# Biolgoical Agents in Autoimmune Rheumatic Diseases

*Essay*

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in Physical Medicine, Rheumatology & Rehabilitation

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بِسْمِ اللّهِ الرّحمَنِ الرّحيمِ

[...رَبِّ أَوزِعنِي أَن أَشكُرَ نِعمَتَكَ
الّتِي أَنْعَمْتَ عَلَيَّ وعَلى والِدَيَّ
وأَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ
وأَدْخِلْنِي بِرَحْمَتِكَ
فِي عِبَادِكَ الصَّالِحِينَ]

صدق الله العظيم

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Abeer Abd El-Fattah Sobhey

# Contents

# List of Abbreviations

| Abbrev. | Full term |
|---|---|
| **ABA** | : Abatacept |
| **ACCP** | : Anti-cyclic citrullinated peptide |
| **ACE** | : Angiotensine converting enzyme |
| **ACR** | : American College of Rheumatology |
| **ADA** | : Adalimumab |
| **ADCC** | : Antibody dependent cytotoxicity |
| **AEs** | : Adverse effects |
| **AICAR** | : Amino imidazole carboxamide ribonucleotide |
| **AIM** | : Abatacept in inadequate responders to MTX |
| **ALT** | : Alanine transaminase |
| **ANA** | : Anakinra |
| **ANA** | : Antinuclear antibody test |
| **ANCA** | : Anti-neutrophil cytoplasmic antibodies |
| **AOSD** | : Adult-onset Still disease |
| **APC** | : Antigen presenting cell |
| **APR** | : Acute phase reactant |
| **APRIL** | : A proliferation-induced ligand |
| **APS** | : Antiphospholipid syndrome |
| **AS** | : Ankylosing spondylitis |
| **ASAS** | : Assessment of Ankylosing Spondylitis International society |
| **AST** | : Aspartate transaminase |
| **ATTAIN** | : Abatacept trial in treatment of anti-TNF inadequate responders |

# List of Abbreviations *(Cont.)*

| Abbrev. | Full term |
|---|---|
| **ATTEST** | : Abatacept Trial for Tolerability, Efficacy and Safety in Treating RA |
| **AZA** | : Azathioprine |
| **B0** | : Naïve B cell |
| **BAFF** | : B-cell activating factor |
| **BASDAI** | : Bath Ankylosing Spondylitis Disease Activity Index |
| **B-CLL** | : B-cell chronic lymphocytic leukemia |
| **BCMA** | : B cell maturation |
| **BCR** | : B-cell antigen receptor |
| **bDMARDs** | : Biologic DMARDs |
| **BLyS** | : B-lymphocyte stimulator |
| **BSA** | : Body surface area |
| **CAPS** | : Cryopyrin-associated periodic syndrome |
| **CB** | : Cannabinoid |
| **CCR** | : Chemokine receptor |
| **CDC** | : Center for disease control and prevention |
| **CDC** | : Compelement dependent cytotoxicity |
| **CK** | : Creatine kinase |
| **COPD** | : Congestive contstructive pulmonary diseases |
| **COX**-2 | : Cyclooxygenase-2 |
| **CPK** | : Creatine phosphokinase |
| **CRP** | : C-reactive protein |
| **csDMARDS** | : Conventional synthetic DMARDs |
| **CSF** | : Cerebrospinal fluid |
| **CSF** | : Colony stimulating factor |

# List of Abbreviations *(Cont.)*

| Abbrev. | Full term |
|---|---|
| **CTLA** | : Cytotoxic T-lymphocyte antigen |
| **CTZ** | : certolizumab |
| **CYC** | : Cyclophosphamide |
| **DAS** | : Disease activity Score |
| **DC** | : Dendritic cell |
| **DHODH** | : Dihydroorotate dehydrogenase |
| **DM** | : Dermatomyositis |
| **DMAR** | : Dsdisease modifying anti-rheumatic drugs |
| **dsDNA** | : Double stranded DNA |
| **EAE** | : Experimental autoimmune encephalitis |
| **EBV** | : Epestine-Barr virus |
| **ELISA** | : Enzyme-linked immune-sorbent assay |
| **EMA** | : European Medical Agency |
| **EMG** | : Electromyography |
| **ER** | : Endoplasmic reticulum |
| **ESR** | : Erythrocyte sedimentation rate |
| **ETN** | : Etanercept |
| **EULAR** | : European League Against Rheumatism |
| **Fc** | : Fragment-crystallizable protein |
| **FCAS** | : Familial cold auto-inflammatory syndrome |
| **FDA** | : Food and Drug Administration |
| **GC** | : Germinal cell |
| **GC** | : Glucocorticoids |
| **GI** | : Gastrointestinal |
| **GOL** | : Golimumab |

# List of Abbreviations *(Cont.)*

| Abbrev. | Full term |
|---|---|
| **gp** | : Glycoprotein |
| **HCQ** | : Hydroxychloroquine |
| **HCV** | : Hepatitis C |
| **hIBM** | : Hereditary IBM |
| **HIV** | : Human immunodeficiency virus |
| **HLA** | : Human leukocyte antigen |
| **HTLV** | : Human T-cell leukemia virus |
| **IBD** | : Inflammatory bowel disease |
| **IBM** | : Inclusion body myositis |
| **ICAM** | : Intracellular adhesion molecule |
| **IFN** | : Interferon |
| **IFX** | : Infliximab |
| **Ig** | : Immunoglobulin |
| **IL** | : Interleukin |
| **ITP** | : Idiopathic thrombocytopenic purpra |
| **IVIG** | : Intravenous immunoglobulin |
| **JAK-STAT** | : Janus kinase-signal transducer and activator of transcription |
| **JRA** | : Juvenile rheumatoid arthritis |
| **LDA** | : Low disease activity score |
| **LDH** | : Lactate dehydrogenase |
| **LFA** | : Leucocyte function associated antigen |
| **LFTs** | : Liver function tests |
| **LN** | : Lupus nephritis |
| **LTA** | : Long term extension |

# List of Abbreviations *(Cont.)*

| Abbrev. | Full term |
|---|---|
| **MAAs** | : Myositis associated antibodies |
| **MAC** | : Membrane attack complex |
| **MCP** | : Metacarpophalanges/phalngeal |
| **MHC** | : Major histocompatibility complex |
| **MI** | : Myocardial infarction |
| **MME** | : Mycophenolate mofetil |
| **MMP** | : Matrix metalloproteinases |
| **MS** | : Multiple sclerosis |
| **MSAs** | : Myositis specific antibodies |
| **MTP** | : Metatarsophalanges/phalangeal |
| **MTX** | : Methotrexate |
| **MWS** | : Muckle-Wells syndrome |
| **NF- κB** | : Nuclear factor kappa-light-chain-enhancer of activated B cells |
| **NICE** | : National institute for health and clinical excellence |
| **NK** | : Natural killer cells |
| **NSAIDs** | : Non steroid anti-inflammatory drugs |
| **PABA** | : Para-aminobenzoic acid |
| **P** | : Placebo |
| **PBO** | : Placebo |
| **pDC** | : Plasmacytoid dendritic cell |
| **PDGF** | : Platelet derived growth factor |
| **PEG** | : Polyethylene glycol |
| **PGE** | : Prostaglandin |

# List of Abbreviations *(Cont.)*

| Abbrev. | Full term |
|---|---|
| **PIP** | : Proximal interphalanges/phalangeal |
| **PM** | : Polymyositis |
| **PML** | : Progressive multifocal leuko-encephalopathy |
| **PMN** | : Polymorph nuclear |
| **PsA** | : Psoriatic arthritis |
| **PSL** | : Prednisolone |
| **pSS** | : Primary Sjögren's syndrome |
| **PUVA** | : Pulse Ultraviolet A |
| **QOL** | : Quality of life |
| **RA** | : Rheumatoid arthritis |
| **RacP** | : Receptor accessory protein |
| **RANK** | : Receptor activator nuclear factor |
| **RANKL** | : Receptor activator nuclear factor ligand |
| **RCTs** | : Randomized clinical trials |
| **RF** | : Rheumatoid factor |
| **RNA** | : Ribonuclear protein |
| **ROR** | : Retioned-related orphan receptor |
| **RTX** | : Rituximab |
| **SAA** | : Serum amyloid A |
| **SARD** | : Systemic autoimmune rheumatic diseases |
| **SDF** | : Stromal derived factor |
| **SEs** | : Side effects |
| **sIBM** | : Sporadic IBM |
| **s-IBM** | : Sporadic inclusion body myositis |
| **SJIA** | : Systemic juvenile idiopathic arthritis |

# List of Abbreviations *(Cont.)*

| Abbrev. | Full term |
|---|---|
| **SjS** | : Sjögren's syndrome |
| **SLE** | : Systemic lupus |
| **SPF** | : Sun protection factor |
| **SSA** | : Anti-Sjögren's syndrome-related antigen |
| **SSc** | : Systemic sclerosis |
| **TACI** | : Transmembrane activator |
| **TB** | : Tuberculosis |
| **TCR** | : T-cell receptor |
| **TCZ** | : Tocilizumab |
| **TGF** | : Transforming growth factor |
| **Th** | : T-helper |
| **Th0** | : Naïve T cell |
| **TLR** | : Toll-like receptors |
| **TNF** | : Tumor necrosis factor |
| **TNF**-R | : Tumor necrosis factor-receptor |
| **Treg** | : Regulatory T cell |
| **TTT** | : Treatment |
| **TYK** | : Tyrosine kinase |
| **UC** | : Ulcerative colitis |
| **URI** | : Ureteric infection |
| **URTI** | : Upper respiratory tract infection |
| **UTI** | : Urinary tract infection |
| **WG** | : Wegener'S granulomatosis |

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# Introduction

Autoimmune diseases are a group of disorders where the immune system malfunctions and attacks tissues. One aspect of these diseases is the formation of antibodies that are directed to self-antigens (autoantibodies). These diseases can be divided into two general groups: organ specific, where the autoantibodies attack a specific organ, such as diabetes mellitus type I, Hashimoto's thyroiditis, Addison's disease, vitiligo, haematologic autoimmune haemolytic anemia and idiopathic thrompocytopenic purpra ***(Davidson and Diamond, 2006).*** Non-organ specific (systemic), where the antibodies attack multiple organ systems. Systemic autoimmune rheumatic diseases (SARD) are a group of systemic autoimmune diseases, which include rheumatoid arthritis (RA), Sjogren's disease, systemic lupus erythromatosus (SLE), polymyositis and dermatomyositis, systemic sclerosis and ankylosing spondylitis. RA is the most prevalent disease in this group ***(Willcocks et al., 2010).***

The goal of treatment (TTT) in systemic autoimmune diseases is to minimize symptoms such as pain, swelling and to prevent bony deformity, improve quality of life (QOL), slowdown progress of the disease and other systems affection. This can often be achieved using the primary TTT, which are 2 main classes, analgesics such as non-steroidal anti-inflammatory