Long-Term Transplant-Free Survival is Improved in Hypoplastic Left Heart Syndrome with Cell-Based Therapy

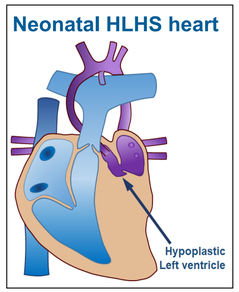
Sunjay Kaushal, Eric Naioti[1], Kevin N. Ramdas[1], Danial Mehranfard[1], Lisa McClain-Moss[1], Michael Davis[2], Shaji C Menon[3], Narutoshi Hibino[4], David Morales[5], Linda M. Lambert[3], S. Adil Husain[3], Kaitlyn Masih[6], Kristopher Deatrick[6], Sarah Speed[5], Joshua M. Hare[1,7], Anthony A. Oliva[1]

[1] Longeveron Inc., Miami, FL. [2] Emory School of Medicine, Atlanta, GA [3] University of Utah, Primary Childrens Hospital [4] University of Chicago [5] Cincinnati Childrens Hospital
[6] University of Maryland, School of Medicine [7] University of Miami Miller School of Medicine.

Background

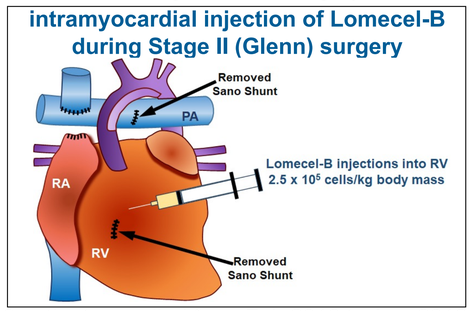
Hypoplastic left heart syndrome (HLHS):

- Congenital heart defect
- Life-saving heart reconstruction
  - Right ventricle (RV) supports systemic circulation.
- Mortality remains high
- Improving transplant-free survival is an important unmet medical need



ELPIS Phase 1 Trial I (NCT03525418) [1]

- Lomecel-B™ as adjunct treatment to standard-of-care HLHS Stage II HLHS surgery



- 10 patients enrolled from Feb 2018 to Aug 2019
  - All received Lomecel-B
- Key enrollment criteria
  - HLHS (all types)
  - No significant coronary artery sinusoids.
  - No required mechanical circulatory support
  - No evidence of arrhythmia requiring anti-arrhythmia therapy
  - No need for aortic coarctation or tricuspid valve repair
- Primary Endpoint: safety
  - Incidence of major adverse cardiac events (MACE) through 1 year post-treatment
  - Infection during first month post-treatment
- Trial met primary endpoint
- We present long-term follow-up results on the patients through 5 years post-treatment.

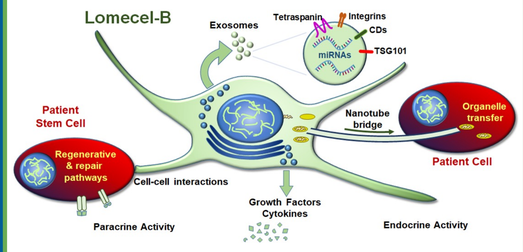
Contacts

Anthony A. Oliva, Ph.D.
aoliva@longeveron.com

Kevin N. Ramdas, MD, MPH
kramdas@longeveron.com

Lomecel-B™

- Allogeneic mesenchymal stem cell (MSC) formulation



- Multiple mechanisms of action favorable to potentially improving HLHS outcomes
  - Pro-regenerative and repair
  - Anti-fibrotic
  - Pro-vascular
  - Anti-inflammatory

SVR Trial Historical Comparator [2,3]

- Initial comparison included all SVR trial patients matching ELPIS enrollment criteria and shunt type.
- Inverse probability of treatment weighting (IPTW, i.e., propensity weighting) performed via:
- Weighting by average treatment effect of the treated patients (ATT)
- Weighting by average treatment effect (ATE).

SVR Trial: 549 patients enrolled
- 139 (25.3%) died prior to Stage II surgery
- 9 (1.6%) received heart transplant prior to Stage II surgery
- 1 (0.2%) missing information on Stage II surgery

SVR Trial: 400 (72.9%) patients underwent Stage II surgery

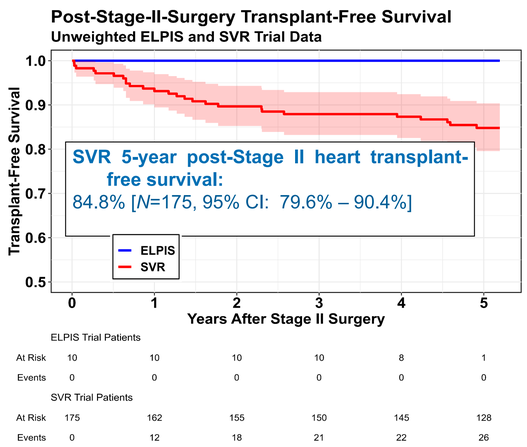
SVR Trial: 175 (31.9%) patients matched ELPIS enrollment criteria *and* received the RVPA (Sano) shunt
- 2 (1.1%) excluded due to missing body measurements

SVR Trial: 173 (31.5%) patients used for IPTW analyses

Post-Stage II Surgery Heart Transplant-Free Survival in ELPIS and SVR Trial

Stage II Baseline Demographics	ELPIS	SVR
Included subjects (*N*)	10	175
Age at Stage II surgery (months)	4.89±0.85	5.07±1.52
Males [*n* (%)]	7 (70.0)	115 (65.7)
Race and ethnicity		
White [*n* (%)]	7 (70.0)	143 (81.7)
Black/African American [*n* (%)]	3 (30.0)	24 (13.7)
Non-Hispanic/Latino [*n* (%)]	10 (100.0)	137 (78.3)
Length at pre-Stage II visit (cm)	61.8±3.7	61.2±4.0
Weight at pre-Stage II visit (kg)	6.1±0.7	5.9±1.0
Duration of injection (min)	5.5±1.78	NA
RVPA shunt at Stage I [*n* (%)]	10 (100)	175 (100)
Total anomalous pulmonary venous connection (TAPVC) [*n* (%)]	1 (10)	2 (1.1)
Moderate or Severe TR [*n* (%)]	0 (0)	39 (22.3)

Scores are mean ± SD) unless otherwise indicated



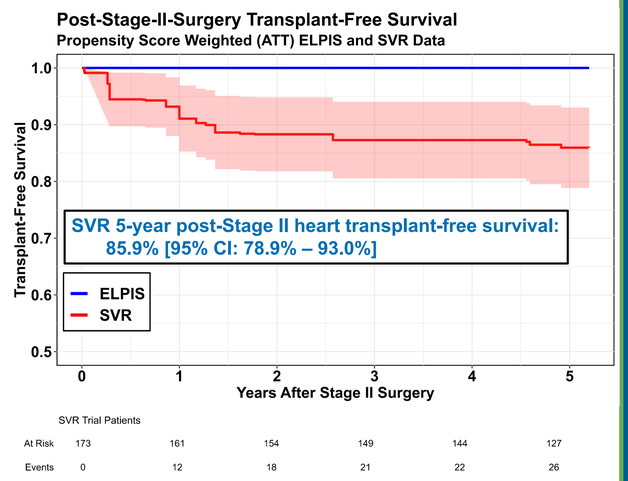
ELPIS Trial
- All 10 patients (*blue line*) alive and transplant-free at last follow-up
- Average age: 4.5 years
  - Min, Max: 3.8, 5.2 years

SVR Trial historical comparison
- 175 patients used for comparison
- 196 patients stating with:
  - HLHS
  - RVPA (Sano) shunt
  - Underwent Stage II surgery
- 21 excluded since would have failed ELPIS enrollment criteria
  - 7 – ECMO at Stage I or II
  - 7 – aortic arch repair at Stage II
  - 7 – AV valve repair at Stage II

Propensity Weighted Analysis

Variable	ELPIS[% or mean (SD)]	SVR [% or mean (SD)]	St. Mean Diff.
Male	70%	67.6%	0.054
African American	30%	24.2%	0.127
Age at pre-Stage II visit (days)	131.8 (23.76)	132.8 (39.51)	-0.043
Weight at pre-Stage II visit (kg)	6.1 (0.72)	6.1 (0.94)	0.101
Height at pre-Stage II visit (cm)	61.8 (3.73)	61.6 (4.07)	0.070
Age at Stage II surgery (days)	147.9 (25.90)	149.4 (39.96)	-0.058
Total anomalous pulmonary venous connection (TAPVC)	10%	2.8%	-0.242
Moderate or Severe TR	0%	0%	0.000

- Calculated using covariates shown in the table
- Yielded 173 SVR Trial patients for analysis.
- Best overall matching using ATT approach
- ATE yielded similar results
  - Mean 84.8%
  - 95% CI: 79.3% – 90.2%



Limitations

- Small sample size of ELPIS trial
- Comparison to an historical control rather than internal control arm.

Conclusions

- Results suggest that, when used as an adjunct to standard-of-care Stage II surgery, Lomecel -B™ may be able to extend the transient short-term transplant-free survival benefits of the RVPA shunt into long-term benefits.
- These results support continued development of Lomecel-B™ for HLHS.
- We are currently enrolling in a double-blinded, Phase 2 trial (ELPIS II) to evaluate Lomecel-B™ efficacy (ClincalTrials.gov: NCT04925024).

Acknowledgements

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References

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