Quoi de neuf ?

Maladies inflammatoires

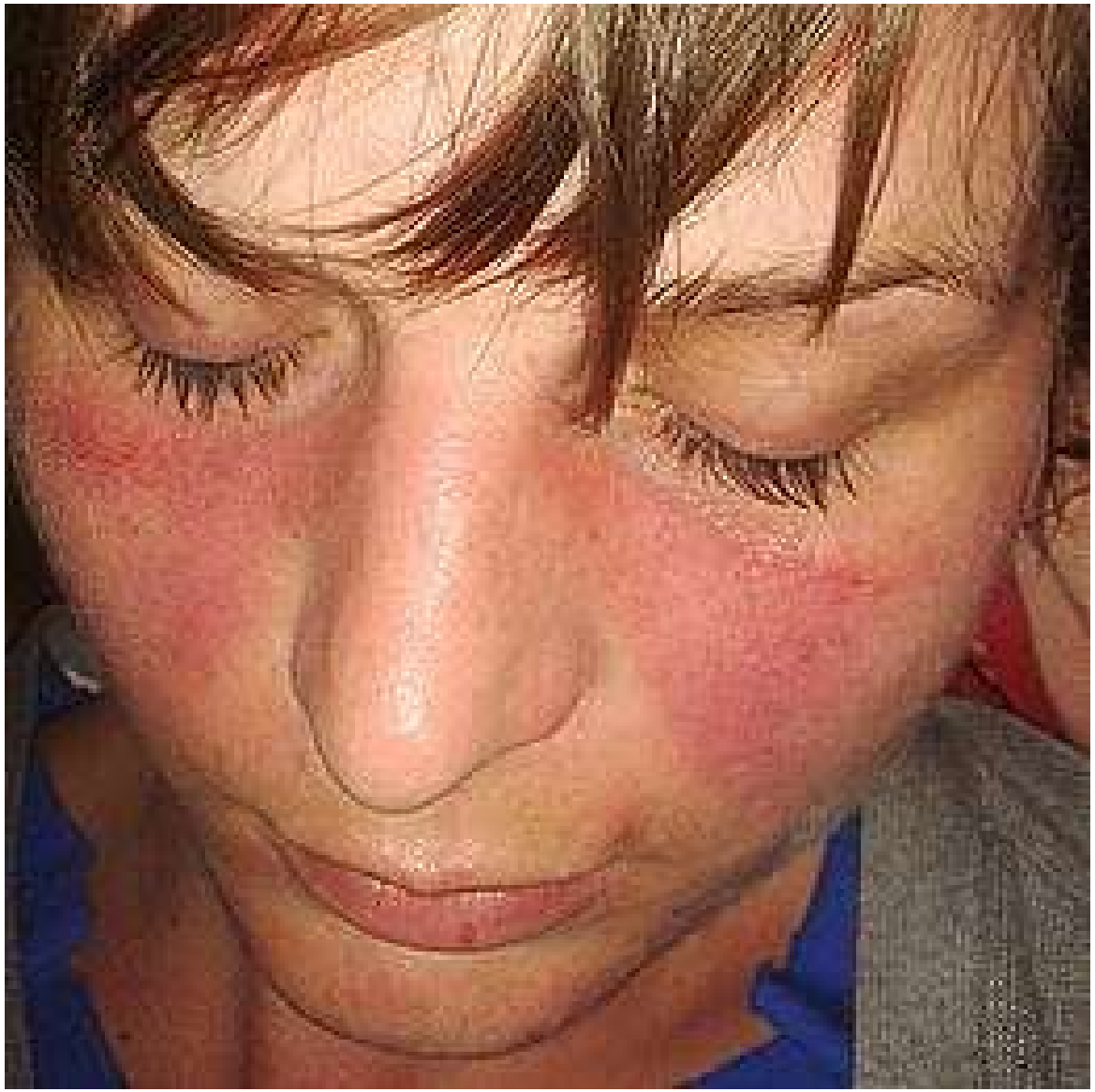
Divi CORNEC

SR0 Septembre 2021 – Saint-Brieuc

Agenda

- De nouveaux traitements pour les maladies systémiques ?

- Mutations somatiques et maladies inflammatoires (exemple du VEXAS)



Lupus systémique

The NEW ENGLAND JOURNAL of MEDICINE

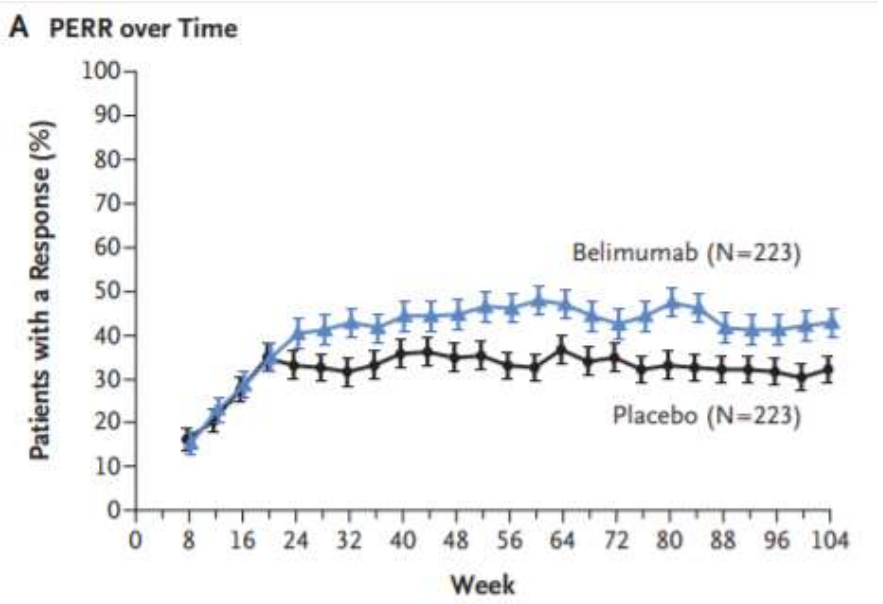
ORIGINAL ARTICLE

Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis

Richard Furie, M.D., Brad H. Rovin, M.D., Frédéric Houssiau, M.D., Ph.D., Ana Malvar, M.D., Y.K. Onno Teng, M.D., Ph.D., Gabriel Contreras, M.D., M.P.H., Zahir Amoura, M.D., Xueqing Yu, M.D., Chi-Chiu Mok, M.D.,

Table 1. Baseline Demographic and Clinical Characteristics of the Patients in the Modified Intention-to-Treat Population.*

Characteristic	Belimumab (N=223)	Placebo (N=223)	Total (N=446)
Female sex — no. (%)	197 (88)	196 (88)	393 (88)
Age — yr	33.7±10.7	33.1±10.6	33.4±10.7
Race or ethnic group — no. (%)†			
Asian	114 (51)	109 (49)	223 (50)
White	73 (33)	75 (34)	148 (33)
Black	30 (13)	31 (14)	61 (14)
American Indian or Alaska Native	4 (2)	6 (3)	10 (2)
Multiple races or ethnic groups	2 (1)	2 (1)	4 (1)
Geographic region — no. (%)			
Asia	106 (48)	105 (47)	211 (47)
Europe	41 (18)	45 (20)	86 (19)
United States or Canada	38 (17)	38 (17)	76 (17)
Americas, excluding United States and Canada	38 (17)	35 (16)	73 (16)



Lupus

ANIFROLUMAB 300 mg, solution à diluer pour perfusion

PUBLIÉ LE 23/07/2021 - MISE À JOUR LE 03/09/2021

A+ A-

Spécialité(s) pharmaceutique(s)

ANIFROLUMAB 300 mg, solution à diluer pour perfusion

Substance active

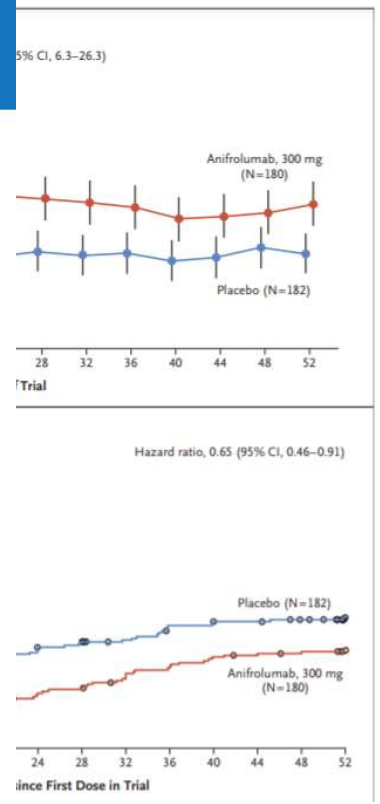
Anifrolumab

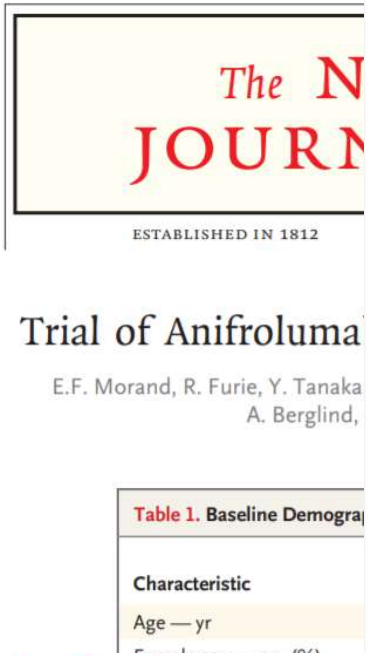
Titulaire

Astra Zeneca

Statut

ATU du 28/06/2021
Début le 09/08/2021





Indications

Traitement de fond additionnel chez les patients adultes atteints d'un Lupus Erythémateux Systémique (LES) insuffisamment contrôlé (ou intolérant) malgré un traitement optimal avec les biothérapies actuellement disponibles

Hispanic or Latino ethnic group — no. (%)†	54 (29.7)	54 (30.0)

Lupus systémique

Efficacy and safety of voclosporin versus placebo for lupus nephritis (AURORA 1): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial

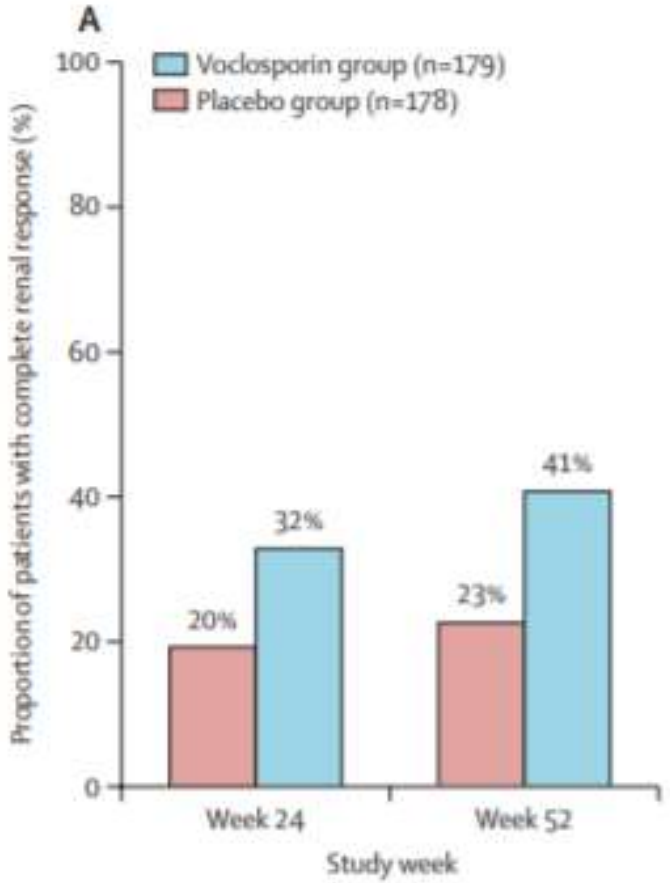
Brad H Rovin, Y K Onno Teng, Ellen M Ginzler, Cristina Arriens, Dawn J Caster, Juanita Romero-Diaz, Keisha Gibson, Joshua Kaplan, Laura Lisk, Sandra Navarra, Samir V Parikh, Simrat Randhawa, Neil Solomons, Robert B Huizinga

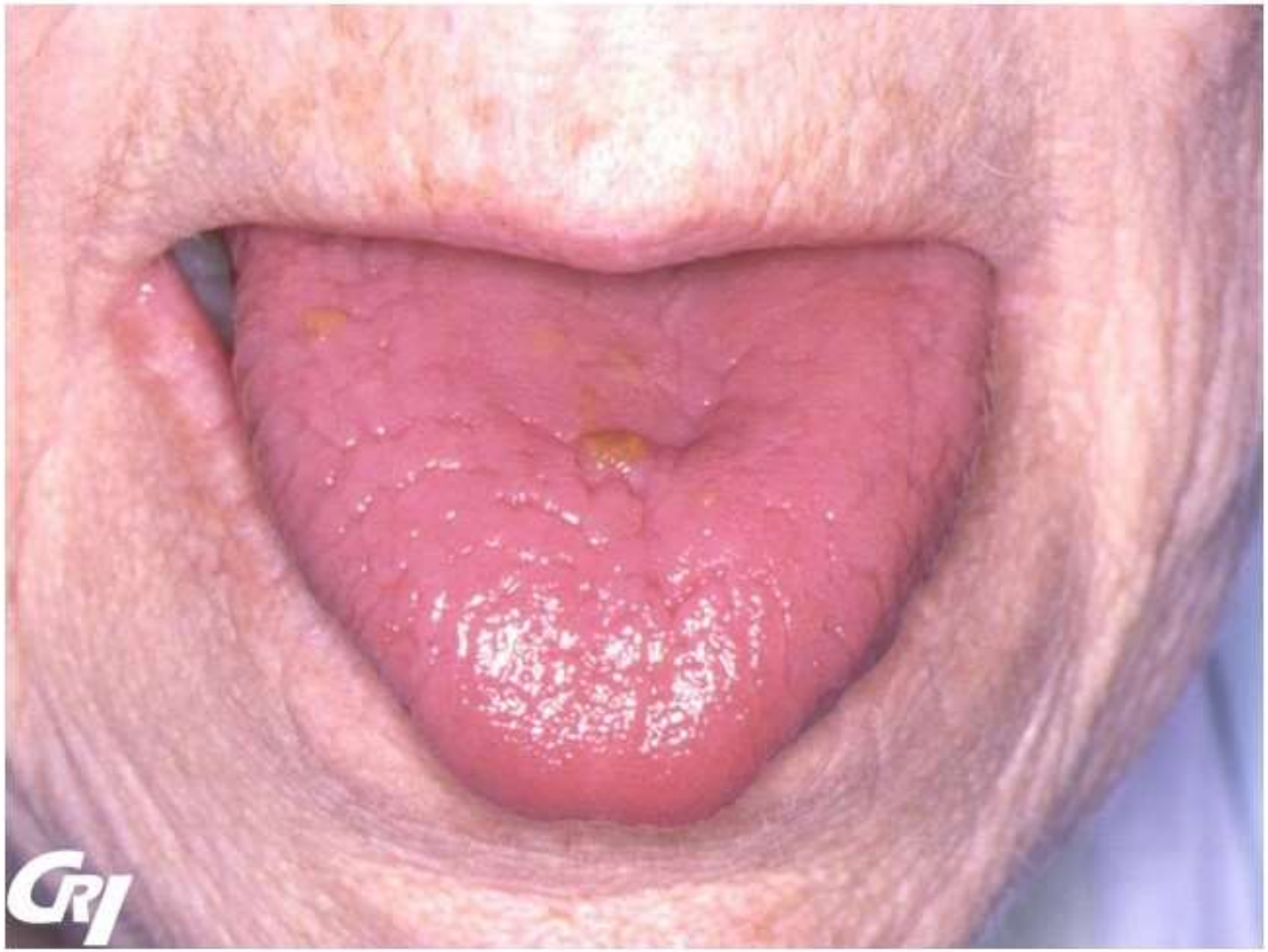
Lancet 2021; 397: 2070–80
Published Online
May 7, 2021
https://doi.org/10.1016/

Summary

Background Voclosporin, a novel calcineurin inhibitor approved for the treatment of adults with lupus nephritis, improved complete renal response rates in patients with lupus nephritis in a phase 2 trial. This study aimed to evaluate the efficacy and safety of voclosporin for the treatment of lupus nephritis.

	Voclosporin group (n=179)	Placebo group (n=178)
Median age, years	31 (18–62)	32 (18–72)
Sex		
Male	18 (10%)	26 (15%)
Female	161 (90%)	152 (85%)
Mean weight, kg	66·49 (17·07)	66·55 (16·11)
Race*		
White	68 (38%)	61 (34%)
Black	26 (15%)	19 (11%)
Asian	53 (30%)	56 (31%)
Other†	32 (18%)	42 (24%)
Ethnicity*		
Hispanic or Latino	57 (32%)	59 (33%)
Non-Hispanic or non-Latino	122 (68%)	118 (66%)
Unknown	0	1 (1%)
Region		
North and Latin America	75 (42%)	74 (42%)
Europe and South Africa	52 (29%)	52 (29%)
Asia-Pacific	52 (29%)	52 (29%)




GRI

Sjögren

- Rituximab : mitigé
- Tocilizumab : aucun effet
- Abatacept : quasi aucun effet

- Plus d’espoir ? On arrête ?

Sjögren

THE LANCET
Rheumatology

Log in

ARTICLES | VOLUME 3, ISSUE 8, E553-E562, AUGUST 01, 2021

Subscribe

Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS): development and validation of a novel outcome measure

Suzanne Arends, PhD * • Liseth de Wolff, MD * • Jolien F van Nimwegen, PhD • Gwenny M P J Verstappen, PhD • Jelle Vehof, PhD • Prof Michele Bombardieri, PhD • Prof Simon J Bowman, PhD • Elena Pontarini, PhD • Alan N Baer, MD • Marleen Nys, PhD • Prof Jacques-Eric Gottenberg, PhD • Renaud Felten, MD • Neelanjana Ray, PhD • Prof Arjan Vissink, PhD • Prof Frans G M Kroese, PhD • Prof Hendrika Bootsma, PhD • Show less

Show footnotes

Published: May 26, 2021 • DOI: https://doi.org/10.1016/S2665-9913(21

Table 2: CRESS response rates at week 24 of abatacept and placebo groups

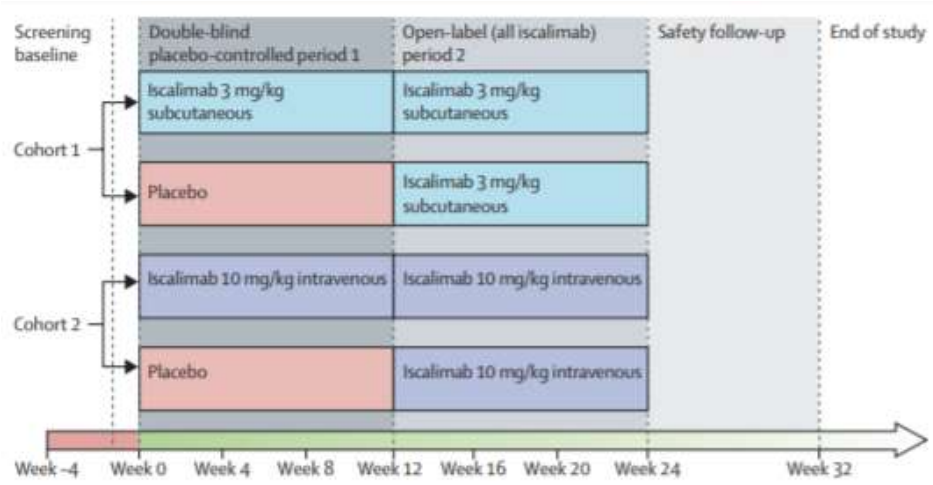
Item	Measurement	Responders abatacept	Responders placebo
Systemic disease activity	ClinESSDAI	45%	27%
Patient-reported symptoms	ESSPRI	58%	22%
Tear gland	Schirmer/OSS	58%	36%
Salivary gland	UWS/SGUS	58%	41%
Serological	RF/IgG	64%	19%
Total CRESS responder	**Response on ≥3 items of 5**	**65%**	**18%**

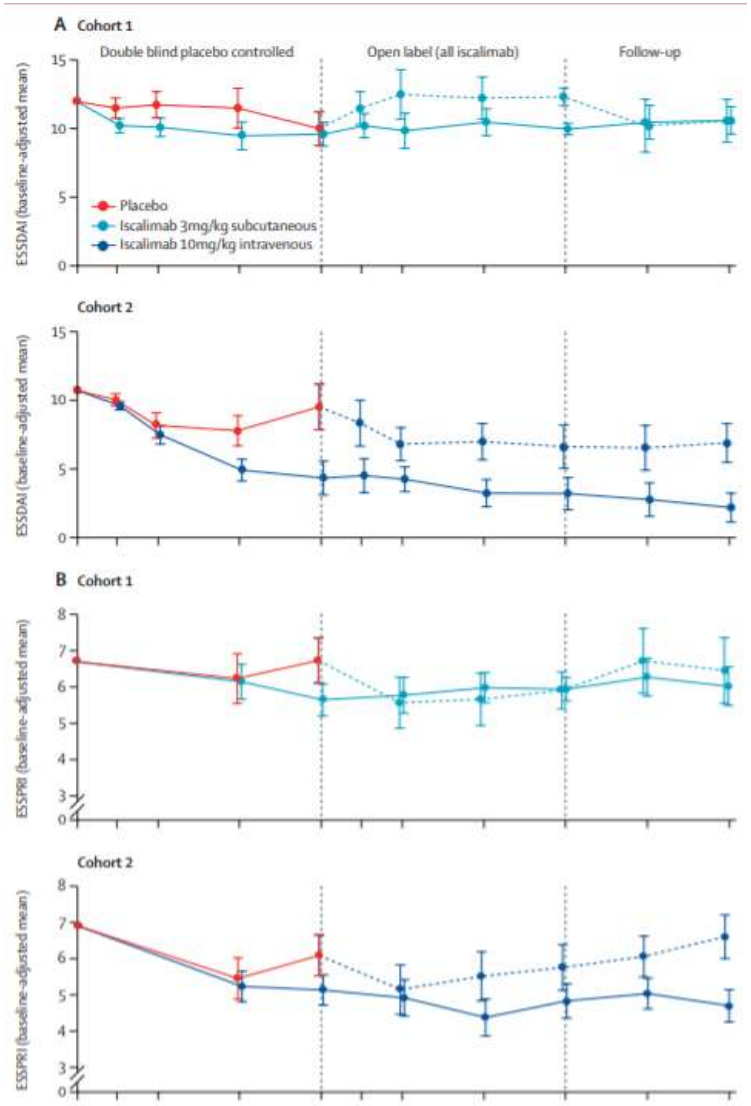
Abbreviations: see Table 1

Sjögren

Assessment of the anti-CD40 antibody iscalimab in patients with primary Sjögren's syndrome: a multicentre, randomised, double-blind, placebo-controlled, proof-of-concept study

Benjamin A Fisher, Antonia Szanto, Wan-Fai Ng, Michele Bombardieri, Maximilian G Posch, Athena S Papas, Arwa M Farag, Thomas Daikeler, Bettina Bannert, Diego Kyburz, Alan J Kivitz, Steven E Carsons, David A Isenberg, Francesca Barone, Simon J Bowman, Pascal Espié, David Floch, Cyrielle Dupuy, Xiaohui Ren, Petra M Faerber†, Andrew M Wright, Hans-Ulrich Hockey‡, Michael Rotte, Julie Milojevic, Alexandre Avrameas, Marie-Anne Valentin, James S Rush§, Peter Gergely§*





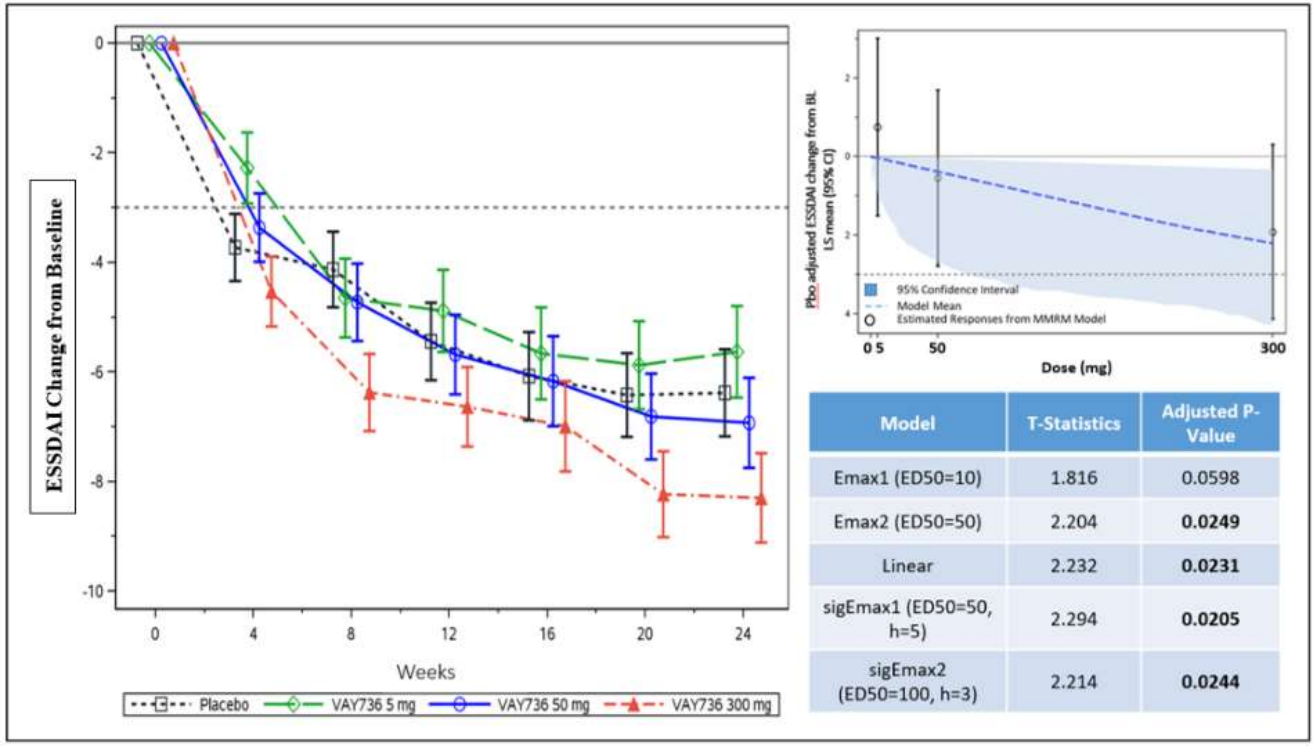
Sjögren

ABSTRACT NUMBER: L19

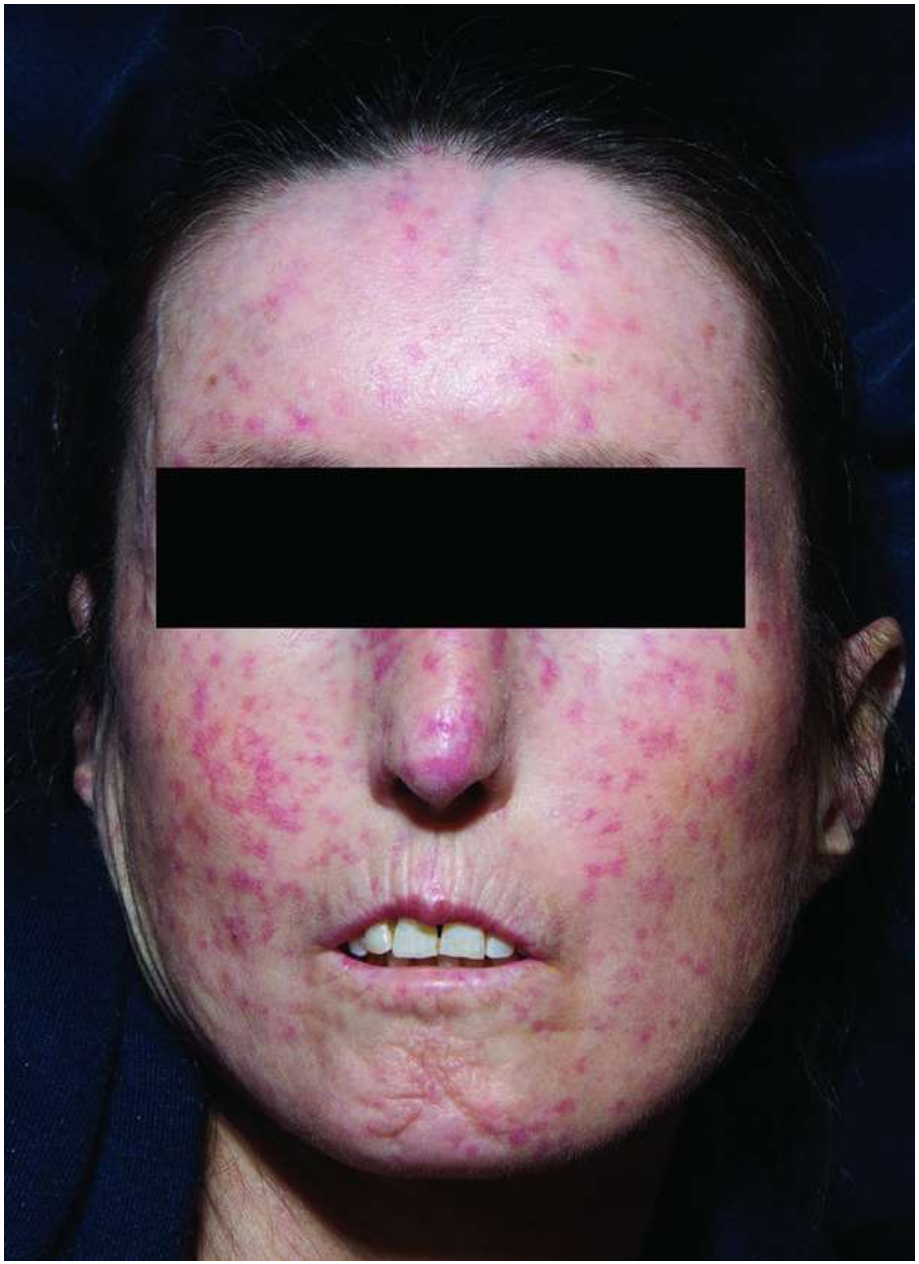
Ianalumab (VAY736), a Dual Mode of Action Biologic Combining BAFF Receptor Inhibition with B Cell Depletion for Treatment of Primary Sjögren's Syndr International Randomized, Placebo Contr Finding Study in 190 Patients

Meeting: 2019 ACR/ARP Annual Me

Date of first publication: October 2



Model	T-Statistics	Adjusted P-Value
Emax1 (ED50=10)	1.816	0.0598
Emax2 (ED50=50)	2.204	**0.0249**
Linear	2.232	**0.0231**
sigEmax1 (ED50=50, h=5)	2.294	**0.0205**
sigEmax2 (ED50=100, h=3)	2.214	**0.0244**



Sclérodermie systémique

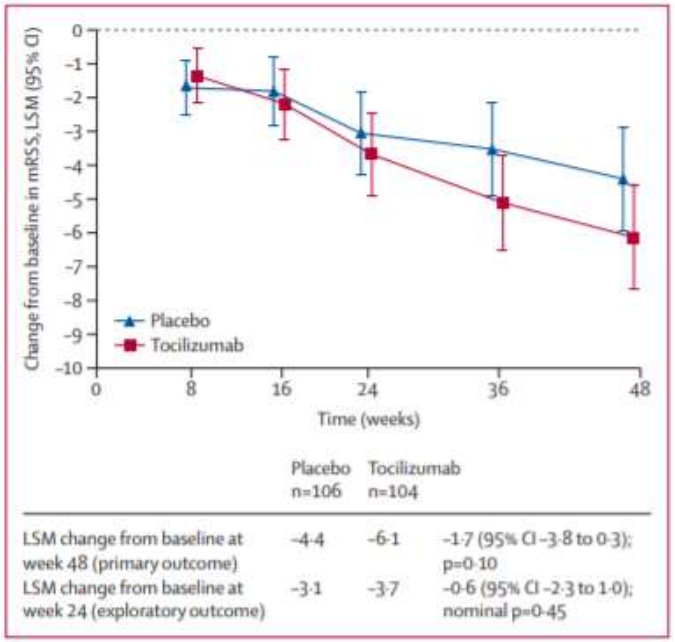
Tocilizumab in systemic sclerosis: a randomised, double-blind, placebo-controlled, phase 3 trial

Dinesh Khanna, Celia J F Lin, Daniel E Furst, Jonathan Goldin, Grace Kim, Masataka Kuwana, Yannick Allanore, Marco Matucci-Cerinic, Oliver Distler, Yoshihito Shima, Jacob M van Laar, Helen Spotswood, Bridget Wagner, Jeffrey Siegel, Angelika Jahreis, Christopher P Denton*, for the focuSSced investigators†*

Summary

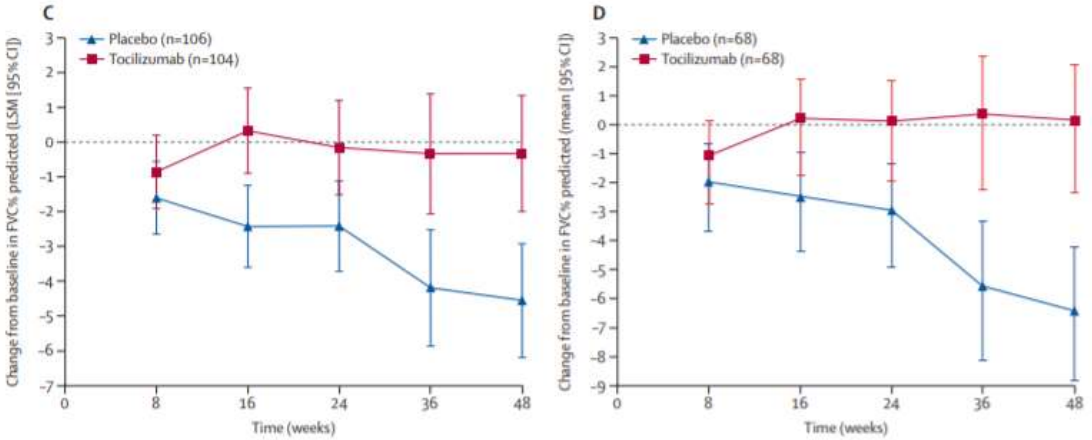
Background A phase 2 trial of tocilizumab showed preliminary evidence of efficacy in systemic sclerosis. We assessed skin fibrosis and systemic sclerosis-associated interstitial lung disease (SSc-ILD) in a phase 3 trial to investigate the safety and efficacy of tocilizumab, an anti-interleukin-6 receptor antibody, in the treatment of systemic sclerosis.

Lancet Respir Med 2020
Published Online
August 28, 2020
https://doi.org/10.1016/



	Placebo n=106	Tocilizumab n=104	
LSM change from baseline at week 48 (primary outcome)	-4·4	-6·1	-1·7 (95% CI -3·8 to 0·3); p=0·10
LSM change from baseline at week 24 (exploratory outcome)	-3·1	-3·7	-0·6 (95% CI -2·3 to 1·0); nominal p=0·45

Figure 2: **Mean change from baseline in mRSS (ITT population)**



	Placebo n=106	Tocilizumab n=104	
LSM change from baseline at week 48	-4·6	-0·4	4·2 (95% CI 2·0 to 6·4); nominal p=0·0002

Sclérodermie systémique

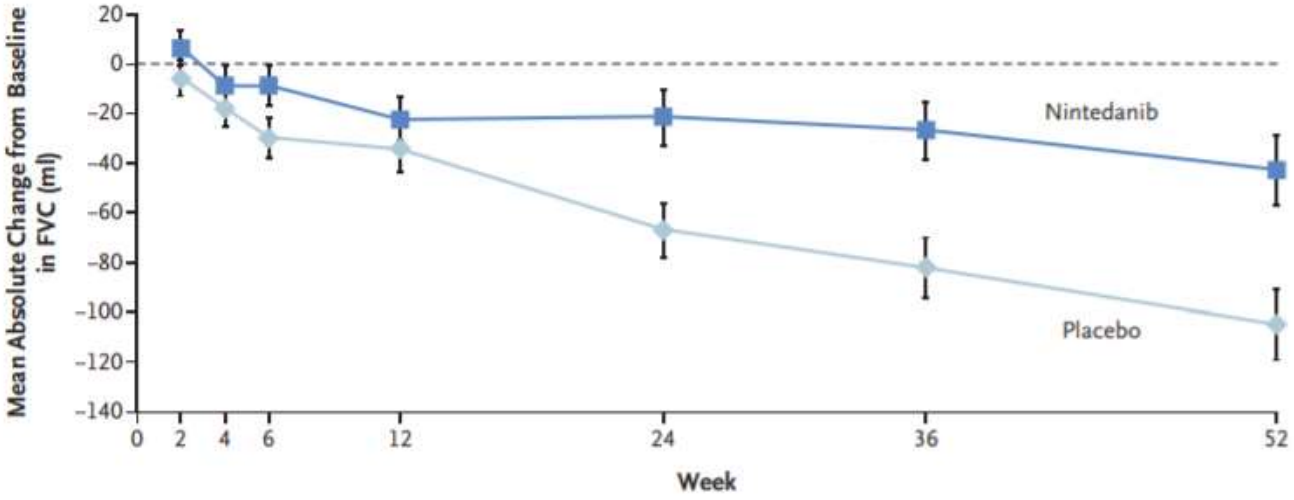
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nintedanib for Systemic Sclerosis–Associated Interstitial Lung I

Oliver Distler, M.D., Kristin B. Highland, M.D., Martina C
Arata Azuma, M.D., Aryeh Fischer, M.D., Maureen D.
Ganesh Raghu, M.D., Wiebke Sauter, Ph.D., Mannaig
Margarida Alves, M.D., Emmanuelle Clerisme-Be
Susanne Stowasser, M.D., Kay Tetzlaff, M.D., Masataka
and Toby M. Maher, M.D., for the SENSCIS Trial In

N Engl J Med 2019;380:2518-28.
DOI: 10.1056/NEJMoa1903076



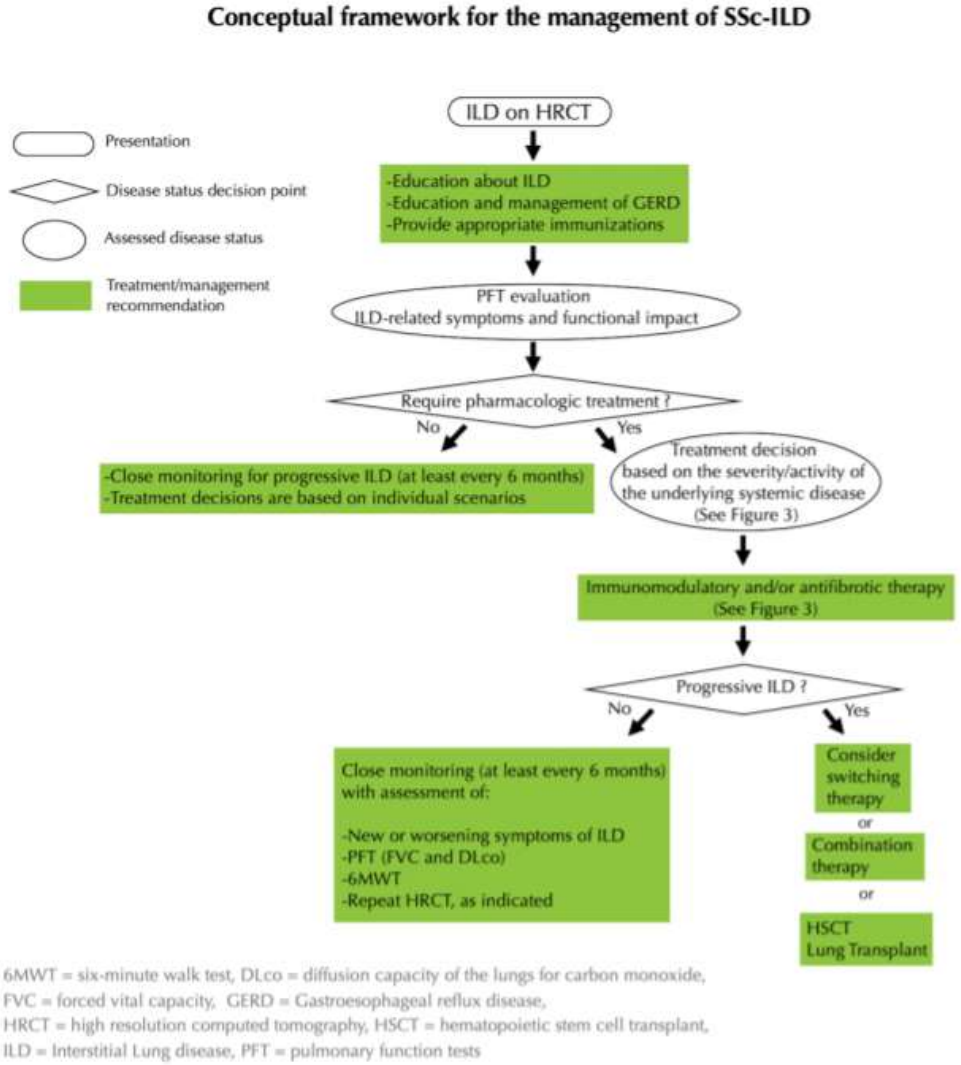
No. of Patients								
Nintedanib	288	283	281	273	278	265	262	241
Placebo	288	283	281	280	283	280	268	257

Sclérodermie systémique

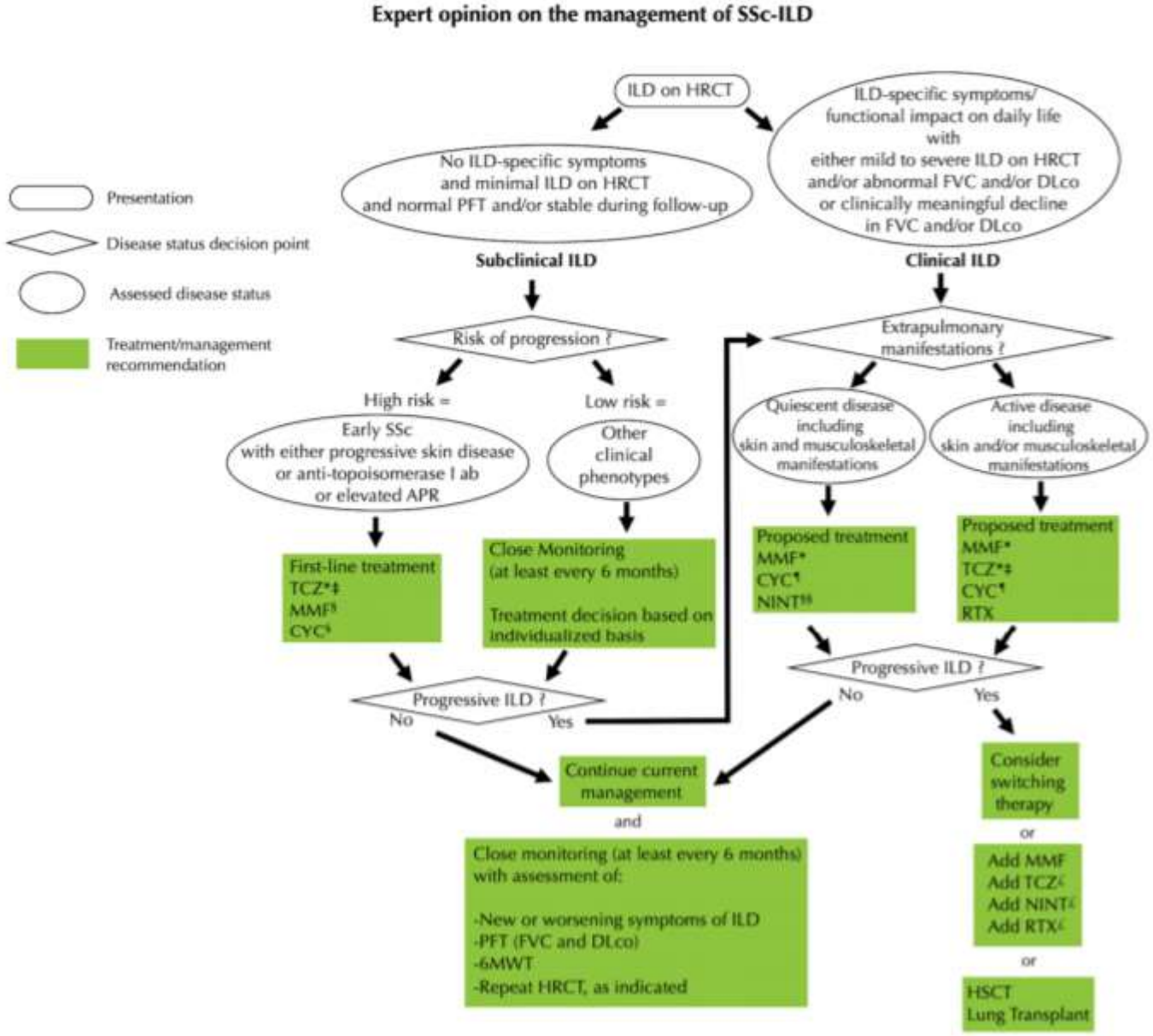
SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE:

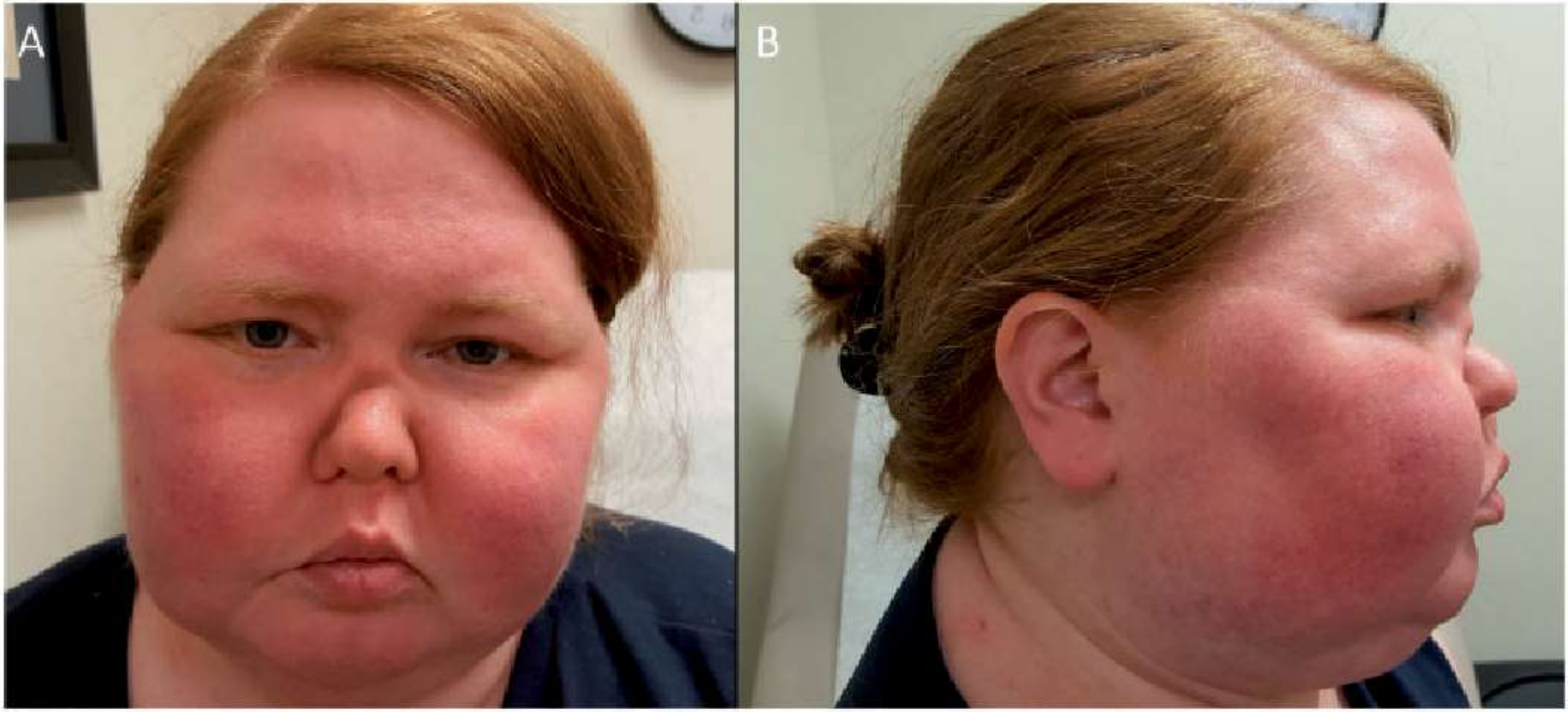
How to incorporate two Food and Drug Administration-approved therapies in clinical pra

Dinesh Khanna MD MSc[1,2]; Alain Lescoat MD PhD[1,3,4]; David Roofeh MD[1,2];
Elana J Bernstein MD MSc[5]; Ella A Kazerooni MD MS[6]; Michael D Roth MD[7];
Fernando Martinez MD MS[8]; Kevin R Flaherty MD MS[9]; Christopher P Denton MD PhI



Sclér


Expert opinion on the management of SSc-ILD
Presentation
Disease status decision point
Assessed disease status
Treatment/management recommendation
ILD on HRCT
No ILD-specific symptoms and minimal ILD on HRCT and normal PFT and/or stable during follow-up
ILD-specific symptoms/ functional impact on daily life with either mild to severe ILD on HRCT and/or abnormal FVC and/or DLco or clinically meaningful decline in FVC and/or DLco
Subclinical ILD
Clinical ILD
Risk of progression ?
Extrapulmonary manifestations ?
High risk =
Early SSc with either progressive skin disease or anti-topoisomerase I ab or elevated APR
Low risk =
Other clinical phenotypes
Quiescent disease including skin and musculoskeletal manifestations
Active disease including skin and/or musculoskeletal manifestations
First-line treatment
TCZ*‡
MMF§
CYC§
Close Monitoring (at least every 6 months)
Treatment decision based on individualized basis
Proposed treatment
MMF*
CYC¶
NINT¶¶
Proposed treatment
MMF*
TCZ*‡
CYC¶
RTX
Progressive ILD ?
No
Yes
Progressive ILD ?
No
Yes
Continue current management
and
Close monitoring (at least every 6 months) with assessment of:
-New or worsening symptoms of ILD
-PFT (FVC and DLco)
-6MWT
-Repeat HRCT, as indicated
Consider switching therapy
or
Add MMF
Add TCZ‡
Add NINT‡
Add RTX‡
or
HSCT
Lung Transplant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B

ANCA

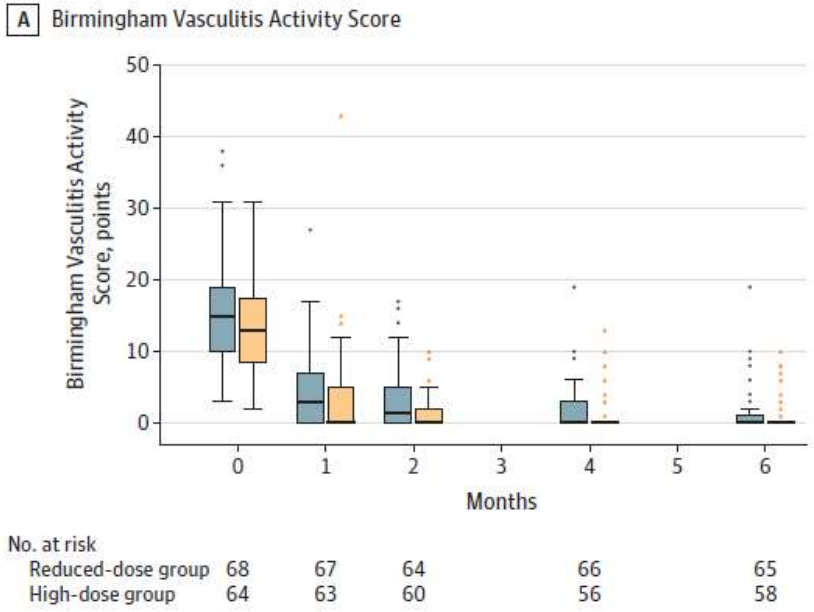
JAMA | Original Investigation

Effect of Reduced-Dose vs Hig on Remission Induction in AN
A Randomized Clinical Trial

Shunsuke Furuta, MD, PhD; Daiki Nakagomi, MD, PhD; Yosl
Takao Sugiyama, MD, PhD; Koichi Amano, MD, PhD; Takesh
Kazuhiro Kurasawa, MD, PhD; Yasuhiko Kita, MD, PhD; Ryu
Keita Ninagawa, MD; Keiju Hiromura, MD, PhD; Shin-ichiro
Hideki Hanaoka, MD, PhD; Kei Ikeda, MD, PhD; Hiroshi Nak

Procedures

Participants were random
high-dose glucocorticoid
lone were 0.5 mg/kg/d ir
group and 1.0 mg/kg/d in t
Prednisolone was stoppe
group, while the dose of p
of 10 mg/d by 5 months i



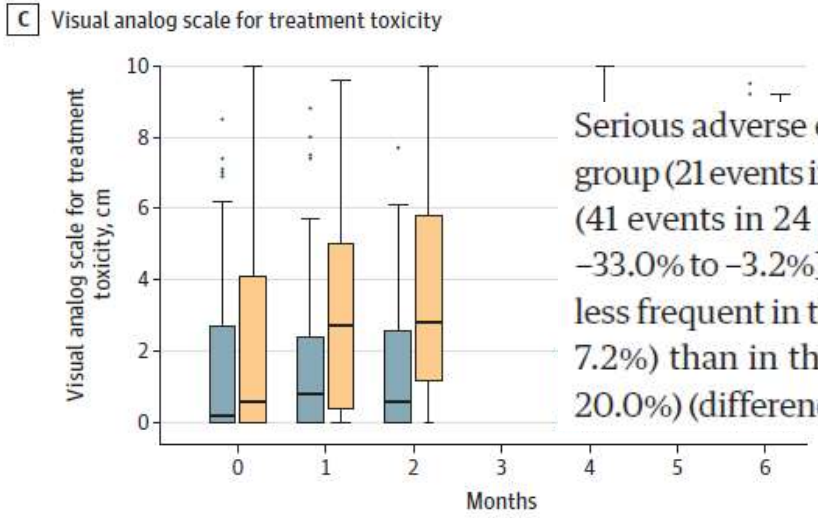


Table 1. Baseline Demographics and Characteristics of Evaluated Patients

	Reduced-dose glucocorticoid plus rituximab (n = 69)	High-dose glucocorticoid plus rituximab (n = 65)
Age, median (IQR), y	73 (66-78)	74 (68-78)
Sex, No. (%)		
Female	43 (62.3)	37 (56.9)
Male	26 (37.7)	28 (43.1)
Diagnosis, No. (%)		
Microscopic polyangiitis	53 (76.8)	51 (78.5)
Granulomatosis with polyangiitis	16 (23.2)	13 (20.0)
Renal-limited vasculitis	0 (0.0)	1 (1.5)
ANCA positivity, No. (%)		
MPO-ANCA[a]	60 (86.9)	55 (84.6)
PR3-ANCA[b]	9 (13.0)	10 (15.4)
Estimated glomerular filtration rate, median (IQR), mL/min/1.73 m^2 (normal limits ≥90 mL/min/1.73 m^2)[c]	52.0 (31.4-74.6)	55.3 (41.2-72.3)

Serious adverse events were less frequent in the reduced-dose group (21 events in 13 patients, 18.8%) than in the high-dose group (41 events in 24 patients, 36.9%) (difference, −18.1% [95% CI, −33.0% to −3.2%]; P = .02) (**Table 3**). Serious infections were also less frequent in the reduced-dose group (7 events in 5 patients, 7.2%) than in the high-dose group (20 events in 13 patients, 20.0%) (difference, −12.8% [95% CI, −24.2% to −1.3%]; P = .04).

ANCA

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 18, 2021 VOL. 384 NO. 7

Avacopan for the Treatment of ANCA-Associated Vasculitis

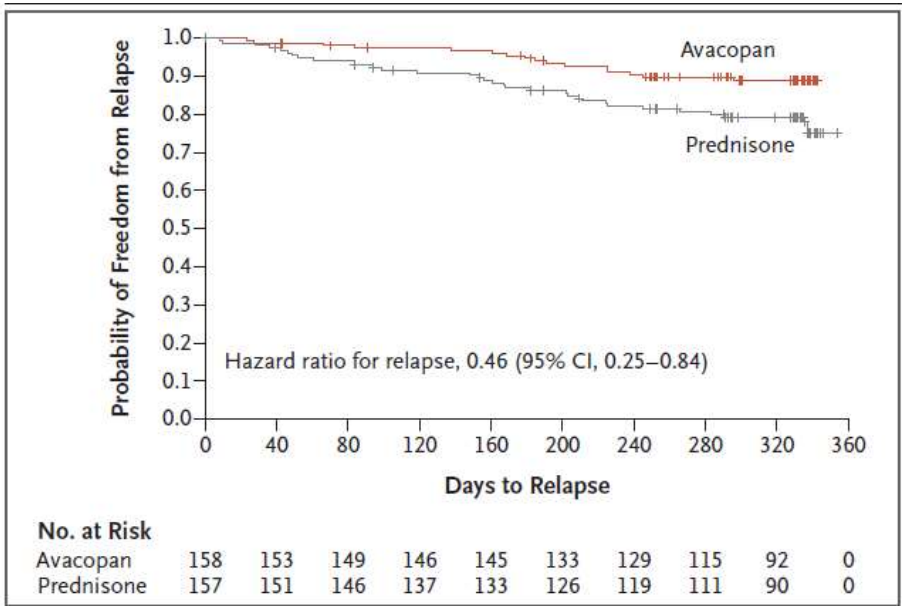
David R.W. Jayne, M.D., Peter A. Merkel, M.D., M.P.H., Thomas J. Schall, Ph.D., and Pirow Bekker, M.D, Ph.D., for the ADVOCATE Study Group*

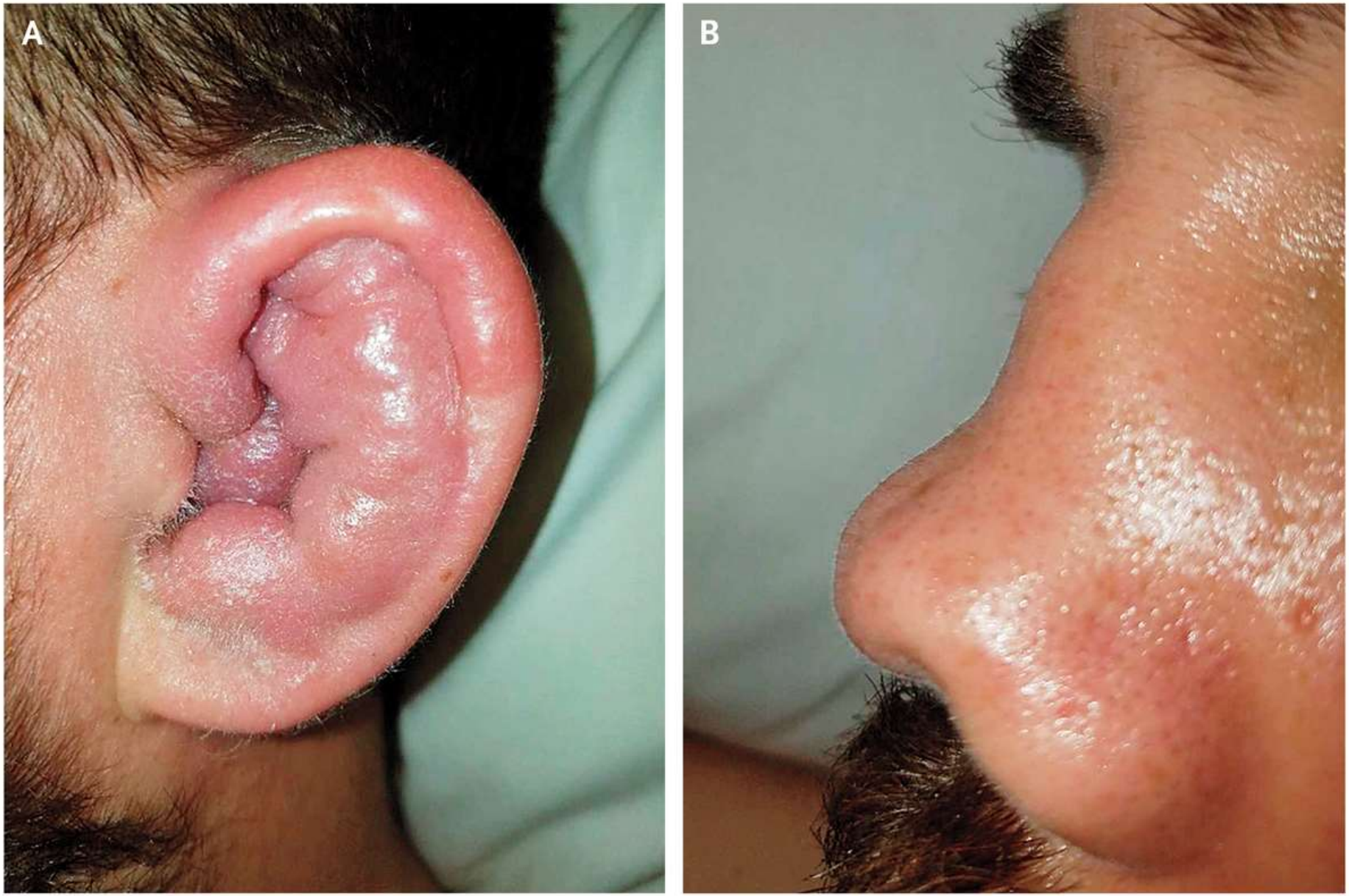
Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Avacopan (N=166)	Prednisone (N=164)
Age — yr	61.2±14.6	60.5±14.5
Sex — no. (%)		
Male	98 (59.0)	88 (53.7)
Female	68 (41.0)	76 (46.3)
Race — no. (%)†		
White	138 (83.1)	140 (85.4)
Asian	17 (10.2)	15 (9.1)
Black	3 (1.8)	2 (1.2)
Other	8 (4.8)	7 (4.3)
Body-mass index‡	26.7±6.0	26.8±5.2
Median duration of ANCA-associated vasculitis (range) — mo	0.23 (0–362.3)	0.25 (0–212.5)
Vasculitis disease status — no. (%)		
Newly diagnosed	115 (69.3)	114 (69.5)
Relapsed	51 (30.7)	50 (30.5)
ANCA status — no. (%)		
Antiproteinase 3 positive	72 (43.4)	70 (42.7)
Antimyeloperoxidase positive	94 (56.6)	94 (57.3)

Table 2. Primary and Key Secondary End Points.*

End Point	Avacopan (N=166)	Prednisone (N=164)	Difference (95% CI)
Primary end points			
Remission at wk 26 — no. (%)†	120 (72.3)	115 (70.1)	3.4 (–6.0 to 12.8)‡§
Sustained remission at wk 52 — no. (%)¶	109 (65.7)	90 (54.9)	12.5 (2.6 to 22.3)‡‖
Secondary end points			
GTI-CWS**			
Wk 13			
Patients evaluated	160	161	
Least-squares mean	25.7±3.4	36.6±3.4	–11.0 (–19.7 to –2.2)
Wk 26			
Patients evaluated	154	153	
Least-squares mean	39.7±3.4	56.6±3.4	–16.8 (–25.6 to –8.0)

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ORIGINAL ARTICLE

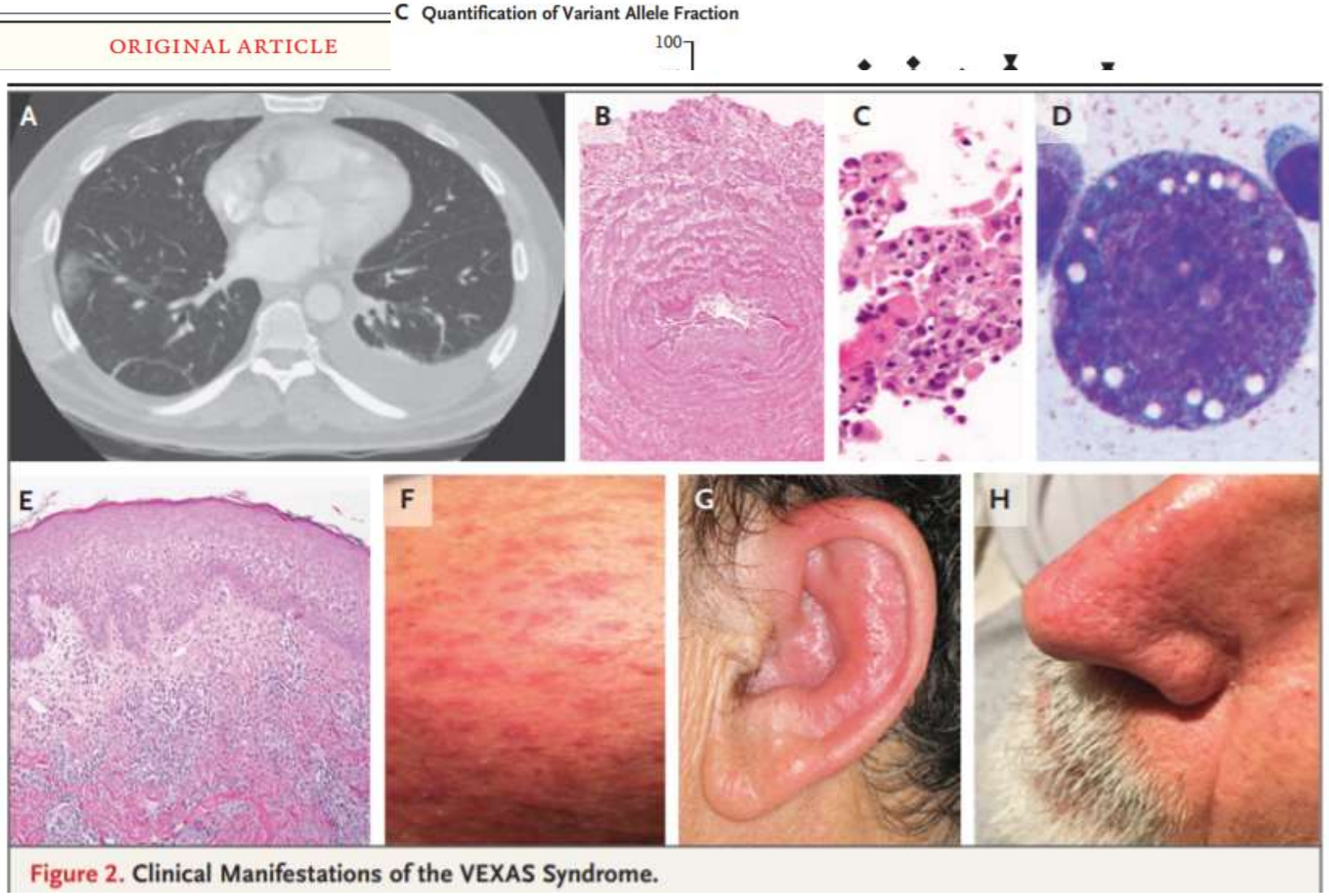

Figure 2. Clinical Manifestations of the VEXAS Syndrome.