How to perform a CAT ?

The CAT (Critically Appraised Topic) is a structured one-page summary and critique of the best available evidence on a focused question. The CAT format requires the writer to:

- 1. Ask a clear, concise and focused question,
- 2. Conduct an efficient and effective search for the highest quality research evidence available,
- 3. Critically appraise the located evidence, and carefully consider the applicability/generalizability of the evidence,
- 4. Write the structured summary (see appendix 4) in 1-4 pages. This is the only document you need to send in.
- 5. Your document should have the name: 999cat.doc, where 999 should be substituted by your exam number you got from our office.
- 6. Make a powerpoint to help you to present your CAT at the exam. This powerpoint should not be sent in and must not contain more then 10 slides (4 slides could be sufficient).

For a formal description see: Wyer PC. The critically appraised topic: closing the evidence-transfer gap. Ann Emerg Med. 1997 Nov;30(5)639-40

Some important points

- A CAT is not presenting original research from yourself or your own institute, it is not a report of one study, it is diving in to literature and comparing a couple (at least three) independent papers dealing with the question you propose. Once you cannot find at least 3 appropriate papers you should reformulate your question or find another topic.
- Your CAT should be original work. We will scan your submission for plagiarism.
- Submit your CAT in word-format, preferentially in Calibri 11 points.
- Give your CAT a clear and informative title.
- Do not forget to write your name and exam number on the top of your document.

An Example

Step 1 Ask a clear, concise and focused question

What's the evidence for the efficacy of Infliximab for generalized myositis without further comorbidity?

So studies on myositis with other concomitant diseases, studies not focusing on therapy and studies with focal myositis should be skipped. I did not make a differentiation between polymyositis and dermatomyositis. Inclusion body myositis will not be traced as this is not treated with Infliximab.

To keep the CAT limited, I confined myself to Infliximab and did not look at TNF- α blocking agents in general.

Step 2 Conduct an efficient and effective search.

Search Strategy:

www.pubmed.org Key-Words Polymyositis AND Infliximab. No filters used.

<u>www.thecochranelibrary.com</u> Polymyositis*, Infliximab* (ti, ab, kw)

Result: 46 Hits to be screened for relevance in Pubmed, 1 hit in Cochrane. See Appendix 1

Step 3 Critically appraise the located evidence

15 Papers remained and have been read. Some notes were made. See Appendix 2.

11 Papers appeared useful. These 11 have been read again to fill the table in Appendix 3.

The problem of this CAT is a very uncommon one. Therefore a couple of case reports have been studied. In more common problems, one can restrict oneself to some bigger studies. A table like in Appendix 3 is not always necessary, it was just my way of approach.

Step 4 Writing the Summary

This is the result of your CAT to be sent in to the exam-committee.

See appendix 4.

I decided to take the 3 multi-patient-Studies to describe and to give a global comment to the single patient cases. You may use another approach.

The only report we want you to send in is the summary following the structure

Titel	Short description of the CAT
Name Author	Your name and the date of the study
Question	Be sure the question is concise and focused!
Search Strategy	Pubmed and Cochrane are satisfactory
Search Outcome	Describe your selection strategy
Results	Make a table as depicted
Comments	Make a sophisticated narrative comment
Clinical Bottom Line	This is the final conclusion
References	Only mention the references studied

Within this frame-work many will be possible and accepted by the examiners.

Be prepared on questions concerning your CAT.

The scoring form as given in <u>appendix 5</u> will be used.

Please do not hesitate to ask for further information: j.b.m.kuks@umcg.nl

Results: 46

Successful treatment of calcinosis with infliximab in a patient with systemic sclerosis/myositis overlap syndrome.

Tosounidou S, MacDonald H, Situnayake D. Rheumatology (Oxford). 2014 May;53(5):960-1. → Skipped, because of further comorbidity

The vitamin D receptor agonist BXL-01-0029 as a potential new pharmacological tool for the treatment of inflammatory myopathies.

Di Luigi L, Sottili M, Antinozzi C, Vannelli GB, Romanelli F, Riccieri V, Valesini G, Lenzi A, Crescioli C. PLoS One. 2013 Oct 30;8(10):e77745. doi: 10.1371/journal.pone.0077745. eCollection 2013. → Skipped, because of not focusing to Infliximab

Bacterial endophthalmitis caused by an intraocular cilium in a patient under treatment with infliximab.

Jin XH, Namba K, Saito W, Iwata D, Ishida S.

J Ophthalmic Inflamm Infect. 2013 Jun 5;3(1):50. doi: 10.1186/1869-5760-3-50. → Skipped, because of no focus on therapeutic effect of infliximab

Efficacy of infliximab in the treatment for dermatomyositis with acute interstitial pneumonia: a study of fourteen cases and literature review.

Chen D, Wang XB, Zhou Y, Zhu XC.

Rheumatol Int. 2013 Oct;33(10):2455-8. doi: 10.1007/s00296-012-2653-4. Epub 2013 May 29. Review.

→ Skipped, because of further comorbidity

Adalimumab for orbital myositis in a patient with Crohn's disease who discontinued infliximab: a case report and review of the literature.

Verma S, Kroeker KI, Fedorak RN.

BMC Gastroenterol. 2013 Apr 4;13:59. doi: 10.1186/1471-230X-13-59. Review. → Skipped, because of no focus on therapeutic effect of infliximab

Raised circulating tenascin-C in rheumatoid arthritis. Page TH, Charles PJ, Piccinini AM, Nicolaidou V, Taylor PC, Midwood KS. Arthritis Res Ther. 2012 Nov 29;14(6):R260. doi: 10.1186/ar4105. → Skipped, because of no focus on therapeutic effect of infliximab

Therapeutic advances in myositis. Aggarwal R, Oddis CV. Curr Opin Rheumatol. 2012 Nov;24(6):635-41. Review. → Not original! Screened for a new link not found in Pubmed

Immunosuppressant and immunomodulatory treatment for dermatomyositis and polymyositis.

Gordon PA, Winer JB, Hoogendijk JE, Choy EH Cochrane Database Syst Rev. 2012 Aug 15;8:CD003643. doi: 10.1002/14651858.CD003643.pub4. Review.

→ Not original! Screened for a new link not found in Pubmed This study came up in both the Pubmed and the Cochrane search Bilateral diffuse orbital myositis in a patient with relapsing ulcerative colitis.

Bennion J, Harris MA, Sivak-Callcott JA, Nguyen J.

Ophthal Plast Reconstr Surg. 2012 Sep-Oct;28(5):e119-20. doi: 10.1097/IOP.0b013e318244a34e. → Skipped, because of no focus on generalized myositis

Anti-tumor necrosis factor inhibitor therapy-induced dermatomyositis and fasciitis.

Riolo G, Towheed TE.

J Rheumatol. 2012 Jan;39(1):192-4. No abstract available.

ightarrow Skipped, because of no focus on therapeutic effect of infliximab

Inflammatory response in human skeletal muscle cells: CXCL10 as a potential therapeutic target. Crescioli C, Sottili M, Bonini P, Cosmi L, Chiarugi P, Romagnani P, Vannelli GB, Colletti M, Isidori AM, Serio M, Lenzi A, Di Luigi L.

Eur J Cell Biol. 2012 Feb;91(2):139-49. doi: 10.1016/j.ejcb.2011.09.011. Epub 2011 Dec 15. → Skipped, because of no focus on therapeutic effect of infliximab

Successful treatment for conventional treatment-resistant dermatomyositis-associated interstitial lung disease with adalimumab.

Park JK, Yoo HG, Ahn DS, Jeon HS, Yoo WH. Rheumatol Int. 2012 Nov;32(11):3587-90. doi: 10.1007/s00296-011-2220-4. Epub 2011 Nov 17. → Skipped, because of concomitant therapy

Tubercular pyomyositis in a case of rheumatoid arthritis being treated with infliximab.

Khosla P, Aroaa N, Jain S.

Int J Rheum Dis. 2010 Feb 1;13(1):82-5. doi: 10.1111/j.1756-185X.2009.01445.x.

ightarrow Skipped, because of no focus on therapeutic effect of infliximab

<u>Coexistent pyoderma gangrenosum and tibialis anterior myositis as presenting manifestations of</u> <u>Crohn's disease: case report and review of the literature.</u> Goldshmid O, Dovorish Z, Zehavi T, Eisen A, Bar-Dayan Y, Amital H. Rheumatol Int. 2011 Apr;31(4):525-7. doi: 10.1007/s00296-009-1168-0. Epub 2009 Oct 22. Review.

ightarrow Skipped, because of no focus on therapeutic effect of infliximab

Dysferlin deficiency treated like refractory polymyositis.

Vinit J, Samson M Jr, Gaultier JB, Laquerriere A, Ollagnon E, Petiot P, Marie I, Levesque H, Rousset H. Clin Rheumatol. 2010 Jan;29(1):103-6. doi: 10.1007/s10067-009-1273-1. → Skipped, because of no focus on myositis

Disseminated Histoplasma capsulatum infection presenting with panniculitis and focal myositis in rheumatoid arthritis treated with etanercept.

Bourré-Tessier J, Fortin C, Belisle A, Desmarais E, Choquette D, Senécal JL. Scand J Rheumatol. 2009;38(4):311-6. doi: 10.1080/03009740902776935. Review. → Skipped, because of comorbity

mAbs in nonlupus autoimmune rheumatic disease.

Whelan BR, Isenberg DA.

Curr Opin Hematol. 2009 Jul;16(4):280-4. doi: 10.1097/MOH.0b013e32832c1f53. Review. → Skipped, because of no focus on therapeutic effect of infliximab

A case of inclusion body myositis responsive to prednisolone therapy.

Kalla R, Soumakiyan M, Tuck S. Clin Rheumatol. 2009 Jun;28 Suppl 1:S21-2. doi: 10.1007/s10067-008-1047-1. Epub 2008 Dec 6.

ightarrow Skipped, because of no focus on myositis and not on therapeutic effect of infliximab

Recurrent posterior scleritis and orbital myositis as extra-intestinal manifestations of Crohn's disease: Case report and systematic literature review.

Culver EL, Salmon JF, Frith P, Travis SP.

J Crohns Colitis. 2008 Dec;2(4):337-42. doi: 10.1016/j.crohns.2008.06.002. Epub 2008 Oct 29.

 \rightarrow Skipped, because of no focus on generalized myositis

Inflammatory muscle diseases.

Mastaglia FL. Neurol India. 2008 Jul-Sep;56(3):263-70. Review. → Not original, however screened to find a new reference

Successful treatment of idiopathic orbital inflammation with infliximab: an alternative to conventional steroid-sparing agents.

Miquel T, Abad S, Badelon I, Vignal C, Warzocha U, Larroche C, Morax S, Dhote R. Ophthal Plast Reconstr Surg. 2008 Sep-Oct;24(5):415-7. doi: 10.1097/IOP.0b013e318182a522. → Skipped, because of no focus on generalized myositis

Treatment of idiopathic sclerosing inflammation of the orbit (myositis) with infliximab. Sahlin S, Lignell B, Williams M, Dastmalchi M, Orrego A. Acta Ophthalmol. 2009 Nov;87(8):906-8. doi: 10.1111/j.1755-3768.2008.01320.x. Epub . → Skipped, because of no focus on generalized myositis

Effectiveness of infliximab in the treatment of refractory juvenile dermatomyositis with calcinosis. Riley P, McCann LJ, Maillard SM, Woo P, Murray KJ, Pilkington CA.

Rheumatology (Oxford). 2008 Jun;47(6):877-80. doi: 10.1093/rheumatology/ken074. Epub 2008 Apr 9.

→ Skipped, because of comorbity

<u>A high incidence of disease flares in an open pilot study of infliximab in patients with refractory inflammatory myopathies.</u>

Dastmalchi M, Grundtman C, Alexanderson H, Mavragani CP, Einarsdottir H, Helmers SB, Elvin K, Crow MK, Nennesmo I, Lundberg IE.

Ann Rheum Dis. 2008 Dec;67(12):1670-7. doi: 10.1136/ard.2007.077974. Epub 2008 Feb 13. → Included

<u>Open-label trial of anti-TNF-alpha in dermato- and polymyositis treated concomitantly with</u> <u>methotrexate.</u>

Hengstman GJ, De Bleecker JL, Feist E, Vissing J, Denton CP, Manoussakis MN, Slott Jensen H, van Engelen BG, van den Hoogen FH.

Eur Neurol. 2008;59(3-4):159-63. doi: 10.1159/000114036. Epub 2008 Jan 29.

→ Included

Autoimmune diseases induced by TNF-targeted therapies: analysis of 233 cases.

Ramos-Casals M, Brito-Zerón P, Muñoz S, Soria N, Galiana D, Bertolaccini L, Cuadrado MJ, Khamashta MA.

Medicine (Baltimore). 2007 Jul;86(4):242-51. → Skipped, because of no focus on treatment of generalized myositis

[Anti TNF-alpha treatment of a refractory polymyositis].

Wendling D, Prati C, Ornetti P, Toussirot E, Streit G. Rev Med Interne. 2007 Mar;28(3):194-5. Epub 2007 Jan 17. French. → Included

Polymyositis associated with infliximab treatment for rheumatoid arthritis. Urata Y, Wakai Y, Kowatari K, Nitobe T, Mizushima Y. Mod Rheumatol. 2006;16(6):410-1. Epub 2006 Dec 20. No abstract available. → Skipped, because of no focus on treatment of generalized myositis

Infectious myositis involving the piriformis in a patient with rheumatoid arthritis. Oda S, Fujinaga H, Takahashi K. Mod Rheumatol. 2006;16(4):260-3. → Skipped, because of no focus on treatment of generalized myositis

<u>Treatment of early and refractory dermatomyositis with infliximab: a report of two cases.</u> Dold S, Justiniano ME, Marquez J, Espinoza LR. Clin Rheumatol. 2007 Jul;26(7):1186-8. Epub 2006 May 31. → Included

Possible role for tumour necrosis factor inhibitors in the treatment of resistant dermatomyositis and polymyositis: a retrospective study of eight patients.

Efthimiou P, Schwartzman S, Kagen LJ. Ann Rheum Dis. 2006 Sep;65(9):1233-6. Epub 2006 Feb 13. → Included

Fatal Mycobacterium peregrinum pneumonia in refractory polymyositis treated with infliximab. Marie I, Heliot P, Roussel F, Hervé F, Muir JF, Levesque H. Rheumatology (Oxford). 2005 Sep;44(9):1201-2. Epub 2005 Jun 7. No abstract available. → Included

Connective tissue disease in children.

Buka RL, Cunningham BB. Pediatr Ann. 2005 Mar;34(3):225-9, 233-8. Review. → Skipped, because of no focus on treatment of generalized myositis

Advanced refractory polymyositis responding to infliximab. Anandacoomarasamy A, Howe G, Manolios N. Rheumatology (Oxford). 2005 Apr;44(4):562-3. Epub 2005 Feb 3. No abstract available. -> Included

Treatment of recalcitrant idiopathic orbital inflammation (chronic orbital myositis) with infliximab. Garrity JA, Coleman AW, Matteson EL, Eggenberger ER, Waitzman DM. Am J Ophthalmol. 2004 Dec;138(6):925-30. → Skipped, because of no focus on generalized myositis

Refractory polymyositis responding to infliximab. Uthman I, El-Sayad J. Rheumatology (Oxford). 2004 Sep;43(9):1198-9. No abstract available. → Included

<u>Refractory adult dermatomyositis with pneumatosis cystoides intestinalis treated with infliximab.</u> Selva-O'Callaghan A, Martínez-Costa X, Solans-Laque R, Mauri M, Capdevila JA, Vilardell-Tarrés M. Rheumatology (Oxford). 2004 Sep;43(9):1196-7. No abstract available. → Skipped, because of comorbidity

<u>Treatment of dermatomyositis and polymyositis with anti-tumor necrosis factor-alpha: long-term</u> <u>follow-up.</u>

Hengstman GJ, van den Hoogen FH, van Engelen BG. Eur Neurol. 2004;52(1):61-3. Epub 2004 Jul 5. No abstract available. → Included

Fatal myositis due to the microsporidian Brachiola algerae, a mosquito pathogen.

Coyle CM, Weiss LM, Rhodes LV 3rd, Cali A, Takvorian PM, Brown DF, Visvesvara GS, Xiao L, Naktin J, Young E, Gareca M, Colasante G, Wittner M. N Engl J Med. 2004 Jul 1;351(1):42-7. No abstract available. → Skipped, because of no focus on treatment of generalized myositis

Successful treatment of alveolar hypoventilation due to dermatomyositis with anti-tumour necrosis factor-alpha.

Korkmaz C, Temiz G, Cetinbas F, Büyükkidan B. Rheumatology (Oxford). 2004 Jul;43(7):937-8. No abstract available. → Included

Refractory polymyositis responding to infliximab: extended follow-up. Labioche I, Liozon E, Weschler B, Loustaud-Ratti V, Soria P, Vidal E. Rheumatology (Oxford). 2004 Apr;43(4):531-2. No abstract available. → Included

Polymyositis associated with infliximab treatment for rheumatoid arthritis. Musiał J, Undas A, Celińska-Lowenhoff M. Rheumatology (Oxford). 2003 Dec;42(12):1566-8. No abstract available. → Skipped, because of comorbidity

Early diagnosis of pyomyositis using clinic-based ultrasonography in a patient receiving infliximab therapy for Behçet's disease.

Kane D, Balint PV, Wood F, Sturrock RD. Rheumatology (Oxford). 2003 Dec;42(12):1564-5. No abstract available. Erratum in: Rheumatology (Oxford). 2004 Feb;43(2):261.

 \rightarrow Skipped, because comorbidity

<u>Successful treatment of dermatomyositis and polymyositis with anti-tumor-necrosis-factor-alpha:</u> <u>preliminary observations.</u>

Hengstman GJ, van den Hoogen FH, Barrera P, Netea MG, Pieterse A, van de Putte LB, van Engelen BG.

Eur Neurol. 2003;50(1):10-5. → Included

Non-Hodgkin's lymphoma in a patient with refractory dermatomyositis which had been treated with infliximab. Roddy E, Courtney PA, Morris A. Rheumatology (Oxford). 2002 Oct;41(10):1194-5. No abstract available. → Skipped, because of comorbity Recent advances in the management of adult myositis. Fam AG. Expert Opin Investig Drugs. 2001 Jul;10(7):1265-77. Review. → Included for screening

Inflammatory muscle diseases. Mastaglia FL. Neurol India. 2008 Jul-Sep;56(3):263-70. Review.

Not Useful

(1)

A high incidence of disease flares in an open pilot study of infliximab in patients with refractory inflammatory myopathies. Dastmalchi M, Grundtman C, Alexanderson H, Mavragani CP, Einarsdottir H, Helmers SB, Elvin K, Crow MK, Nennesmo I, Lundberg IE. Ann Rheum Dis. 2008 Dec;67(12):1670-7.

Open label trial

13 patients with treatment resistant myositis. 3 drop outs because of side effects, 1 because of a tumor. No effect of infliximab in the remaining patients.

Useful

(2)

Immunosuppressant and immunomodulatory treatment for dermatomyositis and polymyositis. Gordon PA, Winer JB, Hoogendijk JE, Choy EH. Cochrane Database Syst Rev. 2012 Aug 15;8.

In this paper I found: Coyle K, Pokrovnichka A, French K, Joe G, Shrader J, Swan L, et al.A randomized, double-blind, placebo- controlled trial of infliximab in patients with polymyositis and dermatomyositis. Arthritis and Rheumatism 2008;58 referred to by Cross-over study

Randomized Controlled Trial

11 patients therapy resistant. Unblinding to an open label study after 16 weeks. No statistical significant effect.

Useful

(3)

Open-label trial of anti-TNF-alpha in dermato- and polymyositis treated concomitantly with methotrexate.

Hengstman GJ, De Bleecker JL, Feist E, Vissing J, Denton CP, Manoussakis MN, Slott Jensen H, van Engelen BG, van den Hoogen FH. Eur Neurol. 2008;59(3-4):159-63.

Open label trial

6 patients 18-70 years old, drug naïve! 4 drop-outs, three because of disease progression, 1 because of a possible infusion reaction. Only 2 had a follow-up of ½ jaar, these patients did respond.

Useful

(4) <u>[Anti TNF-alpha treatment of a refractory polymyositis].</u> Wendling D, Prati C, Ornetti P, Toussirot E, Streit G. Rev Med Interne. 2007 Mar;28(3):194-5.

Case report

30 years old female with Infliximab with moderate success and relapses. After discontinuation an unexpexted improvement occurred. Methotrexate was given as well.

Useful

(5)

<u>Treatment of early and refractory dermatomyositis with infliximab: a report of two cases.</u> Dold S, Justiniano ME, Marquez J, Espinoza LR. Clin Rheumatol. 2007 Jul;26(7):1186-8. Epub 2006 May 31.

Female 40 years, resistant to other therapies, good response, afterward steroids and MTX. Selfdiscontinuation of therapies after 11 months led to death.

Female 29 years, no satisfactory response to steroids. Infliximab for led to improvement. Follow-up 6 months (?)

(6)

Possible role for tumour necrosis factor inhibitors in the treatment of resistant dermatomyositis and polymyositis: a retrospective study of eight patients. Efthimiou P, Schwartzman S, Kagen LJ. Ann Rheum Dis. 2006 Sep;65(9):1233-6. Epub 2006 Feb 13.

Case study

Eight patients with dermatomyositis or polymyositis refractory to corticosteroids and immunosuppressives who were treated with TNF inhibitors between 1998 and 2004. Only one was treated with infliximab. This 73-year old male did not respond to Infliximab.

Useful

<u>Fatal Mycobacterium peregrinum pneumonia in refractory polymyositis treated with infliximab.</u> Marie I, Heliot P, Roussel F, Hervé F, Muir JF, Levesque H. Rheumatology (Oxford). 2005 Sep;44(9):1201-2. Epub 2005 Jun 7. No abstract available.

Case report

68-years old male patient with several immunosuppressive drug failures. Concomitant infection, no information on effect infliximab.

Not useful

(7) <u>Advanced refractory polymyositis responding to infliximab.</u> Anandacoomarasamy A, Howe G, Manolios N. Rheumatology (Oxford). 2005 Apr;44(4):562-3. Epub 2005 Feb 3. No abstract available.

Case Study

66 year old female with a 15 years history, unsatisfactory responses to steroids, azathioprine, IVIG, mycophenolate. Follow-up of 22 Months but still on an 4-8 weeks schedule.

Useful

(8)

Refractory polymyositis responding to infliximab. Uthman I, El-Sayad J. Rheumatology (Oxford). 2004 Sep;43(9):1198-9. No abstract available.

Case Study

33 year old female with a 5 years history, non responding to steroids, azathioprine, methotrexate. Remission with 1 year follow up.

Useful

(9)

<u>Treatment of dermatomyositis and polymyositis with anti-tumor necrosis factor-alpha: long-term</u> <u>follow-up.</u>

Hengstman GJ, van den Hoogen FH, van Engelen BG. Eur Neurol. 2004;52(1):61-3. Epub 2004 Jul 5. No abstract available.

Case Study

2 Patients demonstrated a marked and sustained subjective and objective improvement without the occurrence of any side effects at a first treatment. There was a relapse after 3-4 months with a second successful treatment period, however 1 patients got an anaphylaxis. Concomitant treatment with Methotrexate is advised.

Useful

(10)

Successful treatment of alveolar hypoventilation due to dermatomyositis with anti-tumour necrosis factor-alpha.

Korkmaz C, Temiz G, Cetinbas F, Büyükkidan B. Rheumatology (Oxford). 2004 Jul;43(7):937-8. No abstract available.

19-years old girl with hypoventilation due to myositis. No response to other therapies. Improved.

Useful

 (11) <u>Refractory polymyositis responding to infliximab: extended follow-up.</u> Labioche I, Liozon E, Weschler B, Loustaud-Ratti V, Soria P, Vidal E. Rheumatology (Oxford). 2004 Apr;43(4):531-2. No abstract available.

Case Study

One 63-years old female with polymyositis refractory to steroids, intravenous immunoglobulins, methotrexate, azathioprine. Rapid sustained improvement. Follow-up of two years. Probably additional effect of azathioprine!

Useful

<u>Successful treatment of dermatomyositis and polymyositis with anti-tumor-necrosis-factor-alpha:</u> <u>preliminary observations.</u>

Hengstman GJ, van den Hoogen FH, Barrera P, Netea MG, Pieterse A, van de Putte LB, van Engelen BG.

Eur Neurol. 2003;50(1):10-5.

Case Study

2 Patients demonstrated a marked and sustained subjective and objective improvement without the occurrence of any side effects. Further details are not known.

Not useful

Recent advances in the management of adult myositis.

Fam AG. Expert Opin Investig Drugs. 2001 Jul;10(7):1265-77. Review.

Not useful

	year	#	Side	Other	Concom	Infliximab	Follow-	Other	Effect
			Effects	immune	Immune-	Dose and	Up		
				therapies before?	Suppres sion?	Frequency			
1	2008	13pp	ankle flare	Yes	Yes	5 mg/kg 4*/14 wk	4 mo		-
2	2008	12pp		?? ??	-	5 mg/kg 0,2,6,14	16 wk		-
3	2008	6 рр	Infusion Reaction	No	MTX	10mg/kg 0, 2, 6, 14, 22, 30, 38, and 46 wk	26 wk		3+/3 -
4	2007	F40		Yes	Yes	6*5mg/kg /6 wk	2 yrs		+
5	2007	F40 F29		Yes	Yes ??	3*5 mg/ kg/2 wk	11mo 6 mo		+ +
6	2006	M73		Yes	Yes	3 mg/kg/ 8 wk	4 mo	Contin. Therapy	-
7	2005	F66	Peptic Ulcer?	Yes	??	5 mg/kg/ 4 wk	22 wk	Contin. Therapy	+
8	2004	F33		Yes	??	5x 300 mg/6 wk	1 year		+
9	2004	2 pp	Ana- phylaxis	No	No	10 mg/kg 0,2,4 wk	20 wk	Relapse after 20 wk	+
10	2004	F19	-	Steroids	Yes	8 mg/kg 0, 2, 6 wk	?		+
11	2004	F63	-	Yes	Yes	10 mg/kg 5x each 2 weeks	2 yr		+

Appendix 4 Summary (this is the only document to send in)

Infliximab to treat myositis.

JBM Kuks MD PhD

15th November 2014

Question *What's the evidence for the efficacy of Infliximab for generalized myositis without further comorbidity?*

Search Strategy	Pubmed	[myositis] AND [infliximab]		
		Result: 46 papers, 11 containing direct information relevant for the question: 8 case studies, 2 open label trials, 1 randomized controlled trial. The Cochrane review was included.		
	Cochrane	myositis*, infliximab* (ti, ab, kw) Result: 1 review		

Search Outcome

From the 46 papers, 11 were studied in depth, out of these 3 were selected for this CAT

Results

Ref.	Patient Group	Study	Outcome	Key Results	Study
	& Intervention	Туре			Weakness
Dastmalchi	13 patients	Open label	Improvement	Negative	Concomitant
	5mg/kg Infliximab		of weakness		immunosup-
					pressives.
Coyle	12 patients	RCT	Improvement	Not significant	
	5mg/kg Infliximab		of weakness		
	against placebo				
Hengstman	6 patients	Open label	Improvement	Doubtful, not	Concomitant
	10 mg/kg		of weakness	really	immunosup-
	Infliximab			predictable	pressives
					Low number
					of patients

Comments

The subject is not really topical anymore, as most relevant studies have been written between 2004-2008.

Most studies on Infliximab for Myositis are case reports of patients refractory to other medication and all these case studies report a positive result, so that publication bias is likely. On the other hand the quoted studies with 6-13 patients report negative or at most doubtful effects of Infliximab. Except for in the randomized all patients have been treated with concomitant other immunosuppressive medication, making it difficult to assess the pure effect of Infliximab. This was clearly negative in the RCT-study without concomitant medication, however, the medication dose was relatively low. Finally the effect of Infliximab has been tested in a selected population: nearly all patients have failed in other regimes with immunosuppression. Only one study describes the effect in patients without previous immunomodulation (but with concomitant immunosuppressive medication). The results were equivocal.

Clinical Bottom Line

There is no statistical evidence for the effect of Infliximab in patients with otherwise refractory myositis. Case studies suggest that in individual cases Infliximab may be helpful, but it is not possible to predict this effect. A randomized controlled study with patients using Infliximab without concomitant immunosuppressive medication and without previous immunosuppression would be needed to really assess the effect of Infliximab.

References

<u>A high incidence of disease flares in an open pilot study of infliximab in patients with refractory inflammatory myopathies.</u>

Dastmalchi M, Grundtman C, Alexanderson H, Mavragani CP, Einarsdottir H, Helmers SB, Elvin K, Crow MK, Nennesmo I, Lundberg IE.

Ann Rheum Dis. 2008 Dec;67(12):1670-7. Open label trial

A randomized, double-blind, placebo- controlled trial of infliximab in patients with polymyositis and dermatomyositis.

Coyle K, Pokrovnichka A, French K, Joe G, Shrader J, Swan L, et al. Arthritis and Rheumatism 2008;58 referred to by Cross-over study. *Randomized Controlled Trial*

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Scoring form for CAT

	Item	Maximal	Actual
		Score	score*
1	There is a clear, concise and focused	1	
	question		
2	The question is original and relevant for	2	
	clinical practice		
3	The search strategy is adequate	1	
4	The research outcome is adequate	1	
5	The table with results is correct	2	
6	The comments described are adequate	3	
7	The final conclusion is sound	1	
8	The references are really the current key-	1	
	references for this problem		
9	The answers to the questions are adequate	2	
10	Handling ignorance is adequate	1	
	Total	15	

*There will be a conversion of the score to a mark between 0 and 10