ratio of approximately 52-fold. Spontaneous skin lesions were observed in 90%+ of vehicle-treated mice by 18 weeks of age, with the majority located around the head and nape of the neck. Histologically, lesions were characterized by combined lymphocyte infiltration and epidermal thickening. In contrast, therapeutic INCBO54707 treatment dose-dependently reduced the incidence and severity of cutaneous lesions (p < 0.05). In addition, INCBO54707 treatment abrogated lymphoid tissue and spleen enlargement (p < 0.0001) in a dose-dependent manner. Kidney damage was only partially improved by INCBO54707 at the highest (90 mg/kg) dose. Quantification of anti-dsDNA antibodies by ELISA revealed a profound, statistically significant reduction of antigen-specific autoantibodies IgG immunoglobulins in the serum (p < 0.0001). Total immunoglobulin titers were not reduced.

Conclusion: These data are consistent with immunomodulation and show that oral INCBO54707 treatment, resulting in JAK1-specific inhibition, has the potential to modulate ongoing inflammatory (autoimmune) cutaneous skin disease.

REFERENCES:

Disclosure of Interests: Britany Fay Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Xin He Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Alexander Margulis Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Yen-ou Yang Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Wenging Yao Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Eduardo Huarte Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Monika Scuron Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Yu Li Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Paul Smith Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Keiko Yoshimoto: None declared, Katsuya Suzuki: Employee of: The author is an employee and/or shareholder of Incyte Corporation., Yu Li Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Keiko Yoshimoto, Katsuya Suzuki, Yumi Ikeda, Eriko Takei, Tsutomu Takeuchi.

Abstract

Primary Sjögren syndrome (pSS) is an idiopathic autoimmune disease whose major clinical manifestations are xerostomia and keratoconjunctivitis sicca, and is often accompanied with hypergammaglobulinemia. Several lines of evidence suggest that a focal lymphocytic infiltrate of the exocrine glands is responsible for lesion formation, IgG production and subsequent dysfunction of the glands. It is well known that B cell activating factor (BAFF) and its receptor, BR3, are deeply involved in the pathogenesis of pSS, and hence BAFF and BR3 are promising targets to treat the disease. We have reported that the abnormally elevated expression of BR3 in monocytes is associated with overproduction of inflammatory cytokines, such as IL-6, by monocytes of pSS patients. Our in vitro experiments suggest that BAFF-stimulated monocytes contribute to IgG overproduction by pSS B cells. We also found that the population of a specific subset of B cells overexpressing BR3 was abnormally increased in pSS patients and that the proportion of the subset was positively and significantly correlated with serum levels of autoantibodies and total IgG as well as ESSDAI, one of the indices of disease activity of pSS. Our results collectively suggest that the elevated expression of BR3 in pSS monocytes results in B cell activation and subsequent overproduction of IgG. However, the relationship between the abnormalities of peripheral blood lymphocyte and clinical manifestations of pSS has not been fully understood.

Objectives: To elucidate possible roles of abnormal monocytes in the development of clinical manifestations of pSS.

Methods: The expression level of BR3 in peripheral monocytes of patients with pSS (n = 65) and healthy controls (HC; n = 38) was analyzed by FACS. Peripheral B cells were cultured with BAFF-stimulated monocytes in the presence or absence of an anti-IL-6 receptor antibody, and the proportion of CD38high IgDlow cells and IgG production were analyzed by FACS and ELISA respectively.

Results: The data are consistent with immunomodulation and show that oral INCBO54707 treatment, resulting in JAK1-specific inhibition, has the potential to modulate ongoing inflammatory (autoimmune) cutaneous skin disease.

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OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS) VS. WITH OBSTETRIC MORBIDITY RELATED WITH ANTIPHOSPHOLIPID ANTIBODIES (OMAPS): A SURVEY OF 1650 CASES FROM EUROAPS REGISTRY

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Background: The obstetric antiphospholipid syndrome is an autoimmune systemic disorder related to antiphospholipid antibodies and pregnancy morbidity. There exist many patients that do not fulfill the Sydney classification criteria. Those cases may be defined as Obstetric Morbidity related with antiphospholipid antibodies (OMAPS).

Objectives: To compare clinical features, laboratory data and foetal-maternal outcomes of 1650 women with obstetric antiphospholipid syndrome and 640 women with aPL-related obstetric complications not fulfilling Sydney criteria.

Methods: Retrospective and prospective multicenter study from the European Registry on Obstetric Antiphospholipid Syndrome.

Results: 1650 women with 5251 episodes were included of which 3601 were histologically proven aPL positive. 1000 women with obstetric antiphospholipid syndrome and 640 women with aPL-related obstetric complications not fulfilling Sydney criteria.

Conclusions: Significant clinical and laboratory differences were found between groups. Foetal-maternal outcomes were similar in both groups when they were treated.

REFERENCES:

Disclosure of Interests: None declared

A DUTCH RESEARCH AGENDA DEVELOPED BY PEOPLE WITH RMDs: WHAT ARE THE MAIN PROBLEMS PEOPLE WITH RMDs FACE AND WHAT ARE THEIR MAIN WISHES FOR RESEARCH AND DEVELOPMENT?

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Background: In the Netherlands much progress has been made with regard to patient participation in research. More and more researchers are finding their way to patient organizations for collaboration. This is also the case for the National Association ReumaZorg Nederland where more and more researchers are asking for the opinion of our patient-experts on their written research proposals. However, this happens mostly because ‘asking for the patient’s view’ is an obligatory (last) part of the submission process of their proposal. ReumaZorg Nederland wants to take patient participation in research to the next level. A level where what matters most to patients’ is taken into account before a proposal is written. Only then will the patient’s voice really be heard in the very heart of a research project.

Objectives: To identify the main problems people with RMDs face in their daily lives and to prioritize their wishes for future research and development. To investigate whether these problems and wishes vary between patients with different types of RMDs. To encourage researchers and product-developers to take these wishes into account at the very start of their research proposal or product-plan.

Methods: Independent and professional research was needed to develop this research agenda. NIVEL, the Dutch Institute for Health Services Research, performed a 7 month research project which consisted of several steps. First, a literature search was performed on scientific publications in PubMed, Embase and PsycINFO on search strings focusing on living with RMDs, problems and wishes of people with RMDs and other known research agenda’s for people with RMDs. The second step consisted of 3 focus group sessions: inflammatory RMDs (group 1), osteoarthritis & fibromyalgia (group 2) and soft tissue- & systemic RMDs (group 3). In addition, a combined session of representatives of each focus group (12 participants) was organized to compare and complement the results of the 3 focus groups. In the third step, an online survey (277 respondents) was held to explore how these problems and research wishes were recognized and prioritized within the Dutch community of people with RMDs. After data-analysis in step 4, a stakeholders session was held in step 5 to discuss results amongst patients, researchers, rheumatologists and project-developers.

Results: Among the 89 problems that were recognized, the main problems people with RMDs face are:
1. Uncertainty about their future.
2. Having to cope with fatigue.
3. Having to cope with the unpredictability of RMDs.
4. Preserving boundaries/staying balanced.
5. Having to cope with the impact of RMDs on social life with family and friends.

Among the 85 wishes for research and development, the main wishes of people with RMDs are:
1. To develop treatments of RMDs other than surgery.
2. To develop an accessible and affordable network of physical exercise activities under professional supervision.
3. To investigate the cause of inflammatory RMDs.
4. To investigate the cause of fatigue with RMDs and how to cope.
5. To investigate alternative forms of therapy and their effect on specific types of RMDs.

All results were described in the first Dutch research agenda made by people with RMDs.1

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