대한건선학회
제7회 생물학적제제
심포지엄

일시: 2018년 12월 1일(토) 13:00~17:40
장소: 중앙대학교병원 4층 송봉홀

대 한 건 선 학 회
The Korean Society for Psoriasis

모시는 글

안녕하십니까?

어느덧 올해를 마무리하는 달을 맞게 되었습니다.
대한건선학회에서 주최하는 제7회 생물학적제제 심포지엄에 여러분을 초대합니다.

건선치료에 생물학적제제가 사용되기 시작한 후 건선치료의 패러다임에 커다란 변화가 생겼습니다. 기존 치료의 효과에 만족하지 못하던 환자나 의료진 모두에게 만족스러운 치료효과를 보이고 이전 치료방법에 비하여 장기적 치료가 가능한 장점도 있어 큰 기대를 받고 있습니다.

그러나 생물학적제제를 사용하는 건선치료에는 여러 가지 유념하고 주의해야 할 점들이 많습니다. 이러한 점들을 잘 이해하고 진료에 임하면 환자에게 더 큰 기쁨을 주는 보람이 있을 것이라 생각합니다.

이번 심포지엄은 선생님들께서 생물학적제제를 사용하실 때 사용 전, 사용 중, 그리고 사후에 필요할 가장 핵심적인 내용들의 최신지견을 망라하여 두 가지 세션으로 구성하였습니다.

첫 번째 세션에서는 현재 사용되고 있는 다양한 생물학적제제 중에서 환자에게 가장 적합할 제제를 선택하는 방법, 치료 적합성과 부작용을 줄이기 위하여 시행하는 스크리닝 방법, 각 생물학적제제들의 효과, 그리고 최근 대두되고 있는 특수 부위의 건선 치료에서 생물학적제제의 사용 등에 관한 내용을 다룰 것입니다.

두 번째 세션에서는 생물학적제제 치료 시 경험하실 수 있는 임상적인 문제들에 관하여 집중적으로 살펴보려고 합니다. 생물학적제제의 paradoxical reaction, safety profile, 그리고 drug survival에 대한 좋은 강연이 준비되어 있습니다.

모쪼록, 이번 심포지엄이 선생님들께서 앞으로 환자들을 위하여 생물학적제제를 보다 안전하고 효과적으로 사용하시는 데 많은 도움이 되시기를 바랍니다.

감사합니다.

2018년 12월 1일

대한건선학회 회장 **송 해 준** 배상

대한건선학회
제7회 생물학적제제 심포지엄

PROGRAM

13:00-13:50 Registration

13:50-14:00 Opening remarks **SONG Hae Jun** *(President of KSP)*

14:00-15:20 Session 1: The Efficacy and Screening Test for the Use of Biologics
Chairs: CHOI Jee-Ho *(Ulsan University)*
KIM Kwang-Joong *(Hallym University)*

S1-1 The overview of psoriasis pathogenesis and its application to the selection of biologics **YOUN Sang-Woong** *(Seoul National University)*····· 6

S1-2 Screening test for the use of biologics **SHIN Bong-Seok** *(Chosun Universitiy)*····· 9

S1-3 The efficacy of biologics **KIM Tae-Gyun** *(Yonsei University)*··· 11

S1-4 Site specific psoriasis and biologics **CHOI Yu Sung** *(Ulsan Universitiy)*··· 14

15:20-15:40 Q&A

15:40-16:00 Coffee break

16:00-17:20 Session 2: Safety and Switching Biologics
Chairs: YOUN Jai Il *(Inshine Dermatologic Clinic)*
KIM Tae Yoon *(Catholic University)*

S2-1 Paradoxical reaction of biologics **PARK Hai-Jin** *(Inje University)*··· 18

S2-2 Safety of biologics **KIM Dong Hyun** *(Cha University)*··· 21

S2-3 Drug survival of biologics **BYUN Ji Yeon** *(Ewha Univertisy)*··· 23

S2-4 Switching biologics **KIM Gunwook** *(Pusan National University)*··· 25

17:20-17:40 Q&A

Session 1:
The Efficacy and Screening Test for the Use of Biologics

CURRICULUM VITAE

윤 상 용

Department of Dermatology
Seoul National University College of Medicine, Korea

Education:

1987-1993	B.S. Seoul National University College of Medicine, Seoul, Korea
1995-1997	M.S. Seoul National University, Seoul, Korea (major: Dermatology)
2001-2003	Ph.D. Seoul National University, Seoul, Korea (major: Dermatology)

Appointment:

1993-1994	Internship, Seoul National University Hospital
1994-1998	Residency, Department of Dermatology, Seoul National University Hospital
1998-2001	Army surgeon, Captain, Republic of Korea Army
2001-2002	Clinical Instructor, Department of Dermatology, Seoul National University Hospital
2002-2002	Instructor, Department of Dermatology, Inje University College of Medicine
2002-2003	Instructor, Department of Dermatology, Seoul National University Hospital
2003-2008	Assistant professor, Seoul National University Bundang Hospital
2004-2008	Assistant Professor Seoul National University College of Medicine
2007-2008	Visiting scholar, Division of Dermatology, University of California, San Diego
2008-2016	Associate professor, Seoul National University College of Medicine
2016-present	Professor (Tenure), Department of Dermatology, Seoul National University College of Medicine
2016-present	Chairman, Department of Dermatology, Seoul National University Bundang Hospital

Memberships & Career:

2010-2011	Director of Publication, Korean Society for Psoriasis
2012-2013	Director of Planning, Korean Society for Psoriasis
2013-2017	Treasurer, Korean Society for Psoriasis
2017-present	Academic director, Korean Society for Psoriasis
2016-present	Academic director, Korean Society for Immunodermatology
2013-2016	Section Editor. British Journal of Dermatology
2014-2015	Section Editor, Annals of Dermatology

The overview of psoriasis pathogenesis and its application to the selection of biologics

Sang Woong Youn

Department of Dermatology, Seoul National University College of Medicine, Seoul National University Bundang Hospital

Psoriasis has been known as a chronic dermatosis associated Th17 cell immune reaction since 2009. The first generation biologics for psoriasis block general immunologic reaction related with TNF-α or T cell itself. The inhibitor for p40 subunit of IL-12/IL-23 was firstly designed for Th17 cell blocking along with Th1 blocking. Recently, the Th17 cell pathogenesis has been elaborated. The role of IL-23 for regulatory T cell has been elucidated, and the importance of immune homeostasis was focused. Also, the role of IL-17 in the pathogenesis of psoriasis was discovered. IL-17 also has important role in the maintenance of intestinal integrity and the protection of fungal infection to skin. In addition, the concept of "upstream" regulator and "downstream" regulator was introduced in the pathogenesis of psoriasis. It is very helpful concept for understanding the role of these cytokines and the effect of blocking them.

Finally, I'll suggest my personal opinion about the selection of the biologics according to the pathomechanism of psoriasis.

CURRICULUM VITAE

신 봉 석

Department of Dermatology,
Chosun University College of Medicine, Korea

경력

2000	조선대학교 의과대학 졸업
2004	피부과 전문의
2010	조선대학교 대학원 박사
2008	조선대학교병원 피부과 교수
2011-2012	일본 나고야시립 대학병원 연수
2012-현재	조선대학교 피부과학교실 과장/주임교수

학회활동

2004	대한피부과학회 정회원
2011-	대한여드름학회 평의원
2016-	대한건선학회 간행이사

Screening test for the use of biologics

Bong-Seok Shin

Department of Dermatology, Chosun University College of Medicine, Korea

Biologics for psoriasis approved in Korea are TNF-α inhibitor (etanercept, infliximab, adalimumab), IL-12/23 P40 inhibitor (ustekinumab), IL-23 P19 inhibitor (guselkumab) and IL-17 inhibitor (secukinumab, ixekizumab). These immunosuppressive therapies, while highly efficacious in the treatment of psoriasis and psoriatic arthritis, may be associated with an increased rate of adverse events (reactivation of chronic infection) in patients receiving some of these therapies. So, screening tests before commencement of treatment is of utmost importance when beginning treatment with the biologics.

But to date, no uniform evidence-based guidelines exist regarding screening and monitoring patients who are undergoing biologic therapy. Despite the lack of evidence to support routine testing, current guidelines by professional organizations (AAD, JDA, EADV, and BAD) recommend routine testing. This lecture is intended to provide a review of the literatures on screening tests for biologic agents in patients with psoriasis and psoriatic arthritis

Recommended screening tests for biologics in psoriasis and psoriatic arthritis

Screening tests
CBC with differential, LFTs, Lipid profile*
TST, IGRA, Chest x-ray
Hepatitis B triple serology, Hepatitis C serology
Serum pregnancy test†
Echocardiogram‡

CBC, complete blood cell count; LFTs, liver function tests; TST, tuberculous skin test; IGRA, interferon-gamma releasing assay; Hepatitis B triple serology, HBsAg, HBsAb, HBcAb; Hepatitis C serology, HCV RNA, HCV Ab. *Applies to anti-TNF agents (etanercept, adalimumab, and infliximab) and especially patients with dyslipidemia. †Applies to female patients with psoriasis. ‡Applies to patients with New York heart Association Class I or II, anti-TNF agents(etanercept, adalimumab, and infliximab)

CURRICULUM VITAE

김 태 균

Department of Dermatology,
Yonsei University College of Medicine

Education:

2007	M.D. Yonsei University College of Medicine, Seoul, Korea
2011	M.S. Yonsei University College of Medicine, Seoul, Korea (Dermatology)
2017	Ph.D. Yonsei University College of Medicine, Seoul, Korea (Immunology)

Career/Academic Appointments:

2007-2008	Intern, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
2008-2012	Resident, Department of Dermatology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
2015-2016	Research Fellow, Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
2017-2018	Clinical Fellow, Department of Dermatology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
2018-present	Clinical Research Assistant Professor, Department of Dermatology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Other Research Experience:

2005-2006	Volunteer student, Hae-Jeong Park Lab, Laboratory of Molecular Neuroimaging Technology, Yonsei University College of Medicine, Seoul, Korea
2011	Visiting physician, Krueger Lab, Laboratory for Investigative Dermatology, The Rockefeller University, New York, NY, USA

2018 Visiting fellow, Haniffa Lab, Institute of Cellular Medicine, Newcastle University, Newcastle, UK

Board Certification:

Medical Doctor (Korea)

Board Certified Dermatologist (Korea)

Referee/Reviewer:

Journal of Investigative Dermatology, Journal of Dermatological Science, PLoS One, International Journal of Molecular Sciences, Allergology International, Yonsei Medical Journal, Annals of Dermatology

The efficacy of biologics

Tae-Gyun Kim

Department of Dermatology, Severance Hospital,
Yonsei University College of Medicine, Seoul, Korea

Psoriasis is a chronic inflammatory skin disorder specifically mediated by IL-23/IL-17 cytokine axis. Emerging clinical evidence have demonstrated that antibody-based biological agents which precisely block each pathogenic cytokines or receptors involved in psoriasis pathogenesis lead to a remarkable therapeutic efficacy in psoriatic patients. The major categories of biologics currently utilized in psoriasis treatment include (1) anti-TNF-α, (2) anti-IL-12/23, (3) anti-IL-23, and (4) anti-IL-17 agents. In the wave of biologic era, the efficacy of psoriasis treatment is primarily assessed by achievement of 'clear' or 'almost clear' of the clinical burden of psoriasis severity defined by meaningful reduction of Psoriasis Area and Severity Index (PASI75 or PASI90 responses) and Physician Global Assessment score (PGA0 or PGA1). Biologic agents in psoriasis treatment have shown significantly higher therapeutic efficacy compared to placebo and conventional systemic agents. One can generally expect about 50~80% chance for achieving PASI75 response within 12~16 weeks after starting biologic treatment in patients with chronic plaque psoriasis. It seems that biologics are generally efficacious for a long-term period of treatment, although drug survivor and potential side effect of each biologic agent should be carefully considered. In this presentation, the clinical efficacy of biologic agents currently available in Korea will be discussed.

CURRICULUM VITAE

최 유 성

Associate Professor, Department of Dermatology, Ulsan University Hospital, College of Medicine, Ulsan University

Education

1996-2001	Konyang University College of Medicine (MD), Daejeon, Korea
2010	Korea University Graduate school of Medicine (Ph.D), Seoul, Korea

Training and Fellowship Appointments

2002-2003	Internship, National Medical Center, Seoul, Korea
2003-2007	Dermatology residency, National Medical Center, Seoul, Korea
2007-2008	Fellowship, Seoul National University Hospital, Seoul, Korea

Faculty Appointment

2008-2011	Clinical Assistant Professor, Ulsan University Hospital, Ulsan, Korea
2012-2017	Assistant Professor, Ulsan University Hospital, Ulsan, Korea
2017-	Associate Professor, Ulsan University Hospital, Ulsan, Korea

Memberships

2007-	Korean Dermatological Association
2015-	Director of Planning, Korea Society for Acne Research
2017-	Director of Promotion, Korean Society for Psoriasis
2017-	Director of Publication, Korean Society of Skin Cancer

Site specific psoriasis and biologics

Yu Sung Choi

Department of Dermatology, Ulsan University Hospital
College of Medicine, Ulsan University

1. Scalp psoriasis

The scalp is affected in up to 80% of patients with psoriasis and is the first site of involvement in approximately 25% of cases. Management of scalp psoriasis remains a challenge in regard to both clinical response and patient satisfaction. This is in part attributed to the relative inaccessibility of the scalp to topical treatments, and the inability of patients to reduce scratching and harsh shampooing. Adherence to treatment is another obstacle, as many patients are dissatisfied with the cosmetic properties, treatment regimen, side-effect profile, and inadequate clinical efficacy.

2. Nail psoriasis

Nail psoriasis is a clinical diagnosis made in the context of existing psoriatic skin lesions. It is commonly seen in patients with psoriatic arthritis involving the distal interphalangeal joints. Treatment of nail psoriasis is challenging. First, the anatomical properties of the nail unit pose a barrier to active drug delivery. Next, the naturally slow growth rate of the nail plate often delays noticeable clinical responses by months. Moreover, no standard treatment guidelines exist. All of these issues invariably contribute to poor patient satisfaction and treatment compliance.

3. Palmoplantar psoriasis

Palmoplantar psoriasis (PPP) is a variant of psoriasis vulgaris and can be subdivided into two categories:

1) hyperkeratotic palmoplantar psoriasis (hPPP) : characterized by erythema and keratotic plaques, with or without fissures, affecting the palms and soles with extension to the wrists and margins of the plantar surfaces.
2) palmoplantar pustular psoriasis (PPPP) : known as palmoplantar pustulosis, characterized by the presence of sub-corneal pustules localized to the palms and soles frequently in association with erythema and scale.

4. Inverse/intertriginous and genital psoriasis

Inverse psoriasis involves the axillae, retroauricular region, abdominal, inguinal, gluteal, and inframammary folds, perineum, and perianal area. Given the moist environment of these regions, lesions tend to exhibit less induration and scale.

Session 2:
Safety and Switching Biologics

CURRICULUM VITAE

박 혜 진

Department of Dermatology, Ilsan Paik Hospital,
College of Medicine, Inje University

Education and Training

1994	Ewha Womans University College of Medicine, Seoul, Korea (M.D.)
1998	Ewha Womans University Graduate School of Medicine, Seoul, Korea (M.S.)
2010	Ewha Womans University Graduate School of Medicine, Seoul, Korea (Ph.D.)
1995-1999	Internship and Residency, Ewha Womans University Hospital, Seoul, Korea
2013	International Fellow, Department of Dermatopathology, Hospital of the University of the Pennsylvania, PA, USA

Appointment

2004	Instructor, Department of Dermatology, Ilsanpaik Hospital Inje University College of Medicine
2006	Assistant Professor, Department of Dermatology, Ilsanpaik Hospital Inje University College of Medicine
2011-present	Associate Professor, Department of Dermatology, Ilsanpaik Hospital Inje University College of Medicine
2004-2011, 2014.9-present	Director, Department of Dermatology, Ilsanpaik Hospital Inje University College of Medicine

Professional Societies

Korean Dermatological Association
Member of Korean Society of Dermatopathology
Member of Korean Society for Psoriasis
Member of Korean Society of Nail Research

International Member of American Academy of Dermatology
Member of International Society of Dermatopathology
Member of American Academy of Dermatopathology
International Board of Dermatopathology

Major Committee Assignment

Director of Academy, Korean Society of Dermatopathology
Director of Planning, Korean Society for Psoriasis
Director of Planning, Korean Society of Nail Research

Paradoxical reactions of biologics

Hai-Jin Park

Department of Dermatology, Ilsan Paik Hospital, Inje University

Paradoxical adverse reaction to biologics is a de novo or worsening immune-mediated underlying disease that would normally respond to the biologic agent that causes them. Although the overall safety profile of biologics is acceptable, some patients develop adverse reactions. Most paradoxical reactions have been reported in association with anti-TNF-α therapy. However, cases associated with more recently introduced biologic agents are increasing.

The pathogenesis of TNF antagonist induced psoriasiform lesions involves a disruption in cytokine balance by TNF blockade, allowing unopposed interferon-α (INF-α) production by plasmacytoid dendritic cells (PDCs) in genetically predisposed individuals. Psoriatic skin lesions develop when skin PDCs produce INF-α, stimulating the activation and amplification of pathogenic T-cells, which then generate TNF-α. Also, anti-TNF-α agents could favor granulomatous reactions through imbalance between Th17and Treg cells.

It is likely that paradoxical flare of psoriasis occurs in patients with an underlying genetic predisposition. The polymorphisms in the genes implicated in cytokine production, such as IL-23R, and CTLA-4 or FBXL19 are detected.

Other paradoxical reactions such as paradoxical joint inflammation, inflammatory bowel disease and hidradenitis suppurativa are also reported.

Paradoxical reactions often resolve on discontinuation of the drug or switching to another biologic agent, but occasionally additional therapies are required.

CURRICULUM VITAE

김 동 현

차의과학대학 분당차병원 피부과학교실

약력

1992-1998	연세대학교 학사
1999-2000	신촌세브란스병원 인턴
2000-2003	분당차병원 피부과 레지던트
2003-2004	중앙경찰학교 의무관 (공중보건의사)
2004-2006	국립경찰병원 피부과 과장 (공중보건의사)
2006-2007	신촌세브란스병원 피부과 임상강사
2007-2008	분당차병원 피부과학교실 전임강사
2009-2014	분당차병원 피부과학교실 조교수
2014-	분당차병원 피부과학교실 부교수
2012-2014	캐나다 Laval 대학 LOEX(Laboratoire d'Organogénèse EXpérimental) 연수

학회활동

대한건선학회
대한백반증학회
대한피부병리학회
대한색소학회

Safety of biologics

Dong Hyun Kim

CHA Bundang Medical Center, CHA University

최근 류마티스관절염, 건선, 크론병 등 면역매개 염증성 질환 치료에 생물학적제제가 우수한 효과를 보이고 있다. 생물학적제제마다 각각의 작용기전, 임상효과, 부작용 등이 있으며, 판상건선 치료 목적으로 국내에서 허가된 생물학적제제는 아래와 같다(FDA 허가연도).

1) TNF-alpha 억제제: etanercept (2004), infliximab (2006), adalimumab (2008)
2) IL-12/IL-23p40 단클론항체: ustekinumab (2009)
3) IL-17 단클론항체: secukinumab (2015), ixekizumab (2016)
4) IL-23p19 단클론항체: guselkumab (2017)

기존의 건선 치료는 사용 기간에 비례해서 나타나는 부작용 문제로 한 가지 치료법을 일정 기간 사용 후 부작용이 나타나기 전에 다른 치료법으로 주기적으로 바꾸는 순환치료법을 사용해야 했다. 하지만 기존 치료에 반응하지 않거나 부작용으로 인해 기존 치료를 할 수 없는 중증 건선 환자에서 생물학적제제는 뛰어난 효과와 함께 비교적 높은 안전성을 보여 장기간 사용하는 경우가 많다. 하지만 부작용들이 단기간 또는 1-2년 미만의 임상 자료로 분석되기 때문에 장기간 사용에 대한 안전성에 대해서는 아직 많이 알려져 있지 않다.

Methotrexate와 cyclosporine 처방 시 간기능, 신기능, 혈압상승 등 부작용 발생에 대해 환자에게 설명하고 정기적인 검사를 하는 것에 반해, 생물학적제제는 감염, 특히 잠복결핵, B형간염, 악성종양 등의 부작용에 대한 감시와 치료법에 대한 가이드라인이 아직 부족한 상황이다. 현재 PASI 75 반응이 유지되면 생물학적제제를 장기간 사용을 할 수 있기 때문에 발생 가능한 부작용에 대해 충분히 이해하고 적절하게 대처해야 할 필요성이 높아지고 있다.

모든 생물학적제제 공통으로 나타나거나 일부 생물학적제제에서 특이하게 나타나는 부작용에 대해 최근 논문을 중심으로 요약하였다.

1) 중증 감염 (폐렴, 대상포진 등)
2) 결핵
3) B형간염
4) 악성종양 (림프종, 고형암)
5) 심장질환
6) 칸디다 감염
7) 염증성장질환

CURRICULUM VITAE

변 지 연

Assistant Professor, Department of Dermatology,
Ewha Womans University

Education

1997-2004	M.D., Ewha Womans University College of Medicine
2006-2008	M.S., Ewha Womans University Grauduate School
2009-2012	Ph. D., Ewha Womans University Grauduate School

Training and Fellowship Appointments

2005-2009	Resident, Department of Dermatology, Ewha Womans University Mokdong Hospital
2009-2010	Fellow, Department of Dermatology, Samsung Medical Center
2010-2011	Fellow, Department of Dermatology, Ewha Womans University Mokdong Hospital

Faculty Appointment

2012-2014	Clinical Assistant Professor, Department of Dermatology, Ewha Womans University Mokdong Hospital
2014-	Assistant Professor, Department of Dermatology, Ewha Womans University Mokdong Hospital

Memberships

Korean Dermatological Association
Korean Society for Investigative Dermatology
Korean Society for Immunodermatology
Korean Society for Psoriasis

Drug survival of biologics

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Moderate-to-severe psoriasis frequently requires long-term systemic therapy. Drug survival, also known as 'drug retention' or 'drug persistence', is the rate and duration of adherence to systemic agents, which represent the long-term effectiveness, safety and treatment satisfaction in the real world.

In general, maintenance rates are higher for biologics than for traditional systemic agents. Among biologic agents, the probability of survival was highest for ustekinumab, followed by adalimumab, etanercept, and infliximab. Ustekinumab was associated with the highest drug survival in all and biologic-naïve subjects. The highest value of ustekinumab may be due to the great short-term effectiveness, lower levels of immunogenicity, a lower adverse event rate, and a more patient-friendly administration procedure. Etanercept was most commonly discontinued for loss of efficacy and infliximab was most frequently associated with discontinuation for adverse effects. Switching from one biologic to another is associated with an impairment of drug survival. In one study, higher body mass index (BMI) was a predictor for discontinuation due to ineffectiveness for etanercept and ustekinumab and that female sex was a predictor for discontinuation due to side effects for adalimumab, etanercept and ustekinumab. Because secukinumab and ixekizumab were recently introduced on the market, not enough real-life data for drug survival are available.

Drug survival can be used as a useful reference for choosing a biologic for treating psoriasis in practice. In addition, several courses of different biologics would be required for the long-term disease control because drug survival rates decrease over time.

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Switching biologic agents in the treatment of psoriasis

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■ There is limited information on biological treatment optimization and transitioning in routine clinical practice.

■ Treatment failure

1) Primary failure: not achieved at least a PASI 75
2) Secondary failure: after obtaining a PASI 75 has lost efficacy

■ Washout period

1) If the reason for switching biologics is for lack of efficacy, it would be appropriate to administer the next dose of the new biologics at the next dosing interval.
2) On the other hand, if a biologic agent discontinued because of safety reasons (adverse event), the theoretical washout would be prudent.
3) ex) washout period of ustekinumab
: 2-4 weeks (treatment failure), 8-12 weeks (theoretical washout)

■ Control of flaring patient

1) With more efficacious biologics available (i.e. secukinumab and ixekizumab): revealing 40% of patients obtaining PASI 100 at week 12
2) The high loading doses with these two agents assists in the rapid onset of efficacy which would be helpful in the control of a flaring patient.

■ Switching biologic agents in the treatment of psoriasis

1) For a primary nonresponse, the recommendation is to switch to a different class.
2) For a secondary nonresponse, switching can occur within the same class or to a different mechanism of actions.
3) ustekinumab → secukinumab, secukinumab → ixekizumab, ustekinumab → guselkumab
: reported to be an effective and safe therapeutic options.

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