## The 4<sup>th</sup> Psoriasis Symposium for Biologics and Systemic Agents

## PROGRAM

November 22(Sat), 2014 전남대학교병원 명학회관 대강당



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

### 인사말씀

안녕하십니까?

한 해를 마무리하는 시점에 대한건선학회의 연례 CME 프로그램인 전신치료제 및 생물학적제제 심포지움을 개최하게 되어 기쁘게 생각합니다. 본 프로그램은 금년으 로 3년째를 맞이하고 있습니다. 첫해에는 생물학적제제 심포지움으로 개최하였고 작 년부터는 전신치료제 전반을 아우르는 심포지움으로 확장하였습니다. 그것은 생물 학적제제를 사용하기 위해서는 전신치료제와 자외선 치료의 관문을 통과해야 하는 이유도 있고 또한 건선치료의 새로운 패러다임이 '보다 빠르게', '보다 강하게', '보다 오래' 치료하는 것을 요구하게 되면서 전신치료제의 적극적 사용이 필요하게 되었기 때문이기도 합니다.

전신치료제 전반에 대한 강의와 생물학적제제에 대한 강의에 이어 금년에는 프로 그램의 마지막 부분을 증례 기반의 토론 프로그램으로 구성하여 보다 실질적이고 흥 미로운 진행이 가능하도록 하였습니다. 특히 대학은 물론 개원가에서도 흥미로운 증례를 제시하고 토론을 통해 무엇이 가장 최적의 건선 치료 방안인지를 논의하는 자리를 가지려 하오니 건선에 관심있는 개원회원 여러분의 적극적인 참여를 부탁드 립니다.

이번 심포지움을 준비하면서 많은 분들의 도움이 있었습니다. 연자와 좌장으로 참 여하여 주신 호남지역 피부과 회원 및 대한건선학회 여러분께 감사드립니다. 특별히 광주에서 처음 개최되는 대한건선학회의 행사에 후원기관으로 참여하여 주신 전남 대학교 피부과학교실에 깊이 감사드립니다. 아무쪼록 참여하신 여러분 모두 건선에 대한 치료 역량이 배가되는 계기가 되시길 기원합니다.

#### 2014. 11

#### 대한건선학회 회장 이 주 흥

### PROGRAM

#### **Opening Ceremony**

12:30-13:00	Registration
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12:50-13:00 Opening address; Joo-Heung LEE (*President of KSP*) Congratulatory address; Seong Jin KIM (*Chonnam National University*)

1:00- Chaii	2:10 Session 1 Conventional Systemic Agents rs: Jai II YOUN ( <i>National Medical Center</i> ), Kwang-Joong KIM ( <i>Hallym University</i> )	
S1-1.	Changing paradigm of psoriasis treatment	/ 9
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	Jin PARK (Chonbuk National University)	

#### 2:10-3:00 Session 2 Biologic Agents

Chairs: Nack-In KIM (Kyung Hee University), Young-Ho WON (Chonnam National University)

S2-1.	Biologic agents: When to start? When to stop? And what to choose?	/ 19
	Hai-Jin PARK (Inje University)	
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	Byung-Soo KIM (Pusan National University)	
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	Kun PARK (Wongkwang University)	

3:00-3:30 Coffee break

3:30-	5:00 Session 3 Field Experiences of Problematic Cases & Panel Discuss	ion
Chair	rs: Tae-Yoon KIM (Catholic University), Jee-Ho CHOI (Ulsan University)	
S3-1.	Field experiences with Humira <sup>®</sup>	/ 27
	Yong-Beom CHOE (Konkuk University)	
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	Sang-Woong YOUN (Seoul National University)	
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S3-4.	Field experiences : problematic cases in tertiary hospital	/ 30
	Seung Chul LEE (Chonnam National University)	
S3-5.	Field experiences : problematic cases in private clinic	/ 32
	Shamshik SHIN (Gwangju Clear-skin and Laser Clinic)	
	Panel discussion by Yong-Beom CHOE (Konkuk University),	
	Sang-Woong YOUN (Seoul National University), Jae-We CHO (Daegu Gounmi	
	Dermatologic Clinic), Seung Chul LEE (Chonnam National University),	
	Shamshik SHIN (Gwangju Clear-skin and Laser Clinic)	

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.

## Cyclosporin 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 gin-gival 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.

## Methotrexate in psoriasis treatment

**Bong-Seok SHIN** 

Department of Dermatology, Chosun University College of Medicine, Korea

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

- → 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.

No baseline liver biopsy

Monitor liver function tests monthly for the first 6 months and then every 1 to 2 months thereafter.

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

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- 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

#### **Jin PARK**

Department of Dermatology, Chonbuk National University Medical School, Korea

Acitretin, a synthetic retinoid, is the pharmacologically active metabolite of etretinate. Due to its more favorable pharmacokinetic profile (less lipophilic nature and shorter half-life) than etretinate, it has been established as a systemic second-line therapy for severe psoriasis resistant than topical therapy.

Although its mechanism of action on psoriasis is not exactly known, acitretin is thought to modulate proliferation and differentiation of keratinocyte, to a lesser degree, have immunomodulatory and anti-inflammatory activity.

Acitretin can be used in moderate to severe plaque-type psoriasis, psoriatic erythroderma, generalized pustular psoriasis, palmoplantar psoriasis, and nail psoriasis. Efficacy of actitretin depends on the clinical types of psoriasis. Erythrodermic and pustular psoriasis exhibit good response to acitretin, while it is less effective in plaque-type psoriasis. In monotherapy, acitretin obtains a therapeutic response (PASI 75) in about 40 to 50% of patients. Acitretin can be used in combination with topical therapies, systemic conventional drugs, phototherapy and, recently, in combination with biologics to enhance the efficacy and limit the adverse effects. Compared to other available systemic drugs (methotrexate, cyclosporine, and biologics), acitretin is less effective, but it nonetheless achieves significant clearing and can be used in the long-term without risk of immunosuppression.

Acitretin is available in oral capsule formulation (10, 25 mg). Its bioavailability is increased by intake with fatty food. The best results are achieved when the dose is gradually escalated to achieve the maximally effective dose, which varies in each individual. In general, the optimal therapeutic dose in monotherapy appear to be in the range of 25 to 50 mg/d. Higher-doses (50~75 mg/d) are more effective, but the appearance of the adverse effects usually makes it necessary to reduce the dose or discontinue treatment. While it does not have a rapid onset of action, the value of acitretin in patients with psoriasis lies in its potential for very prolonged use as maintenance therapy after clearing has been achieved, or as a component of combination regimens.

Acitretin does not cause significant end-organ damage compared with its therapeutic counterparts such as methotrexate, cyclosporine; however, it is limited by its teratogenicity and therefore considered inappropriate in most female patients of childbearing age. In addition, it is the oral systemic drugs with the fewest side effects in the long-term treatment of psoriasis. Common side effects included mucocutaneous dryness and elevated triglycerides. Side effects are dose limiting, but they can be minimized by appropriate patients selection and careful monitoring. Physical examination, complete blood count, basic metabolic panel, liver function tests, fasting lipid profiles should be monitored regularly.

In a time where biologics have made their entrance in the treatment of psoriasis, acitretin seems to have reached a background position. However, acitretin continue to be a very important treatment option in the treatment of psoriasis even in the ear of biologics. Since it is only systemic drug for psoriasis that is not immunosuppressive, acitretin could be the drug of choice in patients whom the risk of immunosuppression may limit the use of other anti-psoriatic drugs. In addition, acitretin as a systemic treatment is suitable as a combination treatment with immunosuppressive treatments including biologics. The combination of biologics and acitretin has shown synergistic effects without increasing the risk of toxicity. Therefore, acitretin is not outdated in the treatment of psoriasis, but has an important niche.

## Session 2 Biologic Agents

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

Hai-Jin PARK

Department of Dermatology, Ilsan Paik Hospital, Inje University, Korea

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)-a inhibitors, and interleukin (IL)-12/23 inhibitors. TNF-a 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, reevaluation of confirming drug efficacy at every six month 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. 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. In terms of safety, treatment with ustekinumab for up to 5 years was safe and effective. Patients who have a diminished or loss of response to one biologic agent may respond to switching to another agent.

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- $\alpha$  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- $\alpha$ , they are pharmacologically distinct. Thus failure to respond to one TNF- $\alpha$  antagonist may not preclude response to another TNF- $\alpha$  antagonist. 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- $\alpha$  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, and 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.

## Making sure biologics are safe: Recent update

#### Byung-Soo KIM

Department of Dermatology, Pusan National University School of Medicine, Korea

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.

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

i uolo i. Overview of reported important side effects of biologica	Table	1.	Overview	of	reported	important	side	effects	of	biologics
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- (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  $\rightarrow \uparrow$  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

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**S2-3** 

## **Biologics in special forms of psoriasis**

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Usually psoriasis is defined as follows:"A chronic skin disease that is classically characterized by thickened, red areas of skin covered with silvery scales". As well as skin, the joints, nails, and mucous membranes may also be affected by the disease. Palmoplantar psoriasis it is known to affect approximately 5% of all patients with psoriasis, and it is a disabling unusual variant of psoriasis. Patients with palmoplantar psoriasis use heavy topical prescription than those with plaque psoriasis in the literature.

Some children with refractory, widespread, or incapacitating disease may need systemic or biologic agents. Biologic therapies are attractive options for treating psoriasis in children because they offer the convinence of less frequent dosing and less laboratory monitoring than traditional systemic agents.

The literature shows that close to 50% of pregnant psoriasis patients show improvement during pregnancy, but  $10\sim20\%$  become worse throughout pregnancy. Biologic medications are pregnancy category B. Case reports indicate that etanercept and infliximab have been used safely during lactation.

The most common nail bed feature was onycholysis (70%), and subsequently oil drop discolourations, nail bed hyperkeratosis, and splinter hemorrhages. Infliximab for treating nail psoriasis showed 57.2% nail score improvement versus -4.1% for placebo.

## Session 3 Field Experiences of Problematic Cases & Panel Discussion

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