Factor H preserves alternative complement function during ARDS linked to improved survival

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Supplemental Materials

Table S1: Summary of key characteristics of included cohorts

Cohort	Dates of enrollment	Key Inclusion Criteria	Key Exclusion Criteria	Biospecimens
LARMA	February 1998 - June 1999	ARDS[1]	Chronic medical conditions including respiratory failure; estimated 6-month mortality>50%; age<18	Serum
SAILS	March 2010 – September 2013	ARDS[1] with known or suspected infection	Chronic medical conditions ; >5 times ULN of CK/AST/ALT	EDTA Plasma
ALIR	October 2011 - December 2017	ARDS[2,3]; Age 18-90 years	Chronic respiratory failure; tracheostomy; hemoglobin <8 g/dL	Serum

Abbreviations: ALIR = University of Pittsburgh Acute Lung Injury Registry and Biospecimen Repository cohort; ALT = alanine transaminase; ARDS = acute respiratory distress syndrome; AST = aspartate transaminase; CK = creatine kinase; LARMA = Lisofylline And Respiratory Management of Acute lung injury clinical trial cohort; SAILS = Statins for Acutely Injured Lungs from Sepsis clinical trial cohort; ULN = upper limit of normal.

[1]Acute respiratory distress syndrome was defined in the LARMA and SAILS trials by the 1994 American-European Consensus Conference on ARDS as described in "Bernard GR et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994 Mar;149(3 Pt 1):818-24. doi: 10.1164/ajrccm.149.3.7509706."

[2]Acute respiratory distress syndrome was defined in ALIR by the 2012 Berlin Definition as described in "Acute Respiratory Distress Syndrome: The Berlin Definition**,** JAMA. 2012;307(23):2526-2533. doi:10.1001/jama.2012.5669."

[3]ALIR inclusion criteria are not limited to ARDS. However, the analyses in this paper are limited to those subjectsnin ALIR diagnosed with ARDS, N=107.

Table S2: Comparison of meta-analyses using random and fixed effects models

Meta-Analysis	Fixed Effect HR (95% CI)	I^2	Random Effect HR (95% CI)	I^2
AH50>Median	0.65 (0.45-0.96)	0.00%	0.66 (0.45-0.96)	0.00%
Factor B<25% percentile	1.99 (1.44-2.75)	0.00%	1.98 (1.42-2.77)	4.56%
Factor H<25 percentile	1.52 (1.09-2.11)	0.00%	1.52 (1.09-2.11)	0.00%

Abbreviations: CI = confidence interval; HR = hazard ratio for mortality; I^2 = heterogeneity statistic

Supplemental Figures

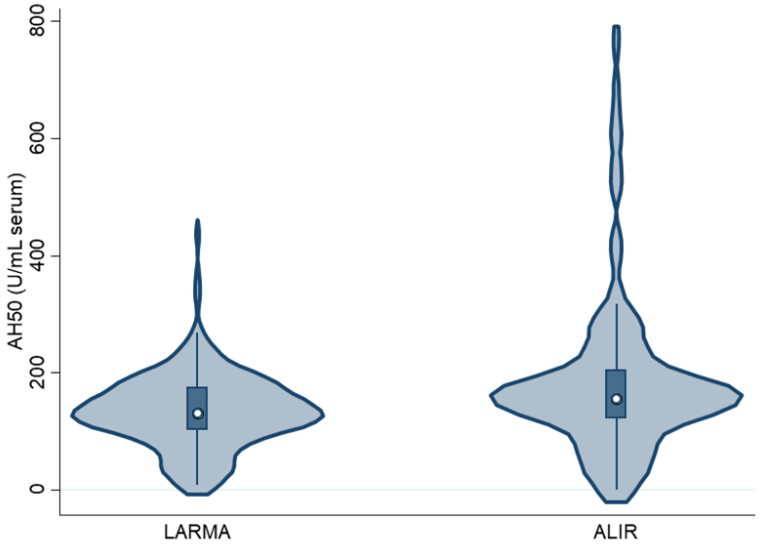

Figure S1. Distribution of AH50 values in the ALIR and LARMA cohorts.

In the LARMA cohort (N=218), median AH50 was 131 U/mL with inter-quartile range 102-175 U/mL. In the ALIR cohort (N=107), median AH50 was 155 U/mL with inter-quartile range 123-206 U/mL.

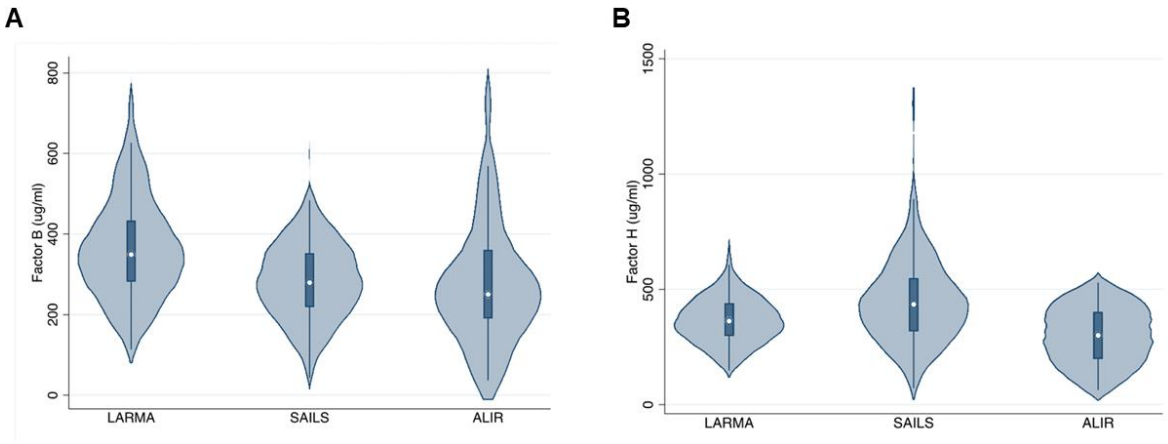

Figure S2. Distribution of circulating levels of Factor B and Factor H in LARMA, SAILS, and ALIR cohorts.

(A) Factor B levels in LARMA (N=218, µg/mL; median 349, IQR 282-433), SAILS (N=224, µg/mL; median 280, IQR 219-353), and ALIR (N=69, µg/mL; median 250, IQR 190-361). The median Factor B level in pooled reference serum from healthy adults was 366 µg/mL (IQR 285-378).

(B) Factor H levels in LARMA (N=218, µg/mL; median 363, IQR 298-440), SAILS (N=224, µg/mL; median 435, IQR 318-549), and ALIR (N=69, µg/mL; median 301, IQR 199-402). The median Factor H level in pooled reference serum from healthy adults was 454 µg/mL (IQR 401-482).