Results: In the three cohorts, 24%, 26% and 12% of the 2010-UA patients fulfilled the 1987 criteria after one year, respectively. Some of these patients fulfilled the 1987 criteria already at baseline. In 1987-and 2010-UA patients aged 40 to 59 who were enrolled in RABBIT at initiation of a biologic or conventional DMARD, these changes in the population have to be taken into account. During the past two decades, the overall incidence of disability pensions (DP) in Germany has decreased tremendously, mainly due to changes in the labour market and in the practice of retirement. In 2010, the rates of new DP in the statutory pension insurance fund were only 52% of those in 1993. When analysing incidence rates of DP among patients with rheumatoid arthritis, these changes in the population have to be taken into account.

Objectives: To compare the incidence of DP in patients enrolled in the German biologics register RABBIT with the expected incidence based upon the general population.

Methods: We used data from 2,385 patients with rheumatoid arthritis (RA) aged 40 to 59 who were enrolled in RABBIT at initiation of a biologic or synthetic DMARD after at least one DMARD failure and did not receive any kind of pension at baseline. Further, we published data on DP by age, sex and from the German statutory pension insurance fund. We applied indirect standardization following the standardized mortality ratio approach.
and divided the cases observed in RABBIT by the number of cases expected for the age and sex matched population leading to a standardized disability pension ratio (SDR). The observation time was censored by either: year of DP; 60th birthday or date of last information on occupational status.

Results: 343 cases with incident DP were observed within 7.437 patient years. The SDR for DP in the RABBIT data compared to the population declined from 10.3 to 3.4 between 2001 and 2010 (Table 1). In the first years of the register, patients who were enrolled at start of a biologic DMARD had a higher risk of DP than those on synthetic DMARDs. This difference disappeared in the last observed years.

Table 1. SDR of receiving a new disability pension in RA patients enrolled in the RABBIT register compared to the age and sex matched general population in the respective year.

| Treatment at baseline | 2001  | 2002  | 2003  | 2004  | 2005  | 2006  | 2007  | 2008  | 2009  | 2010  | Total |
|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Biologic DMARDs      | 12.5  | 10.1  | 5.8   | 5.1   | 3.4   | 3.8   | 3.4   | 4.6   | 4.6   | 4.6   | 5.8   |
| Synthetic DMARDs     | 7.5   | 5.4   | 4.9   | 3.8   | 3.4   | 4.6   |

Conclusions: Taking the overall population trend into account, the risk of early retirement in patients with RA observed in a large cohort has declined tremendously during the last observed years.

Disclosure of Interest: None Declared

THURSDAY, 7 JUNE 2012

Immunological memory

B CELL SUBSETS PHENOTYPE IN AUTOIMMUNITY WITH IMMUNODEFICIENCY: ANALYSIS OF A LARGE COHORT OF PATIENTS WITH APECED SYNDROME

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Background: Autoimmune polyendocrinopathy candidiasis ectodermal dyshidrosis (APECED) is a rare autosomal recessive syndrome due to mutations in AIRE gene, characterized by autoimmune endocrinopathies and mucocutaneous candidiasis. It is accompanied by generation of serum auto-antibodies. Recently the selective susceptibility to C. albicans has been related to the induction of specific IgG antibodies targeting IgA antibodies and IL-22. A 7 cell independent mechanism implicated in peripheral B cell selection, through increased cytokine B-cell activating factor of the TNF family (BAFF), has been proposed. This is of practical importance given the recent advances in immunotherapy targeting B cells.

Objectives: To perform a detailed analysis of B cell subsets in a large cohort of APECED patients compared to age-matched controls, in order to better understand whether an intrinsic alteration in B cell compartment is present. B lymphocytes related cytokines (BAFF, IL-21) were also evaluated in patients' sera and supernatant from monocytes derived dendritic cells (MoDCs).

Methods: Flow cytometric analysis of B cell subsets was performed in 12 patients with APECED from Sardinia, Italy, and compared to age-matched controls. The cohort is characterized by early onset and diagnosis, clinical and hematological heterogeneity, the presence of a wide range of circulating autoantibodies to tissue-specific antigens and genetical homogeneity. The following B cell subsets were analysed: transitional, CD21low B cell subset, naive, IgM memory, switch memory B cells and circulating plasmacells. Serum IL-21 and BAFF levels, and MoDCs supernatant were evaluated by ELISA assay.

Results: APECED patients display with age a reduction of CD19+ peripheral B cells accompanied by a significant decrease in transitional B lymphocytes. Circulating CD21low as well as switch memory B lymphocytes are significantly increased in older patients. Circulating plasma cells are not significantly altered. Serum levels of BAFF as well as BAFF secretion by MoDCs upon stimulation were found increased. No significant difference in IL21 serum levels was observed.

Conclusions: These data show for the first time a significant deregulation of B cell subsets in APECED patients, affecting principally two major subsets: immature transitional, completely absent in older patients and switched memory B cells. Concomitantly up-regulation of BAFF in the absence of functional AIRE was observed. Increasing the knowledge on B cells in APECED patients can improve the comprehension of autoimmunity pathogenesis in immunodeficiency and may also allow the exploration of the possible clinical efficacy of B cell targeted therapy.

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Disclosure of Interest: None Declared

OP0139 A DISTINCT SUBSET OF CD19-NEGATIVE PLASMA CELLS RESIDES IN THE HUMAN BONE MARROW

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Background: Plasma cells (PC) are the unique source of protective and autoreactive immunoglobulin. Mature PC are resting and have downregulated numbers of FACS and the expression of CD19, CD138, K6, HLA-DR, CD95, CD28 and CD56 was studied. Transcriptional analyses of sort-purified plasma cell subsets were performed on an Affymetrix platform. The antibodies expressed by individual plasma cells were characterized using Elispot, cytolsinapic Ig staining, and single-cell RT-PCR.

Results: CD19+ and CD19-negative plasma cells were readily detectable in all human BM samples irrespective of the anatomic site analyzed and co-expressed CD138. At average, 60-70% of the plasma cells expressed CD19 in the BM, while 85% were CD19+ in spleen and tonsils and 95-100% in the blood, respectively. Transcriptional and phenotypical analyses of CD19-negative BMPC suggest their advanced maturity, inasmuch they express CD56 and CD28 while HLA-DR, CD95 and K6-17 are downregulated compared to CD19+ BMPC. CD19-negative BMPC were enriched for IgG-secreting cells which showed surprisingly low mutational load within their VH gene rearrangements. Treatment of RA patients with rituximab significantly reduced numbers of CD19+ BMPC but not CD19-negative BMPC.

Conclusions: Our data indicate an unexpected heterogeneity within the mature plasma cell compartment in the human bone marrow. Detailed characterisation according to CD19 expression suggests that CD19-negative plasma cells acquired a more mature differentiated state and represents rather static population as compared to CD19+ BMPC. A potential anti-CD19 directed B cell depletion approach for therapy of autoimmunity will likely target many but not all plasma cells, while the relationship between CD19 expression by plasma cells and autoantibody production remains to be analysed in order to estimate targeting of autoantibody production. Our data provides new insight into the homeostasis of normal mature plasma cells which opens new perspectives for studies on plasma cells as sources of auto-antibodies in patients with autoimmune diseases.

Disclosure of Interest: None Declared

THURSDAY, 7 JUNE 2012

Comorbidity

OP0140-PARE THE COMPLEXITY OF LIVING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES AND OTHER HEALTH PROBLEMS

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Background: Many people in the UK report they are living with additional health problems to their diagnosed rheumatic or musculoskeletal diseases (RMDs). It is well recognised that ischaemic heart disease and stroke are commoner in acute active rheumatoid arthritis It has been observed that the support and information needs of these people may be higher than those