Figure. Cumulative mortality of patients with idiopathic inflammatory myopathy and matched controls without IIM in early versus late cohorts (1999-2006 versus 2007-2014).

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OP0248 PREMATURE MORTALITY BURDEN FOR SYSTEMIC SCLEROSIS: NATIONWIDE POPULATION-BASED STUDY

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Background: Premature mortality is an important way to quantify disease burden. Patients with systemic sclerosis (SSc) can die prematurely of disease, however, the premature mortality burden of SSc is unknown. The years of potential life lost (YPLL), in addition to age-standardized mortality rate (ASMR) in younger ages, can be used as measures of premature death.

Objectives: To evaluate the premature mortality burden of SSc by calculating: 1) the proportions of SSc deaths as compared to deaths from all other causes (non-SSc) by age groups over time, 2) ASMR for SSc relative to non-SSc-ASMR by age groups over time, and 3) the YPLL for SSc relative to other autoimmune diseases.

Methods: This is a population-based study using a national mortality database of all United States residents from 1968 through 2015, with SSc recorded as the underlying cause of death in 46,798 deaths. First, we calculated the proportions of deaths for SSc and non-SSc by age groups for each of 48 years and performed joinpoint regression trend analysis¹ to estimate annual percent change (APC) and average APC (AAPC) in the proportion of deaths by age. Second, we calculated ASMR for SSc and non-SSc causes and ratio of SSc-ASMR to non-SSc-ASMR by age groups for each of 48 years, and performed joinpoint analysis to estimate APC and AAPC for these measures (SSc-ASMR, non-SSc-ASMR, and SSc-ASMR/non-SSc-ASMR ratio) by age. Third, to calculate YPLL, each decedent's age at death from a specific disease was subtracted from an arbitrary age limit of 75 years for years 2000 to 2015. The years of life lost were then added together to yield the total YPLL for each of 13 preselected autoimmune diseases.

Results: 23.4% of all SSc deaths as compared to 13.5% of non-SSc deaths occurred at <45 years age in 1968 ($p < 0.001$, Chi-square test). In this age group, the proportion of annual deaths decreased more for SSc than for non-SSc causes: from 23.4% in 1968 to 5.7% in 2015 at an AAPC of -2.2% (95% CI, -2.4% to -2.0%) for SSc, and from 13.5% to 6.9% at an AAPC of -1.5% (95% CI, -1.9% to -1.1%) for non-SSc. Thus, in 2015, the proportion of SSc and non-SSc deaths at <45 year age was no longer significantly different. Consistently, SSc-ASMR decreased from 1.0 (95% CI, 0.8 to 1.2) in 1968 to 0.4 (95% CI, 0.3 to 0.5) per million persons in 2015, a cumulative decrease of 60% at an AAPC of -1.9% (95% CI, -2.5% to -1.2%) in <45 years old. The ratio of SSc-ASMR to non-SSc-ASMR also decreased in this age group (cumulative -20%, AAPC -0.3%). In <45 years old, the YPLL for SSc was 65.2 thousand years as compared to 43.2 thousand years for rheumatoid arthritis, 18.1 thousand years for dermatomyositis, 146.8 thousand years for myocarditis, and 241 thousand years for type 1 diabetes.

Conclusion: Mortality at younger ages (<45 years) has decreased at a higher pace for SSc than from all other causes in the United States over a 48-year period. However, SSc accounted for more years of potential life lost than

rheumatoid arthritis and dermatomyositis combined. These data warrant further studies on SSc disease burden, which can be used to develop and prioritize public health programs, assess performance of changes in treatment, identify high-risk populations, and set research priorities and funding.

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OP0249 LONG-TERM EXTENSION RESULTS OF RISE-SSC, A RANDOMIZED TRIAL OF RIOCIQUAT IN PATIENTS WITH EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC)

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Background: RISE-SSc (NCT02283762) was a multicenter Phase IIb trial of riociguat in pts with early (duration ≤ 18 months) dcSSc and modified Rodnan skin score (mRSS) 10–22 units. Pts were randomized double-blind to placebo or riociguat 0.5–2.5 mg t.i.d. for 52 weeks. The primary endpoint, mRSS change from baseline to Week (Wk) 52, did not reach statistical significance ($p = 0.08$, riociguat vs placebo), but there were favorable trends in some other outcomes.

Objectives: To present open-label long-term extension (LTE) results of RISE-SSc.

Methods: Pts who completed Wk 52 of double-blind therapy could enter LTE on riociguat. Endpoints included mRSS, adverse events (AEs), and serious AEs (SAEs).

Results: Of 60 pts randomized to riociguat and 61 to placebo, 42 (riociguat–riociguat group) and 45 (former placebo group), respectively, entered LTE. At LTE start, mean $\pm$ SD mRSS was 16.4 $\pm$ 3.2 and 16.3 $\pm$ 4.2 units, and mean disease duration was 8.9 $\pm$ 7.8 and 8.9 $\pm$ 5.8 months, in the riociguat–riociguat and former placebo groups, respectively. Other demographics/disease characteristics were also comparable. Median duration of riociguat treatment was 1092 d in riociguat–riociguat pts and 649 d in former placebo pts. Throughout the study, mRSS decreased in both groups (Figure 1). From Wk 52 to last visit, mRSS fell by -3.02 ± 5.51 in riociguat–riociguat patients and -3.96 ± 5.43 in former placebo pts. Rates of mRSS regression (decrease by > 5 units and $\geq 25\%$ from Wk 52 to last visit) and of % declines in mRSS were similar in the two groups (Figure 2). mRSS progression (increase by > 5 units and $\geq 25\%$ from Wk 52 to last visit) occurred in 1 pt (2%) in each group. During the entire study, rescue therapy agents were used in 15 (36%) riociguat–riociguat pts and 17 (38%) former placebo pts. AEs were reported from Wk 52 to last visit in 82 pts (94%): 40 (95%) riociguat–riociguat and 42 (93%) former placebo. Most common AEs overall: nasopharyngitis (24%), gastroesophageal reflux disease (17%), diarrhea (15%), and hypotension (14%). AEs of special interest (dizziness, postural dizziness, or hypotension) occurred in 5 riociguat–riociguat pts (12%) and 4 former placebo pts (9%). SAEs were reported in 21 (24%) pts: 10 (24%) riociguat–riociguat pts and 11 (24%) former placebo pts, with no SAE reported in > 1 patient, no SAEs of special interest, and no deaths.

Conclusion: During LTE riociguat treatment, mRSS decreased in both groups from Wk 52 onwards and mRSS progression was uncommon. Riociguat had acceptable safety, similar to the main study, with no new safety signal.