## IPC’s Top Research Priorities 2014

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<thead>
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<th>Rank</th>
<th>Research/Priority Description</th>
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<th>Standard Deviation</th>
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<td>1</td>
<td>Does early aggressive intervention impact the natural history of psoriasis?</td>
<td>3.78</td>
<td>1.13</td>
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<td>2</td>
<td>Identification and validation of biomarkers of psoriasis, including those predicting response to therapy and potential drug-related toxicity.</td>
<td>3.76</td>
<td>1.17</td>
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<td>3</td>
<td>Creation of a complete ‘genetic map’ of psoriasis susceptibility genes to define phenotype-genotype characteristics, focusing on phenotypic variants of psoriasis.</td>
<td>3.65</td>
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<td>4</td>
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<td>5</td>
<td>Effectiveness and safety of systemic treatments in pediatric psoriasis.</td>
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<td>6</td>
<td>Determine whether early aggressive therapeutic intervention (oral therapy vs biologics vs UV phototherapy) reduces the increased cardiovascular risk of psoriasis.</td>
<td>3.53</td>
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<td>7</td>
<td>Mild to moderate psoriasis: developing optimal treatments for localized disease.</td>
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<td>8</td>
<td>Elucidating mechanisms of disease pathogenesis in forms of psoriasis other than psoriasis vulgaris.</td>
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<td>9</td>
<td>Beginning with pediatric patients, develop robust long-term and prospective epidemiological studies to determine the prevalence and natural history of psoriasis and its relationship to other associated diseases.</td>
<td>3.28</td>
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<td>10</td>
<td>Better define effective treatments for patients with exclusively palmoplantar plaque and pustular psoriasis.</td>
<td>3.26</td>
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<td>11</td>
<td>Better define the systemic inflammation associated with psoriasis.</td>
<td>3.26</td>
<td>1.16</td>
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<td>12</td>
<td>Combination therapy in an era with increasing choice of therapeutics.</td>
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<td>13</td>
<td>Identification of psoriasis antigens and auto-antigens.</td>
<td>3.21</td>
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<td>14</td>
<td>What are the biochemical or pathophysiological aspects of uninvolved skin of psoriasis patients that prevent psoriasis? (Research demonstrates that uninvolved skin of subjects with psoriasis is psoriasis “waiting to happen”)</td>
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<td>15</td>
<td>Develop a systematic approach to the relationship between atherosclerosis and psoriasis — is the association primary or secondary?</td>
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<td>3.14</td>
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<td>17</td>
<td>Define the relationship between immunogenicity and clinical response/safety, and develop effective approaches to reduce immunogenicity and correlative loss of response.</td>
<td>3.10</td>
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<td>18</td>
<td>Develop a systematic approach how to choose the best biologic in different clinical scenarios.</td>
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<td>19</td>
<td>Use of biosimilars in psoriasis.</td>
<td>3.06</td>
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<td>20</td>
<td>Better definition of the key biochemical mediators and their downstream pathways in psoriasis pathogenesis.</td>
<td>2.81</td>
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<td>21</td>
<td>Define the effect of early therapeutic intervention and control of psoriasis with prevention of long-term psychological sequelae.</td>
<td>2.77</td>
<td>1.09</td>
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1. Does early aggressive intervention impact the natural history of psoriasis?

Alexa Kimball

Our understanding of the natural history of psoriasis dates back decades; older literature suggests that few complete remissions occur and treatment likely does not affect the course [1]. However, we are now in a different treatment era, where the biology of our therapeutic approaches may result in different outcomes, altering the biologic “march” particularly in young patients with a tendency to develop severe disease. Moreover, even if the course of the disease itself is unaltered by therapy, psoriasis is associated with numerous physical co-morbidities, such as psoriatic arthritis, cardiovascular disease, Crohn’s disease, and other immune-related conditions that accumulate over time [2]. Furthermore, the visible and uncomfortable nature of psoriasis lesions leads to stigmatization and psychological distress, creating a medical, psychological, and socioeconomic burden that can result in “Cumulative Life Course Impairment” (CLCI) [3]. Can this chain of events be mitigated? Early identification of patients who may be most vulnerable to cumulative impact could lead to more aggressive interventions that lessen the progression of CLCIs. Knowing the answers to these questions, while challenging, is likely to substantially inform our treatment choices, the age of the patients we treat, and the severity of the disease that warrant systemic therapy. Therefore, these are questions critical to shaping the guidelines of the future.

References:


2. Identification and validation of biomarkers of disease, response to therapy and relationship to toxicity

Richard B Warren

It has long been known that susceptibility to psoriasis is multifactorial with key genetic variants interacting with environmental insults in predisposed individuals. As pathways of disease susceptibility have been uncovered, it has become clear that effective treatments are targeting these pathways.

It is therefore highly likely that crucial biomarkers of disease susceptibility will also hold the key to stratifying outcomes of treatment effectively. Recent data supports this supposition, with a biomarker of susceptibility for rheumatoid arthritis also being a biomarker predictive of treatment outcome. Such examples are rare however mainly because neither the technologies nor patient cohorts were available to investigate rigorously for biomarkers.
This is no longer the case the technologies to study the genome, transcriptome and metabolome in detail are now available.

This, allied to cutting edge bioinformatics to allow effective analysis of huge datasets, makes it timely to search for biomarkers of psoriasis susceptibility and treatment outcome. The IPC is the perfect conduit to facilitate international collaborations focused around appropriate sample collection and also ensure that all populations are effectively investigated since ethnic diversity will almost certainly mean that differing biomarkers are relevant to different populations.

References:


3. Creation of a complete 'genetic map' of psoriasis susceptibility genes to define phenotype-genotype characteristics, focusing on phenotypic variants of psoriasis

Jonathan Barker

Genetic research has led to dramatic advances in our understanding of psoriasis, its pathogenesis, identification of potential targets for therapeutic intervention and in understanding of the clinical complexity of psoriasis and related diseases. Mostly this has been due to the application of genome wide association studies with identification of common genetic variants associating with psoriasis. The major genetic determinant for psoriasis vulgaris is within the major histocompatibility complex (MHC) but multiple genes, many of which have immunological relevance are also associated. Combining all data indicates that we can explain perhaps 30% of the genetic component of psoriasis. Thus further genetic studies are required to complete the genetic map. To achieve this goal clinicians need to be encouraged and supported to accurately phenotype patients and collect biological samples including DNA. Scientists are essential to use these materials to apply next generation methodologies together with the big data statistics that will be required to allow successful completion of these studies. The clinical gains from this research will be considerable and include providing a platform for prevention strategies, identification of new drug targets and stratifying disease based on outcome – towards the right medicine for the right patient at the right time.

4. Registries - Implementation, feasibility, clinical objectives and outcomes

Arnon Cohen

The introduction of biological agents have increased the options for psoriasis treatment. However, clinical experience with newer systemic therapies is relatively limited. In addition, except for PUVA and cyclosporine, long-term safety data are lacking for conventional treatments.
Registries provide a mechanism to monitor the long-term safety and effectiveness of psoriasis treatment in the 'natural environment'. In addition, registries provide an excellent resource to study health care issues or novel research hypotheses using BIG DATA.

In recent years several registries have been established in the United State, moreover, several European countries, Israel and Australia have established a network of registries to collect data on systemic psoriasis treatment within the PSONET initiative.

Registries are different in many aspects of design. Combining results from registries would increase their power and impact. IPC has a very good position to develop an international collaboration that will call for a worldwide standardization of psoriasis registries.

References:


5. Effectiveness and safety of systemic treatments in pediatric psoriasis

Ruth Murphy

There is very little published evidence about the management of psoriasis in children (1). One third of children present with psoriasis before 18 years of age (2). Those which present early often have more severe disease (2-7). Whilst Etanercept has a license for use in children from 8 years of age, standard systemic agents such as methotrexate, ciclosporin, acitretin and fumaric acid esters are not licensed for use below 16 years of age and there is a paucity of data with respect to both the safety and efficacy of these agents.

Despite this, systemic therapies are used to treat moderately severe psoriasis in the paediatric population (Multi-Site UK Audit of the current treatment of children with psoriasis) (In preparation).

The IPC, through, the Paediatric Dermatology working group, are positioned to identify centres internationally, to participate in an RCT to determine the efficacy of systemic therapies in the paediatric population.

The following databases were searched to identify currently registered RCTs for the treatment of psoriasis in children (PROSPERO; WHO registered trials; Cochrane Database). There was only one registered study, a Cochrane review for the use of ant-TNF therapy in children. There are no registered trials for standard systemic therapies in children.

The IPC need to support work to address this gap in our knowledge about the treatment of psoriasis in children.
6. **Determine whether early aggressive therapeutic intervention (oral therapy vs biologics vs UV phototherapy) reduces the increased cardiovascular risk of psoriasis.**

**Andy Blauvelt**

Psoriasis is associated with systemic inflammation and increased risk of cardiovascular disease, with the extent of skin disease correlating with the degree of risk. Data suggest that methotrexate use decreases risk, whereas it is unclear whether this is true for phototherapy. More so than with methotrexate, TNF blocker use decreases cardiovascular risk in both psoriasis and rheumatoid arthritis patients; ustekinumab therapy may also lower cardiovascular events with chronic use. More and better long-term studies are necessary to prove that anti-inflammatory psoriasis therapies improve cardiovascular function. Such IPC-sponsored studies may include: 1) comparing effects of early life/early disease use vs. later use; 2) comparing effects of various psoriasis therapies head-to-head; and 3) assessing effects on life span. Importantly, results from such studies would need to be effectively disseminated among both patients and dermatologists, so that they could be incorporated into treatment decisions that would greater impact the lives of psoriasis patients.

References:

7. **Mild to moderate psoriasis: developing optimal treatments for localized disease**

*Ulrich Mrowietz*

The majority of psoriasis patients (appr. 75%) present with mild disease (PASI<10, BSA<10, DLQI<10) and is commonly treated outside of specialized centers. During the development of biologic agents over the past decade topical therapy that is the mainstay for mild/localized psoriasis have been widely ignored and innovations are lacking. There is no consented algorithm for topical therapy and no recommendation when to add UV-light and whether narrowband UVB or PUVA should be preferred. In addition, the question about the suitability of UV-light with or without topicals for longterm maintenance management of localized psoriasis has not been sufficiently answered yet.

There is a definite need for harmonization of topical therapy worldwide with a particular focus on longterm management including the definition of treatment goals for non-systemic therapies including topicals and UV-light.

Recommendations on how to treat special localizations such as scalp, face, folds and genitals with topicals should be based on systematic literature searches and, if feasible, supplemented with prospective clinical studies.

8. **Elucidating mechanisms of disease pathogenesis in forms of psoriasis other than psoriasis vulgaris**

*Hervé Bachelez*

**Background**: Physiopathological studies of psoriasis allowed great advances in the understanding of major effector mechanisms operating in the most prevalent clinical form, e.g. plaque psoriasis. On the other hand, limited attention has been given to less frequent clinical phenotypes such as pustular (generalised, palmoplantar, acrodermatitis continua), erythrodermic, or guttate variants. Of note, these latter forms of psoriasis are characterised by limited efficacy of conventional and/or biological antipsoriatic therapies. Finally, recent human immunogenetic studies suggest that a monogenic model underlies the pathogenesis of some of these variants, as recently shown by evidence for mutations of interleukin-36 receptor antagonist-coding genes (IL36RN) in pustular psoriasis.

**Justification**: As the current assumption is that some of these clinical variants result from one major genetic abnormality, and since evidence for genetic heterogeneity has been shown in pustular psoriasis, there is a high need to decipher the immunogenetic scenario operating in very
Feasibility and role of IPC: approval and/or support to the launch of collaborative physiopathological research projects, definition of common clinical databases, and updates of ongoing projects in specific IPC labelled workshops.

References:


9. **Beginning with pediatric patients, develop robust long-term and prospective epidemiologic studies to determine the prevalence and natural history of psoriasis and relationship to other diseases**

Gail Todd

Multiple studies and narrative reviews of the prevalence of psoriasis in different geographical areas have been published. A recent systematic review (Parisi et al., 2013) of general population prevalence studies reported prevalence rates for Europe of 0.73% to 2.9%; North America of 0.7% to 2.3% and Latin American-Indians, Africa (Egypt and Tanzania), Asia (Sri Lanka, Taiwan, China) of 0.0% to <0.5% for all ages. In large areas of the world psoriasis prevalence/incidence is unknown or inferred.

The 2010 global burden of disease project estimates the mortality, morbidity and risk factors for 291 diseases in 187 countries in a systematic collaboration. The DALY psoriasis rank was 144/176 diseases but many non-cutaneous debilitating manifestations were not considered in the disability data (Karimkhani et al., 2014).

A review of African prevalence studies revealed a low prevalence of psoriasis in Western Africa (less than 1% of skin disorders) while higher rates were observed in eastern Africa (Leder et al., 1997). The migration patterns, antigen exposures, and multiple ethnicities of sub-Saharan Africans may offer some explanation.
It is clear that the prevalence of psoriasis varies depending on the population, ethnic group, environment and geographical area studied and the methodology and definitions used (Parisi et al., 2013). We need to improve psoriasis epidemiology nationally and globally with standard protocols and definitions to provide internationally comparable, accurate and consistent data.

**STUDY SIGNIFICANCE AND IMPLICATIONS**

Information will provide figures on global psoriasis prevalence, its distribution within population groups and the associated co-morbidities related in each area. This will assist with cost effective health care planning including the development of health care services that meet the individualized needs of patients with psoriasis as well as the development of health education programs for those affected and the broader community.

The information will inform subsequent basic science and clinical studies. The genetics of psoriasis is complex with evidence that multiple genes are involved. This study allows for an opportunity to discover additional genetic links, co-morbidities and precipitants of psoriasis by comparing populations where psoriasis is rare or does not occur with those in which it does. HLA-Cw6 associated psoriasis has a different phenotype compared to HLA-Cw6 negative psoriasis (GujoÁnsson et al., 2002). The frequency of HLA-Cw6 in Black South Africans is high (35%) but psoriasis prevalence in the general Black population is low (0%) (Leder et al., 1997).

Specific co-morbidities, beyond the metabolic syndrome, and their relationship to psoriasis will lead to new insights. Recent reports on the relationship between HIV and psoriasis suggests that psoriasis has HLA genetic variant enrichment that protects against HIV (Chen et al., 2012; Majorczyk et al., 2014) and open an unexpected door to further understanding of the immunogenetics of psoriasis.

This epidemiology will provide a platform to formulate hypotheses and to determine possible risk factors, genetic factors and ethnic and cultural associations of psoriasis in various environments (rural/urban, latitude, climatic, developed/developing, diet, vector/antigen exposure etc.) populations globally. This will lead to a better understanding of the pathogenesis and natural history of psoriasis and the effect of cultural and other as yet other unidentified influences on its prevalence.

**RESEARCH HYPOTHESIS**

Psoriasis is not one disease.

The prevalence and etio-pathogenesis of psoriasis varies in different ethnic groups and regions of the world.

**METHOD**

We propose prospective population based epidemiological studies in various regions of the world based on a standardized definitions, questionnaires and clinical evaluations to be made freely available, including a disease atlas.

**Phase One** will be to develop internationally standardized, reliable and validated screening tools for psoriasis epidemiology studies.
Phase 2 will see application of the tools in practice for prospective field studies globally to determine psoriasis prevalence.

Phase 3 will run concurrent with the above phases and involve the design, implementation and validation of tools to determine associated co-morbidities, risks and precipitants based on current published data and with input from IPC councilors, patients associations and experts.

References:


5. Majorczyk E, Matusiak L, Nowak I, Pietkiewicz-Sworowska A, Luszczek W, Szepietowski JC, KuÅśnierzcyk P. A single nucleotide polymorphism -35 kb T>C (rs9264942) is strongly associated with psoriasis vulgaris depending on HLA-Cw(*06. Hum Immunol 2014; 75:504-7


10. **Better define effective treatments for patients with exclusively palmoplantar plaque and pustular psoriasis.**

Johan Gudjonsson

Palmoplantar psoriasis is reported to affect approximately 5% of all patients with psoriasis and presents clinically as hyperkeratotic plaques and sometimes as pustules on the palmar and plantar surface of the hands and soles. Recent evidence suggests that the pustular variant of palmoplantar psoriasis may represent a genetically distinct form of psoriasis. However, all variants of palmoplantar psoriasis have a profound impact on quality-of-life and have in several studies been shown to cause greater physical disability than psoriasis without involvement of palms and soles. There is limited evidence for the efficacy of any treatment for palmoplantar psoriasis, although it is generally considered to be difficult to treat, and no published guidelines for its management. Therefore, there is a pressing need to better define effective treatments for patients with palmoplantar psoriasis.
References:


11. Better define the systemic inflammation associated with psoriasis

Wolf-Henning Boehncke

Psoriasis is now considered to be a state of chronic systemic inflammation rather than an inflammatory condition limited to the skin (and possibly joints).

Evidence in favor of this hypothesis comes from studies measuring biomarkers of inflammation in the peripheral blood of psoriasis patients, some of which show good correlation with the clinical course of psoriasis patients under therapy (Ludwig 2007, Strober 2008, Garbaraviciene 2010).

Further exploring this hypothesis is validated as

- it is of general relevance and touches the principal question of whether all (seemingly organ-specific) inflammation might be systemic
- it might pave the way towards biomarkers to measure (objectively) disease activity and severity in psoriasis patients
- it might explain some of the comorbidity observed in psoriasis patients

A methodical approach would be to analyze data sets from clinical trials for biomarkers. A complementary approach would be to determine markers of interest to be studied in a “network” of cooperating IPC groups. Both options are feasible given the contacts of individual IPC members as well as IPC as a collective organization with different pharmaceutical companies, or the role that many IPC members play as heads of active groups in translational research.

References:


12. Combination therapy in an era with increasing choice of therapeutics

Charles Lynde, MD, FRCPC

Traditionally, unlike our rheumatology colleagues, dermatologists have used systemic monotherapy in treating our moderate severe psoriasis vulgaris. Increasingly, however; dermatologists are using systemic combination therapy whether because of suboptimal response, secondary loss of response comorbidities, or immunogenicity issues, etc.
The problem, however; remains that many of the possible systemic comorbidities have either not been studied or only studied in small case studies. Overall guidelines are lacking of evidence to guide the clinician.

A consensus paper on the combinations could be developed and gaps in the literature identified encouragement could then be given to investigators and pharma to investigate the more important gaps.


13. Identification of psoriasis antigens and autoantigens

Prof. Dr. Jörg C. Prinz

Many features of psoriasis are consistent with a T-cell mediated autoimmune disease. Like other autoimmune diseases, psoriasis is linked to a particular HLA class I allele, HLA-Cw*0602, that among various associated gene loci conveys the highest risk for acquiring the disease. The formation of novel psoriatic lesions is associated with an epidermal influx of CD8+ T-cells, which cause the epidermal changes by a T helper (Th) 17-like effector phenotype. Efficient psoriasis treatments are immunosuppressive, interfere with T-cell recruitment and activation or neutralize Th17-related cytokines.

Nevertheless, as for many other T-cell mediated autoimmune diseases, the autoimmune nature of psoriasis has remained hypothetical. While the genetic basis and inflammatory cascade of psoriasis are increasingly well understood the precise mechanisms related to the putatively pathogenic adaptive immune response in the skin are still unknown. Neither the mechanisms of T-cell activation nor the actual role of HLA-Cw*0602 have been elucidated.

Pronounced oligoclonal expansions of CD8+ T cells in the epidermis suggest that the lesional psoriatic T-cell response is antigen-specific. Identification of the potential psoriatic autoantigens and their mode of presentation is therefore crucial for deciphering the pathogenesis of psoriasis.

Antigens of CD8+ T cells are mostly produced in the cytosol from proteins that were degraded by the proteasome, trimmed by amino-peptidases and loaded as short peptides of 8-10 amino acids onto HLA class I molecules.
The HLA class I/peptide complexes are then transported to the cell surface for cognate antigen recognition. CD8+ T cells recognize these complexes by heterodimeric αβ TCRs composed of an α- and β-chain. Both chains are generated by somatic recombination and allow for a huge TCR diversity. Due to this complexity of antigen presentation and T-cell antigen recognition autoantigenic targets of major T-cell mediated autoimmune disorders could not yet be identified.

Due to the accessibility of inflammatory lesions psoriasis should severe as an ideal disease model to characterize the mechanisms of T-cell activation in T-cell mediated autoimmunity. According to the complex experimental challenges related to antigen-presentation and T-cell-antigen recognition, however, the identification of the psoriatic antigens is a major challenge that may require a coordinated approach from different laboratories.

14. **What are the biochemical or pathophysiological aspects of uninvolved skin of psoriasis patients that prevent psoriasis? (Research demonstrates that uninvolved skin of subjects with psoriasis is psoriasis waiting to happen)**

Mark Pittelkow

Psoriasis is a genetic, immune-mediated disease involving skin as well as selected other organs and tissues. Psoriasis demonstrates characteristic patterns of skin involvement, although the disease can become erythrodermic under various conditions. Non-lesional/uninvolved skin of psoriasis may develop active disease induced by injury to the skin, designated the isomorphic or Köbner response. In some cases, lesional/involved skin has been shown to improve or clear following injury, known as the reverse Köbner response. The mechanisms underlying these responses and the observation that psoriasis frequently remains localized and static or occasionally clears spontaneously, indicates that non-lesional skin of psoriasis harbors cellular and molecular pathways that have the potential to prevent the induction of disease as well as normalize and clear active psoriasis. Non-lesional skin of psoriasis exhibits selected abnormalities that reflect evidence of latent (“molecular scar”) disease activity. Clearance of psoriasis by selected skin-directed therapies, such as phototherapy, provides potentially greater resistance to redevelopment of disease than other therapies, providing further evidence of potentially enhanced local resistance to disease development induced by these therapies and inherent in sustaining lesion-free skin. With our current molecular and cellular interrogation technologies, detailed disease identification and the ability to accurately sample, compare and molecularly subclassify skin specimens, there is clear potential to delineate specific biologic and biochemical pathways in skin that resist development of psoriasis and to leverage these findings to better control disease development and recurrence.

References:


15. **Develop a systematic approach to the relationship between atherosclerosis and psoriasis: Is the association primary or secondary?**

Wolf-Henning Boehncke

This topic has large overlap with Topic #2 ("Develop a systematic approach to the relationship between myocardial infarction and psoriasis: Is the association primary or secondary?") because atherosclerosis provides the pathogenetic basis for myocardial infarction, but is the hardest measurable end point (cardiovascular mortality is more closely linked to myocardial infarction and stroke).

Cardiovascular mortality is increased among psoriasis patients. Some epidemiologic and case-control-studies show a “dose effect” of psoriasis in as much as only patients with moderate-to-severe psoriasis show an increased risk for myocardial infarction (Gelfand 2006, Mallbris 2004, Ludwig 2007, Armstrong 2013). While the association as such is readily accepted, the debate on whether or not psoriasis is an independent risk factor for myocardial infarction is ongoing (Boehncke 2011, Nijsten 2009).

Clarifying the role of psoriasis as a possible cardiovascular risk factor has direct implications for the monitoring of the patients and treatment goals of diseases associated with psoriasis (such as hypertension).

This question can be addressed on numerous levels:

A. Experimental research can clarify further the effects of “psoriatic cytokines“ on the biology of endothelial cells, taking into account the phenotypic heterogeneity of these cells depending on the anatomic site (peripheral small arterioles vs. huge vessels such as aorta).

B. Carefully designed cohort studies could use modern imaging to search for developing atherosclerosis in psoriasis patients, ideally in a prospective way

C. Huge prospective cohort studies could investigate the effect of systemic anti-psoriatic (anti-inflammatory) therapies on the patients’ cardiovascular risk

Approaches A and B seem feasible given the scientific competence of numerous groups of IPC members. Approach C would have to be massive and therefore likely not to be pursued by IPC. However, trying to have IPC researchers be linked to such projects (e.g. major cardiology trial in North America on the potential protective effect of MTX on myocardial infarction) might be a way forward.
References:


16. Develop a systematic approach to the relationship between myocardial infarction and psoriasis: Is the association primary or secondary?

Wolf-Henning Boehncke

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B. Carefully designed cohort studies could use modern imaging to search for developing coronary artery disease in psoriasis patients, ideally in a prospective way.

C. Huge prospective cohort studies could investigate the effect of systemic anti-psoriatic (anti-inflammatory) therapies on the patients’ cardiovascular risk.

Approaches A and B seem feasible given the scientific competence of numerous groups of IPC members. Approach C would have to be larger in scope and therefore likely not as easily actionable (by IPC). However, trying to have IPC researchers be linked to such projects (e.g. major cardiology trial in North America on the potential protective effect of MTX on myocardial infarction) might be a way forward.
References:


17. **Defining the relationship between clinical response, immunogenicity and safety of biologic therapy**

April Armstrong

The choice of biologic therapy depends on a combination of different factors including short-term and long-term clinical response, immunogenicity, and safety. Defining the relationship among these factors is important because it contributes directly to therapeutic decision-making. Specifically, we propose to conduct a research project using existing data from clinical trials that examines (a) the relationship between clinical response and immunogenicity, and (b) the relationship between clinical response and safety, using existing data. In determining the relationship between clinical response and immunogenicity, we will gather up-to-date information from the clinical trials on antidrug antibody formation, the type of assays performed, and its correlation with psoriasis severity. With regards to the relationship between clinical response and safety, data from off-label dosing or dose-escalation studies that examined both response and safety events will be informative. The IPC is well equipped to conduct this study; the findings will provide the clinicians with an integrated assessment of a biologics’ clinical response, immunogenicity, and safety.

References:


18. **Develop a systematic approach how to choose the best biologic in different clinical scenarios**

April Armstrong

As the number of biologic medications approved for the treatment of psoriasis continues to rise, the choice of which biologic may be best suited for specific clinical scenarios is a highly clinically relevant topic. Evidence-based, expert-vetted recommendations for biologic choice in real-world scenarios will likely result in improved patient care and outcomes in the long run. We propose to conduct a Delphi exercise that draws on background literature as well as expert opinions to help inform biologic choice for specific clinical scenarios. While biologics can share many common features, the clinical scenarios will emphasize the differences among biologics in treating particular aspects of psoriasis. The IPC is well equipped to conduct this Delphi exercise to develop a systematic approach on how to choose the best biologic in different clinical scenarios. This will provide the clinicians with relevant and useful recommendations for real-world scenarios.

References:


19. **Use of Biosimilars in Psoriasis**

Ron Vender

Biosimilars are biotechnologically processed drugs corresponding to a reference biopharmaceutical (RB) (1). Although they may have comparable outcomes, biosimilarity does not imply interchangeability (2). However, definitions of interchangeability vary. Despite allowing for patients and pharmacists to alternate between the biosimilar and RB without physician intervention in the FDA’s definition (3), this may not be the case for other health-governing bodies. Consequently, extensive investigation is required to support that the biosimilars in psoriasis (BPs) will have indistinguishable outcomes and no greater risk of declining safety or efficacy if used alone or when interchanged with the RB (4). Although it is recognized jointly by some Italian societies (5) that “direct evidence on efficacy, safety, and
immunogenicity of biosimilars is mandatory in psoriasis” (6), the use of biosimilars has been approved for management of all IMIDs (7), including psoriasis, in the EU (6). This provides a solid foundation for determining feasible use of BiPs and determining a consistent definition of biosimilarity and interchangeability in psoriasis internationally, by establishing a consensus based on existing and future comprehensive clinical studies and research.

References:


5. The Italian Society of Rheumatology (SIR), Italian Society of Dermatology (SIDeMaST), and Italian Group of Inflammatory Bowel Disease (IG-IBD)


7. Immune-mediated inflammatory diseases

20. Better definition of the key biochemical mediators and their downstream pathways in psoriasis pathogenesis

Robert Sabat

It is generally acknowledged that soluble extracellular mediators play an essential role in psoriasis pathogenesis. Although members of different chemical classes are involved, current research focuses on proteins like cytokines and chemokines that are abundantly present in psoriatic lesions. The most reliable results regarding these mediators are quantitative mRNA expression analyses and in vitro functional studies. However, the last years shed only first light on downstream pathways of various cytokines. The problem is that convincing knowledge about the significance of a mediator can be achieved currently only by clinical targeting. Suggested activities:

- Organization of consensus meetings to define criteria that should be met by a key mediator

- Organization of conferences to present novel integrative and translational approaches, novel models, and bringing together respective research groups and pharmaceutical companies
Providing of funding for respective research.

The probability to achieve the aim in a short term seems rather low; so what is needed here is long-term commitment. However, achieving the objective is essential for the development of treatments effective in all psoriasis patients and helps to definitely define pathogenetic subgroups of patients.

References:


Marc Bourcier

Psoriasis is a well know common dermatological disease now recognized associated with numerous co-morbidities. While psoriasis can start at any age, it commonly starts early in life. Any chronic medical condition is associated with impairment of Quality of Life. It is well recognized that psoriasis has major impact on physical and mental health domains. Psoriasis starting early in life tends to be more severe. Anxiety and depression are common in psoriatic patients and these can be seen in 24 to 30% of psoriatic patients. Very little is known on the impact of treatment on co-morbidities, namely on the psychological co-morbidities. A publication in 2010 on Cumulative Life Course Impairment addresses this issue and opens the door to further define if early intervention may stop this progression and prevent permanent psychological damage. Further research in this field is needed and may have a major impact in therapeutic decisions. If proven this will confirm that early appropriate treatment is necessary to prevent these permanent sequelae.

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