BIOLOGICS IN RHEUMATIC DISEASES – UPDATE 2018

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Class	Drug	Treatment guidelines and Dosing
ANTI TNF **- cept = receptor molecules** **- mab = monoclonal antibodies** **- omab = murine;** **- ximab = chimeric;** **- zumab = humanized;** **- umab = human.**	infliximab (Remicade*, Inflectra**)	3 mg/kg @ wk 0, 2, 6, then 8 weekly IV over 2 hrs; max 6 maintenance doses per year RA, AS, 2nd line for polyarticular JIA, J SpA . (Also IBD and PsO) LU 469 AS LU 468 RA LU 470 PsA
	etanercept (Enbrel*, Brenzys**, Erelzi)	50mg SC weekly or 25 mg SC twice a week for RA, PsA, AS 0.8 mg/kg per week (up to a maximum of 50mg per week) for JIA (JSpA, JIA poly) LU AS Brenzys 498 Erelzi 513 LU RA Brenzys 499 Erelzi 512 LU JIA poly Erelzi 514
	adalimumab (Humira)	40 mg SC every 2 weeks (dosing for JIA 24 mg per m2) RA, AS, PsA, polyarticular JIA (Also uveitis, IBD and PsO)
	golimumab (Simponi)	50 mg SC every month for RA, AS, PsA or 2 mg/kg over 30 minutes at weeks 0, 4, then every 8 weeks thereafter for RA#
	certolizumab (Cimzia)	400 mg SC at weeks 0, 2, 4 then 200 mg every 2 weeks, or 400 mg every 4 weeks for RA, PsA, AS
ANTI CD20	rituximab (Rituxan)	RA 1000 mg IV day 1 and day 15 - RA (post 1 anti TNF or see list of specific indications for primary use. GPA / MPA 375 mg/m2 once weekly for 4 weeks, see EAP criteria
ANTI IL6 receptor	tocilizumab (Actemra)	IV for RA : 4/mg/kg 4 weekly IV over 1 hr – increase to 8 mg based on response. SC for RA : <100kg, 162 mg every other week; increase to every week based on clinical response; in patients 100 kg or greater, use 162 mg administered every week. See EAP criteria for , sJIA , polyarticular JIA ★★
	sarilumab (Kevzara)#	200 mg s.c. every two weeks (cut to 150 mg if AE) ★★
Selective T Cell Co-stimulatory inhibitor	abatacept (Orencia)	30 min IV at 0, 2, 4 weeks then every 4 weeks after. Dose by weight: 500 mg for patients < 60 kg, 750 mg 60–100 kg, 1000 mg > 100 kg or SC 125 mg weekly RA, 2nd line for polyarticular JIA
ANTI IL17 inhibitor	secukinumab (Cosentyx)	Dose once a week for 5 weeks, then 4 weekly Dosing: AS: 150 mg SC PsA: 150 mg SC for bio-naive patients; 300 mg SC for anti TNF inadequate responders or for patients with moderate to severe PsO; PsO: 300 mg SC (LU code) *[Not useful for Crohn's]*
	ixekizumab (Taltz#)	160mg by subcutaneous injection (two 80 mg injections) at Week 0, followed by 80mg every 4 weeks
JAK 1/3 inhibitor	tofacitinib (Xeljanz**)	5 mg PO BID RA LU 480 RA ★
JAK 1/2 inhibitor	baricitinib#	4 mg daily
Anti IL 1	Anakinra (Kineret)	100 mg SC daily . For cryopyrin associated periodic syndrome 1-2 mg per kg SC daily starting dose
ANTI IL12 and IL23	ustekinumab (Stelara)	45 mg SC at weeks 0 and 4, then every 12 weeks thereafter. Alternatively, 90 mg with body weight > 100 Kg PsA
PDE4 Inhibitor	apremilast (Otezla)#	30 mg PO BID: 2 week starter pack PsO and PsA

EAP Criteria

RA
5 swollen joints, RF/ CCP positive and/or radiographic evidence of rheumatoid arthritis despite the optimal use of DMARDs.
Methotrexate [MTX] (20 mg/week) and Leflunomide [LEF] each 3 months plus one combination with other DMARD OR
LEF (20 mg/day) + MTX for at least 3 months.
OR MTX + Sulfasalazine (SFZ) + OH Chloroquine triple therapy for at least 3 months
Renewal
20% reduction in SJC and a minimum reduction of 2 swollen joints.
Rituximab second line after failing anti TNF (plus see below)

PsA
5 swollen joints and radiographic evidence of psoriatic arthritis despite treatment with MTX (20 mg/week) for at least 3 months and one of LEF (20 mg/day) or SAS(1 g twice daily) for at least 3 months.
If the patient has documented contraindication or intolerance to MTX then only one of LEF (20 mg/day) or SAS(1 g twice daily) for at least 3 months is required.
Renewal
20% reduction in SJC and a minimum of improvement in 2 swollen joints.

AS
Age of disease onset < 50; AND
- Low back pain and stiffness for > 3 months that improves with exercise and not relieved by rest; AND
- Failure to respond to or documented intolerance to adequate trials of 2 NSAIDs for at least 4 weeks each; AND
- BASDAI score of 4 for at least 4 weeks while on standard therapy; AND X-ray or CT scan report stating the presence of "SI joint fusion or erosion" OR MRI report stating the presence of "inflammation" or "edema" of the SI joint(s). Send radiology report with application.

Renewal
50% reduction in BASDAI score or 2 absolute point reduction in BASDAI score.

Other notes:
** Drug has LU code * No new starts for RA # Awaiting ODB coverage

Evaluate need for VZV and HIV serology
Recommend pneumococcal vaccine and annual flu vaccine
RR H. zoster 1.6 with anti TNF and 2 with JAKi

★ BSRBR - 5.1 serious infections per 100 patient years
No increases thromboembolic events with tofacitinib
Lipids at 2 months then 6 monthly

★ Caution in patients at risk of GI perforation

Malignancy – If in doubt consult oncologist
Lymphoma:
Anti-TNF does not increase the risk if lymphoma (BSRBR data)
abatacept, tocilizumab should be used with caution (no evidence).

Non-melanoma skin cancer:
Anti TNF probably does not increase risk. Abatacept, tocilizumab, and Rituximab should be used with caution, ideally after consult with an oncologist (no evidence).

Solid tumors:
Anti-TNF therapy should be avoided in patients with melanoma only; abatacept, tocilizumab, should be used with caution.
Rituximab recommended by ACR for solid tumor and melanoma.

BSRBR 2016: Patients with prior malignancy selected to receive biologics do not have an increased risk of incident malignancy. It remains unknown whether biologics can be used safely in all patients with prior malignancy

Hepatitis B Refer ALL to hepatology for classification

Hep B Status	HbsAg	HbsAb	Total Hbc-Ab	Hbc-IgM	Hbc-IgG	Abnormal LFT +/- symptoms	Additional Testing	Recommendation
Susceptible	-	-	-	-	-	-	None	Consider vaccination, start biologic
Immune due to prev infection	-	+	+	-	+	-	None	Start biologic
Immune due to HBV vaccine	-	+	-	-	-	-	None	Start biologic
Acute Infection	+	-	+	+	-	+	None	Hepatology consult, defer biologic
Chronic infection	+	-	+	-	+	+/-	HBeAg /Ab, HBV DNA	Start biologic + hepatology

In asymptomatic HBsAg+ carriers, antiviral prophylaxis is recommended and should be started 2-4 weeks prior to anti-TNF therapy and continued for at least 6-months. In total Hbc-Ab+ patients, routine prophylaxis is not recommended, although individual factors such as degree of immunosuppression, length of therapy, and degree of local HBV endemicity should be taken into account.
Rituximab should also be avoided in any patient with active or chronic hepatitis B.

Hepatitis C Refer to hepatology - consider pretreatment
There are numerous publications that provide evidence supporting the safe use of anti-TNF biologics in the context of HCV infection. However note: current 2008 ACR recommendations contraindicate use of anti-TNF and abatacept in patients with Hepatitis C with Child-Pugh class B/C liver disease.

Pregnancy

Monoclonal antibodies expose the child to the full adult dose when administered in late pregnancy with a risk for adverse effects in the newborn and perinatally
No increased risk of congenital malformations with anti TNF; should not affect development of baby's immune system after birth; breastfeeding is considered safe because anti TNF poorly excreted

- Do NOT use rituximab; may result in pre-term, miscarriages, hematological abnormalities, congenital malformations, neonatal B cell depletion
- Do NOT use abatacept, JAK inhibition - lack of data
- Tocilizumab may be reasonable for first two trimesters
- Certolizumab might be considered as the anti TNF of choice in this population (biologic rationale)
- Advise NO live vaccines (e.g.rotavirus) until baby is 6 months
- www.mothertobaby.org

Rituximab may be first choice in:
1) Patients with previously treated solid malignancy within the last 5 years
2) Patients with previously treated non-melanoma skin cancer within the last 5 years
3) Patients with previously ever treated melanoma skin cancer
4) Patients with previously ever treated lymphoproliferative malignancy, (e.g., lymphoma, CLL, leukemia)
5) For patients with congestive heart failure NYHA class III or IV with ejection fraction of ≤ 50%
6) For patients with latent tuberculosis with contraindications or intolerance to the use of 2 anti-TB medications
7) For patients with Multiple Sclerosis or family history of MS in first degree relatives
8) For patients with interstitial lung disease where a respirologist opinion is that Methotrexate and Leflunomide are contraindicated, and/ or anti-TNFs are contraindicated.
9) Possibly indicated for Hep C cryoglobulinemic vasculitis.