CanVasc Literature Review

YEAR 2013-14

Rituximab for the treatment of eosinophilic granulomatosis with polyangiitis

This multicenter retrospective chart review study investigated the efficacy of Rituximab in the treatment of EGPA in 41 patients. The majority of them had relapsing or refractory disease; 5 were given the treatment first line. The dose and infusion schedules were variable with some patients receiving 375mg/m2/week for 4 weeks and others receiving 1g every two weeks in 2 doses; around half (19/41) had received only 1 induction infusion, whereas 22 received 2 or 3 infusions at either 6 months and/or 12 months intervals. The primary outcomes were complete response (defined as BVAS = 0) and partial response (defined as BVAS reduction of 50%).

Complete remission was observed in 34% and 49% at 6 and 12 months, respectively. Partial remission was observed in 49% and 39% at 6 and 12 months, respectively. The median BVAS was 11 (6-17.5) at baseline, 2 (0-6.2) at 6 months, and 1 (0-2) at 12 months. BVAS improved in 83% and 88% at 6 and 12 months, respectively. A positive ANCA was associated with increased likelihood of achieving complete remission (80%) versus negative ANCA (38%). Among the 10 renal patients, 7 achieved remission. The median daily prednisone dose reduced from 15mg at baseline to <10mg in 52% and 53% at 6 and 12 months, respectively. Only 2 patients were able to discontinue prednisone. Immunosuppressant drugs were used by 44% of patients at baseline and declined to 28% at 12 months. There was no clinical or demographic feature that was predictive of achieving remission. Similarly, there was no difference in rate of response based on dosing schedule. B cell depletion occurred in all patients. Among the 17 patients that had data, B cell reconstitution occurred in 17%. There was no difference in eosinophil counts although the levels were already low at baseline, possibly due to prednisone and other immunosuppressant drugs. Half the patients had adverse events, the most common of which were infections and infusion reactions. Among the 15 infections in 14 patients, 6 were severe. Among the 10 infusion reactions, 8 were mild and 2 were severe (one was worsening asthma). There was no leukopenia or death.

This important study is of course limited by its retrospective design, the variable dosing and infusion schedules, and its relatively short follow-up period of 12 months. However, it shows that BVAS decreases in most treated patients, although complete remission was achieved in only half of them and the majority remained on prednisone. More data, ideally from prospective studies, are needed to determine the place of rituximab in patients with (refractory) EGPA. – C.Baldwin, December 15, 2014.

AJ Mohammad, A hot, F Arnt, F Moosig, MJ Guerry, N Amudala, R Smith, P Sivasothy, L Guillevin, PA Merkel. Rituximab for the treatment of eosinophilic granulomatosis with polyangiitis (Churg-Strauss). Annals of Rheumatic Disease, 2014. Link

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The place of conventional laboratory tests as biomarkers of disease activity in eosinophilic granulomatosis with polyangiitis

This multicenter retrospective study on a VCRC cohort of EGPA patients investigated the utility of commonly used biomarkers including eosinophil counts, Ig-E, ESR, and CRP, in following patients longitudinally. While these biomarkers are commonly used to follow patients longitudinally, most of the evidence comes from cross-sectional studies of the diagnosis of patients, rather than from individual monitoring of patients.

Overall there were 141 EGPA patients included in this study. Patient demographics at baseline were comparable to those previously reported in the literature with 46% percent being ANCA positive. There were more patients with renal involvement among ANCA positive compared to ANCA negative patients (27% vs. 4%). There was a trend toward more neurological involvement in ANCA positive patients and more cardiac and GI involvement in ANCA negative patients. Absolute eosinophil count, ESR, and CRP did not differ based on the presence or absence of ANCA. ANCA positive patients had higher levels of Ig-E. There was low or no correlation among the biomarkers (absolute eosinophil count, Ig-E, CRP and ESR). Median levels of each biomarker were higher during active disease than during remission; however, this was only statistically significant for absolute eosinophil count and ESR. Using multivariate analysis, only absolute eosinophil count and ESR were associated with disease activity, albeit this association was weak. Absolute eosinophil count was associated with an increased risk of relapse within 3 months but only in patients with BVAS/WG>1. ESR was predictive of a flare within 3 months if the BVAS/WG was >3. There was no difference based on ANCA.

This study highlights the fact that there is little evidence for the usefulness of employing all these tests (IgE, ESR, CRP and eosinophil count) for following patients longitudinally. Only absolute eosinophil count and ESR were shown to predict relapse; however, this was only in patients who had active disease with BVAS/WG > 1 and 3, respectively. The overall conclusion is that patients should be primarily monitored clinically and that IgE level is not useful to predict flares.– C. Baldwin, December 15, 2014.

Grayson PC, Monach PA, Pagnoux C, Cuthbertson D, Carette S, Hoffman GS, Khalidi NA, Koening CL, Langford CA, Maksimowicz-McKinnon K, Seo P, Specks U, Ytterberg SR, Merkel PA; on behalf of the Vasculitis Clinical Research Consortium. Value of commonly measured laboratory tests as biomarkers of disease activity and predictors of relapse in eosinophilic granulomatosis with polyangiitis. Rheumatology, 2014. Link

Rituximab for maintenance in ANCA-associated vasculitis: more effective to prevent major relapse

The treatment of adult patients with severe ANCA-associated vasculitides is staged, first with an induction phase to obtain the remission, then a maintenance phase to maintain the remission. The induction treatment is based on the combination of glucocorticoids and either cyclophosphamide or rituximab (375 mg/m2 x 4, with an infusion every week), based on the results of the previous RAVE and RITUXVAS studies. The results of the multicentric prospective randomized controlled MAINRITSAN study now shows that a treatment with systematic re-infusions of rituximab at a fixed dose of 500mg at day 1 (around an average of 4.5 months after the start of induction therapy), then at day 15, then every 6 months is superior to the "conventional" maintenance treatment with azathioprine (at 28 months, the rates of major relapses was 5% in the 57 rituximab-arm patients versus 29% in the 58 azathioprine-arm patients; p=0.02). The rates and types of adverse events were comparable in both arms, and none was fatal in the rituximab arm. – CPx, 21 NOv 2014.

Guillevin L, Pagnoux C, Karras A, Khouatra C, Aumaitre O, Cohen P, Maurier F, Decaux O, Ninet J, Gobert P et al: Rituximab versus Azathioprine for Maintenance in ANCA-Associated Vasculitis. The New England journal of medicine 2014, 371(19):1771-1780. Link

Markers for work disability in anti-neutrophil cytoplasmic antibody-associated vasculitis

This cross-sectional study of ANCA-Associated Vasculitis patients from 10 hospital-based UK sites assessed the impact of disease on work disability. Patients completed during a follow-up visit a questionnaire comprised of demographic information, psychosocial measures (Hospital Anxiety and Depression Scale, Jenkins Sleep Estimation Scale, ACR definition of chronic wide spread pain, brief COPE measure of coping and the Chalder Fatigue Scale) and employment status. Physicians collected clinical information, including BVAS, VDI, pre-diagnosis comorbidity (Charlson Index), diagnostic status, history of organ involvement, BMI, ANCA status, eGFR, CBC, albumin, CRP, disease duration and immunosuppressant exposure. Retired patients were excluded. Univariate and multivariate logistic regression was employed to determine variables associated with work disability.

Among 208 subjects included, 26% were work disabled. After multivariable analysis, fatigue (OR 7.1), depression (OR 4.4), BMI (OR 3.4) and severe VDI (OR 3.9) were associated with work disability.

This study is relevant because it highlights the need to address important patient factors outside their vasculitis diagnosis and clinical manifestations and beyond the regular "doctor-based" outcomes. Limitations of the study include the inability of the study to assess quality of life measures outside work employment or assess the financial impact on patients. Further studies are required to identify modifiable patient factors impacting patient outcomes such as work disability, lost productivity and the associated financial implications. – C. Baldwin, October 23, 2014.

Basu N, McClean A, Harper L, Amft EN, Dhaun N, Luqmani RA, Little MA, Jayne DRW, Flossmann O, McLaren J, Kumar V, Erwig LP, Reid DM, Macfarlane GJ, Jones GT. Markers for work disability in anti-neutrophil cytoplasmic antibody-associated vasculitis. Rheumatology. 2014; 53:953-956. Link

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Lower doses of rituximab for remission induction in ANCA-associated vasculitides?

Two studies on the use of lower doses of rituximab for induction in ANCA-associated vasculitides have just been published. The first retrospective one (Moog et al.) evaluated the efficacy of a single dose of rituximab (375mg/m2) for remission induction and maintenance in (ANCA)-associated vasculitis in 16 patients. Patients were followed over a period of 24 months. They could be retreated for maintenance with a single dose (every 6 to 9 months) in case of rising antibody titres or B-cell return. Remission (absence of disease activity during the past 3 months with a prednisolone dose of less than 7.5 mg) was achieved in 11 patients (68%) with a mean time to remission of 9.4 months. During the follow-up, 9 patients had a relapse, with a mean time to relapse of 5.3 months (range, 4 to 24 months). At 24 months, 9 of these 11 initial-responders (82%) were in remission, including 2 who had experienced a relapse during their follow-up . Importantly, all patients also continued corticosteroid and/or DMARD (AZA, MMF or LEF for all but 4 of the 16 patients) therapy over the study follow-up.

The second pseudo-prospective study (Tuner-Stokes et al.) included 19 patients with ANCA-associated vasculitides. Induction rituximab also included one single infusion of 375mg per m2. Eight (42%) were on additional immunosuppression at the time of rituximab treatment. Complete remission (defined here as the absence of clinical features of vasculitis for 3 months with a prednisolone dose of less than 10 mg/day) was achieved in 80% of patients at 3 months. There was no difference in the probability of achieving remission between anti-MPO- and anti-PR3- positive patients. Four patients (21%) had a disease relapse. Median time to B cell repopulation was 9.2 months and to disease relapse/redose was 27 months.

Both articles questioned the approved rituximab dosing (375 mg per m2 x 4) to achieve remission in active ANCA-associated vasculitides. Using one single dose seems to achieve remission in an important percentage of patients, but clearly not all. It is difficult to directly compare the results of these two studies to those of the RAVE trial, because of major differences in their study designs, the small number of patients studied here, and the different definitions used to define remission. Moreover, the use of concomitant immunosuppressants complicates the interpretation of the results of these two studies. However, the possibility to use lower doses of rituximab, which remains an expensive drug not superior to the cyclophosphamide-azathioprine regimen according to the RAVE and RITUXVAS trials, deserves further evaluation. - 20 Oct. 2014, A. AlMutlaq (vasculitis fellow, Toronto CanVasc center).

P Moog, M Probst, C Kuechle, C Hauser, U Heemann, K Thuermel, Scandinavian Journal of Rheumatology. Link

Tabitha Turner-Stokes, Eleanor Sandhu, Ruth J. Pepper, Natalie E. Stolagiewicz, Caroline Ashley, Deirdre Dinneen, Alexander J. Howie, Alan D. Salama, Aine Burns and Mark A. Little, Rheumatology 2014;53:1395-1403.Link

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The new histopathologic classification of ANCA-Associated GN and its association with renal outcomes in childhood

In this study the proposed histopathologic classification for adult ANCA associated GN is validated in a retrospective, single center cohort of 40 children diagnosed with ANCA-GN. Renal biopsy specimens were reviewed and classified by a pathologist blinded for renal outcome. Children were followed for a mean of 2.4 years. Biopsy specimens showed the following classification: focal in 13, cresentic in 20, mixed in 2 and sclerotic 5 patients. The composite renal endpoint differed significantly among the biopsy groups. The probability of having a eGFR> 60 ml/min per 1.73m2 at 2 years was 100% in the focal group, 56% in the cresentic/mixed group and 0% for the sclerotic biopsy group.

This study shows the additional clinical utility of the proposed histopathologic classification system and its ability to clearly discriminate kidney outcomes among childhood ANCA GN patients as well as adults. In the future this could permit optimization of treatment strategies and ultimately lead to better evidence for the treatment of this severe disease in children. - M Twilt, 09 Sept 2014.

Noone DG, Twilt M, Hayes WN, Thorner PS, Benseler S, Laxer RM, Parekh RS, Hebert D.The New Histopathologic Classification of ANCA-Associated GN and Its Association with Renal Outcomes in Childhood. Clin J Am Soc Nephrol. 2014 Aug 21. Link

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Adenosine Deaminase " (ADA 2) mutations in Polyarteritis Nodosa vasculopathy and early-onset stroke

Two studies report on ADA 2 mutations in the NEJM in February. The NIH group describes 9 patients with ADA 2 mutations (recessive mutations in CECR1; cat eye syndrome chromosome region, candidate 1). Patients presented with intermittant fevers, early-onset lacunar stroke and other neurovascular manifestations, livedoid rash, hepatosplenomegaly and systemic vasculopathy. Six patients were compound heterozygous for eight CECR 1 mutations, whereas three patients with polyarteritis nodosa or small vessel vasculitis were homozygous for p.Gly47Arg mutation. All patients had marked reduction in the levels of ADA2 and ADA2-specific enzyme activity. Knockdown of a zebrafish ADA2 homologue caused intracranial hemorrhages and neutropenia. These phenotypes were prevented by coinjection with nonmutated (but not with mutated) human CERC1. They conclude loss-off-function mutations in CERC1 were associated with a spectrum of vascular and inflammatory phenotypes, ranging from early-onset recurrent stroke to systemic vasculopathy or vasculitis.

In the second study of Navon Elkan et al, six families were identified with multiple cases of systemic and cutaneous PAN, consistent with autosomal recessive inheritance. Disease onset in most cases was during childhood. In all families the vasculitis was linked to recessive mutations in CECR1, the gene encoding ADA2. The Georgian Jewish patients were homozygous for a Gly47Arg mutation. The German and Turkish patients were compound heterozygous for other substitution-mutations. ADA2 activity was significantly reduced in serum of patients. The authors conlcude recessive loss of function mutations of ADA2 to cause PAN with a highly varied clinical expression.

Both studies show the exciting discovery of a genetic mutation which can enhance the diagnosis of early onset PAN, before life- or organ threatening manifestations occur. - MTwilt, 27 March 2014.

Zhou Q, Yang D, Ombrello AK, Zavialov AV, Toro C, Zavialov AV et al. Early-onset Stroke and Vasculopathy associated with mutations in ADA2. NEJM, online published Febr 19 2014. Link

Navon Elkan P, Pierce SB, Segel R, Walsh T, Barash J, Padeh S, et al. Mutant Adenosine Deaminase 2 in a Polyarteritis Nodosa Vasculopathy. NEJM online published Febr 19 2014. Link

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Is abatacept the next “new” drug for (limited and relapsing) GPA?

The final results of the open-label AGATA study (abatacept for mild relapsing GPA) have been published. Carol Langford reports that abatacept (10mg/kg IV on days 1, 15, 29 then monthly), on top of prednisone (increased to 30mg for the first

weeks than gradually tapered) and, for those 14/20 enrolled patients taken one, the ongoing immunosuppressant (AA, MTX or MMF) achieved remission in 16/20 (80%) of the enrolled patients, at a (very small) median of 1.9 month. At the study closure, 11 patients were off prednisone. Three of the remaining 6 achieved remission but then relapsed under treatment (at month 8.9), and 3 did not respond sustainably or worsened. There were a total of 97 adverse events, including 9 major ones, with infection being the most common recorded one (mainly of the upper airways and 2 serious ocular ones). None was fatal or required study termination.

There is definitely a need to identify an effective and safe treatment for patients with grumbling, lingering, mild but relapsing GPA, at least to spare corticosteroids. Conventional agents, such as AZA or MTX are only partially and often transiently effective. Cyclophosphamide is likely too toxic for limited disease, and does not always prevent relapses of the limited manifestations of GPA (in this study, 15 of the patients previously received cyclophosphamide). Rituximab is considered as an alternative to cyclophosphamide, thus has no approved indication in the treatment of limited GPA. The encouraging (non-discouraging?) results of the AGATA study should lead very soon to a prospective placebo-controlled randomized controlled trial. – CPx, 17 Dec 2013.

Langford CA, Monach PA, Specks U, Seo P, Cuthbertson D, McAlear CA, Ytterberg SR, Hoffman GS, Krischer JP, Merkel PA; for the Vasculitis Clinical Research Consortium. An open-label trial of abatacept (CTLA4-IG) in non-severe relapsing granulomatosis with polyangiitis (Wegener's). Ann Rheum Dis. 2013 Dec 9. Link

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First epidemiological study on renal GPA and MPA in Canada: definitely a good year for the Roughriders!

Dr. Regina Taylor-Gjevre is the CanVasc core member in Saskatoon. With one of her fellows (K. Anderson) and colleagues, she searched the pathology database from the Province for renal biopsy reports suggestive of AAV between January 2007 and December 2011. Thirty-three cases were identified, which corresponds to an annual incidence rate of 11.7 cases/million population (95% CI 7.8, 15.9; GPA 4.6 cases/million/year, MPA: 7.1 cases/million/year). This number is very close to what has been previously reported for GPA and MPA in Europe for example. As only patients with renal disease have been identified in this study, this important result suggests that GPA and MPA are at least as common (if not more!) in Canada than elsewhere in the world! - CPx 25 Nov 2013.

Anderson K, Klassen J, Stewart SA, Taylor-Gjevre RM. Does geographic location affect incidence of ANCA-associated renal vasculitis in northern Saskatchewan, Canada? Rheumatology (Oxford). 2013 Oct;52(10):1840-4. Link

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RAVE: results at 18 months

Another NEJM on vasculitis and this deserves a new party! The RAVE-ITN group reports now the results, already well known in the world of ANCA vasculitis, of the RAVE study at 18 months.

At 18 months, among the 146 patients (197 included) who achived complete remission before or after the term of 6 months (and stopped the steroids), 32% had relapsed in the rituximab arm versus 29% in arm cyc-azathioprine ($p = 0.16$). Those most at risk of relapse are those patients with antiPR3 ANCA, having already relapsed in the past and/or with a diagnosis of GPA. Rituximab was found superior to cyc-azathioprine in relapsers at 6 and 12 months, but at 18 months rituximab is only non-inferior to conventional cyc-aza regimen (complete sustained remission at 18 months in 37% rituximab versus 20% cyc-azathioprine, $p = 0.06$). The monitoring of B CD19 cells (and/or ANCA) is not good at predicting relapses (only 88% of relapsers in the rituximab group had detectable CD19 B cells when they relapsed, versus 55% of those in the cyc-azathioprine arm) . There is still no significant difference in term of side effects between the two regimens (although patients in the cyc-azathioprine arm had more frequent leukopenia, this was not associated with more frequent serious infections).

These results confirm that a course of rituximab 375mg/m2 x 4 gives the same chance of achieving sustained remission at 18 months than the classical scheme cyc-azathioprine. If this is a great new, it remains that the relapse rate at 18 months is still high, and we must do better! The optionsare numerous and need to be evaluated (what to give afterrituximab? azathioprine? nothing andjust wait and see if a relapse occurs? rituximab at regular intervals or based on ANCA and CD19? only for antiPR3 patients?). - CPx 31 July 2013.

Specks U, Merkel P, Seo P, Spiera R, Langford C, Hoffman G, Kallenberg C, St Clair E, Fessler BJ, Ding L, Viviano L, Tchao N, Phippard DJ, Asare AL, Lim N, Ikle D, Jepson B, Brunetta P, Allen N, Fervenza F, Geetha D, Keogh K, Kissin E, Monach P, Peikert T, Stegeman C, Ytterberg S, Mueller M, Sejismundo L, Mieras K, Stone H; for the RAVE-ITN Research Group.Efficacy of remission-induction regimens for ANCA-Associated vasculitis. New England J Medicine 2013 Aug 1, 369(5), p. 417-27. Link

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RAVE: in-depth analysis of therapeutic responses and failures within study first 6 months

The RAVE-ITN groups now reports a more in-depth analysis of the non-responders to induction therapy (with either oral cyclophosphamide or rituximab). In the RAVE trial, 86% of the 197 randomized patients achieved disease remission during the first 6 months (BVAS/WG=0) and 58% achieved the primary study endpoint (BVAS/WG=0 and prednisone dose=0 at month 6). Patients who experienced a severe flare (BVAS/WG>3 or with one major organ involvement) were eligible for blinded cross-over.
Among the 82 (42%; 36 in the RTX group, 46 in the CYC group, p=0.13) of patients who failed to achieve the primary study endpoint, 27 did not reach remission because of an event (such as uncontrolled disease or an adverse events) and 55 entered remission but subsequently experienced an event (such as a flare or an adverse events) within the first 6 months of follow-up. PR3-ANCA+ patients were at higher risk for failing to reach remission in the first 6 months, compared to antiMPO-ANCA+ patients (18% vs 6%; p=0.03), and at a higher risk of relapse (for those who entered remission; 11 (92%) of the 12 patients with severe flares and 17 (68%) of the 25 patients with limited flares were antiPR3+). None of the 14 RTX patients who flared between months 1 and 6 had a preceding ANCA titer rise, and only 43% of the CYC patients who flared had an ANCA titer rise associated with flare. None of the 14 RTX patients who flared between months 1 and 6 had a preceding B cell repopulation, and only 57% of the CYC patients who flared had a preceding B cell repopulation. Fourteen patients were "crossovered": 3 RTX and 8 CYC because of severe relapse, and 3 RTX because of uncontrolled disease. Twelve of them achieved remission within 6 months post-crossover, with 8 of them still in sustained remission at 6 months post-crossover (patient distribution according to received rescue treatment is not provided in the article).

These results clearly confirm previous observations from different cohorts, rather than provide new information. AntiPR3+ patients are at higher risk of relapse, especially if treated with CYC compared to RTX. B cell and ANCA monitoring are not good predictors of relapse, at least within the first 6 months following rituximab treatment. Switching from CYC to RTX, or inversely, is usually effective in those (12/14) patients when the disease is not controlled with the first-line treatment. - CPx, 22 June 2013

Miloslavsky E, Specks U, Merkel P, Seo P, Spiera R, Langford C, Hoffman G, Kallenberg C, St Clair E, Tchao N, Viviano L, Ding L, Sejismundo L, Mieras K, Ikle D, Jepson B, Mueller M, Brunetta P, Allen N, Fervenza F, Geetha D, Keogh K, Kissin E, Monach P, Peikert T, Stegeman C, Ytterberg S, Stone H; for the RAVE-ITN Research Group. Clinical outcomes of remission induction therapy for severe ANCA-Associated vasculitis. Arthritis Rheum. 2013 Jun 10. doi: 10.1002/art.38044. [Epub ahead of print] Link

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Endoscopic surgical technique for the treatment of subglottic stenosis in GPA

A Swedish group report their experience with a new endoscopic surgical technique for the treatment of subglottic stenosis in GPA patients. As this complication tends to be often refractory to systemic treatment and/or in patient otherwise in remission from their other vasculitis manifestations, local treatment takes a major place. Dilations, often repeated, and local

corticosteroid injection are the main local procedures. Some groups also use local application of mitomycin, and few use laser, stenting or tracheal surgery in most severe cases.

This new technique is carried out under general anesthesia using supraglottic JET flow ventilation and grossly consist in the circular incision of the stenosis in its upper part, then the removal of the submucosal fibrous and granulomatous tissue, followed by the reappliance of the mucosa using fibrin sealant (and mitomycine for potential mucosal defects). On the 13 patients who underwent this procedure, sometimes several times (1 to 8 times), there was lamost no perioperative pain or complication. Patient dyspnea improved in all, QoL improved in 11 and remained stable in 2. However, with a mean follow-up of 3.5 years, only 4 patients required only 1 proceedure. Notably, only one of the tissue samples removed from the 13 patients showed granuloma (others only showed non specific inflammation and fibrous tissue). Another interesting technique, which remains obviously not available in all center and with a relatively frequent need to be repeated.- CPx, 18 Mars 2013.

Arebro J, Henriksson G, Macchiarini P, Juto JE. Acta Otolaryngol. New treatment of subglottic stenosis due to Wegener's granulomatosis. 2012 Sep;132(9):995-1001. doi: 10.3109/00016489.2012.674213. Epub 2012 Jun 5. Link

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CD5+ B cell count as a potential predictor for relapse in patients with ANCA-associated vasculitis treated with rituximab??

Bunch et al., from the Chapel hill group, studied the percentage of CD5+ B cells in 33 patients with ANCA-associated vasculitis (20 antiPR3+ and 23 antiMPO+; 24 with active disease and 19 in remission following rituximab treatment). Patients with active disease had lower CD5+ B cell percentage (median 17%; IQR, 10-28) than those in remission (26%; IQR, 21-36, p=0.02) or 68 healthy controls (28%; IQR, 21-35, p<0.001). For patients with paired samples, CD5+ B cells increased from a median of 14% during active disease to 25% at the time of remission. Outcomes of a subset of 19 patients who achieved remission with rituximab, then were followed and tested at serial intervals, including at the time of their B cell reconstitution (CD19+ B cells >1%), were further studied. All these patients were on MMF for maintenance, following their last rituximab infusions. Time to relapse after rituximab infusion was significantly shorter for patients with a CD5+ B cell percentage <30% at the time of their B cell repopulation and were on <1g MMF per day (17 months) as compared to those still receiving >1g/d of MMF (29 months) or those with a CD5+ B cell percentage >30% at the time of B cell repopulation (31 months). The median CD5+ B cell percentages were 16%, 4% and 34%, respectively, at the time proximal to flare.

ANCA status/titer and CD19+ B cell count monitoring and values to predict relapse in patients treated with rituximab showed conflicting results (not reliable in most studies, but 100% of relapses preceded by CD19+ B cell reconstitution in the Mayo Clinic retrospective cohort). The identification of a more reliable biomarker remain thus a major research goal. This study provides very interesting results, which have now to be further investigated prospectively and by other groups.- CPx, 18 January 2013.

Bunch DO, McGregor JG, Khandoobhai NB, Aybar LT, Burkart ME, Hu Y, Hogan SL, Poulton CJ, Berg EA, Falk RJ, Nachman PH. Decreased CD5+ B Cells in Active ANCA Vasculitis and Relapse after Rituximab. Clin J Am Soc Nephrol. 2013 Jan 4. [Epub ahead of print]. Link