

SUPPLEMENTARY APPENDIX 3: Clinical Outcomes

2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

RA Guideline – Outcomes (Green Highlighted Outcomes = Critical)

1. **Disease activity**
 - **Treatment response** ACR50, ACR70, EULAR response
 - Change in disease activity measurement (DAS28, SDAI, CDAI, RAPID3)
2. **Function or functional ability** (ability to function in society, work, etc.; work productivity, employability; disability; work disability)
 - HAQ DI, HAQ II, MDHAQ
 - Work loss, work disability, absenteeism, work retention
3. **Preventing joint damage** (structural damage, e.g., erosion or joint space narrowing, deformity)
 - Radiographic score (e.g., Sharp) or alternate (ultrasound and MRI scoring)
4. **Serious adverse events, including**
 - **Opportunistic infections** (including but not limited to tuberculosis, fungal)
 - **Serious bacterial infections** (non-opportunistic)
 - **Organ damage** (irreversible organ damage (e.g., liver, kidney, bone marrow, lung), ocular toxicity)
 - **Morbidity** (diabetes, cardiovascular morbidity, hepatic disease, cataracts, osteoporosis, fractures, cancer, total joint replacement)
 - **Fetal toxicity**
 - **Death**
5. **Reversible side effects that are not “serious” but that impact QOL or decision-making**
 - **Impact QOL** (cosmetic changes (hair loss, weight gain), mucosal/dermatologic reactions, GI side effects (nausea, diarrhea), depression, other mental status changes (brain fog/dizziness, insomnia, headaches)
 - Important reversible lab abnormalities (e.g., LFTs)
6. **Percent stopping medication because of side effects**
7. **Drug survival** (*only applicable to some PICOs*)
8. **Quality of life** (measures domains including fatigue, sleep, mood, stress, anxiety, depression)
 - Generic/global (SF36 PCS; SF36 MCS; EUROQOL)
 - Disease-specific (RAQOL)
 - PROs not captured in the previous 2 bullets (e.g., fatigue)

Additional outcome for CHF PICOs (#1 critical outcome for these PICOs)

New or worsening congestive heart failure (resulting in hospitalization)

Additional outcomes for Hepatitis B and Hepatitis C PICOs (#1 critical outcome for these PICOs)

Increased viral load

Hepatic disease (a critical outcome for *this* set of PICOs)

Additional outcome for cancer PICOs (all types) (#1 critical outcome for these PICOs)

Recurrence or progression of cancer

Additional outcomes for vaccine PICOs (top critical outcomes for these PICOs)

- Seroconversion or “adequate protection against disease”
- **Herpes zoster incidence**
- **# of influenza cases**

Additional outcomes for tapering/discontinuing PICOs

- % who flare
- % who regain LDA or remissions

Additional outcomes for PICO involving specific medications:

csDMARDs

Methotrexate:

- Pneumonitis
- Nodulosis

Hydroxychloroquine:

- Retinopathy
- Neuropathy/myopathy
- Hemolytic anemia (g6pd deficiency)
- Irreversible dermatologic changes
- CNS adverse effects
- Hypoglycemia

Sulfasalazine:

- Hemolytic anemia (G6PD deficiency)
- CNS/neuromuscular adverse effects
- Fertility

Leflunomide:

- Peripheral neuropathy
- Hypertension
- Pneumonitis

boDMARDs

TNF Inhibitors:

- Demyelinating disease
- CHF exacerbation

Abatacept:

- COPD exacerbation

Rituximab:

- Hypogammaglobulinemia
- Progressive multifocal leukoencephalopathy
- Severe mucocutaneous reactions
- Severe infusion reactions

Tocilizumab/Sarilumab:

- Hyperlipidemia
- GI perforation
- Hypertension

tsDMARDs (Tofacitinib/Baricitinib)

Zoster

- GI perforation
- Hyperlipidemia
- Thrombosis
- Hypertension