Supplementary File A Interpretation of the ACR recommendation schemes

For the interpretation of the ACR-CPG we used the oligoarticular and polyarticular schemes based on the paper itself and after personal communication with the first author of that paper (T.B.).

Patients with systemic arthritis or active sacroiliac arthritis are considered in separate treatment groups. In our study we excluded patients with enthesitis related arthritis, because in our center most of these patients are diagnosed at some point with sacroiliitis which would favor an early anti-TNF start.

Of note, patients with inactive disease were not considered at all in the paper, meaning that the recommendations do not apply to patients with inactive disease. Inactive disease is defined as no active arthritis; no active uveitis; normal ESR or CRP level (if both are tested, both must be normal); and a physician's global assessment of disease activity indicating clinical disease quiescence.[13] Low disease activity was meant to refer to patients for which a majority of clinicians may consider altering the current medication regimen, which we interpreted that the PGA should not be zero if escalating therapy and likewise the active joint count should not be zero in a non-enthesitis, non-uveitic, non-systemic JIA patient. For disease activity levels an ESR or CRP above normal was only considered if this was attributable to the JIA and therefore disregarded in case of 0 active joints and PGA of 0.

OJIA-group

Oligoarticular was defined in the article as "History of arthritis of 4 or fewer joints". This group includes patients with the ILAR categories of persistent oligoarthritis, as well as patients with psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis who have developed active arthritis in only 4 or fewer joints in total throughout the history of their disease course.

The features of poor prognosis (must satisfy 1) are:

- Arthritis of the hip or cervical spine
- Arthritis of the ankle or wrist AND marked or prolonged inflammatory marker elevation
- Radiographic damage (erosions or joint space narrowing by radiograph)

Neither marked nor prolonged ESR were defined in the recommendations.

The cited article for marked ESR refers to an ESR of >100 mm/hr as the only significant predictor of poor prognosis.[14] Hence we used that cut-off value for marked ESR, even though to our opinion such a high ESR is rare in OJIA and warrants further investigations for alternative diagnoses (e.g. Crohn's disease).

The cited articles for prolonged ESR did not contain a cut-off point. We defined a prolonged elevated ESR for our study as a persistently elevated ESR, measured at start of MTX and at least once during the 3 month time-frame.

The disease activity levels for OJIA interpreted on the basis of the ACR recommendations 2011

Disease activity / ***Criteria***	**Inactive**	**Low**	**Moderate**	**High**
Active joints	0	1	≥2	≥2
ESR/CRP	Normal	Normal	>Normal	>twice ULN
PGA	0	>0 and <3	≥3	≥7
Parent/Patient VAS	<2	<2	≥2	≥4
Note	*Must satisfy all*	*No criterion of moderate disease may be satisfied*	*At least 1 of the above, but maximum 2 criteria of high disease activity may be satisfied*	*Satisfy 3 or 4 criteria*

At 3 months escalation to anti-TNF for oligoarthritis was recommended in case of moderate or high disease activity but only in presence of a poor prognostic factor. Therefore for our study we interpreted that the ACR-CPG recommended escalation in an oligoarthritis patient at 3 months when a patient had at least a radiographically damaged joint, arthritis of the hip/ cervical spine or the combination of ankle/wrist arthritis with an ESR >100 mm/hr or ESR>13 mm/hr continuously during 3 months. On top of at least one of these poor prognostic factors a patient should also have ≥2 active joints or a PGA ≥3/10 or a parent/patient VAS ≥2/10 or an ESR >13 mm/hr (due to JIA) or CRP > 10mg/l (due to JIA), although in case of prolonged or marked ESR this item was considered not sufficient for scoring the necessary disease activity level.

At 6 months escalation to anti-TNF for oligoarthritis was recommended in case of high disease activity irrespective of a poor prognostic factor. Therefore for our study we interpreted that the ACR-CPG recommended escalation in an OJIA patient at 6 months when a patient had at least 3 of the following 4 criteria: ≥2 active joints, an ESR >26 mm/hr (due to JIA) / CRP > 20mg/l (due to JIA), PGA ≥7/10 and a parent/patient VAS ≥4/10.

PJIA group

Polyarticular in the ACR-CPG was defined by “a history of arthritis of 5 or more joints”. This group includes patients with the ILAR categories of extended oligoarthritis, rheumatoid factor (RF)–negative polyarthritis, RF-positive polyarthritis, as well as patients with psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis who have developed active arthritis in 5 or more joints in total

throughout the history of their disease. Patients in this group need not currently have 5 or more active joints.

The features of poor prognosis in polyarthritis (e.g. presence of rheumatoid factor) are not relevant for our study, since they are not incorporated in the reasons for escalation to anti-TNF.

The disease activity levels for polyarthritis interpreted on the basis of the ACR recommendations 2011

Disease activity / ***Criteria***	**Inactive**	**Low**	**Moderate**	**High**
Active joints	0	1-4	≥5	≥8
ESR/CRP	Normal	Normal	>Normal	>twice ULN
PGA	0	>0 and <4	≥4	≥7
Parent/Patient VAS	<2	<2	≥2	≥5
Note	*Must satisfy all*	*No criterion of moderate disease may be satisfied*	*At least 1 of the above, but maximum 2 criteria of high disease activity may be satisfied*	*Satisfy 3 or 4 criteria*

At 3 months escalation to anti-TNF for polyarthritis was recommended in case of moderate or high disease activity, irrespective of a poor prognostic factor. Therefore for our study we interpreted that ACR recommended escalation in a polyarthritis patient at 3 months when a patient had ≥5 active joints or an ESR >13mm/hr (due to JIA) or a CRP >10 mg/l (due to JIA) or PGA ≥4/10 or parent/patient VAS ≥2/10.

At 6 months escalation to anti-TNF for polyarthritis was recommended in case of low, moderate and high disease activity, irrespective of a poor prognostic factor. This means that all polyarticular patients not being in inactive disease at 6 months would qualify for anti-TNF. Therefore for our study interpreted that ACR recommended escalation in a polyarthritis patient at 6 months when a patient did NOT satisfy all of the following criteria: active joint count = 0, ESR <13mm/hr and CRP <10 mg/l, PGA = 0 and parent/patient VAS <2.