Scientific Abstracts Friday, 14 June 2019 773

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A SYSTEMATIC LITERATURE REVIEW TO INFORM THE 2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Culminating evidence over the past decade regarding management of systemic lupus erythematosus (SLE) called for an update of the 2008 EULAR recommendations for the treatment of the disease. **Objectives:** Systematic review of the literature (SLR) to inform the 2019 EULAR recommendations for the management of SLE.

Methods: SLR of Pubmed from 01/2007 to 12/2017 for questions (selected through Delphi excercise) regarding: i) efficacy/safety of different drugs used in SLE, ii) treatment of specific manifestations, iii) monitoring and treatment goals and iv) comorbidities and adjunct therapy. Evidence was categorised based on design and validity of available studies [*Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence (LoE)*] and strength of statements was graded [*Grading of recommendation (GoR)*, assessment, development and evaluations, GRADE)].

Results: Main topics supported by strong evidence base included: Association of hydroxychloroquine (HCQ) use with favourable outcomes (LoE 1b,

GoR A), belimumab for extrarenal disease (LoE 1a, GoR A), efficacy of antimalarials in skin disease (LoE 1a, GoR A), mycophenolate mofetil (MMF) for induction and maintenance therapy of lupus nephritis (LN) and cyclophosphamide (CYC) in severe LN (LoE 1b, GoR A). Weak evidence supported the value of repeat kidney biopsy in refractory LN (LoE 4, GoR C), all second-line agents for skin disease (LoE 4, GoR C) and efficacy of most first and second-line treatments for thrombocytopenia (LoE 4, GoR C). Moderate LoE was found for all other questions (Table).

Conclusion: A SLR for the treatment of SLE found the highest LoE for benefits of HCQ, efficacy of belimumab for extrarenal disease and MMF and IV-CYC in LN.

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774 Friday, 14 June 2019 Scientific Abstracts

Table Lovel of avidence for different items regarding treatment of systemic lunus cryth

vidence Base	Topics in SLE treatment
A (strong)	Association of HCQ use with favourable outcomes
	Chronic exposure to GC and risk of organ damage
	Gonadal toxicity of CYC
	Efficacy and safety of belimumab in extrarenal SLE
	Efficacy of antimalarials in skin disease
	MMF for induction and maintenance therapy of LN and cyclophosphamide for severe LI
	Immunosuppressive therapy for inflammatory neuropsychiatric manifestations
	Association of aPL with adverse outcomes
B (moderate)	HCQ cumulative exposure and retinal toxicity
	Efficacy of MTX and MMF in extrarenal SLE
	Comparable efficacy and less toxicity of lower-dose GC regimens
	Efficacy of RTX in renal and extrarenal SLE
	Efficacy of multitarget therapies for induction treatment in LN
	Use of CNIs in refractory LN
	Primary prophylaxis with low-dose aspirin in aPL(+) SLE patients
C/D (weak)	Efficacy of AZA, CsA, and CYC in extrarenal SLE
	Efficacy of second-line treatment in skin lupus
	Efficacy of most first and second-line treatments for thrombocytopenia
	Efficacy of vaccinations in SLE patients
	Efficacy of primary cardiovascular protection with statins and low-dose aspirin in SLE

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2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SYSTEMIC LUPUS **ERYTHEMATOSUS**

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Background: Recommendations for the treatment of systemic lupus erythematosus (SLE) were published by EULAR in 2008. Advances in treatment strategies and goals called for an update of these recommendations, capitalizing on strengths and experience from previous

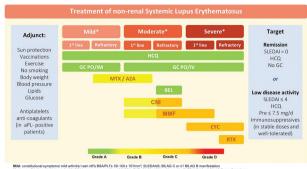
Objectives: To update the EULAR recommendations for the management

Methods: Systematic literature review (01/2007-12/2017) followed by Delphi method to form questions, elicit expert opinions and reach consensus.

Results: Treatment in SLE aims at remission or low disease activity and prevention of flares. Hydroxychloroquine is recommended in all lupus patients, at a dose not exceeding 5mg/kg real body weight. During chronic maintenance treatment, glucocorticoids should be minimized to less than 7.5 mg/day (prednisone equivalent) and, when possible, withdrawn. Prompt initiation of immunomodulatory agents (methotrexate, azamycophenolate) can expedite tapering/discontinuation glucocorticoids. In persistently active or flaring extrarenal disease, add-on belimumab should be considered; rituximab may be considered in organthreatening, refractory disease. Specific recommendations are also provided for the management of cutaneous, neuropsychiatric, haematological

and renal disease (including the use of calcineurin inhibitors). SLE patients should be assessed for their antiphospholipid antibody status, infectious and cardiovascular diseases risk profile, and preventative strategies be tailored accordingly.

Conclusion: Updated EULAR recommendations provide physicians and patients with updated consensus guidance on the management of SLE, combining evidence-base and expert-opinion.



Figure

Acknowledgement: European League against RheumatismDisclosure of Interests: Antonis Fanouriakis Paid instructor for: Amgen, GSK, Speakers bureau: Abbvie, Enorasis, Genesis Pharma, Myrto Kostopoulou: None declared, Alessia Alunno: None declared, Martin Aringer Grant/research support from: Roche, Consultant for: AstraZeneca and Eli Lilly, Ingeborg Bajema Consultant for: GSK, John N. Boletis: None declared, Ricard Cervera: None declared, Andrea Doria: None declared, Caroline Gordon Grant/research support from: Sandwell and West Birmingham Hospitals NHS Trust have received funding from UCB to support research work done by my research group that was unrelated to any pharmaceutical product or clinical trial., Consultant for: I have provided consultancy advice and taken part in scientific advisory boards on the design and analysis of clinical trials and the management of lupus for GSK, EMD Serono and UCB. I have taken part in adjudication and safety monitoring committees for BMS., Speakers bureau: I have been paid by UCB for speaking at meetings., Marcello Govoni Paid instructor for: Pfizer, Roche, Speakers bureau: Pfizer, Abbvie, MSD, Roche, Eli-Lilly, Celgene, Sanofi, Janssen, Frederic Houssiau: None declared, David Jayne Grant/research support from: David Jayne has received research grants from Chemocentryx, GSK, Roche/Genentech and Sanofi-Genzyme. He has received consultancy fees from Astra-Zeneca, Boehringer-Ingelheim, Chemocentryx, Chugai, GSK, Infla-RX, Insmed and Takeda, Marios Kouloumas: None declared, Annegret Kuhn Grant/research support from: Biogen, Galderma, GlaxoSmithKline, LeoPharma, Speakers bureau: La Roche Posav, Janni Lisander Larsen: None declared, Kirsten Lerstrom: None declared, Gabriela Moroni: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Matthias Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Speakers bureau: Chugai, Josef S. Smolen Grant/research support from: Abb-Vie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Elisabet Svenungsson: None declared, Vladimir Tesar: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lillly, Jannsen, Cellgene, Novartis, Anne Troldborg: None declared, Ronald van Vollenhoven Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, GlaxoSmithKline, Pfizer, Roche, and UCB, Consultant for: AbbVie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex., Speakers bureau: Abb-Vie, AstraZeneca, Biotest, Bristol-Myers Squibb, Celgene, Crescendo, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex., Jörg Wenzel Grant/research support from: GSK, Incyte, Consultant for: Biogen, Leo, Paid instructor for: Novartis, George Bertsias: None declared. Dimitrios Boumpas: None declared DOI: 10.1136/annrheumdis-2019-eular.3117