IPC presents most relevant psoriasis research articles

Each year, the International Psoriasis Council (IPC) identifies the top papers in psoriasis research. Papers are nominated for inclusion by our Board of Directors and then circulated to our membership to identify the most important papers. This year’s selection includes articles that enhance our understanding of adaptive and innate immunity in psoriasis, the genes that lead to psoriasis susceptibility, clinical research focusing on a new class of drugs, a TNF-inhibitor studied in children, and a population study that uncovers an increased risk of mortality.

Co-editors Hervé Bachelez, M.D., Ph.D., professor of dermatology at Hôpital-Saint-Louis, Paris; and Mona Ståhle, M.D., Ph.D., professor of dermatology and venereology, Department of Medicine at Karoliska Institutet, Stockholm, provided expert commentary on each article and its value to clinical practice.

**ARTICLES REVIEWED IN THIS ISSUE**


Review of articles begins on page 3.

**INSIDE THIS ISSUE**

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Dear Colleagues,

On behalf of the International Psoriasis Council (IPC) and this issue's co-editors Hervé Bachelez, M.D., Ph.D., and Mona Ståhle, M.D., Ph.D., I am pleased to present the September 2008 edition of our clinical newsletter, *IPC Psoriasis Review*.

Published several times per year, *IPC Psoriasis Review* appraises important current clinical and research publications and provides commentary on those that we believe make the greatest contribution to our understanding of the disease and its treatment. In this issue, we include our annual review of the top research psoriasis papers. We also present select cases from our May 23, 2008, EADV IPC Meet the Experts Program, chaired by Professor Christopher Griffiths, and held in Istanbul.

2008 continues to be a productive year for IPC. Our consensus on topical therapies, led by Professor Peter van de Kerkhof, was published.¹ In September, we held an interdisciplinary conference on psoriasis, comorbidities and lifestyle modification in Dallas, which brought together a group of international experts to critically review the subject and develop a research agenda for IPC. We invite you to attend Psoriasis from Gene to Clinic, chaired by Professors Jonathan Barker and Christopher Griffiths, along with a reception on Wednesday, Dec. 3, at the Royal College of Physicians in London. We hope you are able to attend.

In addition, we introduce a CDROM program, “Psoriasis Review for the Dermatology Clinic,” with details on the back page.

Our CEO and executive director, Malia Tee Lewin, has transitioned out of the day-to-day operations of IPC. We are grateful for Malia’s vision and leadership in serving as our founding CEO and executive director during the past four years, and for helping us secure the appropriate funding, which has led to a significant expansion of our programs. We welcome Karen Rodman as our new CEO and executive director. Karen brings to IPC more than 20 years of successful fund-raising experience in the not-for-profit philanthropic world, and will be a great asset as we plan the organization’s future growth, funding and direction. I am sure you will all enjoy meeting her.

We hope this newsletter is informative and that the knowledge, experience and insights of our faculty are valuable to you in treating your psoriasis patients. For additional copies of *IPC Psoriasis Review*, or to learn more about IPC, please visit www.psoriasiscouncil.org.

Sincerely,

Alan Menter, M.D., President
International Psoriasis Council

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COMMENTARY

Here, the authors demonstrate the predominant contribution of epidermal T cells in psoriatic skin changes. They also show that interactions involving $\alpha_1\beta_1$ integrin, a collagen IV binding receptor at the surface of effector T lymphocytes, is mandatory for the migration of this cellular subset toward the epidermis. This introduces a novel concept that T-cell/extracellular matrix interactions are important in psoriasis development. Finally, injections of an anti-$\alpha_1\beta_1$ integrin monoclonal antibody in a skin xenograft mouse model of psoriasis prevents both the epidermal migration of effector T cells and the onset of the psoriatic phenotype. In addition to their insight into the immunopathology of psoriasis, these findings also identify a potential new therapeutic target.

New pathway drives psoriasis autoimmunity

Plasmacytoid dendritic cells (pDCs) are key mediators of the immune response in psoriasis, but the mechanism of action is not well-understood. Typically, pDCs sense infection through Toll-like receptors (TL7 and TL9) and release type 1 interferons (IFN) like IFN-α. PDCs respond to viral and bacterial DNA, and they do not normally respond to self-DNA. However, recent reports suggest pDCs can respond to self-DNA in autoimmune diseases. This study identifies LL37 as a key activator of pDCs in psoriasis, converting self-DNA into an autoimmune trigger. LL37 is an antimicrobial peptide released by keratinocytes in response to injury or infection. LL37 is expressed by keratinocytes, and is highly upregulated in psoriatic lesions but not normal skin, uninvolved skin of psoriasis patients or other skin disease lesions. LL37 is also released by migratory inflammatory cells such as neutrophils and is thus present in the dermal compartment in association with pDCs. When complexed with DNA, LL37 is taken up by pDCs, and the LL37:DNA complexes activate pDCs through TLR9 and stimulate INF-α production. This is a potential mechanism for self-DNA to trigger autoimmunity in psoriasis.

The anti-psoriatic effect of blocking $\alpha_1\beta_1$ was similar to that of anti-TNF or ciclosporin treatment. These studies suggest the interaction between an extracellular matrix receptor and the T cell plays an integral role in the expansion of T cells into the epidermis and development of psoriasis.


Psoriasis is a complex genetic disease with multiple loci contributing to susceptibility. Genome-wide association (GWA) studies examine genetic variation across the entire genome and can be used to identify new disease loci. This study used GWA scans comprising 311,298 single nucleotide polymorphisms (SNPs) to examine susceptibility to psoriasis (PS) and psoriatic arthritis (PSA). The discovery phase utilized 223 PS cases (132 cases with PS alone and 91 cases with PSA) and 519 controls of European descent. The replication stages examined 577 PS cases and 737 controls from the United States and 578 PSA cases and 480 controls from the UK. The major histocompatibility (MHC) region on chromosome 6p21 showed the strongest association (rs10484554 and rs2395029), as is consistent with multiple psoriasis studies. This study also confirmed associations with previously identified interleukin-23 receptor (IL23R, rs11209026) and interleukin-12 (IL12B, rs6887695 and rs3212227) SNPs. A new SNP that is downstream from IL23R and upstream of IL12RB2 not previously associated with psoriasis was also identified (rs12131065). This GWA scan also provided evidence for novel associations. Four SNPs from 13q13 were identified (rs1186468, rs4514547, rs4569133 and rs7993214) that are found in a region encoding the conserved oligomeric golgi complex component 6 (COG6) gene and a lipoma HMGIC fusion partner (LHFP). Association was also found within a region of the epidermal differentiation complex (EDC) that contains PSORS4, a previously identified psoriasis susceptibility locus. The SNP rs6701216 is located within the late cornified envelope 1C (LCE1C) and is involved in epidermal differentiation. In a separate analysis of the PSA discovery cohort, four SNPS were identified on chromosome 15q21 between ubiquitin specific protease 8 (USP8) and tumor necrosis factor, alpha-induced protein B-like 3 (TNFAIP8L3). Finally, 3 SNPs (rs13151961, rs6822844 and rs6840978) from chromosome 4q27 were identified in a region recently associated with other autoimmune diseases that may represent a novel PSA susceptibility locus.


**COMMENTARY**

This genome-wide scan and SNP-based genetic study was performed mostly in patients with psoriasis and psoriatic arthritis from the United States. This study reveals that the strongest risk factor for psoriasis is associated with genetic variants within the MHC class I region, and that genetic variations in this region also play a key role in PSA. Interestingly, this study reveals association with a SNP in the HCP5 gene in the MHC that has been identified in HIV patients who are elite suppressors and can control their viral load without treatment. Besides confirming the impact of IL23R and IL12B polymorphisms on the incidence of both PS and PSA, this study also identifies novel susceptibility loci, one located on chromosome 4 which harbors putative genes of interest encoding IL2 and IL21 and has been previously associated with rheumatoid arthritis and celiac disease. This large-scale study is a significant step in the completion of the puzzle of susceptibility genes involved in both PS and PSA. Functional studies are needed to understand if these new regions have biologic relevance to psoriasis pathophysiology, although for IL23R, it appears confirmed with novel treatments targeting the p40 molecule.
New psoriasis susceptibility gene identified

A new psoriasis susceptibility locus was identified using a genome-wide association scan (GWA) of more than 408,000 single nucleotide polymorphism (SNP) loci using pooled DNA from 318 British cases and 288 controls. The greatest association was found within the major histocompatibility (MHC) region, as expected, and association with IL23R and IL12B was also confirmed (described below). A region on chromosome 20q13 was identified to show association, and confirmed in two replication sets of 2,679 cases and 2,215 controls of British and German origin. This region contains two genes, (ZNF313/RNF114 and SPATA2). ZNF313 expression in skin, CD4+ T-cells and dendritic cells was confirmed by real-time PCR, while SPATA2 was expressed at very low levels. The rs495337 SNP showed greatest association in this region. The minor allele of SNP rs495337 is associated with an increased expression of ZNF313, suggesting that a ZNF313 regulatory variant tagged by rs495337 may be the psoriasis susceptibility allele. ZNF313 belongs to a family of RING domain E3-ubiquitin ligases, and recombinant ZNF313 was able to bind to ubiquitin in vitro. While the function of ZNF313 is unknown, the process of ubiquitination plays an important role in regulating molecules involved in the immune response.


COMMENTARY

This genetic study uses a whole genome exploration technique to show that psoriasis is associated with a single nucleotide polymorphism on chromosome 20q13. This SNP impacts the transcription of an adjacent gene named ZNF313/RNF114, which is likely to regulate T-cell activation through ubiquitin ligase activity. The function of the ZNF313 gene product needs to be addressed further. However, these findings reveal a new psoriasis susceptibility gene and reinforce the hypothesis of the contribution to disease pathogenesis from multiple genes that share a common role in the regulation of immune responses.

IL-23 receptor variants associated with psoriasis

This report is a detailed analysis of the interleukin-23 receptor (IL23R) gene locus. This locus has been identified as a susceptibility gene for Crohn’s disease, another immune-mediated inflammatory disease. For these studies, a genome-wide association scan (GWA) was performed using pooled DNA from 318 British cases and 288 controls.

The greatest association was seen within the major histocompatibility (MHC) region as expected, but association was also found in the interleukin-23 receptor (IL23R) p.Arg318Gln variant and validated in an additional 519 cases and 528 controls. The IL23R p.Arg318Gln variant was found to be increased in controls, and may confer a protective effect for psoriasis. Other members of the IL23R receptor complex were examined, including interleukin-12 receptor (IL12RB1), IL23A and IL12B genes, which code for the second subunit of the IL23R and the subunits of its ligands. There was no association in any of the markers examined for IL12RB1 and IL23A, but association was noted in two non-coding SNPs (rs10045431 and rs3212227) of the IL12B locus. Rs3212227 was previously identified by Cargill et al and was found to have a modest protective effect in this data set.


COMMENTARY

This genetic study identifies genomic variants in the IL23R gene and single nucleotide polymorphisms in the IL12B gene, associated with a protective effect against psoriasis. This confirms the association of IL12B marker rs3212227 identified by Cargill et al in 2007. Although the functional consequences of these genomic variations remain to be addressed in further studies, these findings emphasize the key role of the IL-23 signaling pathway in the pathogenesis of psoriatic disease, similar to what recently emerged in the setting of chronic gastrointestinal inflammation in Crohn’s disease.
Targeting the IL-12/IL-23 pathway with ustekinumab

Drugs targeting the interleukin-12 (IL-12) and interleukin-23 (IL-23) pathways are of increasing interest in psoriasis. Ustekinumab is a monoclonal antibody to the p40 molecule, shared by both IL-12 and IL-23. In a phase III study, participants were randomized to three experimental groups: 45 mg ustekinumab, 90 mg ustekinumab and placebo (with crossover to ustekinumab at week 12), with approximately 250 patients per group. Each group received an injection at week 0, 4, and every 12 weeks thereafter. The primary endpoint was PASI 75 at week 12, and data were analyzed by intention to treat. At week 12, after receiving two doses of ustekinumab, 67% of patients receiving the 45 mg dose and 66% of patients receiving the 90 mg dose achieved PASI 75, compared to 3% of the placebo group. Patients randomized to the ustekinumab group achieving PASI 75 were again randomized to placebo at week 40 to determine loss of response. During the randomized withdrawal period, there was a gradual recurrence of disease over time. The safety data presented through week 12 were very similar to placebo. Serious adverse events occurred in six patients in the ustekinumab group and two patients in the placebo group.


COMMENTARY

This phase III randomized, placebo-controlled trial focuses on the efficacy and safety of ustekinumab, a monoclonal antibody that binds the p40 subunit of IL-12 and IL-23. Both dosage regimens yielded similar results at week 12, with roughly 63% of patients reaching a PASI 75 response. This trial gives evidence for maintenance of response for at least one year in most patients receiving treatment every 12 weeks with good safety results, notably an apparent absence of skin cancers and severe infections. The favorable efficacy/safety balance of ustekinumab, with minimal constraints regarding the frequency of administration, makes this treatment very appealing for patients with psoriasis. Long-term cohort studies over several years are needed in order to accurately address the safety profiles of IL-12/23-inhibiting compounds, which interfere with cytokines involved in anti-infectious and anti-tumor immunity. Ustekinumab was submitted to the U.S. Food and Drug Administration (FDA) and European Medicines Agency for approval for psoriasis in December 2007, and an FDA Advisory Committee recommended approval of ustekinumab on June 17, 2008.

ABT-874 shows promise in Phase II study

The interleukin-12 (IL-12) / interleukin-23 (IL-23) pathway has gained attention for its role in psoriasis pathogenesis. The monoclonal antibody ABT-874 also targets the p40 molecule shared by both IL-12 and IL-23. In this phase II dose-finding study, 180 patients were randomized to one of six treatment groups with 30 patients each. The following doses were used: 1 dose of 200 mg, 100 mg every other week (eow) for 12 weeks, 200 mg/week for 4 weeks, 200 mg eow for 12 weeks, 200 mg/week for 12 weeks and placebo. The primary endpoint was PASI 75 at week 12. After week 12, all patients who had achieved PASI 75 were enrolled in a 36-week open-label extension study, and that data has not yet been published. At week 12, PASI 75 was achieved by 63% (200 mg dose), 93% (100 mg eow), 90% (200 mg 4 doses), 93% (200 mg eow) and 90% (200 mg/week), compared to 3% of the placebo group. Escalating doses beyond 100 mg eow do not seem to improve efficacy. The treatment was well-tolerated and no serious adverse events were reported.


COMMENTARY

A phase II randomized, placebo-controlled trial provides evidence for the efficacy of ABT-874, a fully human IgG1 monoclonal antibody reacting with the p40 subunit of IL-12/IL-23. Following subcutaneous administration at different dosages and injection number/frequency, the percentage of patients reaching the PASI 75 response at 12 weeks is as great as 93% with an overall good short-term tolerance. However, escalating doses do not seem to improve efficacy beyond 100 mg eow. This study provides a striking validation of inhibition of the IL-23 signaling pathway as a promising therapeutic strategy in patients with moderate to severe psoriasis. Longer-term studies are needed, and phase III studies are ongoing.
Etanercept effective in treating psoriasis in children

Psoriasis is a challenging disease to treat in children, as few therapies are approved and few randomized controlled trials have been performed. The following study was conducted to better understand efficacy and safety of etanercept in children. Etanercept is a soluble tumor necrosis factor receptor that is approved to treat psoriasis in adults and polyarticular juvenile rheumatoid arthritis in children as young as 4. In this study, 211 children (ages 4-17) were randomized to receive etanercept (0.8 mg/kg; maximum 50 mg) or placebo once weekly for 12 weeks followed by an open label extension for 24 weeks. The primary endpoint was PASI 75 at week 12. At week 12, 57% of those receiving etanercept achieved PASI 75 compared to 11% of placebo. At week 36, 138 patients were again randomized to etanercept or placebo to determine the effects of withdrawal and re-treatment. At the randomization, approximately two-thirds of participants had achieved PASI 75. During the 12-week withdrawal period, PASI 75 was lost by 42% of those receiving placebo (29/69). Etanercept was well-tolerated, but four serious adverse events occurred in three patients during the open-label extension, and all resolved without sequelae.


COMMENTARY
This study is the only randomized, placebo-controlled trial that specifically addresses the efficacy and safety of a TNF inhibitor in pediatric patients with moderate-to-severe psoriasis. Although the median age of patients enrolled in this study (14 years) was biased toward adolescence, the results obtained at a weekly dosage of 0.8 mg/kg undoubtedly show evidence for etanercept efficacy over a 48 week period, with an overall good safety record. The PASI 75 rate is higher at week 12 in this population than in trials of adults receiving 25 mg twice weekly but is consistent with trial data of adults receiving 50 mg twice weekly. Given the deleterious impact of severe psoriasis on the quality of life and psychology in childhood, this data has been positively considered by experts for approval of etanercept in pediatric patients in the United States and in Europe. An FDA advisory committee recommended approval of etanercept for children on June 18, 2008.

Severe psoriasis associated with increased risk of mortality

The relationship between psoriasis and mortality was examined using data from the General Practice Research Database (GPRD) in the UK from 1987 – 2002. This large study included 133,568 patients with mild psoriasis, 3,951 patients with severe psoriasis, and 560,358 and 15,075 matched controls for the mild and severe groups respectively. Mild psoriasis was defined as any patient with a diagnostic code of psoriasis but without a history of systemic therapy. Systemic therapy included phototherapy, PUVA, methotrexate, azathioprine, ciclosporin, oral retinoids, hydroxyurea, and mycophenolate mofetil. Severe psoriasis was defined as any patient with a diagnostic code of psoriasis and a history of systemic therapy, while the control group included patients with no history of a psoriasis diagnostic code. There was an increased overall mortality risk in patients with severe psoriasis but not in patients with mild psoriasis, and the increased mortality risk was maintained after adjusting for major risk factors of death. Men with severe psoriasis died 3.5 years (95% CI, 1.2 – 5.8 years; P < .001) younger, and women with severe psoriasis died 4.4 years younger (95% CI, 2.2 – 6.6 years; P < .001) than those without psoriasis.


COMMENTARY
This cohort study provides evidence for an increased risk of mortality in patients with severe psoriasis, defined by patients having received a systemic therapy, but not in those with mild psoriasis. Male and female patients respectively died 3.5 and 4.4 years younger than those without psoriasis, and the risk persisted after adjustment for classical risk factors of mortality. The results are consistent with data from a smaller Swedish study (Mallbris et al 2004). Together, these data support a direct impact of inflammatory disease on mortality. Further studies are needed to understand the cause(s) of increased mortality and if intervention can decrease mortality in these patients.
CASE 1: 39-year-old man with psoriasis

History and presentation
This patient has a 17-year history of psoriasis with 48 percent body surface area involvement, including scalp, trunk and limbs (Figure 1). Prior therapies included multiple courses of topical corticosteroids and narrow-band UVB phototherapy, which produced a moderate response.

What is the most appropriate treatment option?

PANELIST 1: In an individual with this extent of psoriasis, topical therapy is not likely to be successful, and narrow-band was only moderately successful. He is a candidate for systemic therapy, and I would personally initiate methotrexate therapy.

PANELIST 2: This individual may also be at a risk for increased cardiovascular morbidity. I agree that methotrexate is a good treatment option to control his psoriasis and to possibly prevent cardiovascular disease, applying our experience from rheumatoid arthritis. In Germany, we would also consider fumaric acid for this patient.

How do you initiate methotrexate therapy?

PANELIST 1: Initiating methotrexate therapy can be variable. I start with a test dose of 5 mg and then increase to 15 mg per week.

PANELIST 2: We do not typically use a test dose. We start with 15 mg subcutaneous methotrexate. Subcutaneous injection bypasses the gastrointestinal (GI) tract, potentially decreasing GI toxicity and nausea.

PANELIST 3: It is also very important to screen patients for concomitant medications that may interact or interfere with methotrexate. This is an important point for the patient to be aware of, so they can alert other physicians. We also recommend a chest X-ray prior to starting, as some patients develop avoelitis or pulmonitis and having a comparative baseline image is helpful.

Do you use folic acid supplementation with methotrexate?

PANELIST 2: Folic acid supplementation also varies widely, and we use 5 mg every day. We find this schedule improves patient adherence compared to folic acid supplementation six days a week.

PANELIST 3: Some reports in the literature suggest that folic acid supplementation may require a higher methotrexate dose, while other reports don’t find this effect. In our practice, we use folic acid once a week.

PANELIST 1: I think there is literature to suggest you are not mitigating the clinical response while utilizing folic acid. It reduces nausea and probably has protective effects on bone marrow suppression.
**How do you monitor a patient on methotrexate?**

**PANELIST 1:** We are particularly concerned about the hepatotoxic side effects of methotrexate. The guidelines in North America recommend liver biopsy at 1.5 g cumulative methotrexate, and these guidelines are currently being revised. Screening is absolutely critical, and we do liver function tests on a regular basis as well as annual hepatitis B and hepatitis C screening.

**PANELIST 3:** Liver fibrosis can be challenging to diagnose by physical examination or ultrasonography. However, our internal medicine colleagues routinely monitor the liver using ultrasound.

**MODERATOR:** In the UK we monitor serum aminopropeptide of type III procollagen (PIIIP) levels every three months. If there are three consecutive readings higher than the normal level of 4.2, we biopsy the liver. If the liver biopsy is normal but the PIIIP is raised, we go to the standard 1.5 g cumulative dose to trigger a liver biopsy.

**CLINICAL COURSE**

Methotrexate was initiated at 15 mg per week with folic acid supplementation. There was significant improvement in skin symptoms.

**CASE 2:** 65-year-old man with psoriasis co-morbidities and multiple medications

**History and presentation**

This patient has a 30-year history of plaque psoriasis with a PASI of 35 (**Figure 2**). He also has a number of co-morbidities, including congestive heart failure, hypertension, renal insufficiency, hepatic insufficiency and gout. He is taking multiple systemic medications including torasemide, amiodarone, digoxin, ACE-inhibitors and allopurinol.

**What is the most appropriate treatment option?**

**PANELIST 3:** This individual is definitely a candidate for systemic therapy. However, he has a number of co-morbidities that are relative contraindications to several systemic therapies, and he takes a number of drugs that may interact. We would probably not use ciclosporin due to his hypertension and renal insufficiency of congestive heart failure, and we would not use methotrexate due to his liver problems. Therefore, I would consider starting him on UVB phototherapy, as amiodarone is phototoxic within the UVA spectrum. We would start the Ingram regimen, applying dithranol together with low dose phototherapy and if possible, would hospitalize him.

**PANELIST 2:** That is a reasonable approach, but he has very severe psoriasis that contributes to his co-morbidities. I would start him on 7.5 mg methotrexate and 25 mg etanercept.

**PANELIST 1:** I would also consider adding a TNF-inhibitor like etanercept. We would need to know more about his congestive heart failure and whether it was well controlled. We would be working with a cardiologist on these issues. Efalizumab could also be considered, as it does not have a congestive heart failure contraindication.

**CLINICAL COURSE**

The Ingram regimen was started with UVB 311 nm at 0.1 J/cm² with slow dose escalation in combination with dithranol for 30 treatments. Within 8 weeks, his psoriasis was greatly improved, and no phototoxic reactions occurred.

**CASE 3:** 36-year-old woman with inflammatory psoriasis

**History and presentation**

This patient has a 15-year history of inflammatory psoriasis with multiple episodes of erythrodermic psoriasis, including classic generalized pustular disease (**Figure 3**). She currently has one child who was conceived while she was on ciclosporin. She would like to conceive another child without medication.

**When initiating ciclosporin, what dose do you use?**

**PANELIST 3:** The guidelines indicate we have a choice between 2.5 to 5 mg per kilogram body weight. I personally always start with a higher dose, up to 4 to 4.5 mg per kilogram of body weight. It is important to dose ciclosporin to the ideal body weight and not to the actual body weight.

**PANELIST 1:** Ciclosporin is typically used for three or four months to get over an acute crisis. I start at 3 mg per kilogram. I’m very comfortable using ciclosporin in females,
Meet the Experts

and the registry data from transplant patients indicates a potential for a slightly shorter pregnancy term with no other potential problems. If the patient does become pregnant, I would then decide how to taper the ciclosporin. Many experience a spontaneous improvement in their psoriasis during pregnancy, so there is a good chance of minimizing or stopping therapy.

How do you monitor a patient on ciclosporin?

PANELIST 2: In Germany, there are excellent guidelines for ciclosporin that we adhere to. We have patients monitor their blood pressure. We look for renal problems and we ask the patients about neurological symptoms that might develop.

How long do you stop different therapies before a woman should conceive?

PANELIST 2: Our general rule is to stop all systemic treatments if a female gets pregnant or wants to become pregnant. We will use phototherapy and topical treatments.

PANELIST 1: We are very comfortable initiating TNF-α agents in females considering conception, and these agents are all pregnancy category B. There are many patients in registries, and there is no evidence in the literature for teratogenicity.

She is not on any systemic medication, is trying to conceive and has an erythrodermic flare. What is the most appropriate treatment option?

PANELIST 3: One recommendation is to try to avoid becoming pregnant as long as the psoriasis is active. Erythroderma can be life threatening and should be treated aggressively, and I would use a TNF-antagonist. If she wants to become pregnant, I will probably consider one with a short half-life. Etanercept has a serum half-life of three days, and within 10-15 days, most of the drug is eliminated.

PANELIST 2: I think the doctor is facing a potential legal problem if the patient is on systemic therapy and something goes wrong during the pregnancy, as it may be attributed to the drug. If she becomes pregnant, we would hospitalize her and use phototherapy and topical treatments to get the psoriasis under control, which could take 2-4 weeks.

PANELIST 1: In North America we do not have the ability to hospitalize patients with erythroderma due to the cost. We would need to initiate therapy, and in this case probably with infliximab or adalimumab to control her erythroderma as quickly as possible.

CLINICAL COURSE

The decision was made to start infliximab at 5 mg/kg (induction 0, 2, 6 weeks) and every 8 weeks thereafter. The erythrodermic psoriasis abated, but in order to maintain response, the dose was increased. She becomes pregnant while on infliximab.

(Editors note: Infliximab is contraindicated in pregnancy and lactation in Europe and is pregnancy category B in the United States.)

When using infliximab, what is the highest dose you use?

PANELIST 1: We are comfortable increasing infliximab dosages up to 10 mg per kilogram, if necessary. Once she is stabilized, if she is pregnant, I would then start reducing the dose and frequency of infliximab. Unfortunately some patients that taper off infliximab do not respond as well when they are retreated.

PANELIST 3: At doses this high, it will be difficult to get the treatment reimbursed, and I would consider switching to another TNF-antagonist, such as adalimumab.

We hope these three case reviews were informative in your assessment and treatment of psoriasis patients.

IPC gratefully acknowledges our sponsors Abbott Laboratories, Amgen and Wyeth, and Centocor, Inc., for the grants they provided for the Meet the Experts Program. This activity has been planned and implemented in accordance with IPC’s program planning policy. Our sponsors have no control over the program’s content or the cases selected for review.
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FACULTY DISCLOSURES

Professor Bachelez, Ph.D., has served as a consultant for Abbott, Merck-Serono, and Wyeth, and received financial support from Schering-Plough, and Roche laboratories.

Professor Griffiths has received research support or has served as a consultant or speaker for Abbott, Amgen, Biogen-Idec, Centocor, Essex Pharma, Galdema, Leo Pharma, Novartis, Novo Nordisk, Schering-Plough, Merck-Serono, Stiefel, UCB Pharma, and Wyeth.

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Professor Prinz has served as a consultant, investigator, speaker or advisory board member for Biogen-Idec, Novartis, Wyeth, Merck-Serono, Essex Pharma, Galdema, Centocor, and Abbott.

Professor Ståhle is a founder of Lipopeptide AB, a biotech company developing pharmaceuticals for wound healing. Professor Ståhle has served on advisory boards for Wyeth, Abbott, Schering-Plough, Merck-Serono and Mölnlycke Healthcare.

Professor Sterry has served as a consultant, investigator, speaker or advisory board member for Abbott, Schering-Plough, Merck-Serono, Biogen-Idec, Novartis, Isotechnika, Fumedica, Janssen-Cilag, and Wyeth.

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The International Psoriasis Council has developed this CDROM to educate medical professionals about psoriasis and the full spectrum of treatment options, including practical advice for initiating safe and effective psoriasis therapy.

Faculty include Kristine Kucera, PA-C, MPAS, DHS, Craig Leonardi, M.D., Alan Menter, M.D., Mary Wiatrowski, RN, DNC, and Melodie Young, MSN, RN, A/GNP-c.

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