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Biological agents in juvenile idiopathic arthritis: open issues

OP0315 REASONS FOR DISCONTINUATION OF BIOLOGICAL AGENTS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE PORTUGUESE REGISTER, REUMA.PT

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Background: Persistence on medication mainly reflects both effectiveness and safety of a drug. Understanding the reasons to stop bDMARD in routine clinical practice can help to better define the efficacy and safety of biologic medications in children with juvenile idiopathic arthritis (JIA).
Objectives: To investigate persistence on treatment and the reasons for discontinuation of the first biological in patients with JIA.
Methods: Portuguese patients with JIA registered in Reuma.pt who started a bDMARD were analyzed. Persistence was defined as the time between treatment initiation and discontinuation of the first bDMARD. The mean time until discontinuation was calculated using Cox regression survival estimates and the reasons for discontinuation of the first bDMARD were registered.
Results: Of the 1724 JIA patients registered in Reuma.pt, 319 received biological therapy, 62% (198) female. The mean age at disease onset was 7.7±4.8 years and the mean time between the beginning of JIA and the first bDMARD was 8.2±9.4 years. The mean disease duration was 13.7±10.7 years and the mean age at the beginning of biological therapy was 15.8±9.4 years. The distribution of JIA subtypes was: 19.1% polyarticular RF-negative, 17.2% enthesitis-related arthritis, 16.6% polyarticular RF-positive, 16% extended oligoarticular, 13.5% persistent oligoarticular, 12% systemic JIA and 0.9% had undifferentiated arthritis. Considering the whole group, 53.2% have had extra-articular manifestations and 18.4% have or had had uveitis since the beginning of the disease. Persistence on treatment, before discontinuation (due to any cause) was 34.7 months (range: 0.03–182 months) adjusted for gender, biological therapy, JIA subtype, age at the beginning of biological therapy, and disease duration until initiating first bDMARD. The major reasons for drug discontinuation was inefficacy (49.6%), remission (14.2%), adverse events (10.6%), patient decision (1.6%) and pregnancy planning (1.4%). In 22.7% the reason was not specified.
Conclusions: Almost half of the JIA patients stop the first biological agent, due to lack of response, reinforcing the need for the existence of several treatment options fully studied in JIA.
Disclosure of Interest: None declared
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OP0316 DURATION OF CLINICAL REMISSION AND FLARE RATES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AFTER WITHDRAWAL OF BIOLOGICAL TREATMENT (PRELIMINARY DATA)

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Background: Prolonged therapy with biological agents (BAs) may cause adverse events, which leads to the necessity of discontinuation of BAs in patients with juvenile idiopathic arthritis (JIA), once complete disease quiescence has been achieved.
Objectives: To estimate the length of time in clinical remission and time to disease flare after discontinuation of treatment with BAs.
Methods: 83 patients with JIA (33 – with systemic onset, 50 – with oligo- or polyarticular arthritis) were included in the survey. The cohort was 34,9% (29 patients) male and 65,1% (54 patients) female with a mean age of 11±3,69 years (range 5–17 years). All patients with systemic JIA (sJIA) were treated with tocilizumab, 35 (70%) patients with other types of JIA received etanercept, 15 (30%) – adalimumab. 14 (42,4%) patients with sJIA additionally got methotrexate, 5 (15,1%) – cyclosporine, 5 (15,1%) – glucocorticoids, 1 (3,0%) – leflunomide; 9 (25,7%) and 7 (46,6%) patients took combination therapy of etanercept or adalimumab and methotrexate. Patients were randomized into 2 main groups using envelope method: in a first group a BA was discontinued abruptly, while in the second it was tapered gradually by increasing injection/infusion interval.
Results: Duration of inactive disease/clinical remission during tocilizumab treatment was 43±12,16/37±12,16 months, etanercept – 40±13,13/34±13,17 months, adalimumab – 48±11,9/40±12,06 months. Tocilizumab, etanercept, adalimumab were discontinued in 22 (66,6%), 28 (80,0%), 11 (73,3%) patients and were tapered by increasing injection/infusion interval in 11 (33,4%), 7 (20,0%), 4 (26,7%) cases, respectively. After withdrawal of tocilizumab, etanercept and adalimumab 29 (87,9%), 24 (68,6%), 6 (40,0%) patients remained in remission of JIA for 6±10,23 (1–48) months, 6±5,07 (1–20) months and 6±13,33 (4–38) months, respectively. 4 (12,1%), 11 (31,4%), 9 (60,0%) patients flared within 8±5,65 (6–18) months, 5,5±3,49 (1,5–12) months and 4±4,64 (1–13) months after discontinuation of tocilizumab, etanercept and adalimumab, respectively.
Conclusions: Withdrawal of BAs after clinical remission for more than 1,5 years was not associated with a disease exacerbation in more than 70% of patients with JIA. A mean duration of clinical remission after withdrawal of BAs was 6 months.
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Health equity and economy - a vital relationship

OP0317-PARE AN INDEPENDENT REVIEW OF PEOPLE WITH RHEUMATOID ARTHRITIS (RA) AND THEIR CAREGIVER'S LOST WORK TIME

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Background: The National Rheumatoid Arthritis Society (NRAS) is the only patient-led charity in the UK focussing specifically on rheumatoid arthritis (RA) with the key responsibility of raising awareness of the impact and burden of RA. There is a lack of information about the costs and impact of RA on work in the European community; in particular the wider societal costs such as people with RA not being able to perform their job to their best ability, losing days of work due to their RA condition, and the domino effect on caregiver employment.
Objectives: To quantify the burden of RA not only on the healthcare system, but also the wider societal costs associated with RA.
Methods: In 2016 NRAS undertook a partnership with the University of Chester's commercial economics partner HCD Economics who conducted the multinational Burden of Rheumatoid Arthritis: Socioeconomic Survey (BRASS). The study used a bottom-up approach to quantify the burden of disease for people living with RA across 10 European countries including France, Germany, Italy, Spain, Denmark, Sweden, Hungary, Poland, Romania and the UK. The study collected information from patients and physicians on factors associated with managing RA, plus RA sufferers' views on life and workplace impact. It collected information on the resource use and cost of patient care including treatment costs, hospitalisation, tests, and examinations. The wider societal costs included; cost of travel to appointments, requirements for aids/equipment, informal care (non-professional), ability in employment, early retirement due to RA. Work time missed, work and activity impairment were measured using the Work Productivity and Activity Impairment (WPAI) questionnaire.
Results: Voluntary data were collected from 1782 patient forms, of which the average age was 55 years, 1274 (71%) were female and 833 (48%) were currently in work. This study found, on average, persons with RA lose one day of every 4 working days due to not being able to perform their job to their best ability, and completely miss 7% of work time over a 7 day period due to their RA (sample n of 646). In addition to not being able to perform their job to their best ability, almost a third of working persons with RA also had impairment in daily living activities such as shopping and work around the house (sample n of 735). This study also found family/friends have to care for 16% of RA sufferers. This care resulted in reduced employment or inability to work for 25% of family/friend caregivers (sample n of 121).

Conclusions: This study highlights the impact RA has on working life amongst both those with the condition and those providing support. It is hoped these metrics will allow the conversation to open and develop with employers and government on how adapting the workplace can increase productivity. Further research should also be undertaken on the economic impact both to the individuals, their carers and society.
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OP0318-PARE **CONSULTING SERVICES TO EMPLOYERS OF PEOPLE WITH RMDS**

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Background: The Eurobarometer[1] states that RMDs affect 22% of the general population which means that 10 million people are affected in Spain and more than 600.000 people in the autonomous region of Galicia where our organization, LRG, works.
Knowing that 50% of people with RMDs are currently unemployed because of their condition[2], only part of them have the legal work incapacity recognized and receive a pension. This means that RMDs not only affect the health but also the socio-economic status. Most of this people could stay at work and are willing to do so if some arrangements are made like cutting down hours, work place adaptations, flexible schedule, etc.[3]
Most employers are lacking information on how these conditions affect the employee's hability, desire and need to work and how to make the necessary adaptations for not loosing this person from the work force.
Objectives: Making the employer more aware of the positive aspects of keeping all the employees including people with RMDs not just at the work place but at full capacity, avoiding both absenteeism and presenteeism.
Helping the employer knowing about the needs of people with RMDs and the necessary adaptations for each of them.
Keep people with RMDs at work at the best possible conditions both for the employee and the employer, as efficiently and healthy as possible.
Methods: The employee with RMD has 1 session with the psychologist and 1 session with the occupational therapist (OT) to identify the difficulties in continuing to be active into their work place.
LRG HP give personalized advise to the employer about the RMDs, the needs of the employees and how to facilitate them to stay at work and minimize the work incapacity due to their chronic condition. This kind of advise is given by the OT who has treaten the employees and knows all about their needs, goes to their work place to see what are the actual conditions, identifies manageable obstacles and talks to the employers during a pre-scheduled meeting. After, an architect specialized in accesibility offers specific architectural and ergonomic solutions for adapting the work place.
Also peer support is provided by LRG in group meetings and activities of the organization.
Results: The results of this project are shown in the increase of the employees' self-confidence in their capacity to stay at work and also they are more aware of their solvable and non solvable limitations.
During 2016 we advised 14 associates of LRG, 5 of those 14 employees (1/3) stayed at work or returned to work after the consultancy.
Conclusions: This kind of actions are neccesary to make the work places more adaptable and increasing the number of people with RMDs to start a work live, to stay or go back to work.
Peer support within a patient's association is key to create a secure environment for the employees who find relief in seeing other people with RMDs having a sustainable work life.
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Biomarkers in cardiovascular rheumatology - state-of-the-art 2017

OP0319 **HIGH SENSITIVITY CARDIAC TROPONIN T IS A BIOMARKER FOR ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS: A CROSS-SECTIONAL CONTROLLED STUDY**

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Background: Cardiovascular disease (CVD) is the main cause of death in systemic lupus erythematous (SLE) patients. Framingham score underestimates the risk for CVD in this population.
Objectives: Our study aimed to determine whether serum High Sensitivity Cardiac Troponin T (HS-cTnT) helps to identify SLE patients at risk for CVD.
Methods: Presence of carotid plaques was prospectively assessed by ultrasound in 63 consecutive SLE patients asymptomatic for CVD and 18 controls. Serum HS-cTnT concentration was measured using the electrochemiluminescence method. Factors associated with carotid plaques were identified and multivariate analysis was performed
Results: Framingham score was low in both SLE patients (2.1±3.8%) and controls (2.1±2.9%). Nevertheless, 23 (36.5%) SLE patients, but only 2 (11.1%) controls (p=0.039), had carotid plaque detected by vascular ultrasound. In the multivariate analysis, only age (p=0.006) and SLE status (p=0.017) were independently associated with carotid plaques. Serum HS-cTnT concentration was detectable (i.e. >3 ng/L) in 37 (58.7%) SLE patients and 6 (33.3%) controls (p=0.057). Interestingly, 87% of SLE patients with carotid plaques, but only 42.5% in SLE patients without plaques ($p<0.001$), had a detectable HS-cTnT. Conversely, 54.5% SLE patients with a detectable HS-cTnT, but only 11.5% with an undetectable HS-cTnT ($p<0.001$), had a carotid plaque. In the multivariate analysis, only BMI (p=0.006) and HS-cTnT (p=0.033) were statistically associated with carotid plaques in SLE patients. Overall, the risk of having a carotid plaque was increased by 8 (OR [95% CI]: 8.03 [1.41–74.73]) in SLE patients in whom HS-cTnT was detectable in serum.
Conclusions: Detectable HS-cTnT concentration is independently associated with subclinical atherosclerosis in asymptomatic SLE patients at apparent low risk for CVD according to traditional risk factors. These results raise the possibility that this easily obtained biomarker is useful for more rigorous risk stratification and primary prevention of CVD in SLE patients.
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What is behind vasculitis?

OP0320 **DETERMINANTS OF RITUXIMAB PHARMACOKINETICS AND CLINICAL OUTCOMES IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS**

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Background: Response to rituximab (RTX) is variable in patients with ANCA-associated vasculitis (AAV), and predictors of treatment efficacy/relapse risk would be useful. Previous studies have shown that RTX pharmacokinetics (PK) is associated with treatment efficacy in patients with lymphoma.
Objectives: To study the determinants of RTX PK in patients treated for AAV and its association with clinical outcomes.
Methods: This study included 88 patients from the RTX in ANCA-Associated Vasculitis (RAVE) trial who received the full dose of RTX (4 weekly 375 mg/m^2 infusions) and had available serum samples. RTX was quantified using two different assays: a traditional ELISA and a recently developed mass spectrometry-based assay (referred to as miRAMM). We analyzed week (W)2, W4, W8, W16 and W24 serum levels and the trapezoidal area under the curve (AUC) integrating baseline, W2, W4, and W8 levels. We explored potential determinants of RTX PK using univariate and multivariate analysis, and analyzed the association of RTX PK with clinical outcomes: achievement of complete remission at 6 months (defined by a BVAS/WG score of 0 with no prednisone), time to relapse in patients who achieved complete remission, and B-cell depletion duration.