The 3rd Psoriasis Symposium for Biologics and Systemic Agents

PROGRAM

October 26(Sat), 2013
Orchid room, Westin Chosun Hotel 2nd floor
Pusan, Korea
(웨스틴조선호텔 부산점)

Organized by
The Korean Society for Psoriasis
Sponsored by
The Korean Dermatological Association

인사말씀

안녕하십니까?

건선 치료의 패러다임은 최근 수 년간 현저히 변화되었습니다. 이제는 '보다 빨리', '보다 강하게', '보다 지속적으로' 치료가 변화되어야 한다는 목소리가 환자뿐 아니라 의료계 내에서도 쏟아져 나오고 있으며 이러한 요구의 한 가운데에 생물학적 제제의 출현이 자리잡고 있습니다.

이러한 변혁의 시기에 '생물학적 제제와 전신치료제 심포지움'을 개최하게 된 것을 무한한 기쁨으로 생각합니다. 원래 이 심포지움은 작년에 '생물학적 제제 심포지움'으로 부산에서 시작되었습니다. 성공적인 결과에 고무되어 금년에는 전반기와 후반기에 하기로 결정하였고 전반기는 이미 봄에 서울에서 성공적으로 개최되었습니다. 또한 작년에는 생물학적 제제에 국한하였던 심포지움의 범위를 금년에는 전신치료제로 확대하였습니다. 생물학적제제를 사용하기 위해서는 경구용 전신치료제의 단계를 거쳐야 하고 많은 피부과 전문의들이 전신 치료제에 익숙하지 않아서 생물학적 제제와 경구용 전신치료제에 대한 보수교육을 동시에 진행할 필요성을 느꼈기 때문입니다.

이번 심포지움은 세 개의 세션으로 구성되어 있으며 세션 1에서 경구용 전신치료제의 사용방법에 대한 강의를, 세션 2에서 생물학적 제제의 실제 사용에 있어 핵심적인 내용인 '언제 사용을 하고 언제 중단해야 하는가?' 그리고 '안전성을 최대한 지키는 방법은 무엇인가?' 및 '보험과 관련하여 꼭 알아야 할 것은 무엇인가? 등에 대해 집중 조명합니다. 세션 3에서는 생물학적 제제의 실제 사용 경험을 공유하는 시간을 가질 것입니다.

이 심포지움을 위해 좌장, 강사로 참여하신 여러 교수님들, 후원해주신 부산 지역 교수님들, 그리고 운영을 맡아 주신 부산대학교에 감사드립니다. 일본에서 강의를 위해 내한하신 마부치 교수님과 후원하여 주신 여러 회사 관계자들께도 감사드립니다. 준비에 최선을 다한 대한건선학회 임원 여러분과 프로그램 책임자인 전임 및 신임 기획이사 윤상웅, 김병수 교수께 특별한 감사를 드립니다. 참여하신 여러분 모두의 건선 진료 역량이 일취월장하는 계기가 되기를 기원합니다.

2013. 10. 26

대한건선학회 회장 **이 주 흥**

PROGRAM

Opening Ceremony

12:30-12:50 Registration

12:50-12:55 Opening address; Joo-Heung LEE (*President of KSP*)
Congratulatory address; Kee Suck SUH (*Vice President of KDA*)

1:00-2:10 Session 1 Conventional Systemic Agents

Chairs: Jai Il YOUN (*National Medical Center*), Kwang-Joong KIM (*Hallym University*)

S1-1. **Changing paradigm of psoriasis treatment** **/ 9**
Joo-Heung LEE (*Sungkyunkwan University*)

S1-2. **CsA in psoriasis treatment** **/ 10**
Hae-Jun SONG (*Korea University*)

S1-3. **MTX in psoriasis treatment** **/ 13**
Chul-Jong PARK (*Catholic University*)

S1-4. **Acitretin in psoriasis treatment** **/ 15**
Bong-Seok SHIN (*Chosun University*)

Q&A (10 min)

2:10-3:05 Session 2 Biologic Agents

Chairs: Nack-In KIM (*Kyung Hee University*), Kee Suck SUH (*Kosin University*)

S2-1. **Biologic agents: When to start? When to stop? And what to choose?** **/ 19**
Yong-Beom CHOE (*Konkuk University*)

S2-2. **Making sure biologics are safe: Recent update** **/ 21**
Byung-Soo KIM (*Pusan National University*)

S2-3. **Reimbursement strategy** **/ 23**
Jae-We CHO (*Keimyung University*)

Q&A (10 min)

3:05-3:15 *Coffee break*

3:15-4:25 **Session 3 Field Experiences with Biologics**

Chairs: Sang Tae KIM (*Kosin University*), Hae-Jun SONG (*Korea University*)

Q&A (10 min)

Closing

Session 1
Conventional Systemic Agents

S1-1

Changing paradigm of psoriasis treatment

Joo-Heung Lee, MD

Department of Dermatology, Sungkyunkwan University School of Medicine, Samsung Medical Center

Psoriasis treatment paradigm has changed gradually but obviously over the past decades. Core concept of the new paradigm can be summarized as 'higher potency', 'rapid escalation' and 'continuity' of treatment. The advent of the new paradigm was prompted partly because of dramatic impact that biologics have made in the treatment of psoriasis. But main drive of the change came from the strong voices of the patients themselves.

In contrast to several decades ago, fast-acting, potent and relatively safe oral medication such as cyclosporine or methotrexate is now widely used, although long-term treatment with them is not recommended because of major organ toxicities. Innovation in the field of phototherapy for more effective, targeted and even safer devices has also contributed to the emergence of new paradigm. Furthermore, traditional concept of mild to moderate psoriasis has changed. Some even suggests mild psoriasis should be defined as psoriasis involving less than 2% of the total body surface area, much smaller area for mild psoriasis than was suggested a few decades ago. These trends jeopardized the positioning and value of topical treatments that used to be the mainstay for the mild to moderate psoriasis. However, the new trend has not only affected topical treatments. It also undermined the area of conventional systemic agents. While the conventional systemic agents can only offer on-and-off treatment, biologics can allegedly provide long-term or even life-long treatment like other long-term medications in chronic disorders such as diabetes.

Patients' voices are the major driver for more potent, rapid escalating and long-lasting treatment. Recent surveys carried out in Europe and US showed that treatment satisfaction level of psoriasis patients is surprisingly low in contrast to the expectation of dermatologists. Major reasons for the dissatisfaction are time consuming nature and lack of efficacy that are mostly attributed to topical treatments. Many psoriasis patients do not want to waste time and effort in doing apparently ineffective topical treatments. Patients' voices that used to be a 'storm in a teacup' is now spilling over and steering a new paradigm. Their perspective is now being reflected in the treatment guidelines in the form of QoL-based severity measures. S3 European guideline is a great example by incorporating DLQI in the treatment guideline.

In conclusion, we, dermatologists, are being invited to the new world of psoriasis treatment and if we really want to keep our leading role in the management of psoriasis, we should not only be well prepared but also be proactive for the new paradigm.

S1-2

CsA in psoriasis treatment

Hae-Jun SONG

Department of Dermatology, Korea University Guro Hospital

1. Mechanism of action and characteristics

Cyclosporin forms a complex with cyclophilin, which inactives calcineurin phosphorylase, preventing the phosphorylation of nuclear factor of activated T cells and, therefore, the transcription of IL-2. It also down-regulates ICAM-1 on keratinocytes and endothelial cells. It has an effect on dendritics cells, Th17 pathway, and VEGF. Cyclosporin is one of the most effective treatments for psoriasis because of its rapid onset of action.

2. Indication

Indicated for moderate to severe psoriasis unresponsive to other treatments. Although there is limited data regarding its efficacy, cyclosporin can be used for other forms of psoriasis such as chronic palmoplantar pustulosis (PPP), generalized pustular psoriasis (GPP), nail psoriasis, guttate psoriasis and erythrodermic psoriasis. Cyclosporin is contraindicated in uncontrolled hypertension, renal disease, serious infections, and in those with a current and previous history of malignancy, possibly excluding basal cell carcinoma and carcinoma in situ.

3. Efficacy

Efficacy of cyclosporin is dose dependent with a shorter time to remission at higher doses. Cyclosporin at doses of 2.5 to 5 mg/kg/d for a 12- to 16-week period produces rapid and significant improvement in psoriasis in 80% to 90% of patients. At 3 mg/kg/d, PASI 75 is achieved in 50% to 70% of patients and PASI 90 in 30% to 50% of patients. Tachyphylaxis with cyclosporine dose not appear to occur in the treatment of psoriasis

4. Dosage

An initial low-dose approach (starting at 2.5 mg/kg/d) is appropriate for patients with stable psoriasis, whose severity is between moderate and severe. An initial high-dose approach (5.0 mg/kg/d, maximal does) is appropriate for patients with severe psoriasis, patients with psoriasis recalcitrant to other treatments, or for those patients who are highly distressed in a crisis situation. Once a patient's psoriasis is in remission, the goal is to maintain the patient on the minimum effective dose. Intermittent short-term therapy (12~16 weeks) is the most frequently recommended regimen, using short courses of cyclosporin until significant improvement is

achieved, after which treatment is withdrawn. A short course of cyclosporine (starting 5.0 mg/kg/d and gradually decreased after remission by 0.5 mg/kg/day every 2 months) can be used in severe flares of disease as rescue therapy because of its rapid onset of action until an alternative maintenance treatment is instituted. This is particularly useful in the treatment of erythrodermic, or generalized pustular psoriasis. Although long-term maintenance therapy was possible with 3.0 to 3.5 mg/kg/d level, current guidelines limit the continuous use of cyclosporine to 1 year (US), up to 2 years (UK & EU) and prefer intermittent therapy.

5. Combination or rotational therapy

Cyclosporin can be combined with topical therapies, such as corticosteroids or vitamin D3 analogues for an improved response. Systemic treatments, such as methotrexate, acitretin, can also be used in combination with cyclosporin in severe cases, allowing for dose reduction of cyclosporin to minimize toxicity. Rotational therapy with the aforementioned systemic agents can also be used to minimize duration of cyclosporin treatment and toxicity.

6. Safety and monitoring

If serum creatinine increases 30% over the patient's baseline value on two consecutive readings 2 weeks apart, the dose should be reduced. If there is an elevation of serum creatinine of at least 30% over the patient's baseline value, recorded on two consecutive readings 2 weeks apart, the dose should be reduced by 1 mg/kg/day or by 25% to 50% for a minimum of 4 weeks, even if the value lies within the normal reference range. If serum creatinine does not improve after 4 weeks therapy at the reduced dose, cyclosporin should be decreased by another 25% to 50%. If creatinine remains elevated at this stage, cyclosporin should be discontinued. A maximum dose of 5 mg/kg should be used for up to 2 year only. Patients treated continuously for more than 2 years have a significantly higher risk of developing irreversible renal damage. Renal structural changes including slight to moderate interstitial fibrosis were observed in psoriatic patients treated with cyclosporin for 1~2 years, significant lesions such as glomerular sclerosis or severe interstitial fibrosis being observed after 3 years or more. When hypertension develops, the dose should be reduced by 25% to 50% or antihypertensive therapy introduced. Hyperbilirubinemia and increase in transaminase occurs in up to 30% of patients. To assess and monitor the adverse reactions, blood pressure, serum creatinine and blood urea nitrogen should be measured at baseline (two separate measure) and weeks 2, 4, 6, 8, then monthly. CBC, potassium, bilirubin, liver enzymes, fasting lipid profile, uric acid, magnesium (when muscle cramp noted) and urinalysis are recommend at baseline and monthly thereafter. Calcium channel blockers of the dihydropyridine class are the antihypertensives of choice. Experimental studies have shown that cyclosporin is not genotoxic but causes dose-dependent tumor promotion. In skin tumor models, cyclosporin has been shown to enhance the induction of skin tumors by ultraviolet irradiation. Because cyclosporin has been reported to cause the reactivation of latent tuberculosis infection in higher doses used in transplant recipients, and

because cyclosporin is an immunosuppressant, the National Psoriasis Foundation recommends screening for latent tuberculosis infection before initiation of cyclosporin treatment. In addition to above mentioned adverse reactions, there are some more side effects to mention. Nausea, vomiting diarrhea, or flatulence are well known minor complaints. Gingival hyperplasia reported in up to 30% of patients, especially in children. Onset tends to be during 3 to 6 months of treatment and treatment with metronidazole may be useful. 6 months interval monitoring for gingival hypertrophy recommended. It is noteworthy that hypertrichosis, epidermal cysts, keratosis pilaris, acne, folliculitis, sebaceous hyperplasia may be seen as a cutaneous side effects in psoriasis patients under cyclosprorin use.

7. Drug interactions

Because cyclosporin is metabolized by the cytochrome P450 3A4 system, there are important drug interactions that will alter cyclosporin levels. Macrolides, azole antifungals, and calcium channel blockers increase cyclosporin levels. Anticonvulsants, rifampin, and griseofulvin decrease cyclosporin levels. It is also important to note that foods that contain grapefruit juice can increase levels of cyclosporin in the serum. When concomitantly used, some of NSAIDs (diclofenac, naproxen), antifungal such as amphotericin-B, antibiotics (ciprofloxacin, genta & tobramycin, trimethoprim), H2 histamin antogonists, and tacrolimus may increase renal toxicity. Calcium channel blockers (diltiazem, nicardipine), drugs for erectile dysfunction (sildenafil), statins, benzodiazepines, prednisolone, digoxin, colchicine are the medications whose levels increase when used concomitantly with cyclosporin. Cyclosporin crosses the placental blood barrier and is a category C drug in pregnancy.

8. Use of cyclosporin in hepatitis C

Cyclosporin has been contraindicated in patients with chronic hepatitis C infection. But recent studies have shown that cyclosprorin suppresses viral replication and thus not exacerbates hepatitis C infection. Although further investigation on the safety of cyclosporine in HCV infected psoriasis patients, the currently available data indicate that it may be contribute to a good outcome in both safety and efficacy.

S1-3

MTX in psoriasis treatment

Chul-Jong PARK

Department of Dermatology, The Catholic University of Korea College of Medicine

Methotrexate was first used for the treatment of psoriasis over 50 years ago. High-quality data concerning its efficacy and side effects are sparse. Monotherapy and combination therapy with methotrexate continue to be widely used in dermatology primarily in psoriasis and psoriatic arthritis, and for diseases as varied as sarcoidosis, dermatomyositis, and pyoderma gangrenosum.

Methotrexate is a safe and effective drug for the treatment of psoriasis. Appropriate patient selection and monitoring will significantly decrease the risks of side effects. In patients without risk factors for hepatic fibrosis, liver biopsies may not be indicated or the frequency of liver biopsies may be markedly reduced.

Table I. Monitoring for hapatotoxicity in low-risk patients

No baseline liver biopsy
Monitor liver function tests monthly for the first 6 months and then every 1 to 2 months thereafter.
→ For minor elevations (<2-fold upper limit of normal), repeat in 2 to 4 weeks.
→ For moderate elevations (>2-fold but <3-fold upper limit of normal), closely monitor, repeat in 2 to 4 weeks, and dose reductions as necessary.
→ For persistent elevations in 5 of 9 AST levels over a 12-month period or if there is a decline in serum albumin with normal nutritional status below the normal range in the setting of well-controlled disease, liver biopsy should be performed.
Consider continuing to follow according to above ACR guidelines without biopsy
Or
Consider liver biopsy after 3.5 to 4.0 g total cumulative dosage
Or
Consider switching to another agent or discontinuing therapy after 3.5 to 4.0 g total cumulative dosage.

ACR, American College of Rheumatology; *AST*, serum aspartate aminotransferase.

Table II. Monitoring for hepatotoxicity in high-risk patients

Consider the use of a different systemic agent.
Consider delayed baseline liver biopsy (after 2 to 6 months of therapy to establish medication efficacy and tolerability).
Repeat liver biopsies after approximately 1.0 to 1.5 g of therapy.

Decades after its introduction, methotrexate remains an effective treatment in the therapeutic armamentarium of dermatologists. Despite the introduction of biologics, methotrexate is regularly used alone or in combination with biologics for the treatment of psoriasis, and it remains a valuable treatment option in many other dermatologic diseases. Safe and effective use of methotrexate requires rational patient selection and, subsequently, fastidious and appropriate monitoring. Importantly, the clinician must recognize that patients differ in their inherent risks while taking methotrexate, with issues such as comorbidities and concomitant drug use always in need of consideration. Awareness of the risk factors for hematologic toxicity, primarily decreased renal function, will significantly reduce this side effect. Awareness of the risks for hepatic toxicity is also crucial. Patients without hepatic risk factors may not require routine liver biopsies. Folic acid supplementation is recommended to increase the safety and decrease the potential side effects.

References

1. Kalb RE, Strober B, Weinstein G, et al. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. J Am Acad Dermatol. 2009 May;60(5):824-837
2. Montaudié H, Sbidian E, Paul C, et al. Methotrexate in psoriasis: a systematic review of treatment modalities, incidence, risk factors and monitoring of liver toxicity. J Eur Acad Dermatol Venereol. 2011 Suppl 2:12-18

S1-4

Acitretin in psoriasis treatment

Bong-Seok SHIN

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Acitretin, a synthetic second generation retinoid, is the pharmacologically active metabolite of etretinate, and is the only oral retinoid currently approved by the FDA for treatment of severe psoriasis. Acitretin has replaced etretinate in the late 1980s in most countries because of its more favorable pharmacokinetic profile. Bioavailability is enhanced by food, especially fatty food. Acitretin is 50 times less lipophilic than etretinate and binds to albumin, whereas etretinate binds strongly to plasma lipoprotein. Etretinate is stored in adipose tissue from which it is released slowly, so it has a terminal half-life of up to 120 days in contrast to only 2 days in acitretin. But small amounts of etretinate can be formed in patients receiving acitretin if it is taken simultaneously with alcohol. Therefore the time of compulsory contraception in patients receiving acitretin is extended to 2 years (3years in the US)

Acitretin reduces the proliferative activity and favors the differentiation of epidermal keratinocytes. It inhibits keratinocyte production of VEGF, and reduces intraepidermal migration of neutrophils. Also it inhibits IL-6-driven induction of Th17 cells and promotes the differentiation of T-regulatory cells.

Acitretin monotherapy is recommended in the treatment of psoriasis, hyperkeratotic hand eczema, severe Darier disease, severe congenital ichthyosis, keratoderma, lichen planus, lichen sclerosus, discoid LE, and premalignant and malignant skin lesions.

Starting daily dosages between 10 and 25 mg and stepwise escalation are generally associated with higher clinical efficacy and lower incidence of adverse events and are safe in both the short-term and long-term treatments of psoriasis.

Acitretin as single agent therapy appear to show limited efficacy in psoriasis vulgaris (PV). Acitretin appears to provide better efficacy in pustular psoriasis (palmoplantar and generalized von Zumbusch type) than in PV as a single agent treatment. Therefore, combining retinoids with phototherapy appear to be highly effective in patients with PV. These combinations show an increased efficacy compared to monotherapy with acitretin or UVB or PUVA. An additional advantage is that lower doses of acitretin and lower cumulative doses of UV. Also, the possible combination with acitretin is topical agents, but methotrexate with increased hepatotoxicity and cyclosporin with no evidence of increased efficacy are not recommended.

Clinically significant drug interaction may occur with methotrexate, tetracycline, mini-pill, phenytoin, antidiabetic agents, and corticosteroids that should be avoided or used with caution.

Side effects (teratogenicity, mucocutaneous effects, hepatotoxicity, hyperlipidemia, and skeletal abnormalities) are seen in most patients receiving acitretin. But they usually disappear when the drug is reduced or withdrawn, except for hyperostosis. There is no strong evidence of an increased risk of skeletal abnormalities in psoriasis patients treated with retinoids in recent many published studies.

Acitretin therapy should be monitored with liver enzymes, fasting serum cholesterol and TG, blood sugar level, and radiological investigation and this is the responsibility of the supervising dermatologist.

Recently, acitretin has revisited in the era of biologics. Compared with other systemic therapies, acitretin hardly affects the immune system, which explains the unique position of acitretin. This could be an argument to choose acitretin over the other systemic therapies in specific patient populations (immunocompromised patients, patients prone to infection, patients with a history of high cumulative doses of UV or other patients with an increased risk of skin malignancies, HIV-positive patients with psoriasis, and patients living in areas with endemic occurrence of infections such as tuberculosis).

And, acitretin could be an interesting candidate for combination treatment with biologics, since there will be no additional suppression of the immune system and that means there could well be a synergistic effect without increasing the risk of toxicity. Case reports of successful combination of acitretin with infliximab or adalimumab or efalizumab or etanercept have reported in refractory psoriasis recently.

Session 2

Biologic Agents

S2-1

Biologics: when to start? When to stop? And what to choose?

Yong-Beom CHOE

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The advent of biological therapy has revolutionized psoriasis care. Nonetheless, not all patients require biological therapy. Selection of patients depends on clinical characteristics, previous response to other medical therapy, and comorbid conditions. Availability, reimbursement guidelines, and patient preferences guide the choice of therapy for psoriasis. Currently, the biologics approved by the Korean Food and Drug Administration (KFDA) are divided into 2 classes: tumor necrosis factor (TNF)-α inhibitors, and interleukin (IL)-12/23 inhibitors. TNF-α inhibitors (etanercept, infliximab, adalimumab) has the most extensive clinical trial data, but newly developed ustekinumab appear to have similar or better benefits in plaque psoriasis. Moderate to severe psoriasis (PASI>10, BSA>10) not responding to conventional systemic agents for more than 3 months is an indication for starting biological therapy. Patients who respond to therapy (PASI75 response) at 12~16 weeks could get another 6 month treatment. After this point, every six month reevaluation of confirming drug efficacy prolong the use of biologics. Multiple factors will determine which of the four available biologics should be used first in a particular patient. This includes those related to the drug itself and how they relate to the clinical circumstance, patient preferences (e.g. mode of administration) and access, the latter being determined largely by health insurance guideline and patient`s economic status. In the short term, the monoclonal antibodies (infliximab, adalimumab, ustekinumab) seem to have a quicker onset of action, and are more effective than etanercept, although by 1 year the proportion of patients maintaining a PASI 75 may be comparable. With respect to safety, systematic review of data from short-term studies suggests that the risk of adverse events may be slightly higher with infliximab compared with etanercept and adalimumab while registry data indicate that risks of reactivation of tuberculosis and herpes zoster may be greater with adalimumab and infliximab as compared with etanercept. Ustekinumab is more effective than etanercept in the short term and is probably of comparable efficacy to adalimumab and infliximab, but safety data are very limited. Ustekinumab might therefore be reserved for patients who have failed or cannot use TNF-α antagonists. Patients who have a diminished or loss of response to one biologic agent may respond to switching to another agent. There are only limited efficacy data on use of a second biologic therapy in patients with psoriasis where the first has failed. Mechanisms underlying

primary failure (inadequate response following initiation of treatment) or secondary failure (loss of response over time) are poorly understood, although in the case of TNF-α antagonists, development of antidrug antibodies with consequent reduction in circulating drug levels is well described with both infliximab and adalimumab. Further, while infliximab, adalimumab and etanercept all act to block TNF-α, they are pharmacologically distinct. Thus failure to respond to one TNF-α antagonist may not preclude response to a second. This is supported by findings in a small open-label study and retrospective case cohort review which demonstrate efficacy of adalimumab following etanercept failure. Of note, approximately a third of patients entered into ustekinumab RCTs had been previously treated with biologic therapy (predominantly TNF-α antagonists), and this did not influence therapeutic outcome. Careful consideration should be given to the reasons for loss of response when switching to another biologic. There are insufficient data to make recommendations on when to stop biologic therapy. Therapy should be discontinued when patients fail to achieve an adequate response following treatment initiation or when treatment response is not maintained. Withdrawal of therapy is also indicated due to the following events: (i) a serious adverse event. Serious adverse events which may justify the withdrawal of treatment include malignancy, severe drug-related toxicity, severe infection (ii) pregnancy (iii) elective surgical procedures. A possible complication of an abruptly discontinued therapy is a flare of psoriasis. In this scenario, cyclosporine or methotrexate may be used for a few months to suppress disease and same or another biologic may be used subsequently.

S2-2

Making sure biologics are safe: Recent update

Byung-Soo KIM

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Biologic agents targeting specific immune mediators have emerged as an alternative treatment option for patients with moderate-to-severe plaque psoriasis who are unresponsive to, or intolerant of, non-biologic systemic agents. Because they are processed by the same pathways as naturally occurring proteins in the human body, available data generally assert that approved biologic therapies can be considered safe and well tolerated in the short-term and also for longer periods. However, treatment guidelines still recommend them as second- or third-line therapies due to a relative lack of long-term safety data.

Due to their immunosuppressive activity, some anti-TNFs have been associated with a small increased risk of infection in patients with psoriasis and psoriatic arthritis, and studies of TNF antagonist use in other disease areas have raised concerns over a potential link to cardiovascular side-effects, malignancies, melanomas and neurological defects.

Here, I have reviewed the most recent long-term ($\geq$12 months) clinical data for biological agents (etanercept, infliximab, adalimumab, and ustekinumab) that have been approved for the treatment of adults with moderate-to-severe plaque psoriasis.

Table 1. Overview of reported important side effects of biologics

	Etanercept	Infliximab	Adalimumab	Ustekinumab
Common side effects	• URTI • Injection site reactions • Pruritus	• URTI • Acute infusion reaction • Headache • Pruritus • Urticaria • Transaminases	• URTI • Injection site reactions • Headache	• URTI • Headache
Uncommon but severe side effects	• Severe infections • Opportunistic infections • Reactivation of latent TB or progression of recently acquired TB • New onset or exacerbation of CNS demyelinating disorders • Possible increased risk of malignancy (in particular lymphoma) • Drug-induced lupus • Exacerbation of CHF • Vasculitis • Aplastic anaemia	• Severe infections • Opportunistic infections • Reactivation of latent TB or progression of recently acquired TB • New onset or exacerbation of CNS demyelinating disorders • Possible increased risk of malignancy (in particular lymphoma) • Drug-induced lupus • Exacerbation of CHF • Vasculitis • Pancytopenia	• Severe infections • Opportunistic infections • Reactivation of latent TB or progression of recently acquired TB • New onset or exacerbation of CNS demyelinating disorders • Possible increased risk of malignancy (in particular lymphoma) • Drug-induced lupus • Exacerbation of CHF • Vasculitis	• Severe infections • Possible reactivation of latent TB or progression of recently acquired TB • Possible increased risk of malignancy • Myocardial infarction/Stroke

(1) Common side effects
  · significantly higher than placebo, but mostly well tolerated or manageable
  · patients should be fully informed of the risks of their treatments and believe that they have a significant input into their treatment plan
(2) Major adverse cardiovascular events
  · no significant difference in frequency
  · but still, attention should be paid to these pre-existent cardiovascular risk factors
(3) Malignancies
  · potential risk of melanoma, NMSC and non-skin malignancies in patients treated with biologics has been raised by several case reports
  · close monitoring still required before and during the use of biologics
(4) Hepatitis
  · use of biologics limited in patients with chronic infections such as HBV and HCV
  · guidelines recommend to avoid biologics in chronic hepatitis B carriers because of the risk of reactivation
  · data for hepatitis C less clearcut than hepatitis B
  · may allow for the use of etanercept in patients with hepatitis C, provided patients are appropriately monitored during treatment
(5) Tuberculosis
  · agents that block TNF → ↑ reactivation of latent infections such as tuberculosis
  · TB screening before use of TNF inhibitors and also ustekinumab
  · successfully minimized with adequate prophylaxis
(6) Other serious infections
  · no clear association between biologic treatment and an increased risk of serious infection
  · special attention needed in patients on other immunosuppressive agents or had concomitant factors associated with immunosuppression

References

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S2-3

Reimbursement strategy

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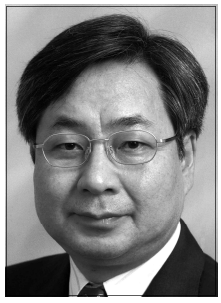
Recently, the introduction of biologics has been making an epoch-marking turning point to the treatment of psoriasis in psoriasis patients. The importance of informations of efficacy-based medication cost, health insurance application criteria, and maintenance as well as discussion on the medication safety have been a growing trend. The insurance coverage for psoriasis patients in Korea entails chronic severe plaque-type psoriasis patients (over 18 years of age) in case it includes all of the followings: plaque-type psoriasis in more than 10% of TBSA; more than 10 points in PASI (Psoriasis Area Severity Index); impossible treatment maintenance out of no- or side-effects even after applying MTX or cyclosporine, or PUVA or UVB phototherapy more than three months each. Biologics available for psoriasis include Stelara® (Ustekimumab), Remicade® (Infliximab), Humira® (Adalimumab), Enbrel® (etanercept), and others, each of which has an individual insurance criteria and it is critically important to be well-informed of the timing and period of application. In addition, current detailed insurance coverage is both clear and vague in the term of use, insurance criteria, irregular visits of psoriasis patients, switching to another medication, and therefore the present author will discuss this matter further.

Session 3

Field Experiences with Biologics

CURRICULUM VITAE



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Research Fellow: Department of Dermatology, University of Michigan, Medical Center, Ann Arbor, Michigan, U.S.A. (September 1994-August 1995)

Teaching Appointments:

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2001-present: Professor, Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Memberships:

- Korean Dermatological Association (KDA) since 1985
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  - Director of Board Certification Examination Committee (2007-2009)
- Korean Society for Investigative Dermatology (KSID) since 1994
  - Director of Scientific & Academic Committee (2003-2005)
  - Secretary General (2005-2007)
- Korean Society for Immuno-Dermatology (KSI) since 2005
  - Secretary General (2005-2012)
  - President (2012-present)
- Korean Society for Psoriasis (KSP) since 1997
  - Director of Scientific & Academic Committee, 1997-2002
  - Secretary General (2002-2007)
  - President (2007-2011)

CURRICULUM VITAE

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Education and Experiences:

1993-1999	Medical Student: Tokai University School of Medicine, Kanagawa, Japan
1999-2001	Resident: Tokai University Hospital, Kanagawa, Japan
2001-2005	Postgraduate Student: Postgraduate School of Internal Medicine (Dermatology), Tokai University School of Medicine, Kanagawa, Japan
2005-2007	Instructor: Department of Dermatology, Tokai University School of Medicine, Kanagawa, Japan
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2011	The research encouragement award of Torii/Teikoku 2011 from the Japanese Society for Psoriasis Research
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CURRICULUM VITAE

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Training

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Licenses

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1986 Medical license: Korean Medical Association (#30469)

Academic Appointments

2009-present Professor and chairman, Department of Dermatology, Sungkyunkwan University School of Medicine, Seoul

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1998-2000 Visiting research fellow (post-Doctorate), Department of Dermatology, University of Michigan, Ann Arbor, MI USA
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Current Positions

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Chairman, Department of Dermatology

Learned Societies

The Korean Dermatological Association
Director for Academic Affairs (2011.10-2013.9)
Director for Insurance & Affairs (2009.10-2011.9)
Member since 1987
The Korean Society for Psoriasis
President (2011-2013)
Secretary General (2007-2011)
Director of Scientific Programs and Affairs (2003.5-2007.4)
Director of Publication (2001.5-2003.4)
Member since 2001
The Korean Society for Investigative Dermatology
Member since 1997
The American Academy of Dermatology, International fellow (since 1998)

Areas of Interest

Psoriasis
Acne & Rosacea
Cosmetic dermatology including laser medicine

CURRICULUM VITAE

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Education:

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Appointment:

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2003-2008	Assistant professor, Department of Dermatology, Seoul National University Bundang Hospital
2004-2008	Assistant Professor, Department of Dermatology, Seoul National University College of Medicine
2007-2008	Visiting scholar, Division of Dermatology, University of California, San Diego
2008-present	Associate professor, Department of Dermatology, Seoul National University College of Medicine, Seoul National University Bundang Hospital

Memberships & Career:

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Specialities:

Acne
Psoriasis
Bioengineering of skin: development of objective diagnostic methods of skin disease
Cosmetic Dermatology