An evaluation of the design of clinical trials conducted for rheumatoid arthritis, 2009-2022

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Objectives

The aim of this study was to evaluate trends in study design and comparators used in clinical trials conducted for rheumatoid arthritis (RA).

Methods

Phase 3 clinical trials in RA with published results and global or cross-continental recruitment between 2009-2022 were identified through ClinicalTrials.gov.

These studies were used to look for trends, including calculating point biserial correlation coefficients and associated p-values to characterise the relationship between trial design and year of study completion.

Results

Of the 100 studies identified, 26 were active comparator-controlled, 35 had a single-arm design, 22 were placebo-controlled, 14 were placebo + background therapy-controlled, and 3 trials were active comparator + placebo-controlled. Between 2009 and 2022, there was a significant increase in the yearly proportion of trials conducted with an active comparator (Figure 1, correlation coefficient 0.6, p = 0.02).

Furthermore, there was a significant decrease in the yearly proportion of trials conducted with a placebo-controlled design (Figure 2, correlation coefficient -0.6, p = 0.01) or a placebo + background therapy-controlled design (Figure 3, correlation coefficient -0.8, p < 0.01).

There was no significant change in the yearly proportion of trials with an active comparator + placebo-controlled design (correlation coefficient 0.0, p = 1.00) or single-arm design (correlation coefficient 0.3, p = 0.22).

Figure 1. Active comparator - controlled trial

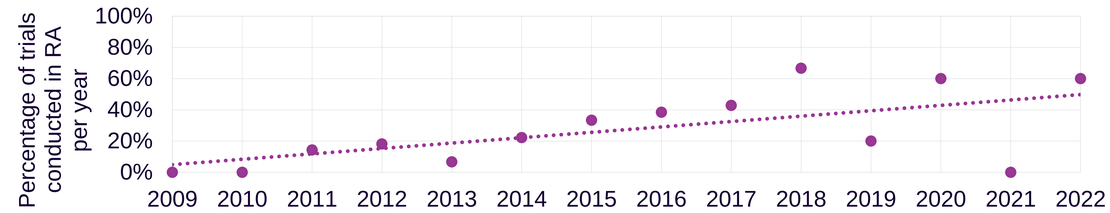


Figure 2. Placebo controlled trial

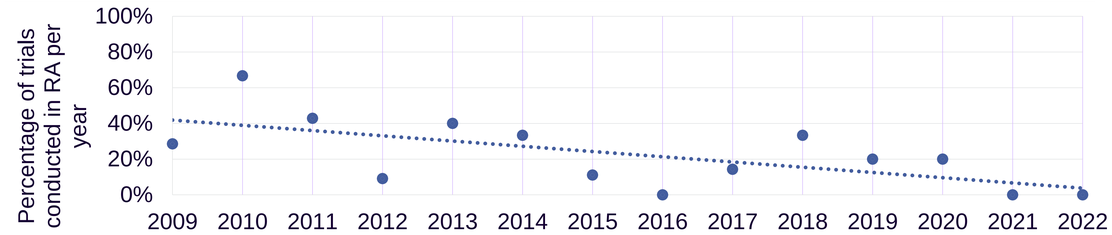
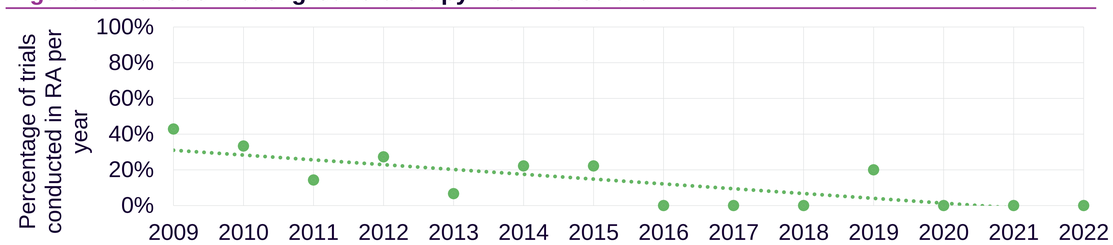


Figure 3. Placebo + background therapy - controlled trial



Conclusion

Although there has been an increase in active comparator-controlled trials and decrease in placebo/placebo + background-controlled trials since 2009, an assessment of European treatment guidelines from 2010-2022 shows there has been little change in the number of recommended treatments for RA patients in that time period. This suggests that treatment availability is not a key driver of increased uptake of active-comparator trial designs.

As such, it can be concluded that the recent shifts in trial design preferences shown in this study may instead reflect the development of a greater focus on medical ethics, with patients increasingly receiving some form of active treatment for their disease.

References: clinicaltrials.gov