Phoenix Children's

# From Phoenix to Philadelphia to Berlin and Back: A Berlin Heart Journey

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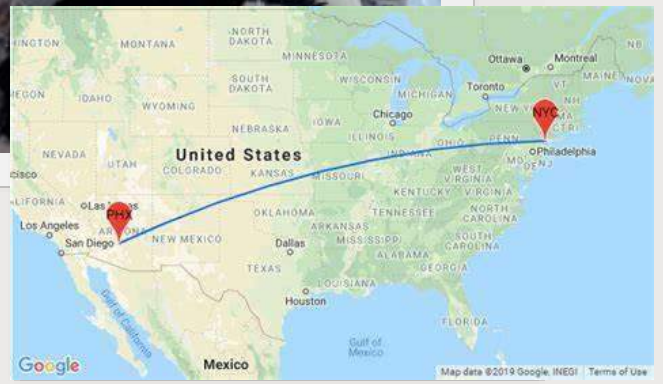
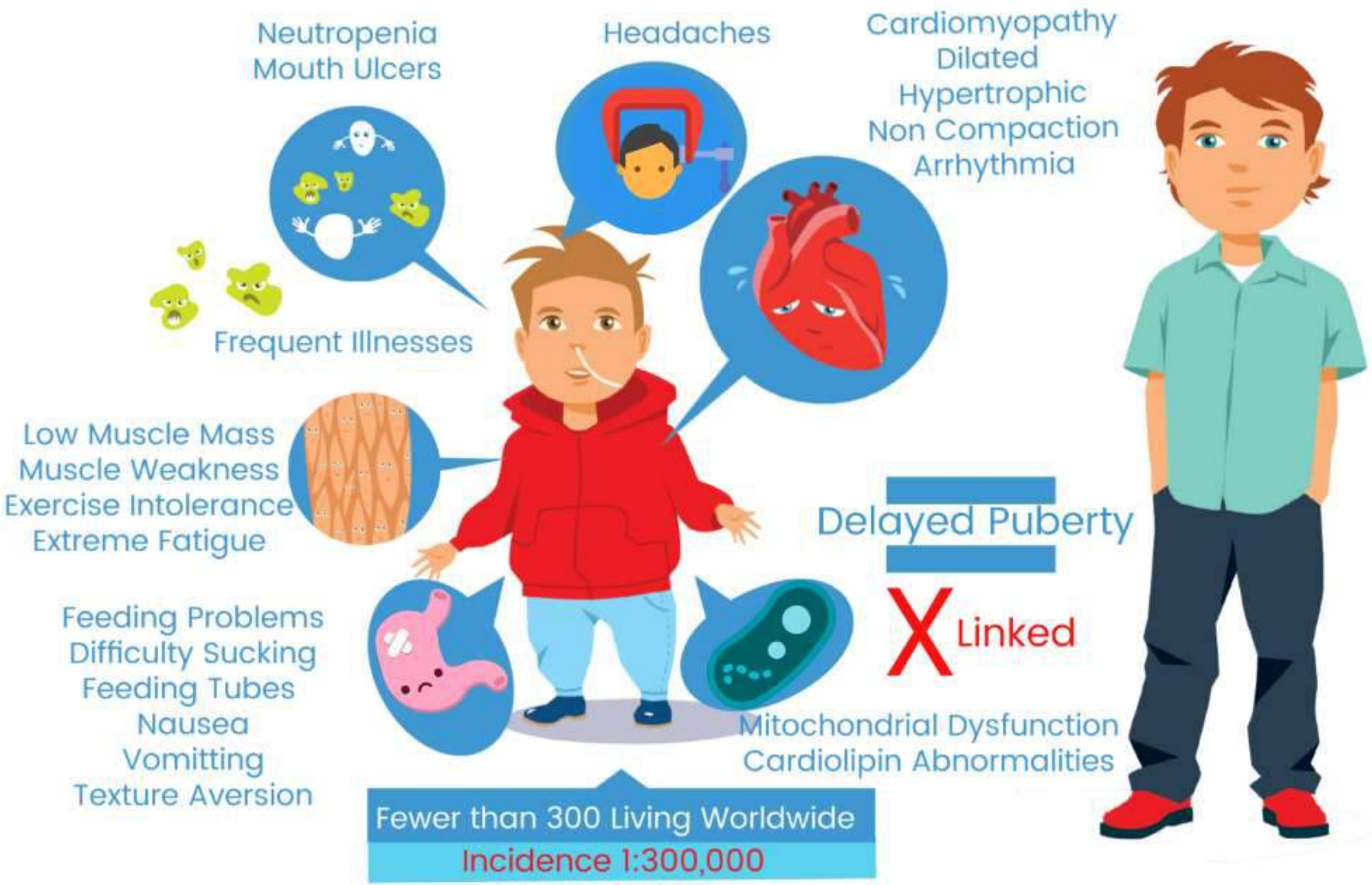
# The Journey Begins

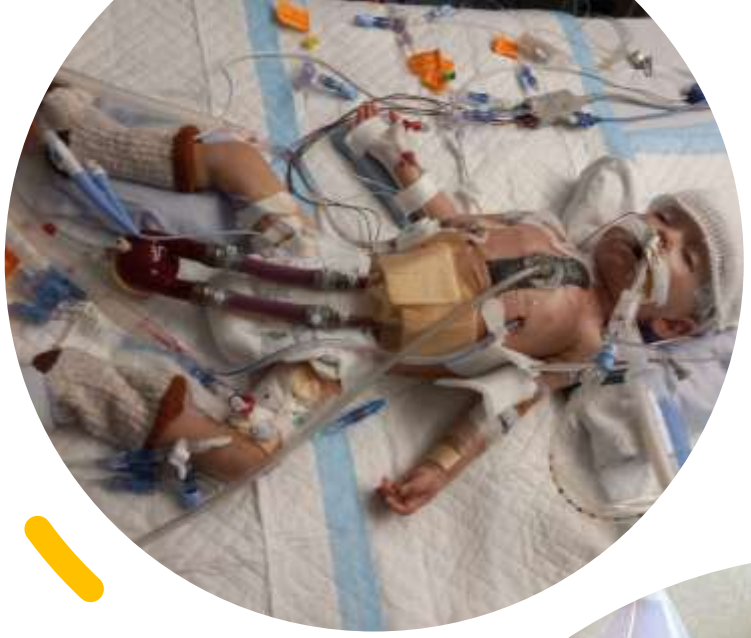
- Low birth weight, but no red flags
  - Happy, playful baby
- At 11 months old, travels with mom from AZ to NJ to visit family for the holidays
- Baby presents to ED
  - Diagnosed with rhinovirus
  - Condition continued to deteriorate
  - Cardiac arrest
- Presented to CHOP in cardiogenic shock
- VA ECMO for 15 days
- Diagnosed with Barth Syndrome and DCM



# What is Barth Syndrome



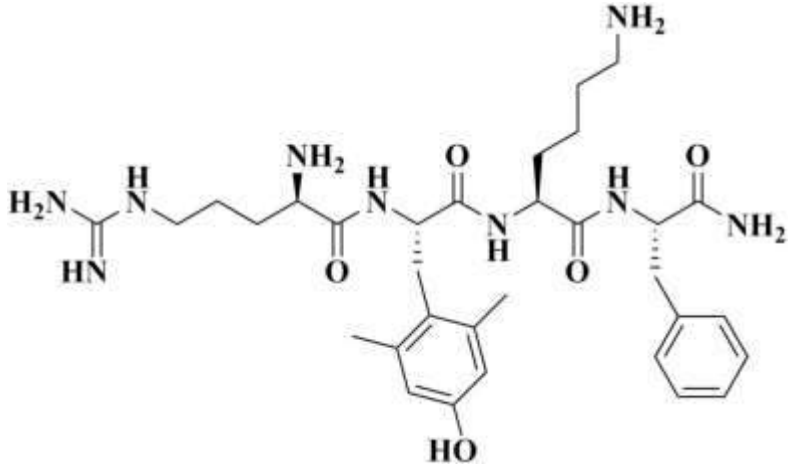
# Onward to Berlin



- 13 days post-VA ECMO
- Berlin Heart LVAD implanted
  - 15 mL pump
  - 5 mm aortic cannula
  - 6 mm LV apex cannula
  - Rate 90 bpm
- Granted compassionate use approval for elamipretide treatment
- Listed for heart transplant at CHOP
- ~5 months (3.5 months on elamipratide) on Berlin Heart, heart starts showing signs of recovery
  - Failed turn-down attempt
- Family wants transferred to Phoenix Children's to be closer to home

# Elamipretide

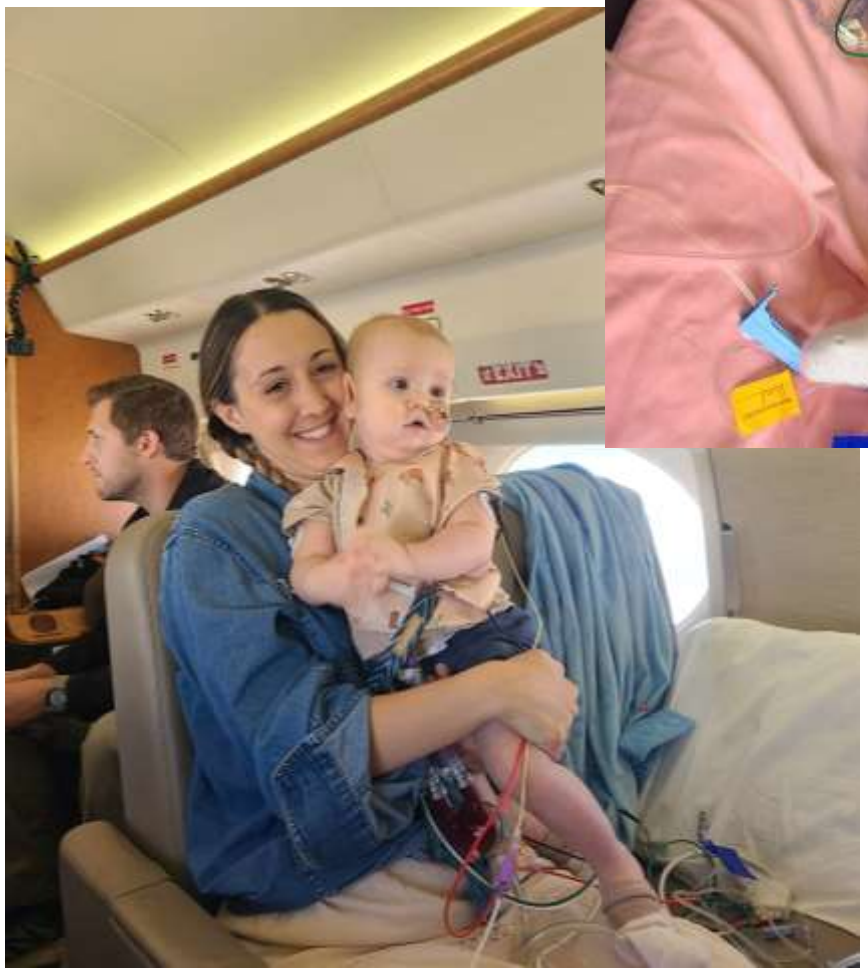
- Investigational drug to treat cardiomyopathy in Barth syndrome patients
- Targets mitochondrial dysfunction in energy-starved myocytes
- Facilitates cell health by improving ATP production and inhibiting oxidative stress and stabilizes cardiolipin
- Improves LVEF
- Lowers LVEDP
- Reduces cardiomyocyte and ventricular hypertrophy
- Limits myocardial fibrosis
- Shown to improve bioenergetics and morphology rapidly (within hours or days) in Barth syndrome patients




- Most Barth syndrome patients do not have access to elamipratide
- FDA has not reviewed data to consider it for approval for Barth syndrome
  - Very small patient population
- Patients lucky enough to have it are at the will of the compassionate use approval
- Advocacy groups have started a petition to FDA for a fair, equitable, and appropriate review for approval in Barth syndrome patients

# Philadelphia to Phoenix

- Very complicated transport
  - Insurance
  - Hospital politics
  - Staffing
  - Equipment
  - Aircraft capabilities
- VitalOne Air Medical Transport
  - Specialize in high-risk medical transport
  - Took care of transportation arrangements when hospital backed out
  - Agreed to transport before having insurance approval
  - Ensured aircraft was capable
  - Team included a nurse practitioner, perfusionist (from Berlin Heart), two flight/aircraft mechanics, critical care flight medic, pediatric cardiac intensivist, and mom
- Air transport with Berlin Heart
  - No special protocol
    - Watch for full fill, full eject
  - Extra IKUS on and running
  - Full set of disposables



# Arrival to Phoenix – BH Day 164, PCH Day 1

- Continued improvement in cardiac function
  - Suction events
    - Rate dropped from 90 to 80 BPM
- BH day 172
  - Successful acute weaning challenge
  - Decreased rate to 60 bpm
  - No change in ventricular function, NIRS, or heart rate
  - Mixed venous blood gas and lactate within normal range
  - Plan for further turn-down test

# Berlin Heart Weaning Procedure

- Weaning may be considered in patients who meet the following criteria
  - LVEDD within normal limits (<98$^{th}$ percentile, or Z-score of +2)
  - EF = 45%
  - Lactate <3 mmol/L
  - No clinical evidence of thromboembolism or bleeding
  - Anticoagulation markers within target parameters
- Weaning can be divided into five steps and generally takes one week to complete
  - Day 0 – acute weaning challenge
  - Day 1-4 – Graduated weaning challenge with echo
  - Day 5 – Pump stoppage with invasive hemodynamic assessment with afterload challenge
  - Day 6 –pump stoppage with invasive hemodynamic assessment in OR (fully anticoagulated)

- Weaning Sequence
  1. Heparinize (75 units/kg, max 5000 units)
  2. After 5 minutes, reduce pump rate from initial rate to 30 bpm in increments of 5 bpm q 5 min. after 5 min at 30 bpm, reassess LV size/function
  3. After a total time of **10 min** at 30 bpm, stop pump for 3 min and reassess LV. Use manual pump to pump twice q30 sec to prevent stagnation/clot formation.
  4. After 3 min pump stop, reconnect pump to Ikus and resume at new reduced rate
- Time spent at 30 bpm (step 3) increases to 20 min, 30 min on subsequent wean trials
- On wean trial days 3 and 4, initiate exercise and gentle age-appropriate play while at 30 bpm
- Final trial – after 3 minutes off pump, initiate norepinephrine infusion at 0.01 mcg/kg/min to MAP 20% above baseline for 5 minutes.
  - If echo and physiological parameters are stable, go forward with explant

# Continued Recovery

- Day 175
  - Rate decreased to 30 bpm for 20 minutes
  - No change in ventricular function, NIRS, heart rate, or blood pressure
  - Mixed venous blood gas and lactate within normal range
  - Rate increased to 60 bpm for the weekend
- Day 179
  - Went to cath lab for clamp-off trial
  - Cannulas clamped
  - No change in ventricular function, NIRS, heart rate, or blood pressure
  - Back up to 60 bpm
- Day 182
  - Repeated pump off trial
  - Again successful trial
  - Plan for explant

# Explant Day – BH Day 187, PCH Day 24

- Patch repair of aorta
- Ventriculotomy closed in layers and buttressed with felt strip
  - CPB: 80 minutes
  - XC: 70 minutes
  - Cool to 32
- Brief run of ventricular tachycardia and ST segment elevation upon cross clamp removal
  - Resolved spontaneously
- TEE showed mild-moderate ventricular dysfunction, but otherwise normal echo
- Returned to CVICU with open chest
  - Significant change in CO when retractor was removed – significant pectus
  - Increased CVP
  - Decreased NIRS
  - Decreased systolic function
  - Decreased BP

# Road to Recovery

- PCH Day 26
  - Chest closed uneventfully
  - Normal physiologic parameters
- PCH Day 27
  - Echo shows normal biventricular function
  - EF ~50-55%
  - Extubated
- PCH Day 31
  - Few tachycardia episodes and fever overnight
    - Concern for infection vs cardiac failure
    - Viral panel negative
    - Echo is reassuring
  - Slowed down transition to oral heart failure meds
  - Possibly over-diuresed
  - Parents felt very strongly about minimizing narcotic and Tylenol use

# Final Approach

- PCH Day 33
  - Transferred to step down unit
  - EF 55%
- PCH Day 37
  - On all oral meds
  - Working on education with family and medication optimization
  - EF 55%
- PCH Day 43
  - DISCHARGED!
  - Family stayed at Ronald McDonald House in immediate-discharge days

# Life At Home

- Multiple follow-up appointments
- Echo continues to be favorable
  - EF ~65% consistently
  - Normal RV and LV size and function
- One event of slightly elevated HR and BP
  - Resolved within 48 hours with no intervention
  - Likely viral illness
- Declan’s mom has become very active in advocating for FDA approval of elamipretide use in Barth syndrome

Thank You!

# References


- https://nottooraretocare.org
- Goldstein, A., MD (2023, December 27). *FDA Okayed Life Saving Drug for Baby, Yet Access for 129 Young Americans with Same Ultra-Rare Disease Hangs in the Balance as FDA Declines Review*. Real Clear Health. Retrieved January 2, 2024, from https://www.realclearhealth.com/blog/2023/12/07/expanded_access_compassion_or_cop-out_997271.html#!
- Barthsyndrome.org