



Welcome!

Advanced Therapy: Biologic DMARDs

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DISCLOSURES

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Disclosure Statement

Planners Jennifer Mandal, MD, Leslie Dexheimer Gleason, RN, and Tabitha Carroway, MPH have stated they have no relationships to disclose. Speaker Wendy Grant, MD has stated she has no relationships to disclose.

Nomenclature

“Biologic” agents are made using recombinant DNA techniques

They are large, unstable proteins that can only be administered parenterally

- **mab** monoclonal antibody
- **ximab** chimeric monoclonal antibody
- **umab** humanized monoclonal antibody
- **cept** fusion protein of a receptor and the Fc portion of IgG

Biologic Agents: Available Mechanisms

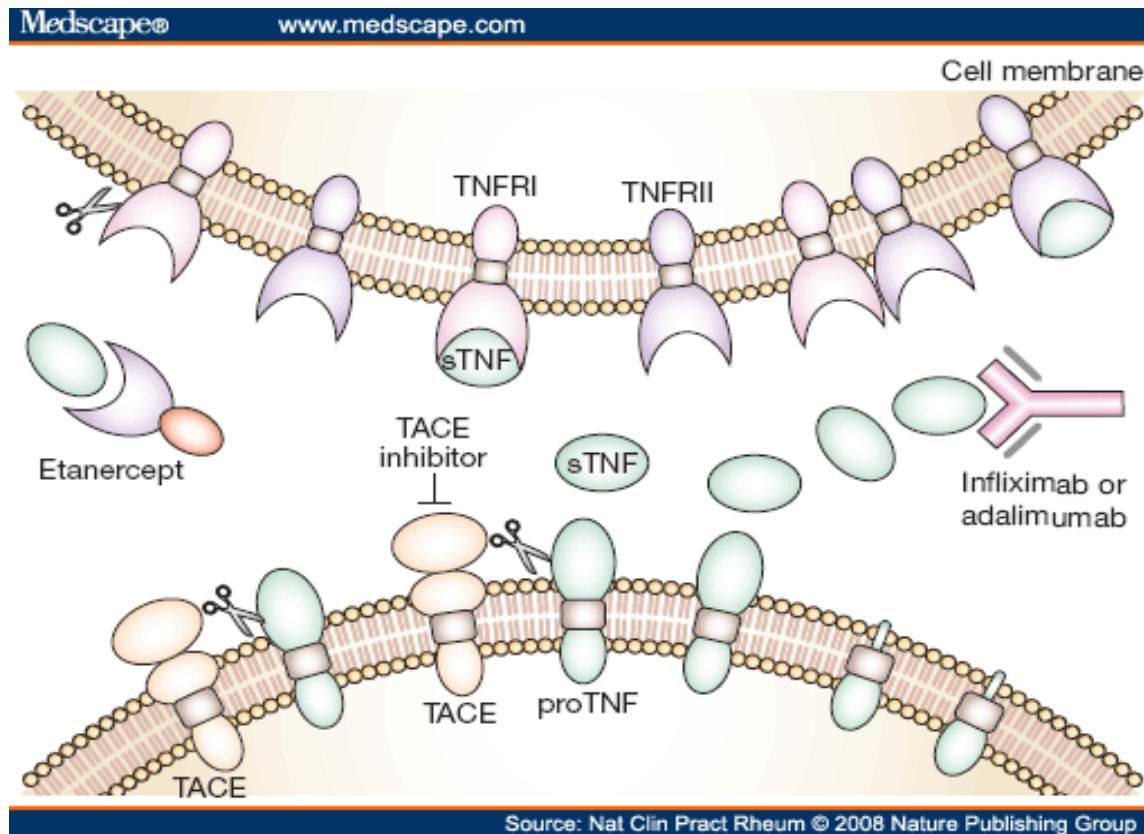
- Cytokine inhibitors
- Costimulatory blockers
- B cell inhibitors
- Kinase inhibitors

Available Biologic Agents for RA

CYTOKINE INHIBITORS

TNF inhibitors

(etanercept, adalimumab, infliximab, golimumab, certolizumab)



Available Biologic Agents for RA

CYTOKINE INHIBITORS

IL-1 inhibitor (anakinra “KINERET”)

IL-6 inhibitors

tocilizumab (“ACTEMRA”)

sarilumab (“KEVZARA”)

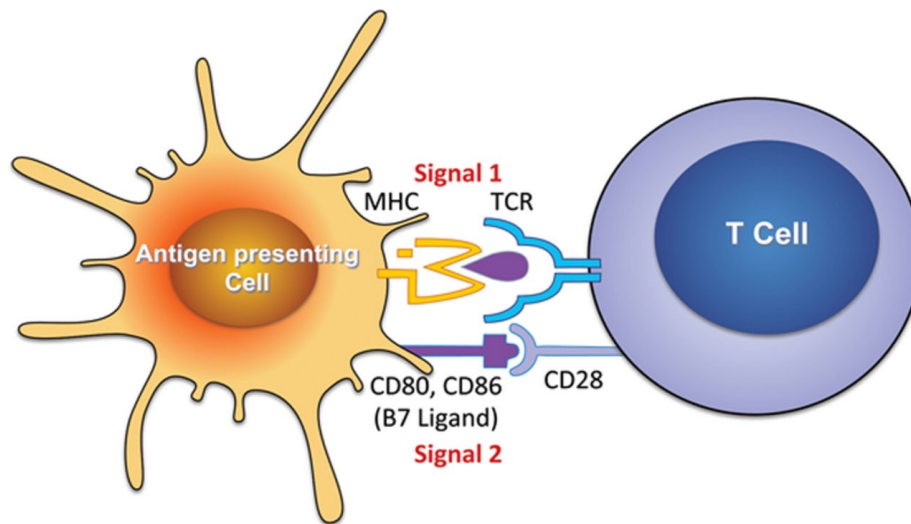
Available Biologic Agents for RA

COSTIMULATORY BLOCKERS

Abatacept (“ORENCIA”)

fusion protein of CTLA-4 and Fc portion of IgG

prevents CD28 binding to CD80/CD86 (blocks second signal binding between T cells and antigen presenting cells)



Available Biologic Agents for RA

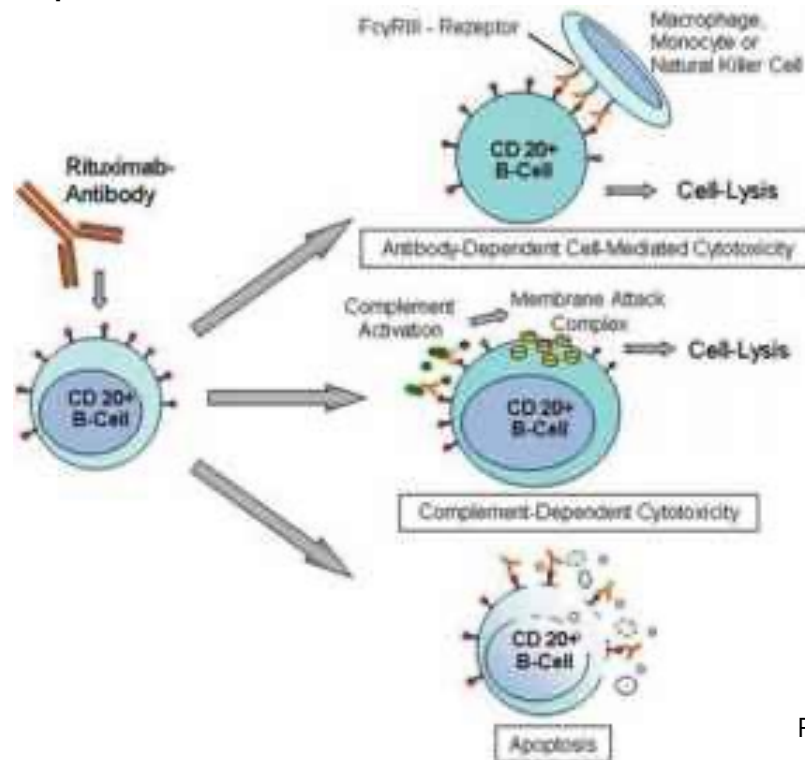
B CELL INHIBITORS

Rituximab

anti CD 20

expressed on pre-B cells and pre-plasma cells

pro-B cells and plasma cells are not affected



Available Biologic Agents for RA

KINASE INHIBITORS

“Small molecules” that are not proteins and technically not biologic agents
but are similar to biologics in that they are highly targeted therapies
and have similar efficacies and side effects

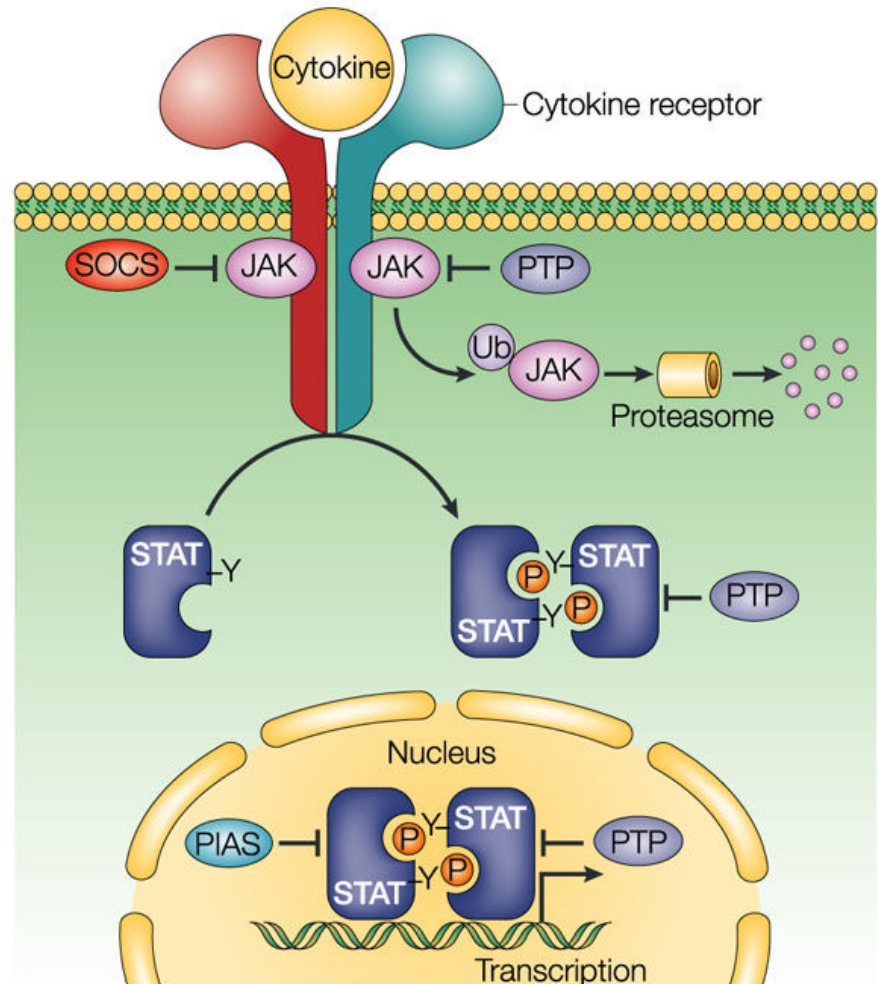
Janus kinases are cytoplasmic proteins that relay information to the nucleus from IL receptors on the cell membrane

JAK inhibitors are oral agents

Tofacitinib, baricitinib, upadacitinib (Xeljanz, Olumient, Rinvoq)

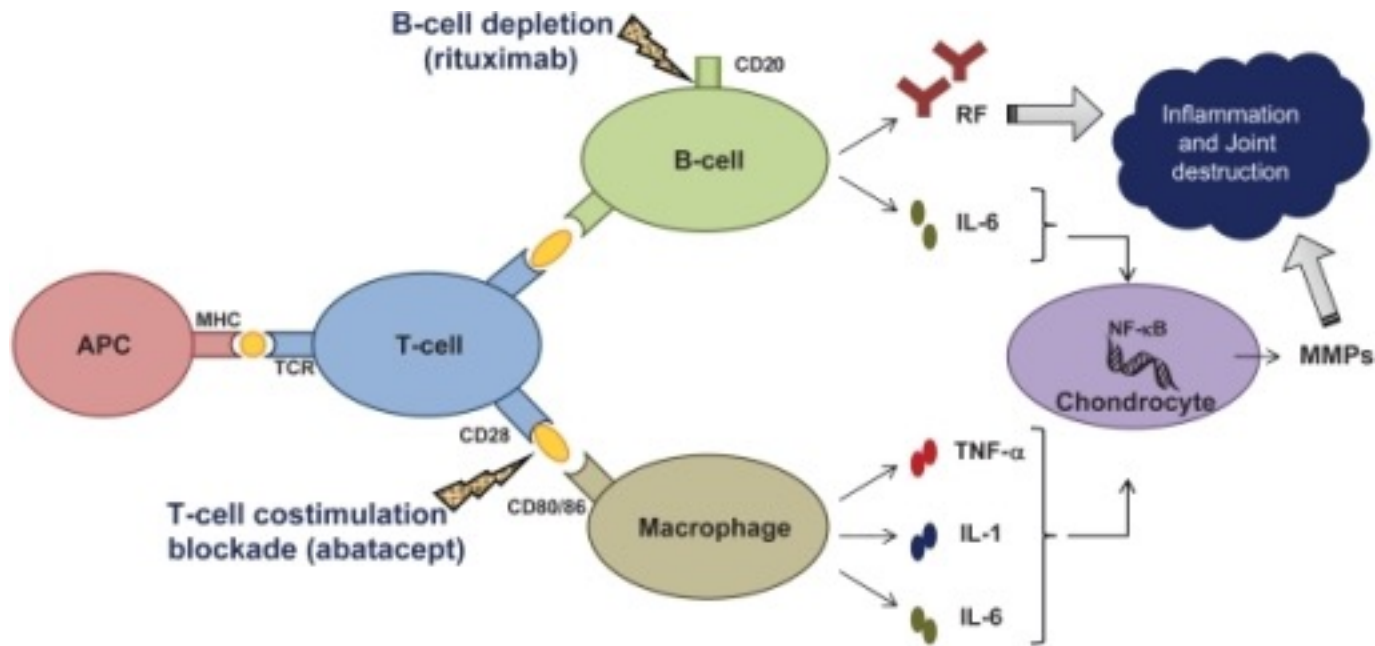
Available Biologic Agents for RA

KINASE INHIBITORS






Available Biologic Agents for RA

Summary of Mechanisms



Inhibitors

- TNF-α  Infliximab, etanercept, adalimumab, certolizumab, golimumab
- IL-1  Anakinra
- IL-6 receptor  Tocilizumab

Available Biologic Agents for RA

Summary

	<u>Trade</u>	<u>Class</u>	<u>Administration</u>	<u>Frequency</u>
Etanercept	Enbrel	TNFi	SQ	weekly
Adalimumab	Humira	TNFi	SQ	Q 14 d
Golimumab	Simponi	TNFi	SQ	monthly
Certolizumab	Cimzia	TNFi	SQ	monthly
Infliximab	Remicade	TNFi	IV	Q 4-8 weeks
Tocilizumab	Actemra	IL-6i	SQ/IV	weekly/monthly
Sarilumab	Kevzara	IL-6i	SQ/IV	
Abatacept	Orencia	Costim blocker	SQ/IV	weekly/monthly
Rituximab	Rituxan	antiCD20 (B cell)	IV	2 IV Q 6 months
Tofacitinib	Xeljanz	JAKi	PO	daily
Baricitinib	Olumient	JAKi	PO	daily
Upadacitinib	Rinvoq	JAKi	PO	daily

Indications for Targeted Therapy in RA

Inadequate response to conventional DMARD therapy

Contraindications to cDMARD therapy

Ongoing corticosteroid requirement (either daily or frequent use for flares)

Erosive disease or progression on imaging

ACR and EULAR Guidelines for Use of Biologics

Both recommend anti TNF therapy as first line agents but recognize that the data supports equivalent efficacy for other biologics

More long-term data exists for TNF inhibitors than for other agents

Most insurances will not approve use of other bDMARDs until anti TNF therapy has been tried

IHS has either etanercept or adalimumab on formulary

ACR and EULAR Guidelines for Use of Biologics

Inadequate response to initial TNF:

- second anti-TNF

OR

- alternative biologic agent (tocilizumab or abatacept)

OR

- tofacitinib

In studies, the efficacies of the above treatment options are equivalent

ACR and EULAR Guidelines for Use of Biologics

When to consider a biologic OTHER THAN a TNF inhibitor as a first line agent

- recent lymphoma history
- h/o demyelinating disease
- LTBI with contra-indications to treatment
- class III/IV CHF
- co-existent lupus or lupus-like illness ("Rhupus")

Pros/cons of Individual Agents Other Than Anti TNF

Abatacept

- PRO** IV - short infusion time
rare infusion reactions; well tolerated
fewer infectious complications
- CON** longer time to efficacy than other agents

Tocilizumab/Sarilumab

- PRO** well-tolerated
- CON** hyperlipidemia
intestinal perforation in elderly and in patients with
prior diverticulitis, steroid use, NSAID use

Pros/cons of Individual Agents Other Than Anti TNF

Rituximab

- PRO** Q 6 month dosing regimen
possible benefit in RA-ILD
- CON** higher rate of infusion reactions
long duration of B cell inactivation (4-6 months +)
decreased response to COVID vaccination

Tofacitinib

- PRO** oral
patient support programs for Medicare (Xelsource)
- CON** higher rate of herpes zoster infection (2X compared with abatacept)
increased risk of CVE/VTE in at-risk patients

Recommendations for High-Risk Comorbidities

CHF

Use combination DMARDs OR non-TNF biologics OR tofacitinib OVER TNFi

Hepatitis B

Received/receiving anti-viral treatment

Same recommendations as in patients without this condition

Hepatitis C

received/receiving anti-viral treatment

Same recommendation as in patients without this condition

untreated

Treat prior to initiating biologic therapy

Recommendations for High-Risk Comorbidities

Treated or untreated skin cancers

Use DMARDs over biologics/tofa in melanoma

Previously treated lymphoproliferative disorders

Use Rituximab over TNFi

Previously treated solid organ malignancies

Same recommendations as in patients without this condition

Previous serious infection

Use combination DMARD over TNFi

Use abatacept over TNFi

Biologic Agents in RA: *References*

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Biologic Agents in RA: *References*

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