0%)	-
11 – 20 years	6 (40%)	-
21 – 30 years	6 (40%)	-
31 – 40 years	2 (13%)	-
41 – 50 years	0 (0%)	-
51 – 60 years	1 (7%)	-
Gender (%)		
Male	6 (40%)	117 (37%)
Female	9 (60%)	199 (63%)
Hurley stage (%)		
Stage 2	7 (47%)	166 (53%)
Stage 3	8 (53%)	150 (47%)
Patient - reported mental health problems (%)		
Depression	4 (27%)	51 (16%)
Anxiety	1 (7%)	-
Smoking (%)		
Baseline		
Yes	9 (60%)	186 (59%)
No	6 (40%)	130 (41%)
End of study		
Yes	7 (47%)	-
No	8 (53%)	-
Relevant co-morbidities		
Polycystic Ovarian Syndrome	3 (33%) *	-
Obesity	4 (27%)	182 (58%)
Metabolic syndrome	5 (33%)	-
Type 2 diabetes mellitus	2 (13%)	29 (9%)
Hyperlipidaemia	4 (27%)	18 (6%)
Follicular occlusion triad	3 (20%)	-
Inflammatory bowel disease	1 (7%)	-
Concomitant medications		
Baseline		
Oral antibiotics	12 (80%)	-
Resorcinol	2 (13%)	-
Isotretinoin	3 (20%)	-
Spironolactone	3 (20%)	-
3 months		
Oral antibiotics	7 (47%)	-

Resorcinol	2 (13%)	-
Isotretinoin	0	-
Spironolactone	0	-
6 months		
Oral antibiotics	3 (20%)	-
Resorcinol	2 (13%)	-
Isotretinoin	0	-
Spironolactone	0	-
9 months		
Oral antibiotics	2 (13%)	-
Resorcinol	3 (20%)	-
Isotretinoin	0	-
Spironolactone	2 (13%)	-
12 months		
Oral antibiotics	2 (13%)	-
Resorcinol	3 (20%)	-
Isotretinoin	1 (7%)	-
Spironolactone	0	-
Family history		
Positive	2 (13%)	78 (25%)
Negative	13 (87%)	245 (75%)
Other risk factors		
Baseline		
Excessive sweating	1 (7%)	-
Tight clothing	2 (13%)	-
End of study		
Excessive sweating	1 (7%)	-
Tight clothing	0	-

*This percentage is derived from the total number of female participants only

- denotes not reported

Table 2.

The mean values of the total abscess and nodule count, DLQI and VAS pain score at baseline, 3-, 6-, 9- and 12-months and the mean difference compared to baseline at each time point.

	Mean	95% CI	Mean difference to baseline	p value
Total abscess and nodule count				
Baseline	25.5	(18.2, 32.8)		
3 months	6.7	(3.9, 9.5)	18.9	<0.01
6 months	4.4	(1.9, 6.9)	21.1	<0.01
9 months	5.3	(0.5,10.1)	20.2	<0.01
12 months	1.5	(0.5, 2.5)	24.0	<0.01
DLQI				
Baseline	14.5	(9.0, 20.0)		
3 months	10.9	(6.8, 15.1)	3.6	0.33
6 months	8.6	(3.9, 13.2)	6.0	0.13
9 months	7.4	(4.3, 10.5)	7.1	0.05
12 months	5.3	(3.0, 7.5)	9.3	0.01
VAS pain score				
Baseline	5.9	(3.5, 8.3)		
3 months	1.1	(0.0, 2.1)	4.8	<0.01
6 months	2.2	(0.6, 3.9)	3.6	0.03
9 months	1.3	(0.1, 2.5)	4.6	0.01
12 months	1.5	(0.5, 2.5)	4.4	0.01

*p value significance is set at 5%

Table 3.

The mean values of the total abscess, inflammatory nodules and fistula count at baseline, 3-, 6-, 9- and 12-months and the mean difference compared to baseline at each time point.

	Mean	95% CI	Mean difference to baseline	p value
Abscess				
Baseline	2.82	(1.15, 4.49)		
3 months	0.59	(-0.05, 1.22)	2.23	0.02
6 months	0.30	(-0.18, 0.78)	2.52	0.01
9 months	1.20	(-0.82, 3.21)	1.62	0.18
12 months	0.38	(-0.06, 0.81)	2.44	0.01
Inflammatory nodules				
Baseline	18.73	(8.35, 29.10)		
3 months	5.17	(2.63, 7.71)	13.56	0.02
6 months	3.90	(1.53, 6.27)	14.83	0.01
9 months	3.00	(1.01, 4.99)	15.73	0.01
12 months	1.13	(0.08, 2.17)	17.6	0.01
Fistula				
Baseline	2.46	(1.07, 3.84)		
3 months	0.92	(-0.02, 2.02)	1.54	0.07

6 months	0.20	(-0.03, 0.65)	2.26	0.01
9 months	1.10	(-0.91, 3.11)	1.35	0.23
12 months	0.00	(0.00, 0.00)	2.46	<0.01

*p value significance is set at 5%