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Targeted Therapies in RA: Real World Comparative Effectiveness Research

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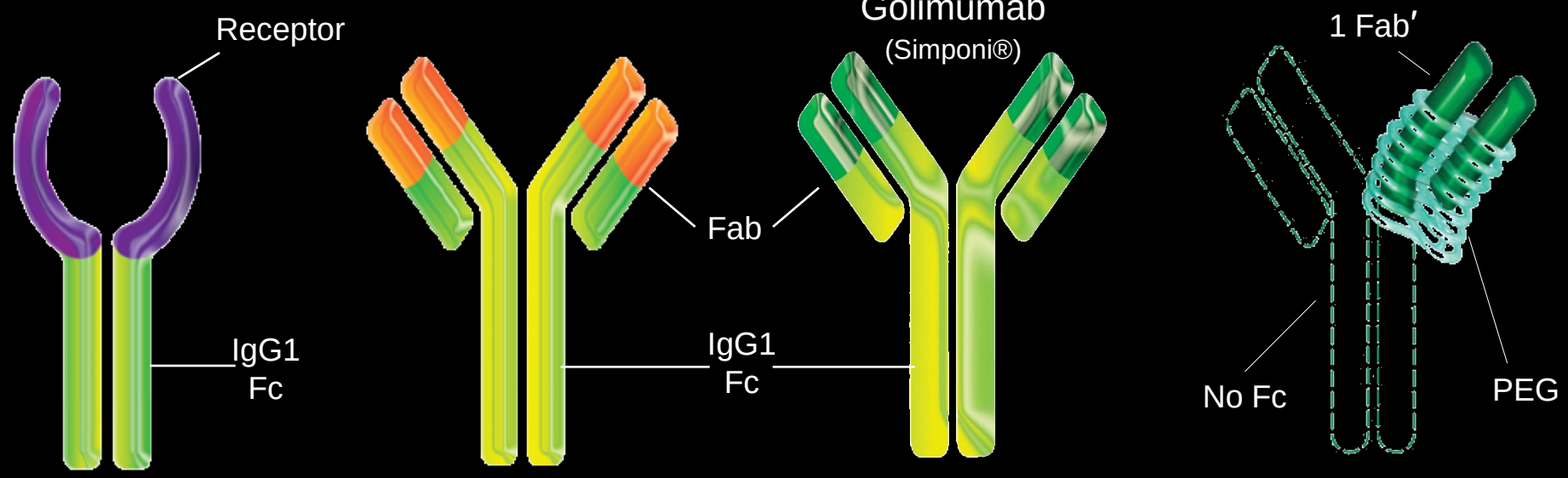
Structure of TNF Antagonists Currently Approved in US

Etanercept
(Enbrel®)

Infliximab
(Remicade®)

Adalimumab
(Humira®)
Golimumab
(Simponi®)

Certolizumab pegol
(Cimzia®)



Recombinant receptor/Fc fusion protein

Recombinant human/mouse chimeric IgG1

Recombinant human IgG1

Recombinant humanized PEGylated IgG1 Fab' fragment

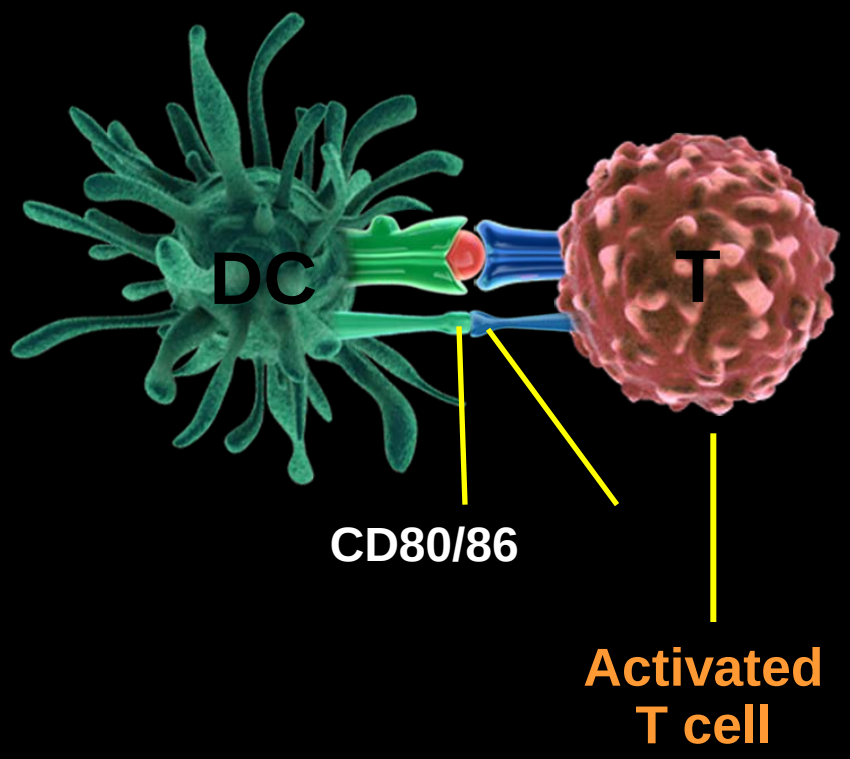
Full Monoclonal Antibody

Monoclonal Fab'

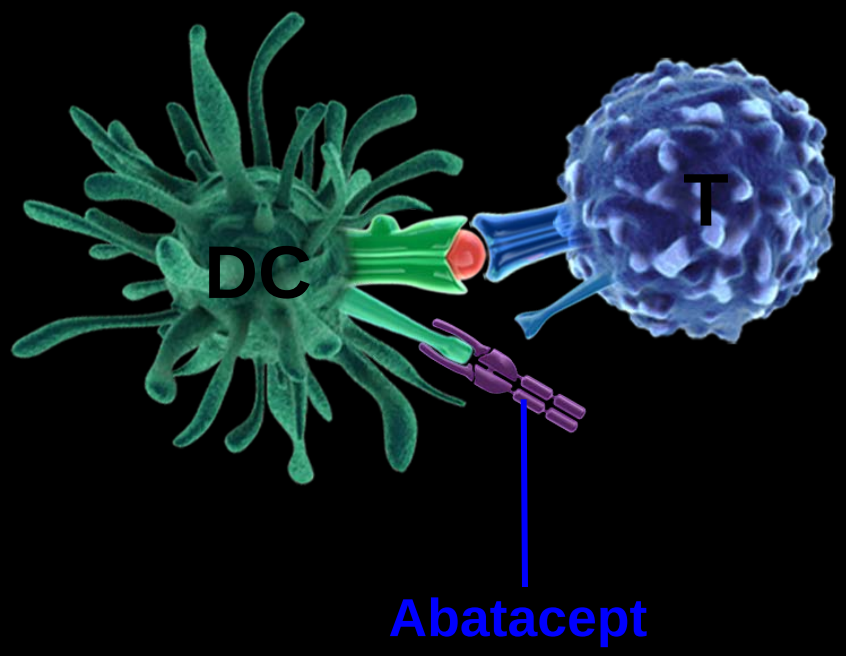
Fc: fragment, crystallizable; Ig: immunoglobulin.

Abatacept Selectively Modulates Co-stimulation via CD80/86:CD28 Pathway

Normal activation



Abatacept blocks activation



Comparative Effectiveness of Abatacept versus Anti-TNF agents in the Treatment of Biologic Naïve Rheumatoid Arthritis Patient Using the CORRONA Registry

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CORRONA

CORRONA

Consortium of Rheumatology Researchers of North America (CORRONA)

- Gathers information on arthritis, comorbidities, functional status, medications, adverse events and outcomes from both patients and providers
- Includes over 100 practice sites
- 37 states across the US
- 80% private practice and 20% academic

OBJECTIVES

- The objective of this study was to compare the effectiveness of abatacept to anti-TNFs using the following:
  - Change in disease activity based on the Clinical Disease Activity Index (CDAI)
  - Achievement of remission based on the CDAI

METHODS

- **Study setting:** The Consortium of Rheumatology Researchers of North America (CORRONA) registry is a prospective observational cohort of >20,000 RA patients

- **Study Population:**
  - Visits between 2/20/02 and 12/14/09
  - Biologic naïve
  - Not in remission at baseline
  - Follow-up visit 1 year after initiation.
  - Patients who initiated abatacept or an anti-TNF were identified
  - Anti-TNF initiators were matched to abatacept initiators (3 to 4:1 match) based on age, disease duration, use of methotrexate at time of initiation, initiation time frame (at or prior to index visit) and baseline CDAI

METHODS

- **Outcomes**: Comparative effectiveness was examined by comparing abatacept initiators to anti-TNF initiators 1 year after initiation on the following:
  - Treatment response based on change in CDAI
  - Achievement of remission based on the CDAI
- **Analyses:**
  - Three analytic approaches were used
  - Intention to treat (ITT): all initiators were included in these analyses
  - Nonresponder imputation: nonresponse was imputed for those who discontinued for reasons other than toxicity and last response if due to toxicity
  - Completers analysis: included only those who remained on drug
  - Regression models were performed to adjust for clustering by physician and by matched clusters as well baseline differences.

Table 1. Baseline characteristics of abatacept and matched anti-TNF initiators

Characteristic	Abatacept initiators N=36	Anti-TNF initiators N=139	P value
Female (%)	81	78	0.81
Age (in years)	66	65	0.41
Private insurance (%)	71	71	1.00
Medicaid (%)	6	7	1.00
Medicare (%)	65	55	0.41
No insurance (%)	3	1	0.42
Disabled (%)	3	13	0.19
Duration of RA (mean years, ±SD)	11.5 (10.1)	10.6 (8.6)	0.65
CDAI (mean, ±SD)	16.5 (11.0)	18.0 (10.0)	0.44
Tender joint count (mean, ±SD)	4.7 (5.9)	5.1 (5.0)	0.72
Swollen joint count (mean, ±SD)	5.8 (4.4)	6.0 (4.6)	0.86
Physician global (mean, ±SD)	24.9 (18.3)	32.3 (19.0)	0.04
Patient global (mean, ±SD)	34.7 (20.2)	37.0 (24.9)	0.60
Morning stiffness RA (mean hours, ±SD)	1.1 (1.6)	1.3 (1.8)	0.46
ESR (mean mmHg, ±SD)	22.6 (11.6)	28.4 (25.9)	0.49
Prior number of DMARDs (mean, ±SD)	1.2 (0.9)	1.2 (1.2)	0.73
Current methotrexate use (%)	71	72	1.00

Table 2. Comparison of response based on change in CDAI in abatacept (ABA) initiators as compared to anti TNF initiators

	Intention to Treat*	Completers analysis*
Mean change in CDAI in abatacept vs. anti-TNF initiators	-6.51 vs. -7.89	-8.25 vs.-9.28
Adjusted difference	0.81 (-2.54 to 4.15)	-0.70 (-4.41 to 3.01)

*Not statistically significant: models adjusted for clustering by physician, matched clusters and baseline CDAI

CORRONA

Table 3. Comparison of CDAI remission in abatacept (ABA) initiators as compared to anti-TNF initiators

	Intention to Treat	Nonresponder imputation	Completers analysis
Remission (%)	36 vs 25	36 vs 19	45 vs 27
Adjusted likelihood of remission	1.62 (0.63-4.17)	2.21 (0.80-6.12)	1.87 (0.68-5.18)

CORRONA

CONCLUSIONS

- Among this small sample of RA patients in a real-world setting, treatment with abatacept was not associated with any differences in response or remission rates from those seen with anti-TNFs based on mean change in CDAI and achievement of CDAI remission.
- This study suggests similar effectiveness of abatacept and anti-TNFs in biologic naïve RA patients.
- Further research with a larger sample size is needed to confirm these findings.

Clinical Trials: Investigator Initiated Teriparatide for Joint Erosions in RA

- Randomized, controlled, 12-month open-label study of teriparatide in patients with RA and T-scores between -1.0 and -2.5 who have joint erosions
  - Subjects will be randomized to receive:
    - Teriparatide + TNF antagonist
    - TNF antagonist alone.
- Hypothesis: Combination of teriparatide + TNF antagonist will be much more effective at retarding erosion progression in RA then a TNF antagonist alone and may allow for healing of erosions
  - Joint erosion scores will be significantly improved at study completion in patients taking teriparatide
  - Teriparatide will significantly increase
  - RA disease activity measures will remain stable during the study year
- Conducted at UMass Memorial Medical Center & Brigham and Women's Hospital
- Funded by a grant from Lilly

Clinical Trials: Sponsored Multi-center

Rheumatoid Arthritis

- Tocilizumab (anti-IL-6R mAB) - Hoffmann-La Roche Inc.
  - Randomized, Double-blind, Parallel Group Study of the Safety, Disease Remission and Prevention of Structural Joint Damage During Treatment with Tocilizumab , as a Monotherapy and in Combination with MTX, Vs. MTX in Patients with Early Moderate to Severe RA (Hoffmann-La Roche Inc. - WA19926)

Ankylosing Spondylitis

- SAR153191 (anti-IL-6R mAB) - Sanofi-Aventis
  - Randomized, Double-blind, Placebo-controlled, Dose Ranging Study to Evaluate Efficacy and Safety of SAR153191 in Patients with AS (ALIGN)
  - Uncontrolled Extension Study Evaluating the Long Term Safety and Efficacy of SAR153191 in Patients with AS (SUSTAIN)

Osteoarthritis

- Hymovis™ (Hyluronic acid) - Fidia Farmaceutici S.p.A.
  - Parallel, Double-blind, Blinded Evaluator, Randomized, Placebo-controlled, Study to Evaluate the Safety and Effectiveness of a New Viscoelastic Hydrogel (Hymovis™) in the Treatment of Knee OA with an Open-label Extension