Personalized dose reduction based on serum TNF-inhibitors concentration do not lead to changes in disease activity in chronic arthritis: A randomized controlled trial

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Abstract

OBJECTIVES: We hypothesized that Therapeutic Drug Monitoring (TDM) decreased drug consumption or accelerated switch of biologics in chronic arthritis patients undergoing TNF-alpha inhibiting (TNFi)-therapy. Primary outcome was dose reduction, secondary outcomes included clinical scores DAS28-CRP or ASDAS-CRP, self-reported outcome and experienced adverse events. METHODS: 48-week prospective, randomized open-label trial investigating TDM in participants (n=239) treated with infliximab (IFX), etanercept (ETN) or adalimumab (ADA), receiving standard of care or standard of care plus TDM, the latter based on serum-trough concentration measurements of IFX, ETN and ADA. Independent of clinical status, adults treated for their rheumatoid arthritis (41%), psoriatic arthritis (20%), or spondylarthritis (39%), were included in a tertiary outpatient clinic. Serum TNFi trough-values were determined at inclusion and every 16 weeks and used proactively in the TDM-group to evaluate whether participants were within the therapeutic window or not, consequently leading to maintained TNFi-therapy, dose-reduction, or switch to other biologics. RESULTS: In comparison to standard of care, TDM reduced doses for IFX (- 12% [CI: -20; -3] p=0.001); ETN (-15 % [-29; 1]; p=0.01) and prolonged the inter-dosing interval in ETN (+ 235 %;[38;432] p=0.02) and ADA (+ 28%;[6; 51] p = 0.04) and accelerated switch of biologics ($\chi 2$= 6.03, p=0.01). No group-differences were shown in clinical assessment CRP, DAS28-CRP or ASDAS-CRP, nor in self-reported outcome or experienced adverse events, indicating sustained disease control. * CONCLUSIONS – TDM improved clinical decision making and caused earlier and targeted dose-reduction and accelerated switch of biologics, thereby preventing over- and under medication.

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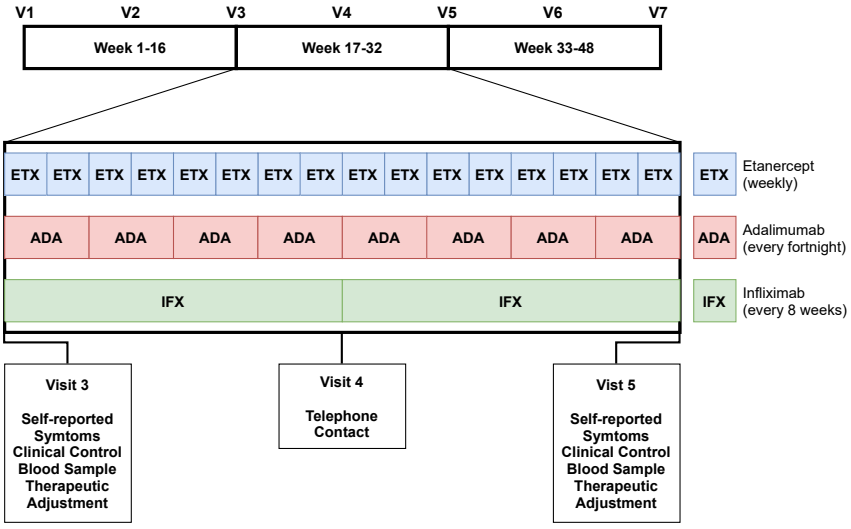

Figure 2: Drug consumption

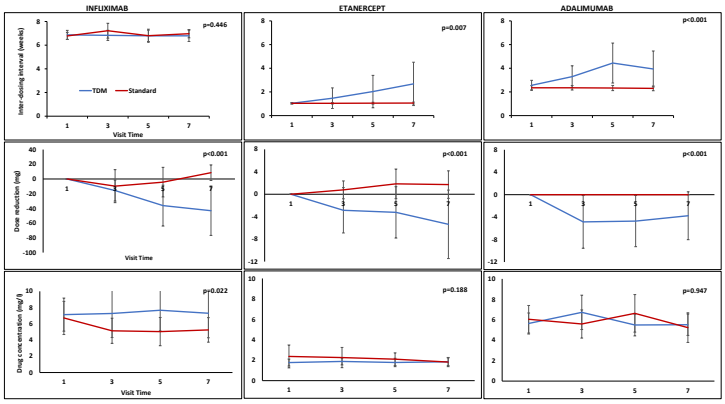

Figure 3: Clinical outcomes

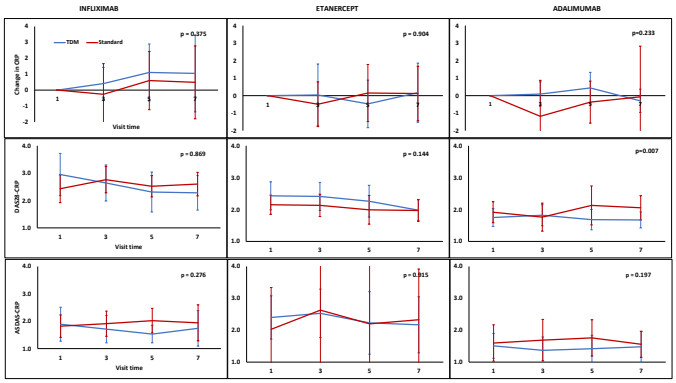

Figure 4: Self-reported outcomes