LONG TERM DRUG-FREE CLINICAL-REMISSION IN PATIENTS WITH RA ON cDMARDs

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NEW DELHI INDRAPRASTHA APOLLO HOSPITALS

- Followed prospectively over 2 years
- Single center, northern India, single investigator

INTRODUCTION

- "Developments in the clinical understanding of rheumatoid arthritis"

Ten clinical facts ("principals of management")-

- Composite disease indices
- LDA and CR- tight control-T2T
- MTX etc and Biologics

- *Review article-Smolen JS and Aletaha D. http://arthritis-research.com/content/11/1/204. 2009*

INTRODUCTION

- 2015 ACR Guidelines For RA

- *Singh JA, Saag KG et al Arthritis care and research-DOI 10.1002/acr.22783*

INTRODUCTION

- COMPLETE REMISSION ACHIEVED-WHAT NEXT?

1) One year duration (also 6 months!!) in CR for rheumatoid patients- reduction of doses

2) 2015- ART-no synovitis yet MR positive

3) PRIZE (NEJM2014) and RETRO (ART-2014)- some continued doses of DMARDs better than no treatment at all and

INTRODUCTION

- "Predictors and Persistence of New Onset Clinical Remission in Rheumatoid Arthritis Patients"

-CORRONA

-8% (2105individuals) point prevalence of CR

-CHF, Prednisolone use

-about 50% of pts with One year CR managed to remain in CR over the next year

-cDMARDs only 2% point prevalence CR, 11% for Anti-TNF+cDMARD

- Navarro-Milalan IY, Chen L et al. *Semin Arthritis Rheum.* 2013 October;43(2):137-143

INTRODUCTION

- "Sustained rheumatoid arthiritis remission is uncommon in clinical practice"

-"BRASS"- pts not in remission at baseline- atleast 2 yrs followup

-Survival analysis performed on 871 RA subjects

-394 in CR point prevalence-revealed less than 50% CR rates remained in remission at 1 year

-Median duration of remission 1year

IN CLINICAL PRACTICE ONLY A MINORITY OF PATIENTS ARE IN SUSTAINED REMISSION

- Prince FHM, Bykerk VP et al *Arthritis Research & Therapy* 2012; 14:R68

Objective-To evaluate prospectively the durability of Complete Remission (CR) in RA patients (CR of at-least 6 months) when all their cDMARDs have been discontinued

Not a DBCT or intervention

Data only- no ethical issues

Standard of care followed for treatment OPD care RA

Methods

- 2012-2015- pts in CR over a follow-up of six months at-least
- OPD visits at 1, 2 and 3 months and followed-up over two years to determine the length of CR (durability of CR)
- Definition remission – “less or equal to one active joint”
- cDMARDs (cDMARD treated RA pts only- no Biologic treated patient)

RESULTS

- Demographics- 567 RA patients in the 18-67 age range (females 92%)
- 27 RA patients (42-58 age) achieved CR of at-least 6months while on follow-up on treatment with cDMARDS
- Consent verbal and written for drug discontinuation (also standard practice in India)

Results -Continued

- cDMARDs used were- Methotrexate(MTX)+ Leflunomide (24) and MTX+HCQ (3);induction phase all were also on low dose steroids
- Doses varied all through the treatment

RESULTS-DURABILITY OF CR

- 6 patients-18months
- 6 patients-21 months
- 2 patients- 15 months
- 3 patients –continue in remission >2 yrs
- 10 pts – relapsed between 6-12 months

Discussion

- AVERT-Evaluating drug free remission with Abatacept in early rheumatoid arthritis: results from the phase 3b, multicenter, randomized, active- controlled AVERT study of 24 months, with a12 month double blind treatment period.

Emery P, Burmester GR et al. Ann Rheum. Dis;74:19-26

DISCUSSION

- MTX especially multiple actions as follows-
  Nucleotide pathway

  AICAR and ADENOSINE PATHWAY

  IL-6, IL-1, TNF and “immune reconstitution”

Clinical ramifications: for combination MTX with other biologics, bispecific biologics and MTX with

Discussion

- Discontinuation of infliximab after attaining low disease activity in patients with rheumatoid –RRR (remission induction by Remicade in RA) study

- *Tanaka Y, Takeuchi T et al. Ann Rheum. Dis 2010;69:1286-1291.*

CONCLUSION

- COMBINATIONS OF DMARDs MTX, LEFL, LOW-DOSE STEROIDS MORE LIKELY TO ACHIEVE CR (MULTIPLE CELLULAR AND CYTOKINE TARGETS) and particularly potent!
- EVEN cDMARD TREATED PATIENTS MAY BE SUBJECTED TO DE-ESCALATION AND STOPPING OF ALL TREATMENTS (MINORITY ONLY)