New Agents in Treatment of Psoriatic Arthritis

Essay

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Physical Medicine, Rheumatology and Rehabilitation

By

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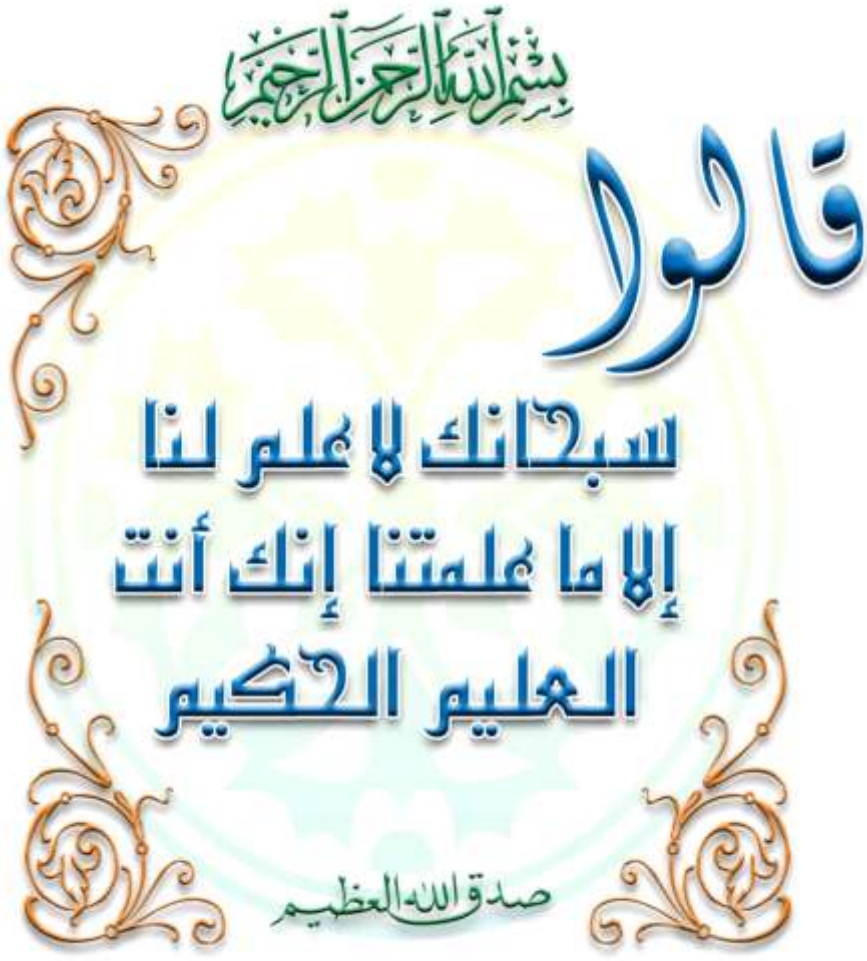

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Marwa Mahmoud Ahmed Abdellatif

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List of Abbreviations

Abbr.	Full-term
ADCC	**:** Antibody-dependent cell cytotoxicity.
anti-TNF	**:** Antitumor necrosis factor.
AP-1	**:** Activator protein 1.
APC	**:** Antigen-presenting cells.
AZA	**:** Azathioprine.
bDMARD	**:** Biological DMARD.
C/EBP	**:** CCAAT-enhancer-binding protein.
CARD15	**:** Caspase recruitment domain-containing protein 15.
CASPAR	**:** Classification Criteria of Psoriatic Arthritis.
CBC	**:** Complete blood count.
CIA	**:** Collagen-induced arthritis.
Cmax	**:** Maximum serum concentration.
CQ	**:** Chloroquine.
CREB	**:** CAMP-responsive element binding protein.
CRP	**:** C-Reactive Protein.
csDMARDs	**:** Conventional synthetic DMARD.
CT	**:** Computed tomography.
CTLA-4	**:** Cytotoxic T-Lymphocyte Antigen 4.
DCs	**:** Dendritic cells.
DIP	**:** Distal interphalangeal.
DKK-1	**:** Dickkopf-1.
DMARDs	**:** Disease Modifying Anti Rheumatic Drugs.
EDEM	**:** ER degradation-enhancing α-mannosidase-like protein.
EOW	**:** Every other week.
ER	**:** Endoplasmic Reticulum.
ERAD	**:** Endoplasmic reticulum-associated degradation.
ESR	**:** Erythrocyte Sedimentation Rate.
EULAR	**:** The European League against Rheumatism.
FDA	**:** Food and Drug Administration.

Grp78 : Glucose Regulate Protein 78.
GST : Gold sodium thiomalate.
H_2O_2 : Hydrogen peroxide.
HCQ : Hydroxychloroquine.
HIV : Human Immunodeficiency Virus.
HLA : Human leukocyte antigens.
IBD : Inflammatory bowel disease.
IFNγ : Interferon gamma.
IgG1 : Immunoglobulin G_1.
IL : Interleukin.
ISR : Integrated Stress Response.
IκBα : Inhibitory subunit of nuclear factor kappa B alpha.
JaK : Janus kinases.
JAK : Janus Kinase Inhibitor.
KIR : Killer-cell immunoglobulin like receptor.
KIR3DL2 : Killer cell immunoglobulin-like receptor 3DL2.
LCE : Late Cornified Envelope.
LFA-3 : Lymphocyte function–associated antigen 3.
mAb : Monoclonal antibody.
MCP : Metacarpophalangeal.
MDA : Minimal disease activity.
MHC : Major histocompatibility complex.
MRI : Magnetic Resonance Imaging.
MTX : Methotrexate.
NF-κB : Nuclear factor of kappa-light-chain-enhancer of activated B cells.
NK : Natural Killer cells.
NKG : Natural Killer Group.
NSAIDs : Non-steroidal anti-inflammatory drugs.
OMERACT : Outcome Measures in Rheumatology Clinical Trials.
OPG : Osteoprotegerin.
PDE : Phosphodiesterase.
PDE4 : Phosphodiesterase Four Inhibitor.
PDI : Protein disulfide isomerase.

PIP : Proximal interphalangeal.
PS : Psoriasis.
PsA : Psoriatic arthritis.
PSORS1 : Psoriasis susceptibility gene 1.
RA : Rheumatoid Arthritis.
RANKL : Receptor activator of nuclear factor-κB.
RANKL : Receptor activator of nuclear factor kappa-B ligand.
ROS : Reactive oxygen species.
rs : The ringelschwantz.
SEFIR : Similar expression to fibroblast growth factor genes and IL-17R.
SH2 : Src homology 2 domain.
SLE : Systemic lupus erythematosus.
SOM : Somatostatin.
SOMR : Somatostatin receptor.
SP : Substance P.
SpA : Spondyloarthropathy.
STAT : Signal transducer and activator of transcription.
TB : Tuberculosis.
TBK1 : TANK binding kinase 1.
TCR : T-cell receptor.
Th : T helper.
TICOPA : Tight Control of PsA.
TNAIP3 : TNF α-induced protein 3.
TNF : Tumor Necrosis Factor.
TNFAIPI : TNFAIP3-interacting protein 1.
TNFi : Tumour necrosis factor inhibitor.
TRAF : Tumor necrosis factor receptor-associated factor.
TRAP : T-cell receptor activating protein.
tsDMARD : Targeted synthetic DMARD.
UGGT : UDP-glucose: glycoprotein glucosyltransferase.
UPR : Unfolded Protein Response.
US : Ultrasonic.
λ_S : The recurrence risk.

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ABSTRACT

Background: psoriatic arthritis is a long term inflammatory arthritis. Psoriatic arthritis is leading to bone erosion, joint destruction and associated with nail diseases, dactylitis, enthesitis, sponnylitis and uveitis.

Aim of this study was to review the new lines of treatment for psoriatic arthritis with or without skin affection. **Treatment**, the underlying process in psoriatic arthritis is inflammation; so, treatments are directed to reduce and control inflammation. Although no clear correlation exists between joint inflammation and the skin in every patient, the skin and joint aspects of the disease often must be treated simultaneously. However, only certain therapies are effective for psoriasis and psoriatic arthritis. Systemic agents, can be used for both skin and joint manifestations, it includes methotrexate and ciclosporin. For the biologic agents, the tumour necrosis factor inhibitors such as adalimumab, etanercept, infliximab, golimumab and certolizumab are effective. Ustekinumab is a recently agent belonging to the group of anti-IL-12p40 antibodies and has been shown to be efficacious. Newer drugs in the treatment which have shown efficacy for both psoriasis and psoriatic arthritis consist of the anti-IL-17 agent, secukinumab, and a phosphodiesterase-4 inhibitor, apremilast. As well as the oral JaK inhibitor, tofacitinib, have very limited but promising data.

Keywords: psoriasis, psoriatic arthritis, anti- TNF, anti-IL-17, small molecules inhibitors.

Introduction

Psoriasis is a chronic immune-mediated inflammatory disorder characterized by uncontrolled proliferation of keratinocytes, activated dendritic cells, release of pro-inflammatory cytokines, and recruitment of T-cells to the skin ***(Harrington et al., 2017)***.

Psoriasis is a multisystemic disease which affects 2–3 % of the population. It usually presents with skin and joint manifestations. The proportion of patients of psoriasis who develops psoriatic arthritis (PsA) ranges from 6 to 42 % in different studies ***(Choi et al., 2017)***.

Psoriasis usually presents 8–10 years before PsA, although some patients present with PsA sine psoriasis. Both of them are immune-mediated chronic inflammatory diseases with a similar pathogenesis, concurrent treatment should be undertaken to minimize side effects and financial burden of medications ***(Springate et al., 2017)***.

The peak of PsA incidence occurs between 30 and 50 years of age. It is characterized clinically by edema, pain, tenderness, and stiffness of the joints, ligaments and tendons (dactylitis and enthesitis) ***(Ajesh and Vinod, 2017)***.

Both the innate and adaptive immune systems are involved in the pathogenesis of psoriasis and PsA. T cell