INTRODUCTION

- Treatment benefit is demonstrated by evidence that interventions have positive impacts on how patients feel, function, and/or survive (FDA Regulation 21CFR314.510).
- The ACR CRIS is a composite endpoint for trials in diffuse systemic sclerosis (dcSSc) with outcome assessments that are direct measures of patient symptom/function/survival.
- Understanding the relationship and magnitude of effects on these indirect assessments would provide confidence that each component of CRIS would reliably predict an effect on direct measures of patient benefit.

OBJECTIVE

To provide data to support evaluation of CRIS using patient-reported outcomes (PRO’s) anchors, i.e. HAQ-DI and PGA.

METHODS

- We evaluated 2 cohorts: an early diffuse cutaneous SSC (dcSSc) cohort used for development of ACR CRIS (CRIS cohort [1]) and a phase 2 trial of tocilizumab vs. placebo in dcSSc [faSScinate trial cohort (2)].
- We assessed the effect size (ES) at the patient-level for non-PRO variables (mRSS, MDGA, and FVC%)
- We defined “responders” as subjects who met minimal clinically important differences (MCID) estimates for HAQ-DI (improvement of ≥ 0.22) and PGA (improvement of ≥ 1.0, range 0-10). We also explored MCID estimates of PGA improvement ≥ 2.0.
- We interpreted the ES using the Cohen’s criteria [< 0.20 = negligible, 0.20-0.49 = small, 0.50-0.79 = medium, >0.80 = large] (3).
- We assessed whether ES in subjects classified as responders (HAQ-DI and PGA) in the faSScinate trial was associated with larger improvements in the ACR CRIS score at week 24 and 48.

RESULTS

- In the CRIS cohort - (a) ES were generally of greater magnitude for responders vs. non-responders (Table 2), except for HAQ-DI and FVC% when using PGA as an anchor, (b) ES for MDGA was non-significant for responders vs. non-responders, despite large magnitude likely due to the small sample size.
- In the faSScinate trial cohort, statistically significant improvements in the median ACR CRIS scores were seen in those who attained MCID vs. patients who did not.

CONCLUSION

- In a dcSSc cohort, patients who achieved MCID in HAQ-DI and PGA were associated with larger magnitude of improvement in ACR CRIS non-PRO variables.
- HAQ-DI and PGA are part of the ACR CRIS score. This is a limitation of this analysis.
- Ongoing trials should confirm the relationships between non-PRO variables (mRSS, MDGA, and FVC%) vs. PRO anchors.

REFERENCES