Abstract OP0044 – Figure 1 Adjusted HR (solid black line) and 95% CIs (grey line) for all-cause mortality, over time since cohort entry

Conclusions: In 2 large Canadian RA population-based inception cohorts, a small increased mortality risk appeared after 6 years of RA duration and increased to a 14% (in BC) and 13% (in ON) increased risk after 10 years. While these findings represent an improvement in the mortality risk associated with RA compared to previous reports in older historical cohorts, the increasing mortality risk associated throughout the disease course suggests increased efforts to prevent disease progression and optimise comorbidity management are needed.

Disclosure of Interest: None declared

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OP0045 ADVERSE EVENT REPORTING RATES AND PLACEBO/STANDARD-OF-CARE-ARM ACR RESPONSES VARY BY REGION IN RHEUMATOID ARTHRITIS TRIALS

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Background: Clinical trials are increasingly globalised, with more trials conducted in Asia, Latin America, and the Russian Federation and Eastern Europe (RFEE).¹ Adverse event (AE) reporting rates and placebo (or standard-of-care-arm) response may differ by geographic region and level of economic development²⁻⁴; efficacy and safety may not be generalizable across regions. This potential heterogeneity and its implications for rheumatoid arthritis (RA) trials have not been studied in detail.

Objectives: To assess potential regional differences in rates of ACR responses and AE reporting using patient-level data (PLD) from RA trials in the TransCelerate initiative.⁵

Methods: We obtained PLD for all 17 RA trials available through TransCelerate as of August 2017 and analysed data from 7 trials with geographic information available (NCT01198002, NCT01202760, NCT01202773, NCT01404585, NCT00605735, NCT00048581, NCT00647270). We grouped patients by region and evaluated differences in demographics, AE reporting rates, and ACR response. Pairwise comparisons were made between regions using Fisher's exact test, with false discovery rate (FDR) correction for multiple comparisons. All patients were included in analyses of AE reporting. Only patients with data sufficient to calculate ACR scores were included in analyses of ACR response. Demographics for patients in each region are shown in table 1.

Results: The lowest rates of AE reporting and ACR50 response were seen in RFEE. The highest rate of ACR20 response was seen in Asia. After FDR

correction, significantly lower 12 week and 52 week AE reporting rates were seen in RFEE than in Asia, Latin America, or the United States. Only the ACR50 response difference between RFEE and Latin America survived FDR correction; however, ACR20 rates in Asia remained significantly higher than in RFEE and the United States (table 2).

Abstract OP0045 – Table 1 Patient demographics by region

Region	AE Analysis, n	ACR Response Analysis, n	Female, %	Median Age, y (SD; range)
US	369	268	81	55 (11; 21-78)
RFEE	213	160	81	51 (12; 25-79)
Latin America	167	132	89	51 (12; 22-76)
Asia	164	107	88	52 (12; 18-83)

Abstract OP0045 – Table 2 Proportions of patients attaining ACR50/20 response at 12 week and/or reporting ≥ 1 AE at 12 and 52 weeks across regions

Attaining ACR50	6	9 ^a	7	1
Attaining ACR20	17	24	29 ^{a,b}	15
With AE at 12 weeks	53 ^a	49 ^a	51 ^a	22
With AE at 52 weeks	68 ^a	58 ^{a,b}	65 ^a	39

^ap < 0.05 vs RFEE. ^bp < 0.05 vs US. All p values corrected for multiple comparisons.

Conclusions: Patient-level data from placebo arms in the TransCelerate initiative revealed significant regional differences in AE reporting rates and ACR50/ACR20 response rates. Differences in Latin America, RFEE, and Asia were especially notable; future patient populations from these regions may show distinct efficacy/safety profiles regardless of treatment. Given ongoing globalisation of clinical trials, country- and region-specific treatment patterns, patient populations, and safety issues should be explored to avoid misguided inferences across regions. Capping recruitment by region to balance these factors may be warranted.

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WEDNESDAY, 13 JUNE 2018: Immunobiology of vasculitis

OP0046 EFFECT OF A SELECTIVE C5aR ANTAGONIST, AVACOPAN (CCX168), ON PLASMA COMPLEMENT LEVELS IN ANCA ASSOCIATED VASCULITIS (AAV)

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Background: The interaction between primed neutrophils and anti-neutrophil cytoplasmic autoantibodies (ANCA) releases factors that activate the alternative complement pathway, initiating an amplification loop that is thought to sustain necrotizing inflammation during flares of AAV.¹ Avacopan (CCX168), a selective, orally available, small molecule C5aR1 antagonist, was associated with rapid clinical benefit in the Phase 2 CLEAR trial in patients with AAV,² indicating that therapeutic intervention in this pathogenic process can be accomplished by inhibiting the C5aR1-dependent cellular response to C5a, without broad inhibition of upstream complement functions important to host defense.

Objectives: The present study was designed to confirm the reported elevated levels of complement activation products in AAV,² demonstrate that inhibiting cellular (e.g. neutrophil) activation by C5a with avacopan is effective in AAV while preserving upstream functions of complement, and compare effects of avacopan to those of high dose prednisone.

Methods: The CLEAR trial compared 3 regimens in 67 patients with AAV:¹ full dose prednisone (60 mg daily, tapered);² avacopan 30 mg twice daily plus low dose prednisone (20 mg, tapered);³ avacopan 30 mg twice daily plus no