Rapporteur Analysis –
Afternoon session (23-11-24) Hall B

2023 ACR ILD Guidelines - What is new?

- 70 percent may have ILD in SSc, only 25-40 percent have “clinically significant” disease.
- HRCT chest - mandatory for diagnosis
- Standard HRCTprotocol radiation - 3-5 msv.
- Screening - 3-6 months in 1st year - with PFT . Ambulatory desaturation should be done once a year.
- First line treatment is always immunosuppressant, needs to be continued life long.
- No role of anti fibrotic upfront. In case of progression - change immunosuppressant + add antifibrotic
- Moderate to high steroids are strongly recommended against scleroderma ILD, 30 percent are RNA polymerase 3 positive - high risk for renal crisis.
- Nintedinib more beneficial in UIP OR Fibrotic NSIP
- Advised to add PCP prophylaxis if using steroid > 20mg or dual immunosuppressant

Autoimmunity and fibromyalgia - At Crossroads

- SSRIs don’t work well in fibromyalgia
- Glycine, an inhibitory pain neurotransmitter, is downregulated in Fibromyalgia.
- Kcc2 is the key to chronic pain.
- Sex dimorphism in pain- pain in females in T cell mediated whereas in males, microglia and TLR 4 mediate pain. Estrogen upregulates nociceptor trpv1 and Nav1.7(Nav1.7 SCN9A - is a gatekeeper of pain - key voltage gated Na channel in hypothalamus)
- Autoantibodies in FM - Few studies have proposed the association - voltage gated potassium channels, antibodies to extracellular domains of LGI -1, CASPR 2,Plexin - D1, anti FGF 23 antibodies

Impact of Ro52 in clinical phenotypes of CTDs

- Isolated anti-Ro52 positivity - primary sjogren (SjS) , myositis , SLE, scleroderma , even without autoimmune disease .

    1. SjS - glandular involvement, higher ILD
    2. SLE - Less data, more sicca and cytopenia
    3. Scleroderma - ILD, limited scleroderma, PAH, joint involvement

4. Myositis- anti Jo Ab,Anti MDA5 antibody association,
5. Juvenile myositis - severe lung disease.

- Pathogenic role or epitope spreading ? Yet to be established .

Sjögren's Syndrome Symposium

- Novel agents in SjS target different pathways - B cell pathway, costimulation blockade, pDC -IFN pathway.

- B cell depleter - Ibelimumab, anti BAFF, sequential use with rituximab results in better treatment outcome with decrease in total and memory B cells.

- Ianalumab, an anti BAFF receptor, has dual action - BAFF block with ADCC .(NEPTUNUS study).

- Costimulation blockade - Anti CD40 antibody iscalimab (TWINSS study) , anti CD40 ligand(dazodalibep) ,anti CD80/86 - abatacept

- Target IFN pathway - Jak stat pathway(tofacitinib, filgotinib)

- Primary Sjogren Syndrome (SjS) with ACA have Raynaud's phenomenon and sclerodactyly while Anti Ro has high extraglandular manifestations .

- Lanalumab anti BAFF-R showed improvement in a dose dependent manner in Sjogren syndrome patients in a RCT.
- T cells including both CD4 and CD8 drive pathogenesis and have been shown in labial biopsies. Domain 5 of E-Cadherin is critical for binding by aEb7 integrin on CD8 T cells.

- CXCL13, CD48, TNF R-2 in addition to BAFF is significantly correlated with ESSDAI.

- Multiomics analysis showed significant association of interferons and ADAMs substrates to SjS , implying that these cells are induced by various stimuli like viruses & CD8 T Cells.

- Atlas of human antibodies is very essential as often the diseases are polyclonal.

- Building a comprehensive database of autoantibodies associated with autoimmune disease- helps in multiple ways.
- Auto antigens expression is not as tissue specific as we think
- Interactive network models help us to understand how different diseases are connected by shared antibodies.
- Autoimmune diseases vary in magnitude and diversity of autoantibodies profile, by leveraging network analysis algorithms, we can predict such variations or associations.

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