

RA

Indicators:

- c-reactive protein. test in venous blood, measure conc in plasma. If elevated: active infection/inflammation
- Rheumatoid factor: auto-antibody against self proteins Fc part of IgG (not to be confused with anti-drug-antibodies)
- Citrullination: Arginine converted to citrulline, affects the joints. Triggers immune response
- anti-CCP is antibodies against these citrullinated peptides
- Sänka (white blood cell count)
- anti-nuclear auto-antibodies
- + clinical factors (swelling etc)

test: ELISA, nephelometry (for immunocomplexes)

Treatments:

Lefunomide: antireumatisk, hämmar ett enzym (dihydroorotatdehydrogenas) → B-celler, T-celler, NK-celler
→ hindrar celler (ffa. lymfocyter) från att dela sig = mindre inflammation

Hydroxychloroquine: anti-malaria
- pH increased in lysosomes => less lysis in APCs => less antigen presentation on MHC II
- Inhibits stimulation of Toll Like Receptors which are important for activation of innate immune cells by recognition of bacteria/viral specific motifs

Next course of treatment:

- annan verkningsmekanism
- biverkningar: adverse effects

→ "reumatics": the symptoms

Biologics

Adalimumab:

- hämmar TNF- α som är ett transmembranprotein som uttrycks på ytan och är pro-inflammatoriskt
- binds specifikt, block binding to P55 and P75 receptors
- fully human antibody, not chimeric this can affect how well the body tolerates the drug. ADA = AntiDrug Antibodies - developed against parts of drug that is recognized as foreign.

Combinatory treatment:

TNF α : ett cytokin som frisätts vid inflammation,
+ Metotrexate: Folic acid antagonist = behövs för DNA-syntes = suppressed replication = less immune cells
This decreases the risk of ADA as well => can use biodrugs for longer

PCP

Immunförsvaret försvagas av adalimumab, vilket gör Mary känslig för opportunistisk infektion av bakterie och parasitinfektion, fungi.

Common for AIDS patients

Anmäl behandlande läkare?

Insurance issues
(USA case)

Vad göra?

Anses vara vanlig biverkning.
Rapportera ändå? - ja, pga föremål för utökad övervakning

Monitorera läkemedel efter klinisk prövning (post-marketing surveillance)

Hålla koll på patienter som tar immunosuppressiva:
- tell patient to be aware of risk and symptoms
- screena innan behandling för latent (TBC, HepB mm)
- profylaktisk behandling mot
- ta bort metotrexate? I så fall ersätt med annan som dämpar humoral svaret för att få bättre effekt av TNF α -hämmare

Alternative biological drugs:

Inhibit interleukins:

- tocilizumab, anti-IL6 receptor = prevents the binding of IL6 to it's receptor
- IL-1 blocker

Rituximab: anti-CD20, binds B-cells, makes NK-cells kill the B-cells

T-cell suppressor by binding CD80 and CD86 on APC => decrease activation of T-cells

anti-CD4 on T-cells

Design strategies:

- fab-region affects binding to target
- effect selectivity: target one or more variants
- Fc-region: different effector functions depending on which Fc-receptor it binds
- "Isotype": Byt konstanta delen
Nästan alltid subklasser av IgG
- Mouse/chimeric/fully human
- Antibody-drug conjugates
- Bispecific antibodies: two targets in one protien

