Title: Juvenile dermatomyositis: novel treatment approaches and outcomes

Review for Current Opinion Rheumatology May 2018
Journal Ref.: Ms. No. BOR3006 B

Authors: Giulia C Varnier[1], Clarissa A. Pilkington[1], Lucy R.Wedderburn[1, 2, 3]

Affiliations:
1. Great Ormond Street Hospital for Children NHS Foundation Trust, London
2. UCL Great Ormond Street Institute of Child Health, 30 Guilford St, London WC1N 1EH, UK
3. NIHR GOSH Biomedical Research Centre (BRC), London, UK

Corresponding author:
Giulia Camilla Varnier MD
Paediatric Rheumatology Department,
Great Ormond Street Hospital for children NHS Foundation Trust, London WC1N 3JH
020 7405 9200 ext. 7887
giulia.varnier@gosh.nhs.uk

Abstract:

Purpose of review:
The aim of this paper is to provide a summary of the recent therapeutic advances and the latest research on outcome measures for juvenile dermatomyositis (JDM).

Recent findings: Several new international studies have developed consensus-based guidelines on diagnosis, outcome measures and treatment of JDM to standardise and improve patient care. Myositis specific antibodies together with muscle biopsy histopathology may help the clinician to predict disease outcome. A newly developed magnetic resonance imaging-based scoring system has been developed to standardize the use of MRI in assessing disease activity in JDM. New data regarding the efficacy and safety of rituximab, especially for skin disease, and cyclophosphamide in JDM support the use of these medications for severe refractory cases.

Summary: International network studies, new biomarkers and outcome measures have led to significant progress in understanding and managing the rare inflammatory myositis conditions such as JDM.

Keywords: juvenile dermatomyositis, outcome measures, advanced treatment

Current word length from Intro to end of conclusions: 2170

Text of review:

Introduction:
Juvenile dermatomyositis (JDM) is a rare systemic autoimmune disease characterised by a vasculopathy that primarily affects muscle and skin, but may involve the lung, bowel, heart and other organs[1,2]. JDM is the most common inflammatory myopathy of childhood, affecting 1.9 cases per million children in UK [3] and 2.4-4.1 cases per million children in USA [4]. In this review we will summarise the recent developments in the clinical assessment, treatments and outcomes in JDM.

Clinical outcomes and Core Set Criteria
International collaborations have been undertaken to unify and standardize assessments and treatments of rare diseases such as idiopathic inflammatory myositis (IIM). The Paediatric Rheumatology International Trials Organization (PRINTO) and the International Myositis Assessment & Clinical Studies Group (IMACS) initial preliminary response criteria considerably improved clinical assessment and therapeutic response of JDM patients, but were lacking in sensitivity and still presented several differences in the individual core set measurement [5-7]. To overcome these issues these two international organisations joined forces and developed a new set of consensus-driven response criteria for adult dermatomyositis/polymyositis and children with JDM. This new tool is based on a continuous model, with a total improvement score of 0-100, and with different thresholds for minimal (≥30), moderate (≥45) and major (≥70) clinical response based on weighted scores applied to an absolute percentage improvement [8••]. The core set measures were identified by consensus among expert paediatric and adult rheumatologists, neurologists and dermatologists, using the Delphi method. The agreed measures were the following: Physician global activity; Parent or Patient global activity; Manual Muscle testing (MMT) or Childhood myositis Assessment Scale (CMAS); Childhood Health Assessment Questionnaire (CHAQ); Muscle enzymes (creatine kinase, aldolase, alanine aminotransferase, aspartate aminotransferase and lactate dehydrogenase) or Physical Summary Score of the Child Health Questionnaire-Parent Form 50 (CHQ-Phs) and Extramuscular activity or Disease Activity Score. These new response criteria provide a quantitative measurement of disease improvement and resolve the differences between PRINTO and IMACS criteria, enabling an easier comparison between different datasets and facilitating future trials.

Another important step towards effective communication between different study groups by using standardised clinical data has been created by International group of experts (McCann *et al*), who have defined an optimal dataset for JDM to capture disease subphenotype, activity, comorbidity, and damage over time [9]. Both an international panel of experts took part in a Delphi process, but also parents and patients with JDM participated in the survey, enabling the group to highlight what patients and families feel are essential items of the clinical assessment in JDM, with good agreement with the health care professionals**.**

A recent large analysis of the Euromyositis registry, which includes both adult and paediatric onset cases of all types of Idiopathic Inflammatory myositis (IIM) has highlighted the differences between JDM and adult dermatomyositis and polymyositis, the former being less associated with interstitial lung disease and malignancy and having different skin disease characteristics [10].

Little is known regarding long term outcome in JDM, but two recent studies shed some light on this extremely important aspect of -care. Silverberg *et al* evaluated over 14 million hospitalisation of patients with JDM over a 10-year period and showed significantly higher odds for cardiovascular and cerebrovascular comorbidities in this US cohort of patients, especially for girls and ethnic minorities [•11]. Ethnicity and lower family income were found to be associated with worse outcome, increased morbidity and decreased function in another large American cohort study [12]. A further study showed worse cardiovascular outcome in JDM patients (tested with a 6-minute walk test, timed "up and go" test, CMAS, echocardiography, lung function test, thoracic high resolution computed tomography scan and magnetic resonance imaging and health related quality of life questionnaire) with a mean of 17 years of disease history when compared with sex-and age-match controls, especially those with active disease [13].

One of the ongoing challenges of the management of JDM has been identifying a reliable, practical tool to measure the skin disease. A prospective study tested the PRINTO proposed criteria for clinically inactive disease, which stated that at least three of four conditions should be met: creatinine kinase (CK) ≤150 U/L, Childhood Myositis Assessment Scale (CMAS) ≥48, Manual Muscle Testing of 8 groups (MMT8) ≥78 and physician global assessment of overall disease activity (PGA) ≤0.2.) [14]. This analysis by Almeida *et al* showed the importance of incorporating the physician global assessment of overall disease activity as an essential criterion of clinically inactive disease, as this helps prevent the misclassification of patients with active skin disease [15]. Subsequent to this study the same study group tested three different skin scoring tools in JDM, the Myositis Intention to Treat Activity Index (MITAX), abbreviated Cutaneous Assessment Tool (CAT) and Disease Activity Score (DAS) and correlated them with the physician's 10-cm skin visual analogue scale (VAS). All three tools were easy and quick to use, and this study showed that the DAS best correlated with the physician VAS. However all three skin tools had limitations, suggesting that future studies should design a new tool with all the strengths of the existing ones [16].

Antibodies

Juvenile myositis is a highly heterogeneous disease ranging from profound muscle weakness and visceral involvement to normal muscle strength. In recent years autoantibodies have been identified in 60-70% children with myositis and have been able to identify clinically homogeneous groups [17-21]. This concept has been recently further validated in a large study including 379 juvenile myositis patients, which confirmed that the myositis specific autoantibodies (MSA) are exclusively found in children with IMM, and not in healthy children or patients with other autoimmune diseases (including arthritis or lupus) or muscular dystrophy. Therefore this study suggested that the presence of MSA should be considered highly suggestive of the diagnosis of myositis [19]. In this study specific MSA such as anti-TIF1y was shown to be associated with the use of more powerful medication; in addition anti-HMGCR and anti-SRP antibodies were also found in patients with profound muscle weakness and slow/poor response to treatment.

These findings will help the clinician to predict disease features and outcome and to guide the treatment. Furthermore, Deakin *et al* showed that the severity of the muscle biopsy (defined using a standardised score tool), in combination with MSA subtype can predict the risk of remaining on treatment in patients with JDM. Surprisingly, children with anti-Mi2 antibody were associated with a better prognosis, despite the severity of the muscle biopsy in these cases, whilst in patients with anti–NXP-2, anti–TIF-1 g , or no detectable antibodies , the biopsy score was predictive of the probability of remaining on treatment over time [22••].

Imaging

The use of magnetic resonance imaging (MRI) has played an increasingly important role to help clinicians with diagnosis and follow up of children with inflammatory myositis, especially as it does

not involve ionizing radiation. It helps with selection of the muscle biopsy site; and it is not invasive, unlike electromyography or muscle biopsy [23-24]. A recent study showed that where a flare was questioned, if the MRI showed active myositis, the physician would change or escalate treatment. This biomarker can be useful especially as up to 75% of patients suspected of having a flare had no abnormal muscle enzymes [25].

To date the use of MRI is not standardised and might differ significantly in different centres, for example in terms of which part of the body is assessed, which planes to perform, the protocol used, and the usefulness of intravenous contrast. To overcome these limitations Thyoka *et al*. recently improved the previously published MRI-based scoring system for JDM [26]. Nine paediatric radiologists with an interest in musculoskeletal imaging and two paediatric rheumatologists reviewed and modified the previously developed criteria and tested it on a set of MRI scans from 20 patients with s JDM. The resulting new scoring system showed good inter-observer reliability with no significant difference when using either the coronal or the axial planes. The study showed that various combinations of techniques can be useful, T1-weighted to assess muscle atrophy and T2-weighted/fat suppression or STIR to visualize inflammatory changes of the skin and soft tissue oedema. The panel considered MRI of gluteal and thigh muscle optimal to assess disease activity and severity and, also, was more easily available than whole body MRI, and gadolinium contrast was not needed [27•].

Consensus treatment plans

In recent years several international efforts have been undertaken to achieve evidence-based guidelines with the aim to standardize outcome measures and management of children with JDM. The Single Hub and Access point for paediatric Rheumatology (SHARE) group has been working on harmonizing the care of paediatric rheumatology patients in Europe since 2012 and have recently published consensus-based recommendations for the management of JDM developed by an evidence –informed consensus process involving systematic literature review, online survey and final consensus meeting between 21 expert in paediatric rheumatology and physical therapy [28••].

In parallel, the Childhood Arthritis and Rheumatology Research alliance (CARRA) has developed consensus treatment plans for several paediatric rheumatologic diseases including juvenile localised scleroderma, systemic juvenile idiopathic arthritis (JIA), polyarticular JIA, lupus nephritis and JDM [29]. With respect to JDM the CARRA group has recently proposed a consensus-based treatment plan for JDM with predominant skin disease consisting of three different options for the clinician: option A included hydroxycloroquine alone, Option B included hydroxycloroquine and methotrexate and option C consisted of hydroxycloroquine, methotrexate and corticosteroids [30]. The same study group also proposed a consensus treatment plan for JDM with persistent skin disease despite the resolution of the muscle disease with three different Plans: Plan A to add intravenous Immunoglobulin (IVIG), Plan B to add mycophenolate mofetil and Plan C to add cyclosporine [31]. Continuation of previous treatments including corticosteroids, methotrexate and IVIG was allowed in Plan B and C. The next step in both studies will be to collect prospective data to understand which treatment option is the most effective.

Advances in treatment

To date, only two randomized controlled trials were performed including JDM patients. These were the PRINTO trial which showed that corticosteroids plus methotrexate was the most effective and safest treatment option in new onset JDM when compared to prednisolone alone and prednisolone and cyclosporine [••32], and the Rituximab in Myositis (RIM) trial which, although it did not meet its primary endpoint, showed an overall good response rate and ability to taper corticosteroids in adult and juvenile DM [33]. In the same cohort of patients the efficacy of rituximab in treating the cutaneous disease was subsequently assessed. The disease activity was evaluated using the cutaneous assessment of the Myositis Disease Activity Assessment tool and the damage using the Myositis damage index (MDI). In JDM, Rituximab treatment significantly improved skin disease

activity, especially cutaneous ulcerations, erythroderma, heliotrope rash and Gottron's sign/papules. No major changes were seen among damage items, including calcinosis [34].

Cyclophosphamide is currently used to treat malignancy, systemic lupus erythematosus and vasculitis. Clinicians may be reluctant to give cyclophosphamide in JDM because of the lack of evidence and its side effects. Recently, the efficacy on skin, muscle and global disease activity of cyclophosphamide has been reported in 56 severe and refractory cases of JDM. The long term side effects are still unknown but its short-term safety profile in this study is encouraging [35].

A combination of cyclophosphamide, IVIG and Rituximab has proven to be effective in anti –signal recognition particle (anti-SRP) myositis, a very rare inflammatory myopathy characterised by profound muscle weakness, raised CK and no skin rash with a much improve outcome compared with the very little literature available [36]. The CARRA group in North America conducted a survey regarding the use of biologic agents in treating JDM which showed that biologics were used only for refractory cases of JDM with the general belief that these were effective in reducing complications, particularly calcinosis, and therefore were an appropriate step when corticosteroids, methotrexate and IVIG fail to control the disease. The most common biologics used were Rituximab, Abatacept, anti-TNF and Tocilizumab suggesting that these agents could be considered for future studies [37]. An anecdotal report described a successful use of Ustekinumab (human monoclonal antibody against IL-12/23) in treating a case of juvenile amyopathic dermatomyositis with psoriasis and active skin disease [38]. An analysis of a large number of JDM patients treated with TNF blockade, to date published in abstract form, suggests efficacy of blocking TNF for severe cases of JDM [39].

Future treatment options

Promising options are coming from the world of adult DM, including a RCT of Infliximab in 12 refractory PM and DM which showed some benefit and good safety profile [40]. Another RCT concluded that 50% of patients with adult dermatomyositis and polymyositis treated with Abatacept had lower disease activity [41]. In addition Rituximab has been successful in improving respiratory symptoms and lung function tests, but also in reducing the daily corticosteroid dose in refractory progressive interstitial lung disease in anti MDA5 positive amyopathic dermatomyositis, infection was the main side effect reported [42].

Conclusions:

In conclusion, in the recent years several international efforts have achieved important goals with the ultimate aim to harmonise and standardise the management of children with juvenile inflammatory myopathies. Collaborative networks are essential to facilitate research in rare diseases and provide evidenced based treatments for JDM.

Key points:

- European and American study groups proposed a consensus for optimal dataset and criteria of minimal, moderate and major response to treatment in JDM.
- New consensus based guidelines are available for diagnosis and management of children with JDM, and particularly with predominant skin disease and persistent skin disease.
- New autoantibody association, especially combined with muscle biopsy histopathology, and a new MRI scoring system may help the clinician with treatment choice and disease prognosis.

Acknowledgements:

Financial support and sponsorship: LW is supported by grants from the UK NIHR through the NIHR Biomedical Research Centre at GOSH and Arthritis Research UK (20164, 21593)

The Authors declare no conflict of interest.

References and recommended reading:
Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest
•• of outstanding interest

1. Rider LG, Lidsley CB, Miller FW. Juvenile dermatomyositis. In: Petty RE, Laxer RM, Lindsey CB, Wedderburn LR, editors. Textbook of pediatric rheumatology. 7th ed. Philadelphia: Elsevier Saunder; 2016. p. 351–84.
2. Feldman BM, Rider LG, Reed AM, Pachman LM. Juvenile dermatomyositis and other idiopathic inflammatory myopathies of childhood. Lancet. 2008;371:2201–12.
3. Symmons DP, Sills JA, Davis SM. The incidence of juvenile dermatomyositis: results from a nation-wide study. Br J Rheumatol 1995;34:732–6.
4. Mendez EP, Lipton R, Ramsey-Goldman R *et al*. for the NIAMS Juvenile DM Registry Physician Referral Group. US incidence of juvenile dermatomyositis, 1995–1998: results from the National Institute of Arthritis and Musculoskeletal and Skin Diseases Registry. Arthritis Rheum 2003;49:300–5.
5. Rider LG, Giannini EH, Brunner HI, *et al*. International consensus on preliminary definitions of improvement in adult and juvenile myositis. Arthritis Rheum. 2004 Jul;50(7):2281-90.
6. Ruperto N, Pistorio A, Ravelli A, *et al*. The Pediatric Rheumatology International Trials Organization provisional criteria for the evaluation of response to therapy in juvenile dermatomyositis. Arthritis Care Res (Hoboken). 2010 Nov;62(11):1533-41.
7. Ruperto N, Pistorio A, Ravelli A, *et al*. Criteria to define response to therapy in paediatric rheumatic diseases. Eur J Clin Pharmacol. 2011;67(Suppl 1):125–31.
8. ••Rider LG, Aggarwal R, Pistorio A, *et al*. 2016 American College of Rheumatology/European League Against Rheumatism Criteria for Minimal, Moderate, and Major Clinical Response in Juvenile Dermatomyositis: An International Myositis Assessment and Clinical Studies Group/Paediatric Rheumatology International Trials Organisation Collaborative Initiative. Ann Rheum Dis. 2017;76:782–91. *This report shows the new response criteria for JDM, with thresholds for minimal, moderate and major improvement*.
9. • McCann LJ, Pilkington CA, Huber AM, *et al*. Development of a consensus core dataset in juvenile dermatomyositis for clinical use to inform research. Ann Rheum Dis. 2018;77(2):241–250. *This study introduces an internationally agreed dataset for JDM that is designed to capture disease activity and damage over time.*
10. Lilleker JB, Vencovsky J, Wang G, *et al*. The EuroMyositis registry: an international collaborative tool to facilitate myositis research. Ann Rheum Dis. 2018 Jan;77(1):30-39.
11. Silverberg JI, Kwa L, Kwa MC, *et al*. Cardiovascular and cerebrovascular comorbidities of juvenile dermatomyositis in US children: an analysis of the National Inpatient Sample. Rheumatology (Oxford). 2018 Apr 1;57(4):694-702.
12. Philippi K, Hoeltzel M, Byun Robinson A, *et al*. Race, Income and Disease Outcomes in Juvenile Dermatomyositis. J Pediatr. 2017 May; 184:38-44.
13. Berntsen KS, Tollisen A, Schwartz T, *et al*. Submaximal Exercise Capacity in Juvenile Dermatomyositis after Longterm Disease: The Contribution of Muscle, Lung, and Heart Involvement. J Rheumatol. 2017 Jun;44(6):827-834.
14. Lazarevic D, Pistorio A, Palmisani E, *et al*. The PRINTO criteria for clinically inactive disease in juvenile dermatomyositis. Ann Rheum Dis. 2013 May;72:686-93.

15. Almeida B, Campanilho-Marques R, Arnold K *et al*. Analysis of published criteria for Clinically Inactive Disease in a large Juvenile Dermatomyositis cohort shows that skin disease is underestimated. Arthritis Rheumatol. 2015 Sept;67(9):2495-502.
16. Campanilho-Marques R, Almeida B, Deakin C, *et al*. Comparison of the Utility and Validity of Three Scoring Tools to Measure Skin Involvement in Patients With Juvenile Dermatomyositis. Arthritis Care & Res (Hoboken). 2016 Oct;68(10):1514-21.
17. Tansley SL, Betteridge ZE, Shaddick G, *et al*. Calcinosis in juvenile dermatomyositis is influenced by both anti-NXP2 autoantibody status and age at disease onset. Rheumatology (Oxford). 2014 Dec;53(12):2204-8.
18. Tansley SL, Betteridge ZE, Gunawardena H, *et al*. Anti-MDA5 autoantibodies in juvenile dermatomyositis identify a distinct clinical phenotype: a prospective cohort study. Arthritis Res. Ther. 2014 Jul 2;16(4):R138.
19. Rider LG, Shah M, Mamyrova G*, et al*. The myositis autoantibody phenotypes of the juvenile idiopathic inflammatory myopathies. Medicine (Baltimore). 2013 Jul;92(4):223-43
20. Gunawardena H, Wedderburn LR, North J, *et al*. Clinical associations of autoantibodies to a p155/140 kDa doublet protein in juvenile dermatomyositis. Rheumatology (Oxford). 2008 Mar;47(3):324-8.
21. Gunawardena H, Betteridge ZE, McHugh NJ. Myositis-specific autoantibodies: their clinical and pathogenic significance in disease expression. Rheumatology (Oxford). 2009 Jun;48(6):607-12.
22. •• Deakin CT, Yasin SA, Simou S, *et al*. Biopsy Findings in Combination With Myositis-Specific Autoantibodies Aid Prediction of Outcomes in Juvenile Dermatomyositis. Arthritis Rheumatol. 2016 Nov;68(11):2806-2816. *This was the first study to demonstrate that the muscle biopsy and the MSA can help the clinician to predict the outcome in JDM.*
23. Maillard SM, Jones R, Owens C, *et al*. Quantitative assessment of MRI T2 relaxation time of thigh muscles in juvenile dermatomyositis. Rheumatology (Oxford) 2004;43:603-8.
24. Park JH, Vansant JP, Kumar NG, *et al*. Dermatomyositis: correlative MR imaging and P-31 MR spectroscopy for quantitative characterization of inflammatory disease. Radiology 1990;177:473-9.
25. Abdul-Aziz R, Yu CY, Adler B *et al*. Muscle MRI at the time of questionable disease flares in Juvenile Dermatomyositis (JDM). Pediatr Rheumatol Online J. 2017 Apr 12;15(1):25.
26. Davis WR, Halls JE, Offiah AC, *et al*. Assessment of active inflammation in juvenile dermatomyositis: a novel magnetic resonance imaging-based scoring system. Rheumatology (Oxford) 2011;50:2237-44.
27. •Thyoka M, Adekunle O, Pilkington C, *et al*. Introduction of a novel magnetic resonance imaging-based scoring system for assessing disease activity in children with juvenile dermatomyositis. Rheumatology. Article in press. *This new scoring system will help standardise the use of MRI in JDM.*
28. ••Enders FB, Bader-Meunier B, Baildam E, *et al*. Consensus-based recommendations for the management of juvenile dermatomyositis. Ann Rheum Dis 2017;76:329–340. *This international effort is an important step towards an unified and standardised management of JDM.*
29. Ringold S, Nigrovic PA, Feldman BM, *et al*. The Childhood Arthritis and Rheumatology Research Alliance Consensus Treatment Plans. Arthritis Rheumatol. 2018 May;70(5):669-678.
30. Kim S, Kahn P, Robinson AB, *et al*. Childhood Arthritis and Rheumatology Research Alliance consensus clinical treatment plans for juvenile dermatomyositis with skin predominant disease. Pediatr Rheumatol Online J. 2017 Jan 11;15(1):1.
31. Huber AM, Kim S, Reed AM, *et al*. Childhood Arthritis and Rheumatology Research Alliance Consensus Clinical Treatment Plans for Juvenile Dermatomyositis with Persistent Skin Rash. J Rheumatol. 2017 Jan;44(1):110-116.

32. ••Ruperto N, Pistorio A, Oliveira S, *et al*. Prednisone versus prednisone plus cyclosporine versus prednisone plus methotrexate in new-onset juvenile dermatomyositis: a randomised trial. Lancet. 2016 Feb 13;387(10019):671-8. *A randomized controlled trial showing the superiority of prednisone plus methotrexate over prednisone alone or prednisone plus cyclosporine.*
33. ••Oddis CV, Reed AM, Aggarwal R, *et al*. Rituximab in the Treatment of Refractory Adult and Juvenile Dermatomyositis and Adult Polymyositis: A Randomized, Placebo-phase Trial. Arthritis Rheum. 2013 February; 65(2): 314–324. *RCT evidence that Rituximab may help to taper corticosteroids with good clinical response in adult and juvenile DM.*
34. Aggarwal R, Loganathan P, Koontz D, *et al*. Cutaneous improvement in refractory adult and juvenile dermatomyositis after treatment with rituximab. Rheumatology (Oxford). 2017 Feb;56(2):247-254.
35. Deakin CT, Campanilho-Marques R, Simou S, *et al*. Efficacy and Safety of Cyclophosphamide Treatment in Severe Juvenile Dermatomyositis Shown by Marginal Structural Modeling. Arthritis Rheumatol. 2018 May;70(5):785-793.
36. Binns EL, Moraitis E, Maillard S, *et al*. Effective induction therapy for anti-SRP associated myositis in childhood: A small case series and review of the literature. Pediatr Rheumatol Online J. 2017 Oct 31;15(1):77.
37. Spencer CH, Rouster-Stevens K, Gewanter H, *et al*. Biologic therapies for refractory juvenile dermatomyositis: five years of experience of the Childhood Arthritis and Rheumatology Research Alliance in North America. Pediatr Rheumatol Online J. 2017 Jun 13;15(1):50.
38. Montoya CL, Gonzalez ML, Ospina FE, Tobón GJ. A rare case of amyopathic juvenile dermatomyositis associated with psoriasis successfully treated with ustekinumab. J Clin Rheumatol. 2017 Mar;23(2):129-130.
39. Campanilho-Marques R, Deakin C, Simou S, *et al*. Annals of the Rheumatic Diseases, volume 75, supplement 2, year 2016, page 140. DOI: 10.1136/annrheumdis-2016-eular.5062
40. Shiffenbouer A, Garg M, Castro C, *et al*. A randomised, double blind, placebo-control trial of infliximab in refractory polymyositis and dermatomyositis. Semin Arthritis Rheum. 2018 Jun;47(6):858-864.
41. Tiarnlund A, Tang Q, Wick C, *et al*. Abatacept in the treatment of adult dermatomyositis and polymyositis: a randomised, phase IIb treatment delayed-start trial. Ann Rheum Dis. 2018 Jan;77(1):55-62.
42. So H, Wong VTL, Lao VWN, Pang HT, *et al*. Rituximab for refractory rapidly progressive interstitial lung disease related to antiMDA5 antibody positive amyophatic dermatomyositis. Clin Rheumatol. 2018 Apr 30. doi: 10.1007/s10067-018-4122-2. [Epub ahead of print].