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OF NEW JERSEY

UNIVERSITY HOSPITAL
Newark, New Jersey

VTL-308 A Randomized, Open-label, Multicenter, Controlled, Pivotal Study to Assess Safety and Efficacy of ELAD® in Subjects with Alcohol-Induced Liver Decompensation (AILD)

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- The speaker's views are entirely his own and do not necessarily reflect the views of Rutgers – The State University of New Jersey, Rutgers New Jersey Medical School or Vital Therapies, Inc.

- The speaker has accepted payment for bona fide services from Vital Therapies, Inc. within the preceding five years.

Epidemiology

- Recently accepted manuscript on the burden of illness associated with sAH: accepted for publication in the peer-reviewed journal *Alcohol*
  - Evaluates data set encompassing commercial insurance claims from 2006 to 2013 representing over 40 million insurance enrollees per year†
  - Key Conclusions:
    - Nearly 30,000 patients in the U.S. each year are estimated to suffer from a particularly debilitating form of severe alcoholic hepatitis associated with significant mortality and a hospital stay of at least 3 days.
    - The annual cost for treatment of sAH population is extraordinarily high.
      - The average annual per-patient costs for an alcoholic hepatitis patient were found to be higher than those for heart failure and diabetes patients
    - High rate of re-hospitalization, with over 50% of the survivors re-hospitalized within a year and nearly 75% through the second year

Source: Mortality and Costs Associated with Alcoholic Hepatitis: A Claims Analysis of a Commercially Insured Population, *Alcohol* (2018), Thompson et al

† This research was supported by Vital Therapies

Epidemiology

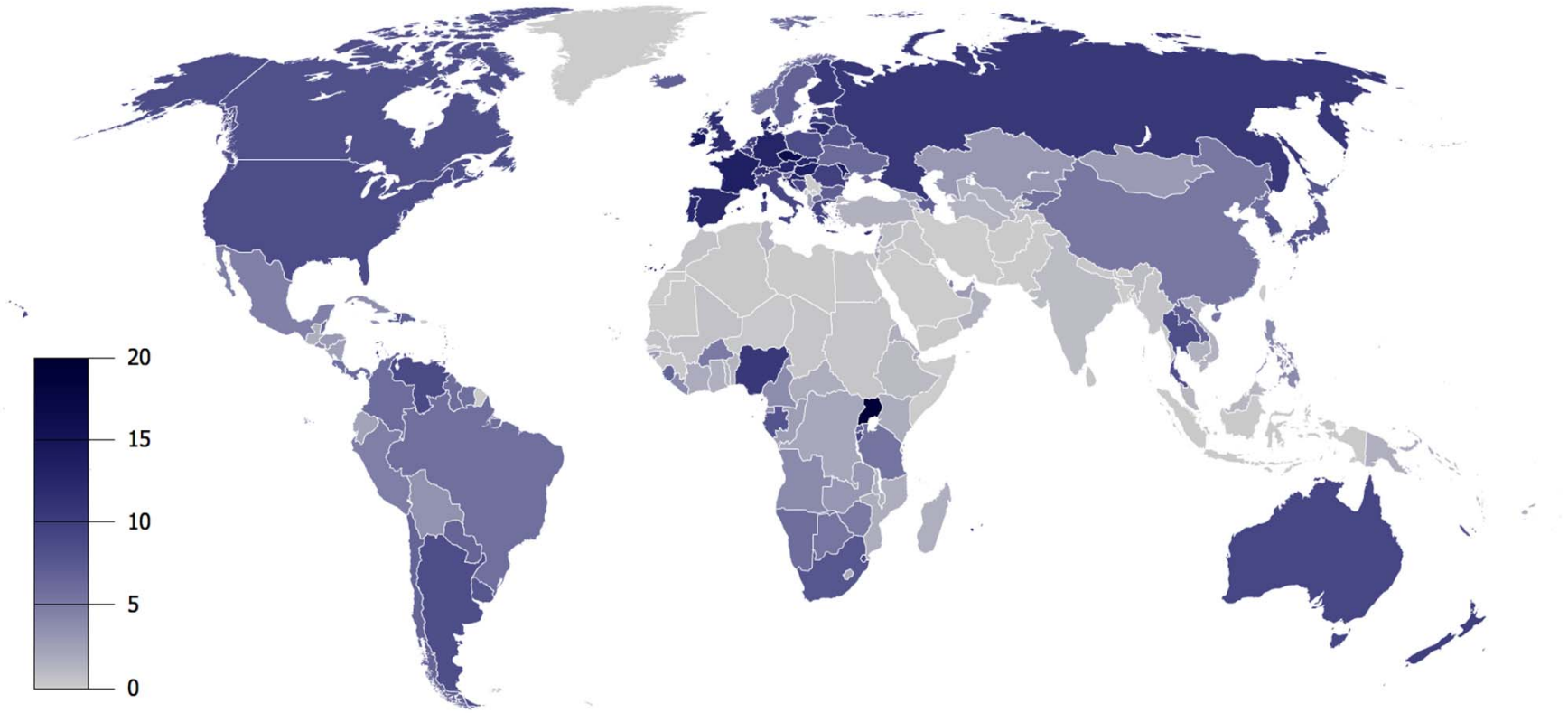
- Department of Health and Human Services (https://hcupnet.ahrq.gov/#setup) estimates that for 2014 the number of hospital admissions related to sAH in the U.S. was approximately 102,000, with approximately 15,000 of these admissions identifying sAH as the primary diagnosis

- In addition, approximately 323,000 hospital admissions occurred in 2014 related to alcoholic cirrhosis, alcohol liver damage not-otherwise-specified or alcoholic fatty liver, with approximately 50,000 hospital admissions identifying these conditions as the primary diagnosis

Epidemiology

- Alcoholic Liver Disease may well be the oldest form of liver injury: fermented beverages were present as early as 10,000 BC.
- Approximately 2/3 of adult Americans drink some alcohol.
- Alcoholic liver disease encompasses a spectrum of injury from simple steatosis to frank cirrhosis.
- Excessive alcohol consumption is the third leading preventable cause of death in the United States.

Total Recorded Alcohol Per Capita Consumption (15+), in Liters of Pure Alcohol



Treatment

- Abstinence
- Corticosteroids
- Pentoxifylline
- Antioxidants
- Nutritional Supplementation

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VTI-208

Major Inclusion / Exclusion Criteria

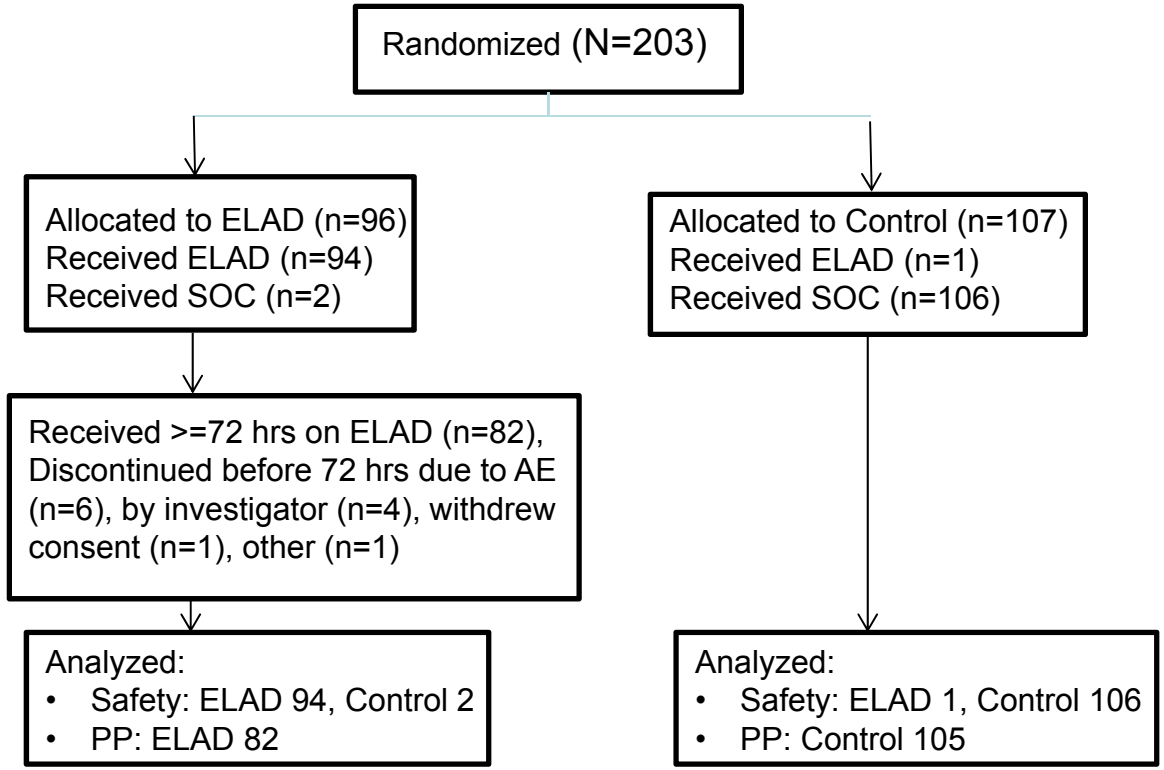
Inclusion

- Age >18
- Total bilirubin ≥8 mg/dL
- EtOH within 6 weeks of onset of symptoms
- Group A (sAAH)
  - Maddrey DF ≥32
  - Liver biopsy or
  - At least 2 out of:
    - Hepatomegaly
    - AST>ALT
    - Elevated WBC
    - Ascites
- Group B (AILD)
  - MELD 18 – 35
  - Histological / laboratory / medical evidence of underlying disease

Exclusion

- Platelets <40,000/mm^3
- INR >3.5
- MELD >35
- AST >500 IU/l
- Bilirubin reduction of >20% in prior 72 hours
- Uncontrolled infection, bleeding or hemodynamic instability
- Small liver size (by imaging)
- Chronic dialysis

Summary of Analysis Populations



Baseline Demographics: ITT Population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)
Randomization Stratum, n (%)			
Subject has AILD that is classified as severe Acute Alcoholic Hepatitis	92 (95.8)	101 (94.4)	**193** (95.1)
Subject has AILD that is not classified as severe Acute Alcoholic Hepatitis	4 (4.2)	6 (5.6)	**10** (4.9)

Baseline Demographics: ITT Population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)
Age (years)			
Mean (SD)	**46.5 (9.06)**	**44.8 (10.66)**	45.6 (9.95)
Median	48.0	45.0	46.0
Min, Max	25, 68	25, 67	25, 68
Age Category, n (%)			
18-35 years	**12 (12.5)**	**25 (23.4)**	37 (18.2)
36-50 years	48 (50.0)	49 (45.8)	97 (47.8)
≥51 years	36 (37.5)	33 (30.8)	69 (34.0)
Sex, n (%)			
Male	55 (57.3)	65 (60.7)	120 (59.1)
Female	41 (42.7)	42 (39.3)	83 (40.9)

Baseline Disease Characteristics: ITT population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)	p-value [1]
Baseline Model for Endstage Liver Disease (MELD) score				
Mean (SD)	**27.6 (3.94)**	**27.1 (3.79)**	27.3 (3.86)	0.371
Median	**27.0**	**27.0**	27.0	
Min, Max	20, 35	20, 35	20, 35	
Category, n (%):				**0.100**
MELD Score <28	**51 (53.1)**	**69 (64.5)**	120 (59.1)	
MELD Score ≥28	**45 (46.9)**	**38 (35.5)**	83 (40.9)	
Serum Creatinine (mg/dL) at Baseline				
Mean (SD)	**1.09 (0.887)**	**0.93 (0.500)**	1.01 (0.712)	**0.116**
Median	0.89	0.80	0.84	
Min, Max	0.2, 6.2	0.1, 3.2	0.1, 6.2	
Total Bilirubin (mg/dL) at Baseline				
Mean (SD)	**26.21 (9.678)**	**24.07 (8.317)**	25.08 (9.027)	**0.092**
Median	25.80	25.00	25.70	
Min, Max	9.3, 56.8	8.6, 44.6	8.6, 56.8	
INR at Baseline				
Mean (SD)	2.01 (0.567)	2.05 (0.489)	2.03 (0.526)	0.580
Median	1.84	1.98	1.90	
Min, Max	1.0, 3.5	1.2, 3.4	1.0, 3.5	
Subject had dialysis at least twice in the past week, n (%)				
Yes	2 (2.1)	0	2 (1.0)	
No	94 (97.9)	107 (100)	201 (99.0)	

Study Disposition: ITT Population

Characteristic	ELAD Treatment (N=96) n (%)	Control (N=107) n (%)	Total (N=203) n (%)
Completed Study to End of Study Day 91			
Yes	50 (52.1)	57 (53.3)	107 (52.7)
No	46 (47.9)	50 (46.7)	96 (47.3)
Primary Reason for Early Discontinuation from the Study			
AE/SAE	0	1 (0.9)	1 (0.5)
Lost to follow-up//non-compliance	5 (5.2)	4 (3.7)	9 (4.4)
Withdrew consent	1 (1.0)	7 (6.5)	8 (3.9)
Death	37 (38.5)	37 (34.6)	74 (36.5)
Liver transplant	0	0	0
Other	3 (3.1)	1 (0.9)	4 (2.0)

Treatment group in the ITT population. Subject 05-02 was randomized to Control but received ELAD Treatment; this subject was included in the denominator for the Control group in the ITT population.

Primary Endpoint
Overall Survival, ITT population, including VTI-208E through 7/30/15

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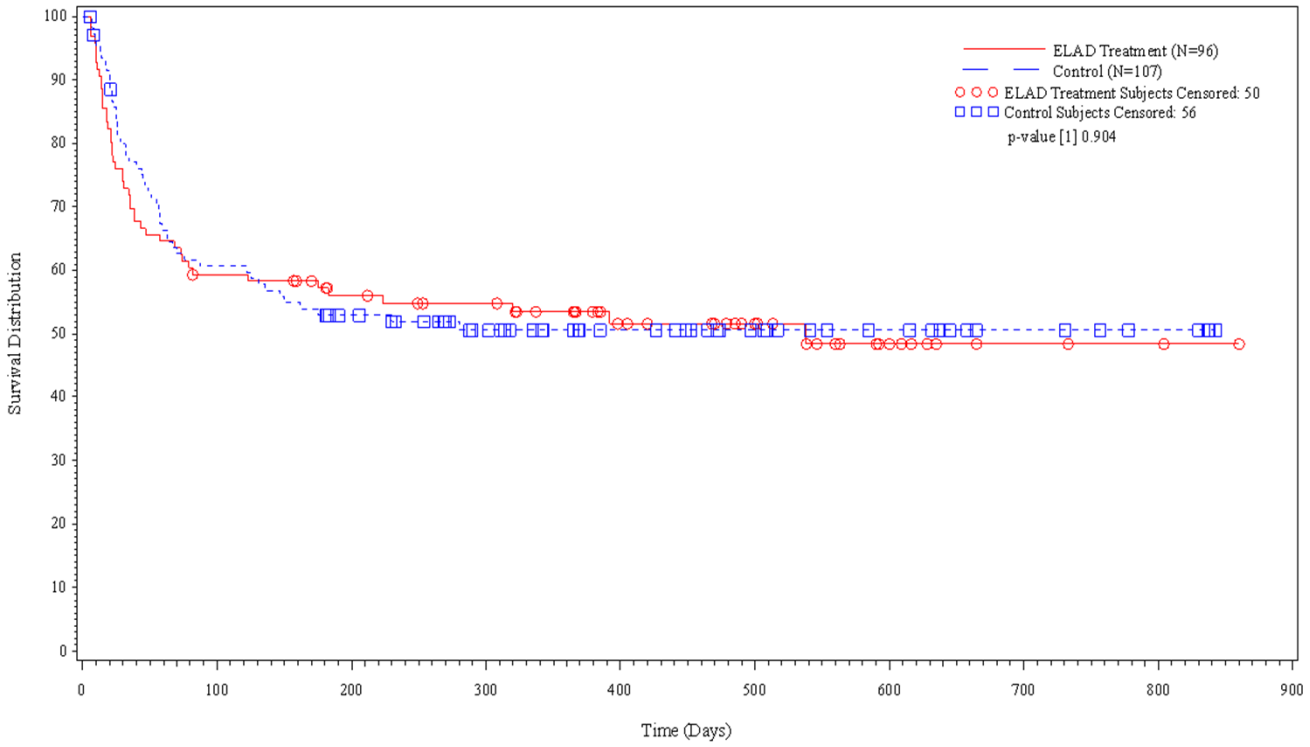
Figure 14.2.1a
Summary of Kaplan-Meier Analysis of Overall Survival
ITT Population



Note: Overall Survival includes data up to at least Study Day 91, with follow-up Protocol VTI-208E providing additional survival data up to a maximum of 5 years.
Subjects with last contact day <91 are considered lost to follow-up.
[1] p-value obtained from log-rank test, stratified by randomization strata.

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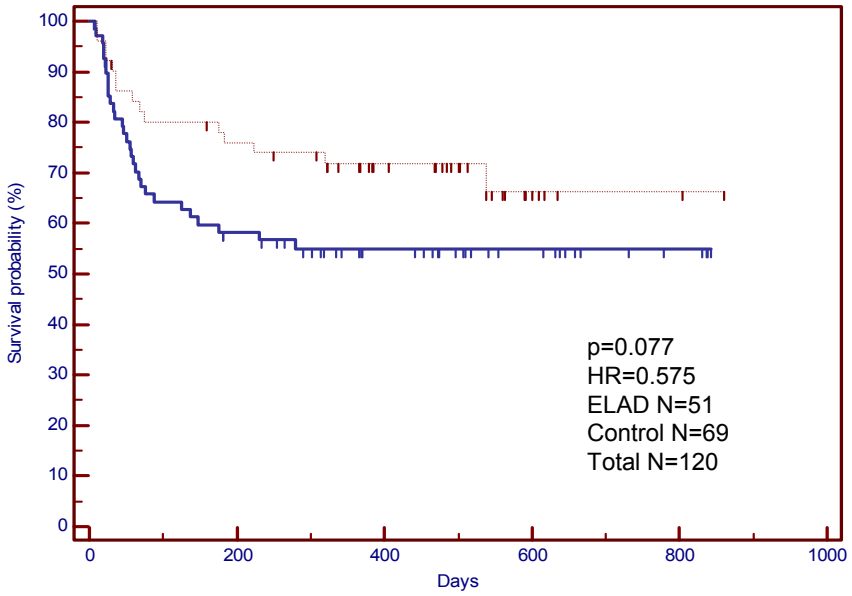
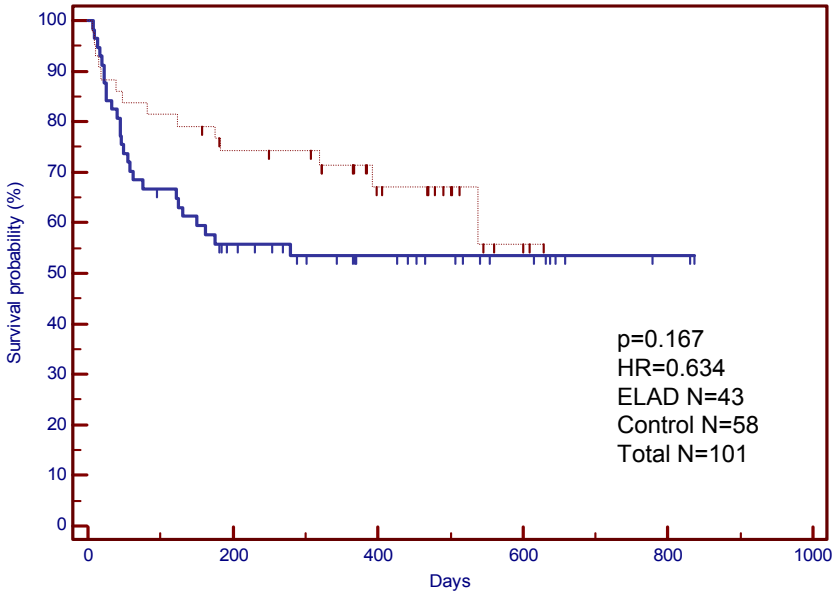
Pre-defined Sub-Group Analyses of VTI-208

MELD <28

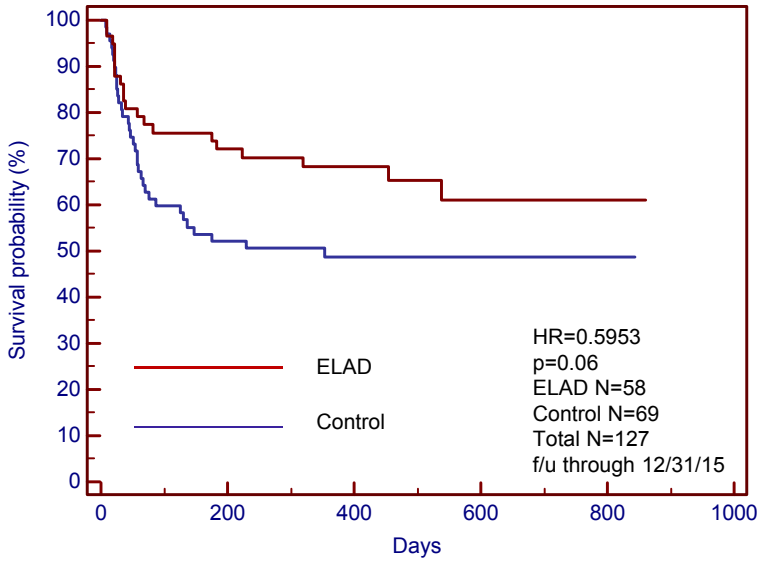


Age <median

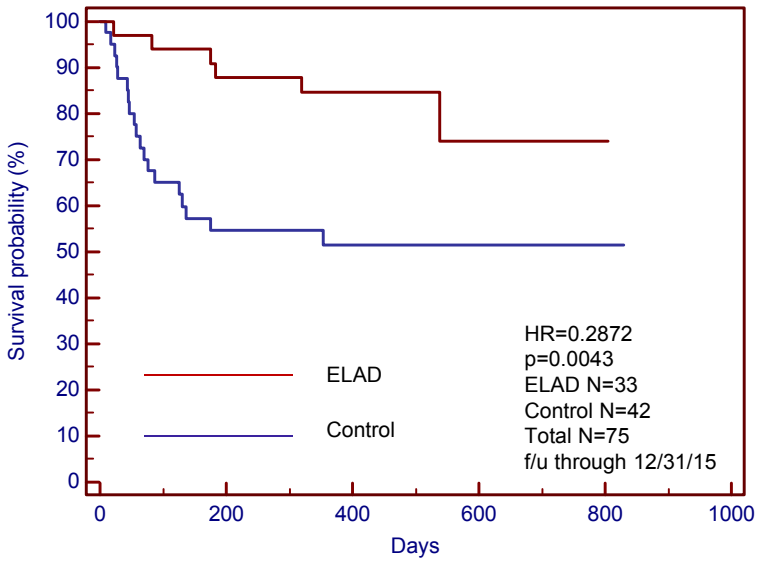


Combined Sub-Group Analyses of VTI-208

Overall Survival: No Multi-organ Failure

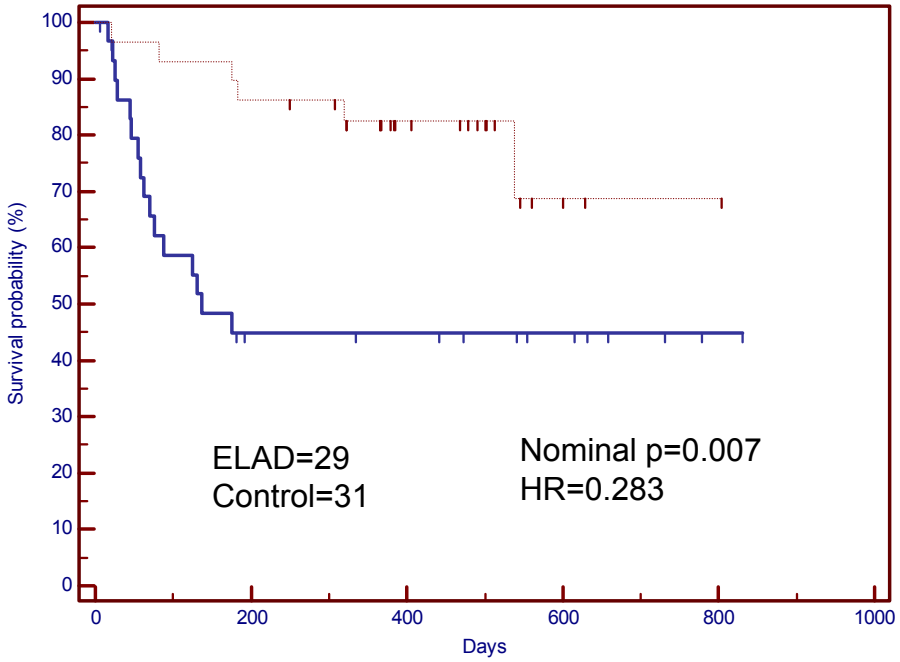


Overall Survival: Younger with no Multi-organ Failure



Post-Hoc Sub-Group Analysis (Hypothesis generating) Age <50, MELD <30, INR ≤2.5, creatinine <1.3mg/dL, bilirubin ≥16mg/dL (proposed VTL-308 study population)

Overall Survival:
(including follow up data through July 31, 2015)



Proportions of Survivors

	91d			180d		
	Alive	LTFU/ WC	Dead	Alive	LTFU /WC	Dead
ELAD	27 (93%)	0	**2 (7%)**	26 (90%)	0	**3 (10%)**
Control	17 (61%)	2	**12 (39%)**	13 (48%)	2	**16 (52%)**
Nominal p-value	**0.004**			**0.0002**		

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VTL-308

Major Inclusion / Exclusion Criteria

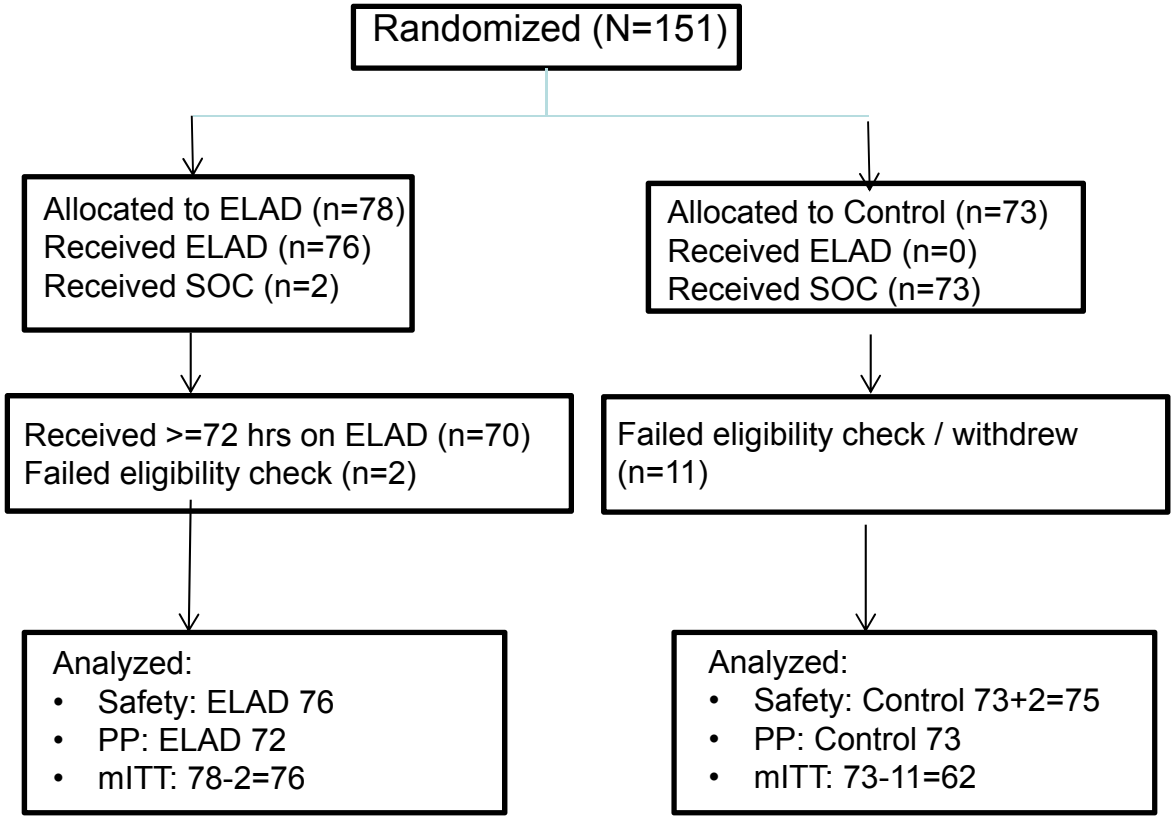
Inclusion

- Age ≥18 and **<50**
- Total bilirubin **≥16** mg/dL
- EtOH within 6 weeks of onset of symptoms
- Clinical Diagnosis of sAH
  - Maddrey DF ≥32
  - Liver biopsy or
  - At least 2 out of:
    - Hepatomegaly
    - AST>ALT
    - Elevated WBC
    - Ascites

Exclusion

- Platelets <40,000/mm^3
- INR **>2.5**
- Creatinine **≥1.3 mg/dL**
- MELD **≥30**
- AST >500 IU/l
- Bilirubin reduction of >20% in prior 72 hours
- Uncontrolled infection, bleeding or hemodynamic instability
- Small liver size (by imaging)
- Chronic dialysis

Summary of Analysis Populations



Demographics / Baseline Characteristics

- Demographics
  - No difference in: Age, ethnicity, sex, race, height, weight
- Baseline Characteristics
  - MELD : ELAD – 24.8 vs 25.6 (p=0.06)
  - No difference in time from hospital admission to randomization, ascites, liver volume, Child-Pugh score,
  - No difference in kidney function, HE grade, sedation, coagulopathy, lung function, CLIF-SOFA score
  - SIRS – slightly higher in ELAD than Control, does not seem to impact mortality

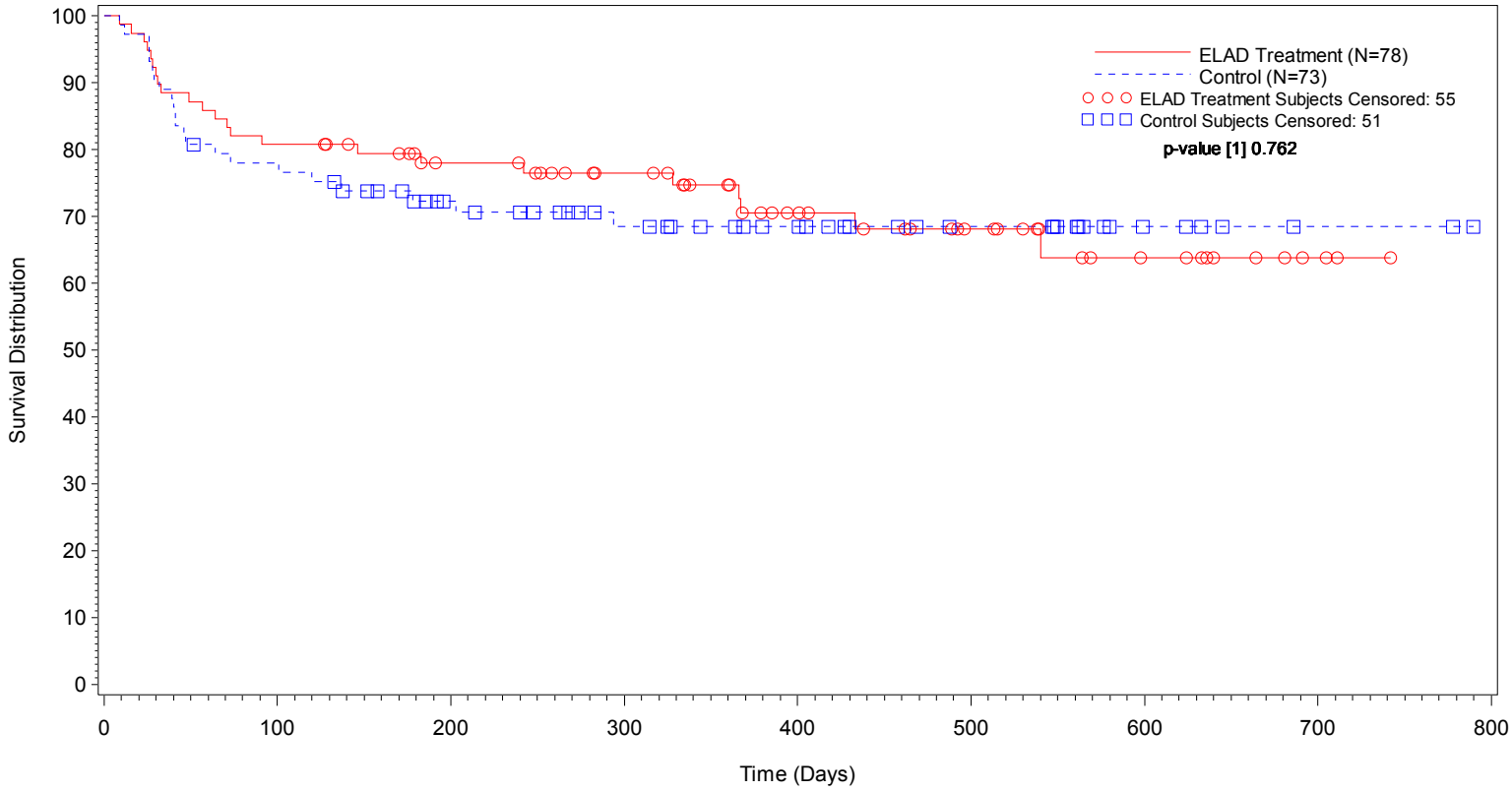
Baseline Demographics: ITT Population

Characteristic	ELAD Treatment (N=78)	Control (N=73)	Total (N=151)
Age (years)			
n	78	73	151
Mean (SD)	39.1 (6.26)	39.5 (7.20)	39.3 (6.71)
Median	40.0	41.0	40.0
Min, Max	25, 49	23, 49	23, 49
Age Category, n (%)			
18-35 years	23 (29.5)	22 (30.1)	45 (29.8)
36-<50 years	55 (70.5)	51 (69.9)	106 (70.2)
Sex, n (%)			
Female	31 (39.7)	29 (39.7)	60 (39.7)
Male	47 (60.3)	44 (60.3)	91 (60.3)

Baseline Disease Characteristics: ITT population

Characteristic	ELAD Treatment (N=78)	Control (N=73)	Total (N=151)	p-value [1]
Baseline model for end stage liver disease (MELD) score				
n	78	73	151	
Mean (SD)	24.8 (2.37)	25.6 (2.35)	25.2 (2.38)	0.0556
Median	25.0	25.0	25.0	
Min, Max	19, 29	21, 29	19, 29	
Serum Creatinine (mg/dL) at Baseline				
n	78	72	150	
Mean (SD)	0.701 (0.2169)	0.753 (0.2515)	0.726 (0.2348)	0.1760
Median	0.640	0.762	0.690	
Min, Max	0.36, 1.24	0.30, 1.27	0.30, 1.27	
Serum Bilirubin (mg/dL) at Baseline				
n	78	73	151	
Mean (SD)	24.236 (6.8789)	25.626 (5.7106)	24.908 (6.3584)	0.1804
Median	21.872	26.270	24.152	
Min, Max	16.00, 44.70	16.10, 41.00	16.00, 44.70	
INR at Baseline				
n	78	73	151	
Mean (SD)	1.794 (0.3457)	1.855 (0.3383)	1.823 (0.3424)	0.2758
Median	1.770	1.810	1.800	
Min, Max	0.95, 2.50	1.30, 2.50	0.95, 2.50	

Primary Endpoint
Overall Survival, ITT population, including VTI-308E (through 8/28/18)

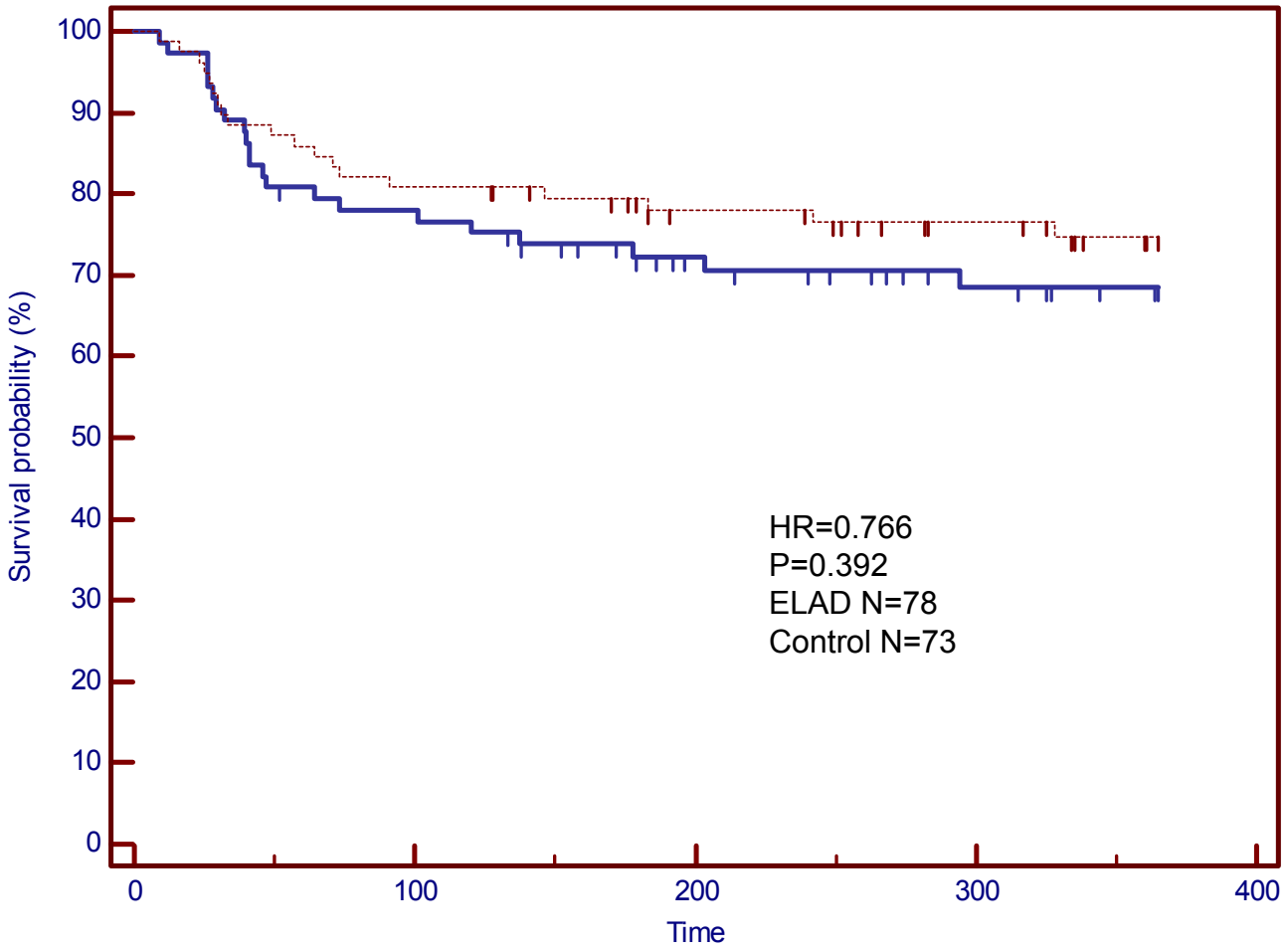


Primary Endpoint
Overall Survival, ITT population, including VTI-308E (through 8/28/18)

Survival Estimates	ELAD Treatment (N=78)		Control (N=73)
Number (%) of Subjects who Died	**23 (29.5)**		**22 (30.1)**
Number (%) of Subjects Censored	55 (70.5)		51 (69.9)
Censored reason: Still Alive	51 (65.4)		49 (67.1)
Censored reason: Lost to Follow-Up	4 (5.1)		2 (2.7)
Min, Max (days)	9, 742		9, 790
Min, Max for Non-Censored Subjects (days)	9, 540		9, 294
Percentiles [95% CI] (days) [1]			
25th	328 [64, NE]		137 [41, NE]
Median	NE		NE
75th	NE		NE
Hazard Ratio [95% CI]		**0.913 [0.509, 1.640]**	
p-value [2]		**0.762**	

Note: Overall Survival includes data up to at least Study Day 91, with follow-up Protocol VTL-308E providing additional survival data up to a maximum of 5 years.
Subjects with last contact day <91 are considered lost to follow-up.
[1] Kaplan-Meier product limit estimates.
[2] p-value obtained from log-rank test.
NE = Not Evaluable.

Primary Endpoint
Overall Survival, ITT population, including VTI-308E (through 365 days)



Secondary Endpoint: Proportion of Survivors at d28/91 ITT Population

Characteristic	ELAD Treatment (N=78)		Control (N=73)	Total (N=151)
Study Day 28 Number (%) of Subjects who Died	**6 (7.7)**		**6 (8.2)**	12 (7.9)
Number (%) of Subjects Still Alive	72 (92.3)		67 (91.8)	139 (92.1)
p-value [1]		0.9048		
p-value [2]		0.9051		
Study Day 91 Number (%) of Subjects who Died	**15 (19.2)**		**16 (21.9)**	31 (20.5)
Number (%) of Subjects Still Alive	57 (80.8)		66 (78.1)	120 (79.5)
p-value [1]		**0.6829**		
p-value [2]		0.6839		

[1] p-value obtained from Pearson chi-square test.
[2] p-value obtained from Cochran-Mantel-Haenszel (CMH) test.

Survival Status d180/365: ITT Population

Characteristic	ELAD Treatment (N=78) n(%)	Control (N=73) n(%)	P – value (Chi-squared)	Total (N=151) n(%)
Status at time of **Day 180** [2]				
Death	**16 (20.5)**	**20 (27.4)**	**0.321**	36 (23.8)
Alive	56 (71.8)	46 (63.0)		102 (67.5)
Unknown [1]	6 (7.7)	7 (9.6)		13 (8.6)
Status at time of **Day 365** [3]				
Death	**19 (24.4)**	**22 (30.1)**	**0.425**	41 (27.2)
Alive	36 (46.2)	26 (35.6)		62 (41.1)
Unknown [1]	23 (29.5)	25 (34.2)		48 (31.8)
Status at time of database lock				
Death	**23 (29.5)**	**22 (30.1)**		45 (29.8)
Alive	55 (70.5)	51 (69.9)		106 (70.2)
Ongoing [4]	49 (62.8)	43 (58.9)		92 (60.9)
Withdrew Consent [4]	**2 (2.6)**	**6 (8.2)**		8 (5.3)
Lost to Follow-up [4]	**4 (5.1)**	**2 (2.7)**		6 (4.0)

Note: Percentages are based on the number of subjects randomized into VTL-308 within each treatment group, unless otherwise specified.
[1] Subjects last known alive day is less than the corresponding study day and no death is reported.
[2] Includes subjects where database lock date – randomization date +1 is greater than or equal to 180. Percentages are based on these subjects.
[3] Includes subjects where database lock date – randomization date +1 is greater than or equal to 365. Percentages are based on these subjects.
[4] Percentages are based on number of subjects alive at database lock.

Overall Summary of Treatment Emergent Adverse Events: Safety Population

Characteristic	ELAD Treatment (N=76)	Control (N=75)	Total (N=151)
Number (%) of Subjects Reporting Any TEAE	76 (100)	74 (98.7)	150 (99.3)
Number of TEAEs	1205	911	2116
Number (%) of Subjects Reporting Any TESAE	47 (61.8)	42 (56.0)	89 (58.9)
Number of TESAEs	116	113	229
Subjects with TEAEs by Highest Severity [1], n (%)			
Mild	4 (5.3)	15 (20.0)	19 (12.6)
Moderate	39 (51.3)	25 (33.3)	64 (42.4)
Severe	33 (43.4)	34 (45.3)	67 (44.4)
Missing	0	0	0
Subjects with TESAEs by Highest Severity [1], n (%)			
Mild	0	1 (1.3)	1 (0.7)
Moderate	18 (23.7)	9 (12.0)	27 (17.9)
Severe	29 (38.2)	32 (42.7)	61 (40.4)
Missing	0	0	0

Note: TEAE = treatment emergent adverse event (based on randomization date/time); TESAE = treatment emergent serious adverse event (based on randomization date/time), note that TESAEs are a subset of TEAEs; N/A = not applicable.
[1] Patients reporting more than one adverse event are counted only once using the highest severity.
[2] Patients reporting more than one adverse event are counted only once using the closest relationship to ELAD treatment. “Related” events included all events reported with “possible”, “probable”, “related” or missing relationship to study treatment.

Summary of Treatment Emergent Serious Adverse Events (Safety Population)

Characteristic	ELAD Treatment (N=76)	Control (N=75)	Total (N=151)
Number of TESAEs	116	113	229
TESAEs by Severity, n (%)			
Mild	4 (3.4)	2 (1.8)	6 (2.6)
Moderate	55 (47.4)	34 (30.1)	89 (38.9)
Severe	57 (49.1)	77 (68.1)	134 (58.5)
TESAEs by ELAD Relationship, n (%)			
Not Related	109 (94.0)	N/A	222 (96.9)
Possibly Related	0	N/A	0
Probably Related	0	N/A	0
Related	7 (6.0)	N/A	7 (3.1)
TESAEs by Type of ELAD Relationship, n(%)			
Related to ELAD C3A Cells	4 (3.4)	N/A	4 (1.7)
Related to ELAD System	0	N/A	0
Related to ELAD Procedure	5 (4.3)	N/A	5 (2.2)
Unknown	0	N/A	0
Number (%) of TESAEs Leading to Premature Discontinuation of ELAD Treatment	11 (9.5)	N/A	11 (4.8)

TESAE = treatment emergent serious adverse event (based on randomization date/time).

Note: At each level of summation (overall, preferred term), subjects reporting more than one serious adverse event are counted only once. The descending order of incidence of TESAEs was based on the Total column.

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Subjects with at least one TESAE by Preferred Term: Descending Order

Preferred Term	ELAD Treatment (N=76) n (%)	Control (N=75) n (%)	Total (N=151) n (%)
Subjects Reporting at Least One TESAE	47 (61.8)	42 (56.0)	89 (58.9)
Multi-organ failure	7 (9.2)	13 (17.3)	20 (13.2)
Acute kidney injury	7 (9.2)	6 (8.0)	13 (8.6)
Gastrointestinal haemorrhage	6 (7.9)	7 (9.3)	13 (8.6)
Hepatorenal syndrome	7 (9.2)	5 (6.7)	12 (7.9)
Hepatic failure	6 (7.9)	5 (6.7)	11 (7.3)
Hepatic encephalopathy	2 (2.6)	7 (9.3)	9 (6.0)
Pneumonia	4 (5.3)	5 (6.7)	9 (6.0)
Septic shock	4 (5.3)	4 (5.3)	8 (5.3)
Acute respiratory failure	3 (3.9)	4 (5.3)	7 (4.6)
Anaemia	4 (5.3)	3 (4.0)	7 (4.6)
Hepatitis alcoholic	3 (3.9)	4 (5.3)	7 (4.6)
Bacteraemia	3 (3.9)	3 (4.0)	6 (4.0)
Ascites	1 (1.3)	4 (5.3)	5 (3.3)
Abdominal pain	3 (3.9)	1 (1.3)	4 (2.6)
Hypotension	1 (1.3)	3 (4.0)	4 (2.6)
Hypovolaemic shock	1 (1.3)	2 (2.7)	3 (2.0)
Renal failure	2 (2.6)	1 (1.3)	3 (2.0)
Systemic inflammatory response syndrome	2 (2.6)	1 (1.3)	3 (2.0)
Acute respiratory distress syndrome	2 (2.6)	0	2 (1.3)
Alcohol abuse	1 (1.3)	1 (1.3)	2 (1.3)
Alcohol withdrawal syndrome	2 (2.6)	0	2 (1.3)
Alcoholic liver disease	1 (1.3)	1 (1.3)	2 (1.3)
Anaphylactoid reaction	2 (2.6)	0	2 (1.3)
Epistaxis	2 (2.6)	0	2 (1.3)
Generalised oedema	1 (1.3)	1 (1.3)	2 (1.3)
Hepatic hydrothorax	1 (1.3)	1 (1.3)	2 (1.3)

Subjects with at least one TESAE leading to Discontinuation of ELAD Treatment

System Organ Class / Preferred Term	ELAD Treatment (N=76) n (%)
Subjects Reporting at Least One TESAE Leading to Discontinuation of ELAD Treatment	11 (14.5)
General disorders and administration site conditions	2 (2.6)
Medical device site haematoma	1 (1.3)
Medical device site haemorrhage	1 (1.3)
Hepatobiliary disorders	1 (1.3)
Alcoholic liver disease	1 (1.3)
Immune system disorders	2 (2.6)
Anaphylactoid reaction	2 (2.6)
Infections and infestations	2 (2.6)
Bacteraemia	1 (1.3)
Pneumonia	1 (1.3)
Respiratory, thoracic and mediastinal disorders	3 (3.9)
Acute respiratory distress syndrome	2 (2.6)
Pulmonary oedema	1 (1.3)
Vascular disorders	1 (1.3)
Haematoma	1 (1.3)

TESAE = treatment emergent serious adverse event (based on randomization date/time).
Note: At each level of summation (overall, system organ class, preferred term), subjects reporting more than one adverse event are counted only once.

RUTGERS

Subgroup Analyses: Overall Survival incl. VTI-308E: ITT

By Region: US vs ROW

	US				Non-US		
Survival Estimates	ELAD Treatment (N=57)		Control (N=52)		ELAD Treatment (N=20)		Control (N=20)
Number (%) of Subjects who Died	**15 (26.3)**		**17 (32.7)**		**8 (40.0)**		**4 (20.0)**
Number (%) of Subjects Censored	42 (73.7)		35 (67.3)		12 (60.0)		16 (80.0)
Censored reason: Still Alive	40 (70.2)		35 (67.3)		10 (50.0)		14 (70.0)
Censored reason: Lost to Follow-Up	2 (3.5)		0		2 (10.0)		2 (10.0)
Min, Max (days)	23, 742		9, 790		9, 624		12, 633
Min, Max for Non-Censored Subjects (days)	23, 540		9, 294		9, 433		12, 178
Percentiles [95% CI] (days) [1] 25th	367 [71, NE]		68.5 [39, NE]		74 [9, 433]		NE
Median	NE		NE		433 [57, NE]		NE
75th	NE		NE		NE		NE
Hazard Ratio [95% CI]		0.723 [0.361, 1.448]				2.098 [0.629, 6.999]	
p-value [2]		0.357				0.218	

Note: Overall Survival includes data up to at least Study Day 91, with follow-up Protocol VTL-308E providing additional survival data up to a maximum of 5 years. Subjects with last contact day <91 are considered lost to follow-up.
[1] Kaplan-Meier product limit estimates.
[2] p-value obtained from log-rank test.
NE = Not Evaluable.

Analyses of Overall Survival-Cox Regression Analysis Univariate Model: ITT Population

Covariate	Hazard Ratio [95% CI]	P-value [1]
Age (years) (continuous)	1.052 [1.004, 1.103]	0.0318
Age (< median years vs ≥median years)	0.541 [0.293, 0.997]	0.0489
Baseline MELD score (continuous)	1.255 [1.092, 1.441]	0.0013
Baseline MELD (<median cutoff vs ≥median cutoff)	0.421 [0.208, 0.855]	0.0167
Hepatic encephalopathy (0 vs 1/2 vs 3/4)		0.7128
Hepatic encephalopathy (0 vs 1/2)	1.153 [0.566, 2.347]	0.6956
Hepatic encephalopathy (0 vs 3/4)	0.548 [0.072, 4.160]	0.5611
Hepatic encephalopathy (1/2 vs 3/4)	0.278 [0.029, 2.692]	0.2694
Baseline total bilirubin level (mg/dL) (continuous)	1.047 [1.003, 1.092]	0.0359
Baseline total bilirubin level (<median cutoff vs ≥median cutoff)	0.590 [0.319, 1.091]	0.0924

Note: Overall Survival includes data up to at least Study Day 91, with follow-up Protocol VTL-308E providing additional survival data up to a maximum of 5 years.
Note: When the covariate is dichotomous (ex: A vs B), B is used as the reference group. NE = Not Evaluable
[1] p-values obtained from individual univariate cox regression models including covariate and treatment group

Analyses of Overall Survival-Cox Regression Analysis Univariate Model: ITT Population

Covariate	Hazard Ratio [95% CI]	P-value [1]
Baseline PT ratio (sec) (continuous)	1.080 [1.002, 1.166]	0.0454
Baseline white blood cells (x10^3/mL) (continuous)	1.004 [0.963, 1.046]	0.8622
Baseline BUN (mg/dL) (continuous)	1.039 [1.011, 1.067]	0.0053
Baseline creatinine (mg/dL) (continuous)	2.433 [0.707, 8.373]	0.1587
Steroid Use (Yes vs No)	0.504 [0.275, 0.923]	0.0265
Baseline Weight (kg) (continuous)	0.989 [0.972, 1.006]	0.1867
Baseline Weight (kg) (<median cutoff vs ≥median cutoff)	2.248 [0.944, 5.353]	0.0674
Baseline Height (cm) (continuous)	0.983 [0.954, 1.013]	0.2621
Baseline Height (cm) (<median cutoff vs ≥median cutoff)	1.420 [0.768, 2.626]	0.2634
Region (US vs Non-US)	0.889 [0.456, 1.732]	0.7289

Note: Overall Survival includes data up to at least Study Day 91, with follow-up Protocol VTL-308E providing additional survival data up to a maximum of 5 years.
Note: When the covariate is dichotomous (ex: A vs B), B is used as the reference group. NE = Not Evaluable
[1] p-values obtained from individual univariate cox regression models including covariate and treatment group

Analyses of Overall Survival-Cox Regression Analysis Multivariate Model: ITT Population

Covariate	Hazard Ratio [95% CI]	P-value [1]
Age (years) (continuous)	1.033 [0.981, 1.089]	0.2159
Baseline MELD score (continuous)	1.198 [1.012, 1.417]	0.0354
Baseline total bilirubin level (mg/dL) (continuous)	1.020 [0.968, 1.074]	0.4577
Baseline BUN (mg/dL) (continuous)	1.025 [0.999, 1.052]	0.0599
Steroid Use (Yes vs No)	0.415 [0.188, 0.915]	0.0293

Note: Overall Survival includes data up to at least Study Day 91, with follow-up Protocol VTL-308E providing additional survival data up to a maximum of 5 years.
Note: When the covariate is dichotomous (ex: A vs B), B is used as the reference group. NE = Not Evaluable
[1] p-values obtained from multivariable cox regression model including top 5 most significant covariates (p-value <0.1 in univariate models) and treatment group.

Exploratory Endpoint: Proportion of Transplant-Free Survivors at Study Day 91 (ITT Population)

Excluding Liver Transplant from both denominator and the numerator

Characteristic	ELAD Treatment (N=76)		Control (N=71)	Total (N=147)
Study Day 91 Number (%) of Subjects who Died	**15 (19.7)**		**16 (22.5)**	31 (21.1)
Number (%) of Subjects Still Alive	61 (80.3)		55 (77.5)	116 (78.9)

Note: The subjects lost to follow up were included in subject still alive in the analysis.

Counting Liver Transplant as an Event

Characteristic	ELAD Treatment (N=78)		Control (N=73)	Total (N=151)
Study Day 91 Number (%) of Subjects who Died	**17 (21.8)**		**18 (24.7)**	35 (23.2)
Number (%) of Subjects Still Alive	61 (78.2)		55 (75.3)	116 (76.8)

Tx in first 91d:

ELAD = 2
Control = 2
No deaths

Key Conclusions

- ELAD did not meet its primary endpoint
  - Overall survival, ITT analysis
    - Hazard ratio: 0.913
    - p-value: 0.762
- ELAD did not meet the secondary endpoints
  - Mortality at 28 days:
    - ELAD: 7.7% Control: 8.2% p-value: 0.9048
  - Mortality at 91 days:
    - ELAD: 19.2% Control: 21.9% p-value: 0.6829
- Safety and Per-protocol population had slightly better results for ELAD: HR=0.797 and HR=0.876 respectively
  - No significant differences between ELAD and Control
- mITT population had slightly worse results for ELAD: HR=1.193
  - No significant differences between ELAD and Control
- Population demographics were generally well balanced
  - Mortality was generally about 20% at Day 91 (somewhat less than planned)
- No new safety concerns
  - Treatment emergent serious adverse events similar in incidence, severity
  - Hepatic encephalopathy, Anemia, Diarrhoea, Acute kidney injury, Ascites