Cutting Edge Therapeutic Approaches

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Cutting Edge

- Identify and treat early
- Treat to target
- Remission
- Remission induction
- Prevention

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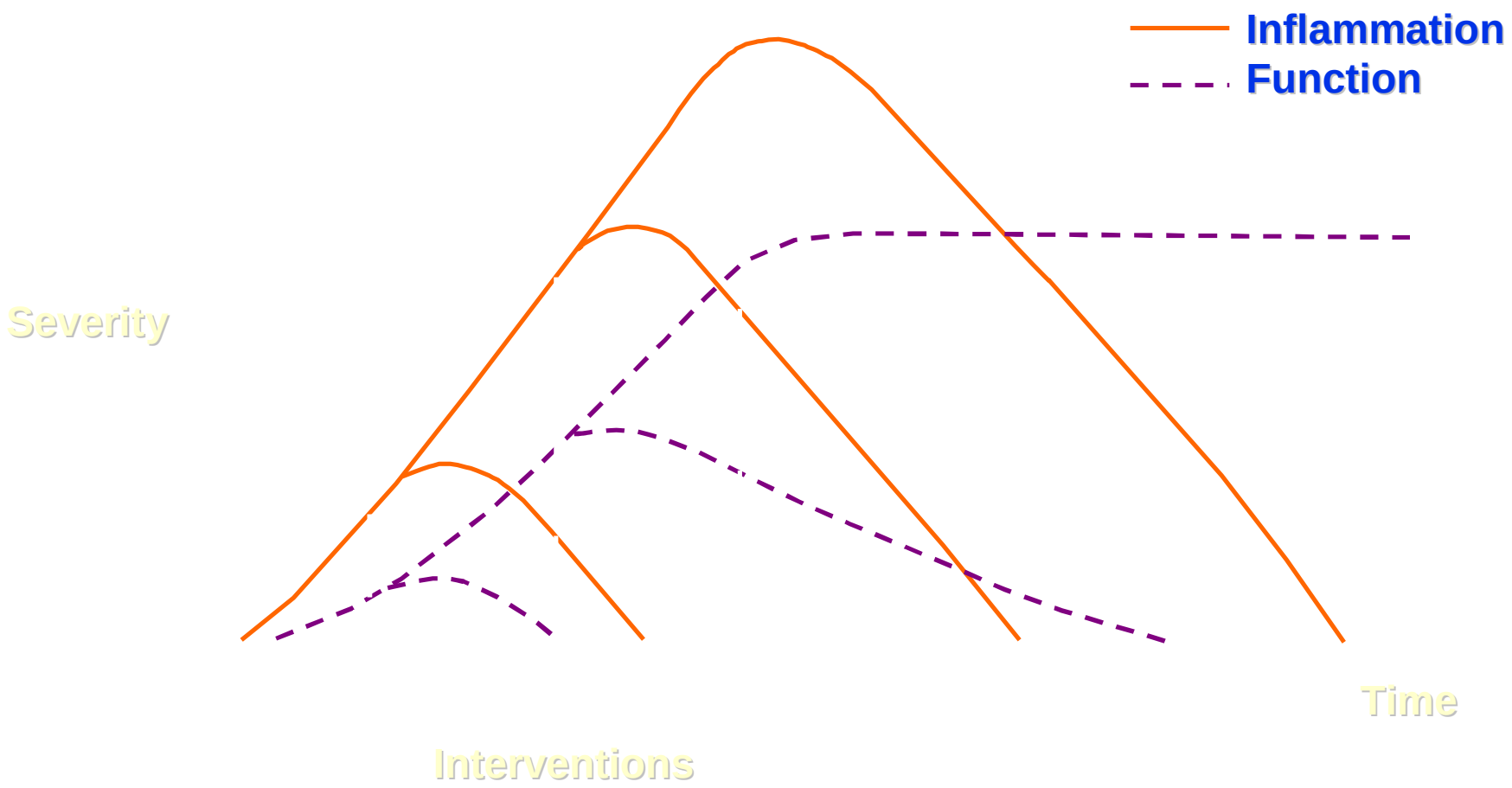
Effect of RA Disease Duration on Inflammation and Function



Emery P. *Ann Rheum Dis.* 1995;54:944

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The T2T-Initative

What Should be the Target and Why?

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Recommendations: Overarching principles

- The treatment of RA must be based on a shared decision between patient and rheumatologist.

- The primary goal of treating the patient with RA is to maximize long term HR-QOL through control of symptoms, prevention of progressive structural damage, normalization of function and social participation.

- Abrogation of inflammation is the most important means to achieve these goals.

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Main goal of therapy

Remission on DMARDs

Brown A et al Arthritis and Rheum 2006
Brown A et al Arthritis and Rheum 2006

- DMARDs can produce clinical remission
- DMARDs rarely produce imaging remission
- Hence DMARDs rarely produce true remission
- Explains progression of damage in patients in clinical remission on DMARDs

New Goals

- **True remission, biologic-free**
- **True remission, drug-free**

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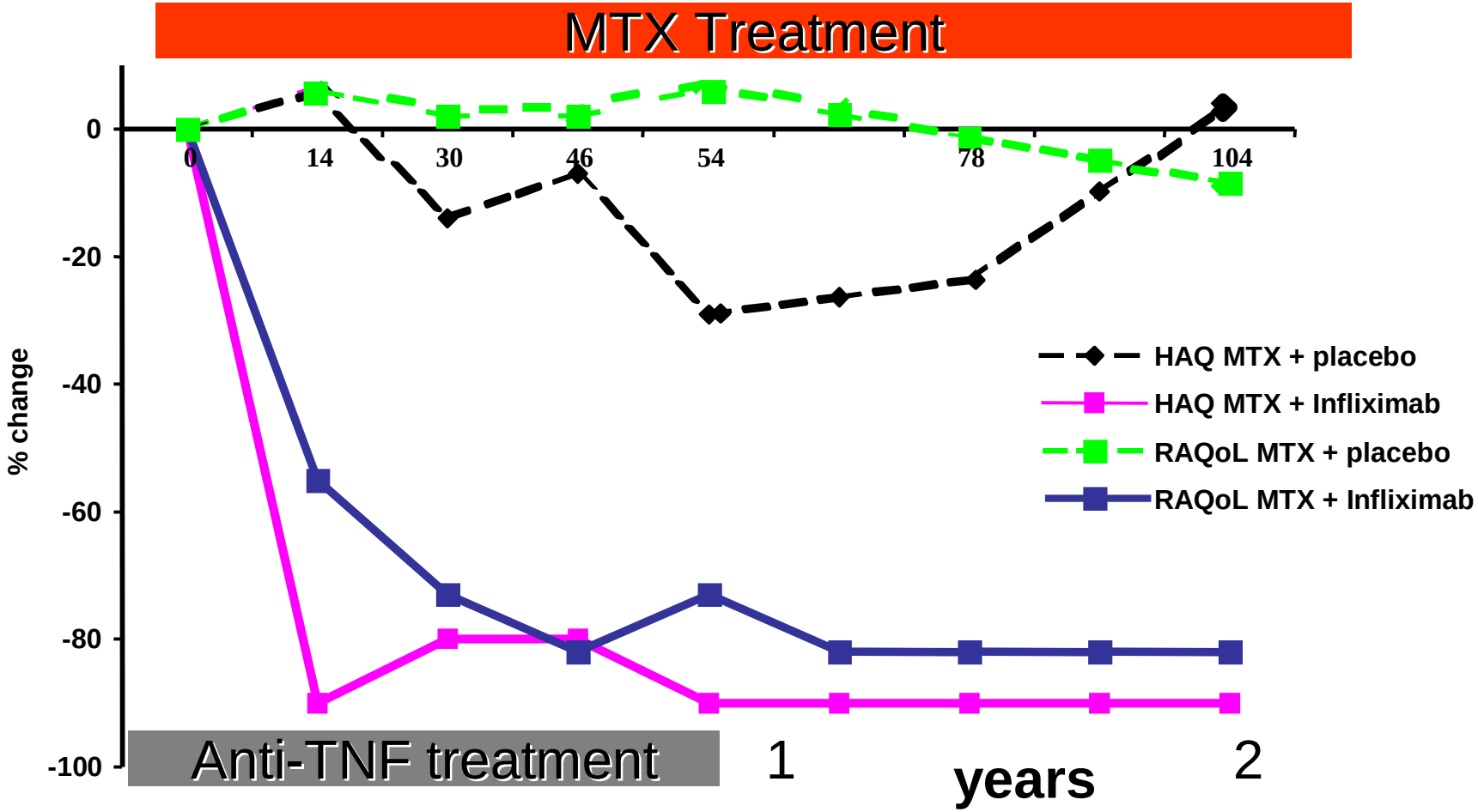
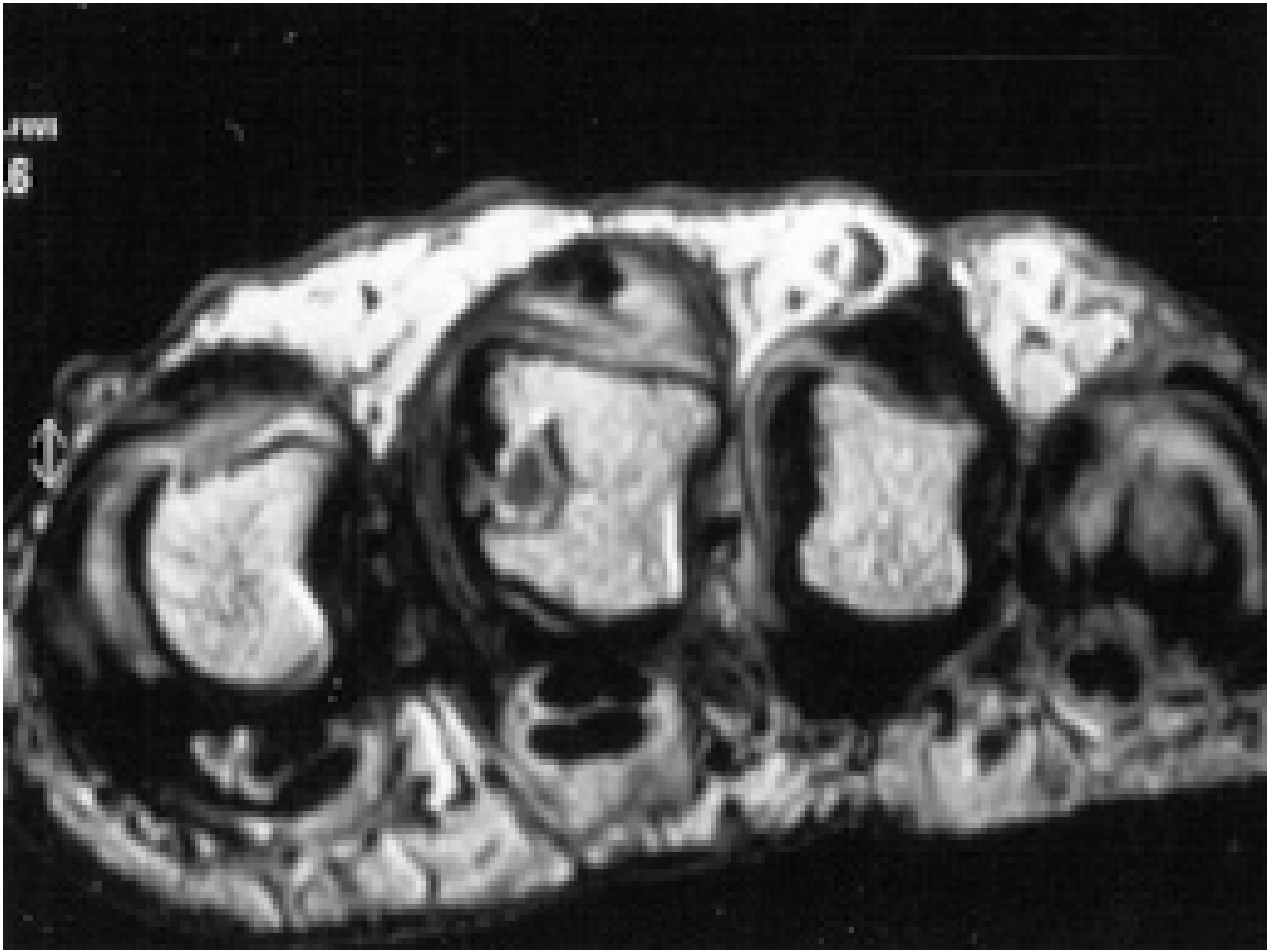
anti-TNF at presentation produces long-lasting benefit (one year after stopping therapy)

Quinn et al Arthritis & Rheum 2005





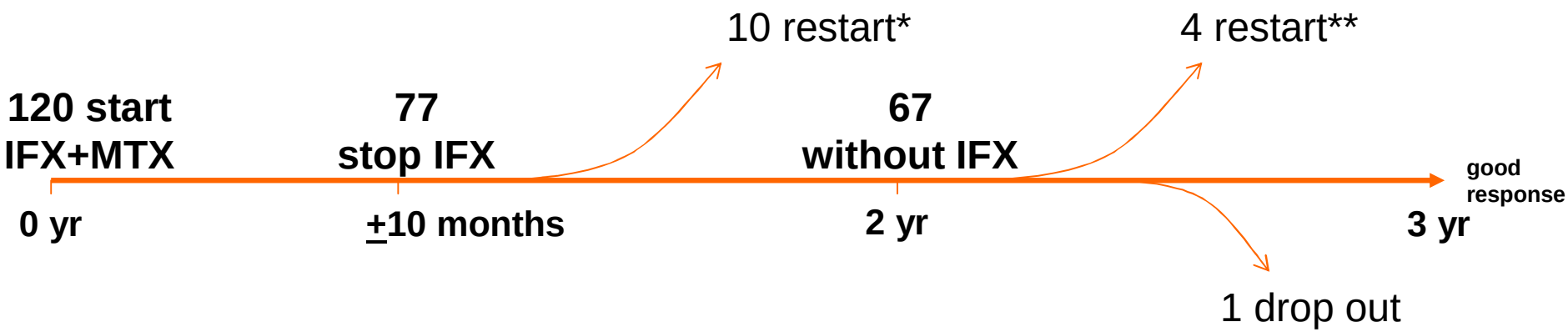
8 year follow-up of 1 year remission-induction regime in early RA

Bejarano et al 2009

- **DAS28** was significantly lower 2.7 vs. 4.3, p=0.02
- **Remission** 4/9 patients(1 off all drugs) vs. 0/9 control patients
  - RAQoL 3 vs. 8, p=0.18;
  - HAQ 1.0 vs. 1.5, p=0.12

BEST Study: long-term Outcome anti-TNF arm

62 without IFX:
44 MTX mono
2 SSA mono
16 **nothing**



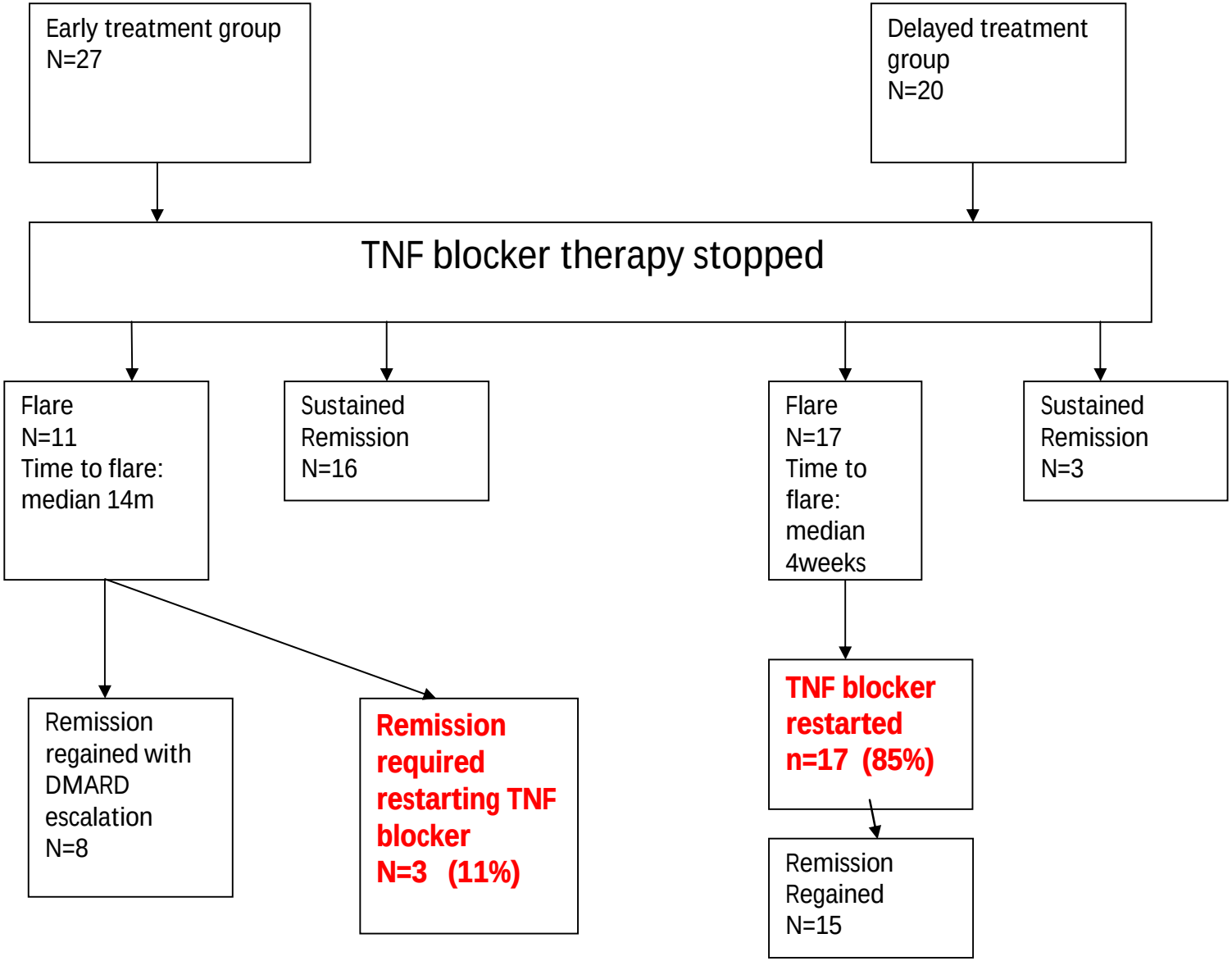
* 8 within 4 months after stop IFX, all within 1 year
** 2 patients restarted IFX, 19 and 24 months after stop IFX. In the other 2 patients, after tapering of MTX, IFX was restarted because no MTX increase was possible (MTX 10 mg/wk was max. tolerated dose).

All patients who restarted IFX again had a good response on IFX, although some needed dose increase.

Remission Questions

- Is there sub-clinical synovitis in patients in remission on DMARDs?
- Does sub-clinical determine structural progression?
- Timing of suppression of synovitis with anti-TNF occur?
- Can clinical findings predict imaging findings?
- What are features of early vs late treatment?
- What are features that allow successful cessation of TNF blockade?
  - Take patients in remission on TNF blockade stop TNF
  - Long-term follow-up

Study Flow chart: Follow-up



Predictive Value of Short Duration and Immunology

- If treated <6 months symptoms:85% stop therapy successfully

- If *both* short duration (<6 months) and normal immunology (T regs) present PPV= 94%

- Window of opportunity for re-setting immunology approx 5 months from symptom onset

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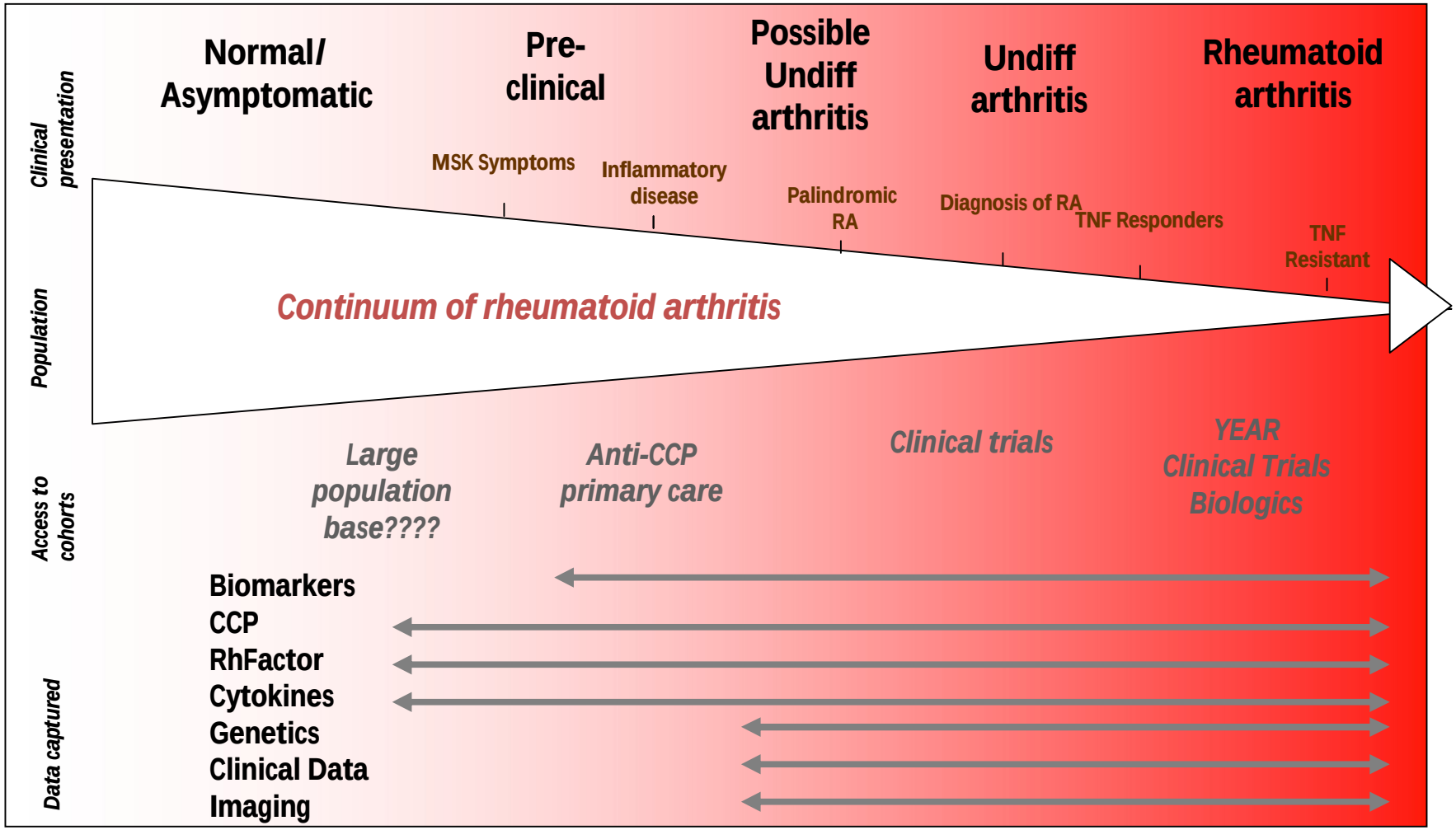
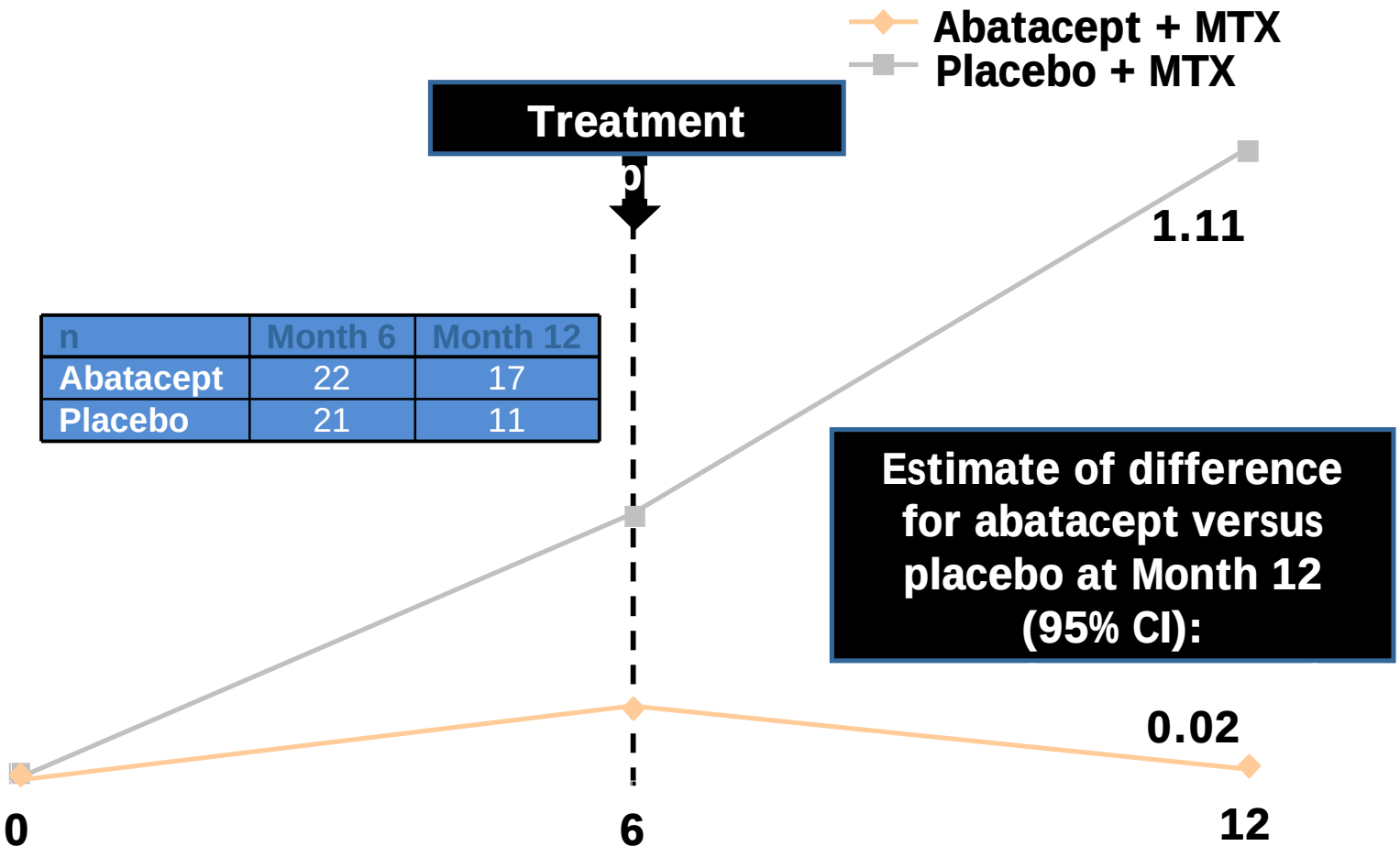
Defining the RA Phenotype



Abatacept Provides Radiographic Benefits Which Persist Beyond Therapy Cessation: Total Sharp Score

ADJUST



n	Month 6	Month 12
Abatacept	22	17
Placebo	21	11

Population: all randomized and treated patients with available data at the visit of interest (as-observed)

Key Messages

- RA is treatable, damage is preventable
- Most patients are not treated optimally
- Changing paradigms
  - Acceptable outcome has changed
- Conventional DMARDs rarely produce true remission

- Remission off drugs now possible and is the current optimal aim
- Will not be achieved under NICE guidelines