BIOLOGIC THERAPY : A NEW OPTION FOR TREATMENT JUVENILE IDIOPATHIC ARTHRITIS

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INTRODUCTION

- JIA is the most common chronic rheumatic inflammatory disease of childhood. If not successfully treated, it can lead to severe disability.
- Juvenile idiopathic arthritis (JIA) is a collective term for arthritides that are diagnosed before the age of 16 years.Diagnosis requires disease duration of at least 6 weeks and the exclusion of other causes of arthritis.

CLASSIFICATION

Classification of JIA

Based on symptoms presented during 1st 6 months of ds -

1. Systemic onset JIA (10-15%)
2. Oligo-articular JIA (50 %)
    a. Persistent oligo-articular JIA
    b. Extended oligo-articular JIA
3. Polyarticular JIA (RF negative) (15-20%)
4. Polyarticular JIA (RF positive) (≤5%)
5. Psoriatic arthritis (5-10%)
6. Enthesitis related arthritis (5-10%)
7. Undifferentiated arthritis (10-15%)

Principles of management

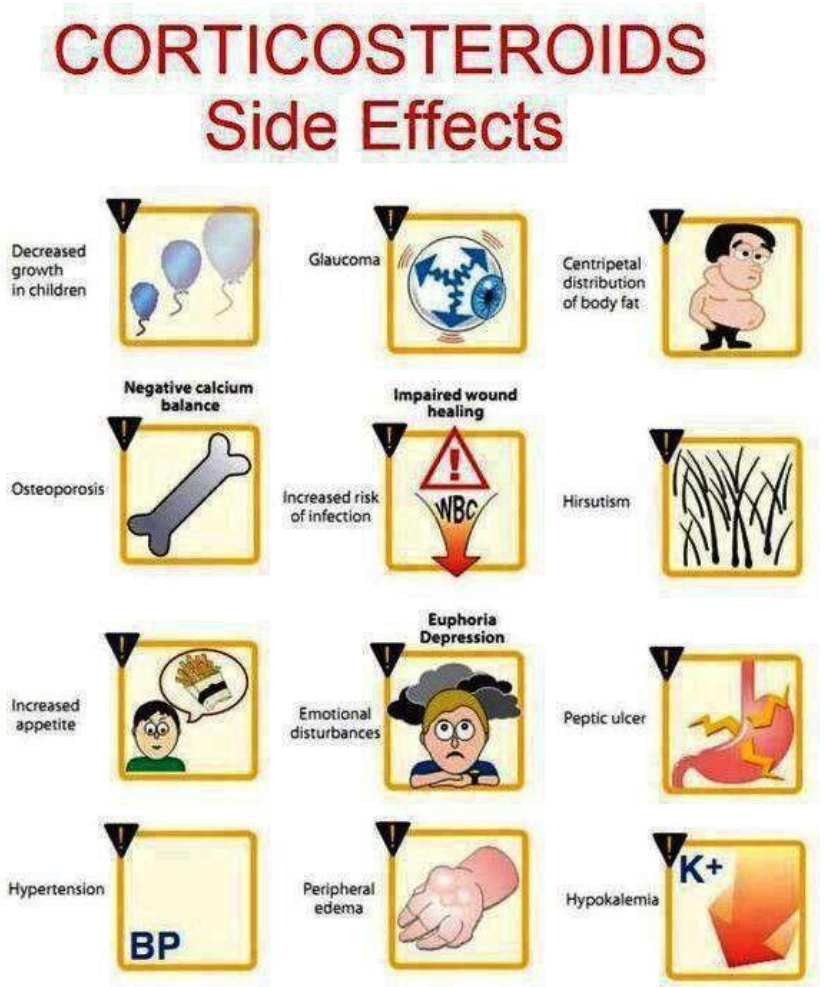
- Two major trends :
  - “Window of opportunity”: literature suggests that treating inflammatory disease early and aggressively to ‘switch off’ the immune process leads to better longterm.
  - “Treat to target” : This concept has arisen in the era of biological agents, when treatment goals have become more ambitious and patient outcomes vastly improved.

Principles of management (cont…)

- **The first treatment :**
  - Anti-inflammatory drugs : NSAIDs, Steroids
  - Classical DMARDs : Methotrexate, Sulfasalazine, Hydroxycloroquin
- **But :**
  - 30% patients reponse to NSAIDs.
  - 50% patients nonresponse to Methotrexate (*)

(*) Silverman E, Mouy R, Spiegel L *et al.* Leflunomide in juvenile rheumatoid arthritis (JRA) investigator group. Leflunomide or methotrexate for juvenile rheumatoid arthritis. *N. Engl. J. Med.* 352, 1655–1666 (2005).

Side effects of Corticosteroids



Biologic therapies

- Biologic therapies : are treatments which utilise either monocloral antibodies or soluble cytokine receptors, to specifically target individual components of the immune system(*)
- Biologics should not be used unless a patient is intolerant to, or has failed optimised treatment with MTX; this is defined as 15mg/m2 given subcutaneously once-weekly for at least 3 months; higher doses have no evidence to suggest increased efficacy (**)

(*) Ungar W, et al. Sem Arth Rheum 2013;42:597-618. The use of biologic response modifiers in polyarticular course juvenile idiopathic arthriits: a systematic review.
(**)Dueckers G, Guellac N, Arbogast M, Dannecker G, Foeldvari I, Frosch M, et al. Evidence and consensus based treatment guidelines 2010 for juvenile idiopathic arthritis by the German Society of Paediatric Rheumatology. Klin Padiatr. 2011;223:386–94. doi:10.1055/s-0031-1287837.

History of biologic agents

- Biologic agents: “bench to bedside” medicine.
- Biologic agents are approved by FDA for treatment JIA
  - Anti TNF-α : Etanercept (1999), Adalimumab (2008)
  - Anti IL-1 : Anakinra
  - Anti IL-6 : Tocilizumab (2011)
  - Rituximab
  - Abatacept

Comparison of treatment response, remission rate and drug adherence in polyarticular juvenile idiopathic arthritis patients treated with etanercept, adalimumab or tocilizumab

Honeff et al, Arthritis & Therapy (2016) 18:272

Background : Treatment response, remission rates and compliance in patients with polyarticular juvenile idiopathic arthritis (polyJIA) treated with adalimumab, etanercept, or tocilizumab were analyzed in clinical practice.

Methods:

- Treatment response, remission rates and compliance in patients with polyarticular juvenile idiopathic arthritis (polyJIA) treated with adalimumab, etanercept, or tocilizumab were analyzed in clinical practice.
- 236 patients started adalimumab, 419 etanercept and 74 tocilizumab, with differences in baseline patient characteristics

Improvement in patients using etanercept, adalimumab or tocilizumab according to the ACRpedi30

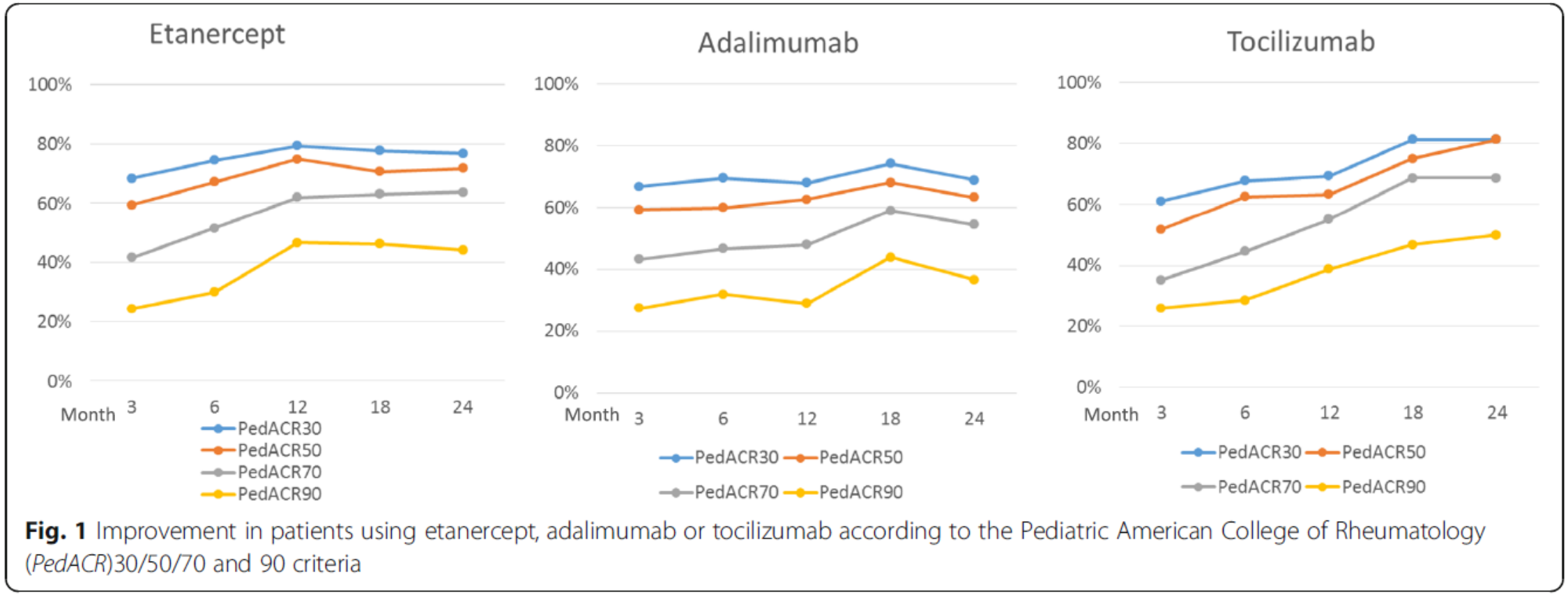


Fig. 1 Improvement in patients using etanercept, adalimumab or tocilizumab according to the Pediatric American College of Rheumatology (*PedACR*)30/50/70 and 90 criteria

Improvement in patients following etanercept, adalimumab or tocilizumab treatment according to Juvenile Disease Activity Score 10 at baseline compared with the last observation

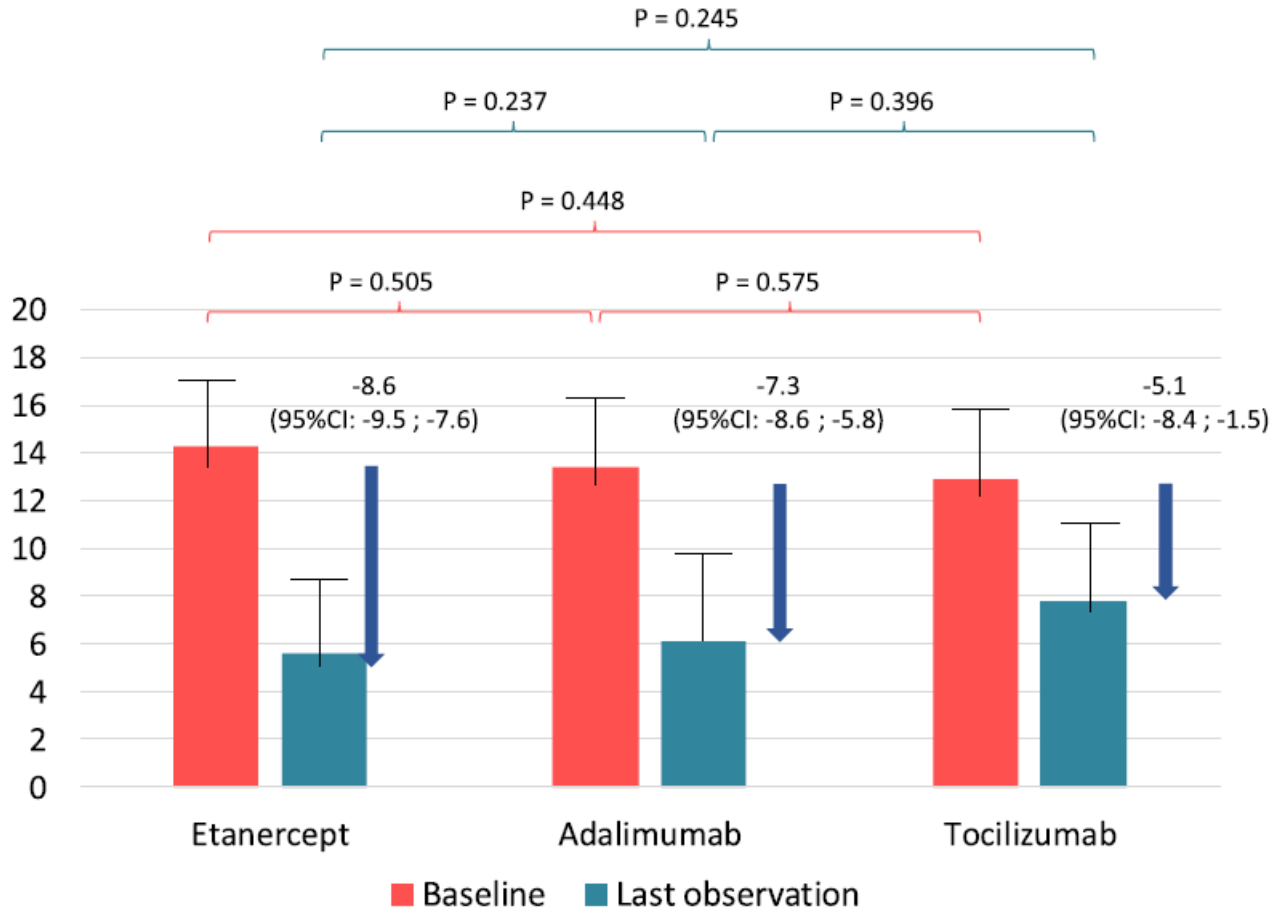


Fig. 2 Improvement in patients following etanercept, adalimumab or tocilizumab treatment according to Juvenile Disease Activity Score (*JADAS*)10 at baseline compared with the last observation on a study drug

Rates of Juvenile Disease Activity Score (JADAS)10 remission and minimal disease activity in patients taking etanercept, adalimumab or tocilizumab

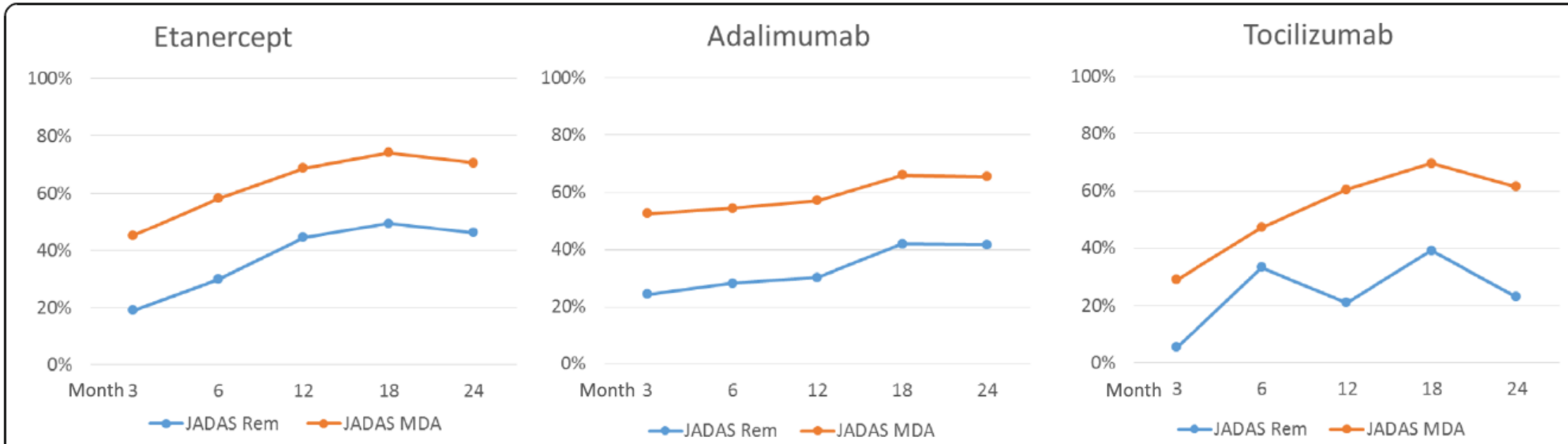


Fig. 3 Rates of Juvenile Disease Activity Score (*JADAS*)10 remission and minimal disease activity in patients taking etanercept, adalimumab or tocilizumab

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Table 2 Rates and reasons for discontinuation

	Etanercept cohort	Adalimumab cohort	Tocilizumab cohort	Adalimumab versus etanercept[a]	Tocilizumab versus etanercept[a]	Tocilizumab versus adalimumab[a]
	n = 419	*n* = 236	*n* = 74	OR (95% CI); *p* value	OR (95% CI); *p* value	OR (95% CI); *p* value
Discontinuations, *n* (%)	207 (49.4)	142 (60.4)	23 (31.1)	1.57 (1.03; 2.41); 0.037	0.20 (0.09; 0.45); <0.001	0.13 (0.06; 0.29); <0.001
Inefficacy, *n* (%)	50 (11.9)	52 (22.0)	9 (12.2)	1.65 (0.88; 3.08); 0.118	0.34 (0.11; 1.00); 0.050	0.20 (0.07; 0.60); 0.004
Remission, *n* (%)	54 (12.9)	22 (9.3)	2 (2.7)	0.78 (0.43; 1.40); 0.404	0.12 (0.02; 0.79); 0.027	0.16 (0.02; 1.05); 0.056
Intolerance, *n* (%)	15 (3.6)	15 (6.4)	2 (2.7)	2.28 (1.03; 5.04); 0.042	0.84 (0.18; 4.01); 0.826	0.37 (0.08; 1.79); 0.216
Details	Hypersensitivity (5), uveitis (3), vasculitis (1),	Infections (4)[b]	Impetigo (1)			
	Lymphoma (1)	Hypersensitivity (3)	Neutropenia (1)			
	Elevated transaminases (1), neuro-psychiatric (4)[b]	Pustulosis (1), neuro-psychiatric (5)[b]		0.2	5	
Others*, *n* (%)	88 (16.0)	53 (22.4)	10 (13.4)	1.21 (0.74; 1.96); 0.443	0.27 (0.10; 0.72); 0.009	0.22 (0.08; 0.60); 0.003

[a]Analyses weighted by an inverse probability of treatment estimated by a generalized propensity score. [b]Infections included pneumonia and soft tissue infections; Neuropsychiatric included headache, nausea, aggressiveness, anxiety, and vertigo. *beta* regression coefficient for continuous variables, *CI* confidence interval, *OR* odds ratio for categorical variable

Conclusions

- ❑ Adalimumab/etanercept/tocilizumab showed comparable efficacy toward polyJIA.
- ❑ Tolerance was acceptable.