

Journal Watch

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A systematic review and meta-analysis of the prevalence and phenotype of adult-onset atopic dermatitis

Lee HH, Patel KR, Singam V, Rastogi S, Silverberg JL. *J Am Acad Dermatol* 2019;80:1526-32.

Atopic dermatitis (AD) has been traditionally considered as a paediatric disease. Previous studies have suggested that 50% of childhood AD cases begin in the first year of life and 85% began in the first five years of life. However, recent cohort studies of adult patients showed high rates of AD beginning at an older age. This systematic review and meta-analysis studied the proportion of adult-onset AD and its clinical characteristics.

Cross-sectional or cohort studies that contained analyses on the age of AD onset after 10 years of age and a sample size of at least 100 AD patients were included in the analysis. There were 25 observational studies included. There were six (24%) studies with prospective cohorts, 4 (16%) studied retrospective cohorts, and 15 (60%) with cross-sectional cohorts. There were 10 out of 25 studies were conducted in Asia.

Adult-onset AD was defined as onset of AD after 16 years of age. The pooled proportion of adult-onset AD was 26.1% (95% confidence interval

[CI] 16.5%-37.2%). There was no difference between women (29.2%, 95% CI 15.0%-45.9%) and men (29.9%, 95% CI 14.0%-48.8%) had adult-onset disease. Concerning the area of habitation and age of onset of AD, one study reported a higher proportion (87.5% vs 82.3%) in contrast to another study found a lower proportion (70.6% vs 83.4%) of AD patients living in urban areas had adult-onset versus child-onset disease. Conjunctivitis, facial dermatitis, cheilitis, eyelid dermatitis, pruritus after sweating, xeroderma or xerosis, hand and foot dermatitis, Dennie-Morgan folds, and nipple dermatitis, were phenotypic features that were consistently present in child-onset AD. A history of allergic rhinitis was more common in child-onset AD than adult-onset AD in some individual studies, although the frequency of asthma between the two groups. A personal or family history of food or medication allergies and adverse reactions was more common in patients with child-onset AD than adult-onset AD.

In conclusion, onset of AD occurred in adulthood in one in four adults with AD. There was an equal male:female ratio in the proportions of adult-onset disease across different regions. Adult-onset AD was associated with distinct clinical characteristics. Further prospective studies on adult-onset AD are required.

Potential of narrow-band ultraviolet B to induce sustained durable complete remission off-therapy in patients with stage I mycosis fungoides

Pavlotsky F, Dawood M, Barzilai A.

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Narrow-band ultraviolet B (NBUVB) is considered to be treatment of choice for stage I mycosis fungoides (MF). In a previous study of stage I MF patients treated by NBUVB, 84% of stage IA and 78% of stage IB patients achieved complete response (CR). Despite the high initial CR rate, there is limited data on long term disease-free survival (DFS) after phototherapy. This retrospective cohort study aimed to examine the DFS rate at ≥ 5 years in stage I MF patients after CR induction with NBUVB.

A total of 117 stage I MF patients started NBUVB thrice weekly during 2003-2010. Ninety-three patients (80%) achieved a CR. They were followed-up for period of five years or more. Of these, 56 (60%) cases had no recurrence as of March 2017 and the mortality rate was zero. There were 22 clinically clear-cut recurrences and recurrence was confirmed by biopsy in another 15 cases.

In the univariate analysis, a younger age (patients < 50 years 124 months vs 91 months for patients ≥ 50 years), early stage of MF (stage IA: 131 months vs stage IB 87.6 months), lower total cumulative dose (total dose $< 40\text{J}/\text{cm}^2$: 123 months vs 91 months for total dose $\geq 40\text{J}/\text{cm}^2$) and fewer sessions (118 months vs 93 months for total of < 50 and ≥ 50 sessions respectively) of NBUVB were associated with a longer DFS. In the multivariate analysis, when stratified by stage and age (106-142 months) the DFS was significantly shorter for stage IB patients aged ≥ 50 years (72 months) than for the other three patient groups. There was no difference in the recurrence rate in terms of sex and skin phototype.

The main limitation of this study was the retrospective nature. There may have been recall error about topical steroid usage and intentional tanning. Moreover, the morphology of the lesions (i.e. patches or plaques or both) could not be assessed.

In conclusion, 80% CR and 60% were disease-free for ≥ 5 years stage I MF patients could be achieved by NBUVB. Younger patients with stage IA have a higher chance of achieving this.

Benefit-risk profile of tofacitinib in patients with moderate-to-severe chronic plaque psoriasis: pooled analysis across six clinical trials

Strober BE, Gottlieb AB, Van de Kerkhof PCM, Puig L, Bachelez H, Chouela E, et al.

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Biological therapy in general, has better response rate than traditional systemic therapy in treatment of moderate-to-severe chronic plaque psoriasis. Current biological therapies for psoriasis are all administered parenterally. On the other hand, tofacitinib is a Janus kinase inhibitor which is administered orally and is therefore more advantageous in terms of convenience. This study investigated the benefit-risk profile of tofacitinib in treatment of moderate-to-severe chronic plaque psoriasis. In the study 745, 741 and 373 patients received oral Tofacitinib 5 mg and 10 mg twice (bd) daily and placebo over 52 weeks respectively. Psoriasis Area and Severity Index (PASI) 90 was achieved in patients receiving tofacitinib 5 mg or 10 mg bd than placebo at week 16 (PASI 90: 22.2%, 39.1% and 3% respectively; $P < 0.001$). The response was maintained in more than 65% of tofacitinib group patients with PASI 90 at week 16 at week 52. A greater number of patients receiving tofacitinib 5 mg or 10 mg bd achieved Higher Nail Psoriasis Severity Index (NAPSI) 75 than placebo at week 16 (16.9%, 28.1% and 6.8%, respectively; $P < 0.001$). More patients in the tofacitinib group had a lower Dermatology Life

Quality Index (DLQI) (score ≤ 1) than placebo group at week 16: tofacitinib 5 mg bd (27.7%), tofacitinib 10 mg bd (44.3%), placebo (5.3%). More patients in tofacitinib group had a lower Itch Severity Item (ISI) (score ≤ 1) than placebo group at week 16: tofacitinib 5 mg bd (43%), tofacitinib 10 mg bd (60.9%), placebo (10.5%) and a higher number of patients in tofacitinib group had a lower Hospital Anxiety and Depression Scale (HADS) score (score < 8) than placebo group at week 16: tofacitinib 5 mg bd (52.4%), tofacitinib 10 mg bd (61.6%), placebo (35.8%).

Tofacitinib 5 mg bd and 10 mg bd were generally well-tolerated and except for a higher rate of herpes zoster (mild or moderate), side effects were generally comparable with other biological agent or systemic psoriasis treatment. The most frequently observed serious infections were pneumonia (0.4%), herpes zoster (0.2%) and appendicitis (0.2%). No renal toxicity, hepatic toxicity or bone marrow suppression was reported.

In conclusion, oral tofacitinib 10 mg bd is more effective than tofacitinib 5 mg bd and both have a favourable benefit-risk profile for treatment of moderate-to-severe chronic plaque psoriasis.

Efficacy and safety of brodalumab in patients with psoriasis who had inadequate responses to ustekinumab: subgroup analysis of two randomized phase III trial

Langley RG, Armstrong AW, Lebwohl MG, Blauvelt A, Hsu S, Tyring S, et al.

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Brodalumab is a human anti-interleukin 17 receptor A monoclonal antibody that block IL-17 cytokines. It is a new biological agent approved for treatment of moderate or severe psoriasis. This study compared the therapeutic response of brodalumab with another biologic treatment: ustekinumab.

Patients aged 18 to 75 years were randomised to receiving brodalumab 210 mg or 140 mg every 2 weeks (subcutaneous injection on day 1 and weeks 1, 2, 4, 6, 8, 10), ustekinumab or placebo in induction phase (first 12 weeks). At week 12, maintenance therapy with brodalumab 210 mg every 2 weeks, brodalumab 140 mg every 2 weeks, brodalumab 140 mg every 4 weeks or brodalumab 140 mg every 8 weeks was given. In ustekinumab group, ustekinumab dose was given according to body weight (45 mg if ≤ 100 kg, 90 mg if > 100 kg) every 4 weeks initially and then every 12 weeks. Patients treated with either brodalumab or ustekinumab with inadequate response at week 16 received brodalumab treatment 210 mg every 2 weeks.

The efficacy of psoriasis treatment (PASI 75, PASI 90 and PASI 100) at week 52 for following two groups were compared: inadequate response to ustekinumab at week 16 but with brodalumab rescue treatment group vs. inadequate responses to ustekinumab at week 16 with continuation of ustekinumab group. At week 52, inadequate ustekinumab response with brodalumab rescue group had higher response rates than inadequate ustekinumab response with continuation of ustekinumab group: PASI $\geq 75\%$ (72.6% vs 61.7%), PASI $\geq 90\%$ (58.1% vs 25.5%), PASI 100% (36.3% vs 5.4%). Side effects were similar between two groups: headache, fatigue, upper respiratory tract infection, nasopharyngitis, and arthralgia. In conclusion, brodalumab was effective in treating moderate-to-severe psoriasis patients who did not achieve an adequate response with ustekinumab.

University students' behaviours towards accessing sexual health information and treatment

Gray BJ, Jones AT, Couzens Z, Tracey Sagar T, Jones D.

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In general, young people under the age of 25 years are at a relatively greater risk of getting sexually transmitted diseases, including university students. A cross sectional study was conducted in UK through a territory wide online survey between 2012 and 2015. The majority of the responding students were heterosexual and were aged 24 years or younger. The study aimed to explore where these students collected information on sexual health and where they received treatment. Results of the survey showed that most of the participants received sexual health information and advice from the Internet (49.1%) and general practitioners (GP)/family doctors (38.9%). Some obtained information from local sexual health (SH) clinics. Apparently males appeared less likely to seek sexual information than females. Young and older students in contrast to teenagers, were more likely to seek advice from their GP/family doctors and local SH clinics (young students: (AOR 1.47; CI: 1.23-1.75; older students: AOR 2.18; CI: 1.70-2.81) and local SH clinics (young students: AOR 1.49; CI: 1.23-1.81; older students: AOR 2.20; CI: 1.70-2.90). The most favoured facilities for treatment were local SH clinics (24.9%) and GP/family doctors (20.2%). Students who had their first sexual encounter before 16 years old were more likely to seek sexual health treatment at a either local SH clinic (AOR 2.8; CI: 2.31-3.39) or GP/family doctor (AOR 1.73; CI: 1.21-1.83) Males tended to receive treatment less frequently than females (AOR 1.37; CI: 1.17–1.60) and were also less inclined to ask for advice (AOR 2.74; CI: 2.24-3.35). The study also found that bisexual males were more likely to have required sexual health treatment than heterosexual males (AOR 0.65; CI: 0.5-0.86).

Diagnostic determination of Norovirus infection as one of the major causes of infectious diarrhea in HIV patients using a multiplex polymerase chain reaction assay

Yang S, Li M, Cheng J, Wan G, Zhou Y, Jia H, et al.

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In human immunodeficiency virus (HIV)-infected or acquired immunodeficiency syndrome (AIDS) patients, infective diarrhoea is not uncommon. It is known that Norovirus is the commonest contagious pathogen causing gastroenteritis. A 1-year study was conducted in Beijing to look for the occurrence of Norovirus causing diarrhoea in HIV-infected patients. A multiplex polymerase chain reaction was utilised as a diagnostic tool to detect Norovirus in stool specimens. Samples were obtained from 81 HIV-infected patients with diarrhoea (55 with known pathogens, 26 without identifiable pathogen). Norovirus was detected in 13 (50%) stool specimens from 26 patients having diarrhoea of no identifiable aetiology among which one specimen showed both Norovirus and enterotoxigenic *Escherichia coli* infection. For the remaining 55 patients with identifiable pathogens, 9 (16.4%) of them were also detected positive for Norovirus infection. The study concluded that Norovirus infection is an important cause of diarrhoea among HIV-infected patients.

Association of Disease Recurrence With Survival Outcomes in Patients With Cutaneous Squamous Cell Carcinoma of the Head and Neck Treated With Multimodality Therapy

Sun L, Chin RI, Gastman B, Thorstad W, Yom SS, Reddy CA, et al.

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The aim of this study was to report survival outcomes in patients with cutaneous squamous cell cancer of the head and neck (cSCC-HN) after disease recurrence after surgery and postoperative

radiotherapy and to investigate the association of immune status with disease-related outcomes. This was a multi-institutional study of 205 patients who had received surgical resection and postoperative radiotherapy for primary or recurrent cSCC-HN between January 1, 1995, and December 31, 2014. Patients with any disease recurrence (local, regional, and/or distant failure) were included. Patients were categorised as immunosuppressed if they were diagnosed with of chronic haematological malignancy, HIV or AIDS, or had been treated with post-transplant immunosuppressive therapy for 6 months or more before diagnosis.

There were 205 patients in the study cohort, of which there was disease recurrence after surgery and post-operative radiotherapy in 72 patients (63 men, 9 women; (median age, 71 years; range, 43-91 years) and 32 patients (44.4%) were immunocompetent and 40 patients (55.6%) were immunosuppressed. The most common manifestation of treatment failure was locoregional recurrence in both groups (immunosuppressed, 31 [77.5%]; and immunocompetent, 21[65.6%]).

The one-year overall survival after any recurrence was 43.2% (95% CI, 30.9%-55.4%) with a median survival time of 8.4 months. Compared to those who were amenable to surgical salvage, patients who were not amenable to surgical salvage had significantly poorer median cumulative incidence of survival (4.7 months; 95% CI: 3.7-7.0 months vs 26.1 months; 95% CI: 6.6 months to not reached; P=0.01).

The authors concluded that regardless of immune status, patients with recurrence of cutaneous squamous cell carcinoma of the head and neck after definitive treatment with surgery and postoperative radiotherapy have poor survival rates.

Association of Ustekinumab vs TNF Inhibitor Therapy With Risk of Atrial Fibrillation and Cardiovascular Events in Patients With Psoriasis or Psoriatic Arthritis

Lee MP, Desai RJ, Jin Y, Brill G, Ogdie A, Kim SC. *JAMA Dermatol*. Published online, March 27, 2019. doi:10.1001/jamadermatol.2019.0001.

This study evaluated the risk of atrial fibrillation (AF) and major adverse cardiovascular events (MACE) associated with use of ustekinumab vs tumour necrosis factor inhibitors (TNFi) in patients with psoriasis or psoriatic arthritis. This cohort study included data from a nationwide sample of 78162 commercially insured patients in two US commercial insurance databases, Optum Clinformatics and Truven MarketScan (Truven Health Analytics) from September 25, 2009, through September 30, 2015. Patients included had psoriasis or psoriatic arthritis, and initiated ustekinumab or a TNFi therapy.

The study included a total of 60028 patients with psoriasis or psoriatic arthritis (9071 ustekinumab initiators and 50957 TNFi initiators) in the analyses. The mean age was 46 +/- 13 years (Optum) and 47 +/- 13 years (MarketScan) and 49.1% of cases were male. The overall crude incidence rates (IRs) (per 1000 person-years) for AF were 5.0 (95% CI: 3.8-6.5) in ustekinumab initiators and 4.7 (95% CI: 4.2-5.2) in TNFi initiators. In addition, for incident AF, the combined adjusted hazard ratio for ustekinumab initiators was 1.08 (95% CI, 0.76-1.54) as compared to TNFi initiators.

For MACE, the overall crude IRs were 6.2 (95% CI, 4.9-7.8) in ustekinumab initiators and 6.1 (95% CI, 5.5-6.7) in TNFi initiators. In patients treated with ustekinumab. Compared to TNFi initiators, in ustekinumab initiators, the combined adjusted hazard ratio for MACE was 1.10 (95% CI, 0.80-1.52).

The authors concluded that, in patients with psoriasis or psoriatic arthritis, the risks of AF and MACE associated after starting ustekinumab vs TNF inhibitors were similar.