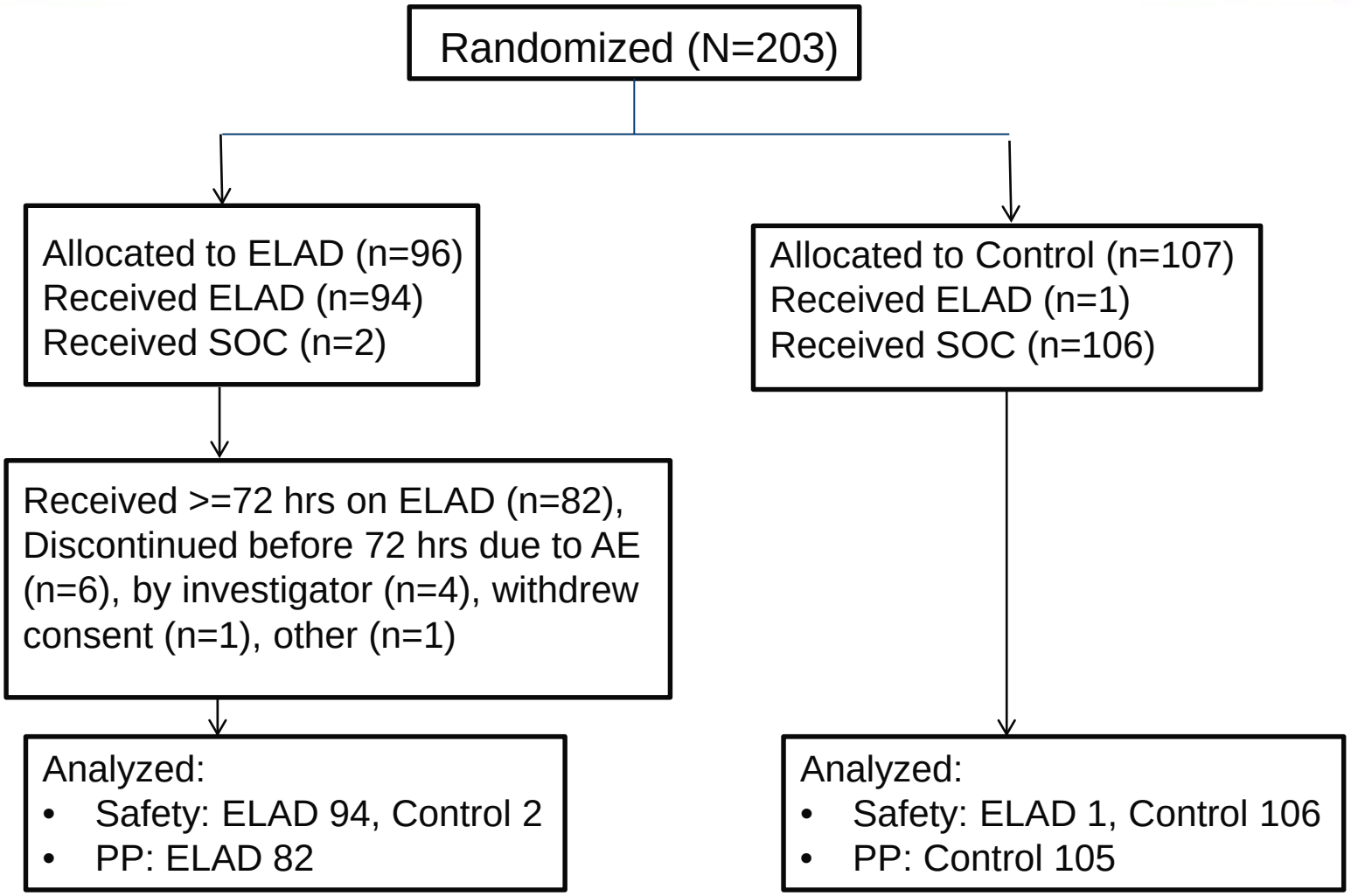
VTI-208 Clinical Study

Data Analysis August 27 2015

Summary of Analysis Populations



Key Conclusions (1)

- ELAD failed to meet its primary endpoint
  - Overall survival, ITT analysis
  - Hazard ratio: 1.027
  - p-value: 0.904
- ELAD failed to meet the secondary endpoints
  - Mortality at 28 days:
    - ELAD: 24% Control: 19.6% p-value: 0.46
  - Mortality at 91 days:
    - ELAD: 40.6% Control: 38.3% p-value: 0.74
- Per-protocol population had slightly better results for ELAD
  - No significant differences between ELAD and Control
- Population demographics were generally well balanced
  - Mortality was generally about 40% (somewhat less than planned)
  - ELAD group was slightly older, slightly higher MELD (bilirubin and creatinine)
- No new safety concerns
  - Treatment emergent adverse events similar in incidence, severity
  - Anemia, thrombocytopenia, coagulopathy

Key Conclusions (2)

- Subgroup analyses reveal:
  - Lower MELD (< 28) associated with better outcome for ELAD vs Control
  - Younger age (< 46.9) associated with better outcome for ELAD vs Control
  - Patients with acute kidney injury (crea >1.5mg/dL) did poorly on ELAD
  - Patients with blood thinning problems (INR > 2.5) did poorly on ELAD

Key Conclusions (3) Data Summary

- Overall Study Population

ITT Total N=203 ELAD: N=96 Control: N=107

- HR: 1.027 (0.98) p=0.90
- Proportion survivors (91d): ELAD: 59.4% Control: 61.7% p=0.74

PP Total N=187 ELAD: N=82 Control: N=105

- HR: 0.871 (1.15) p=0.52
- Proportion survivors: (91d): ELAD: 64.6% Control: 61.9% p=0.70

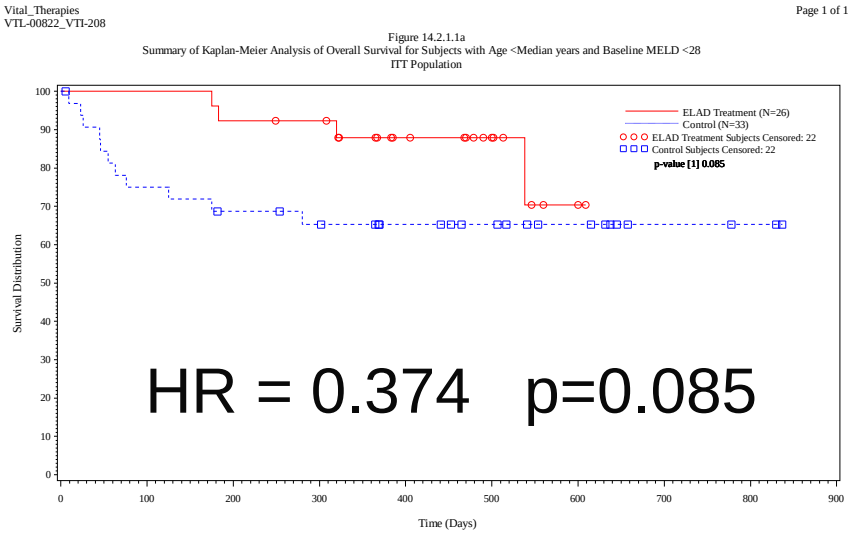
Key Conclusions (4) Data Summary Key Sub Groups

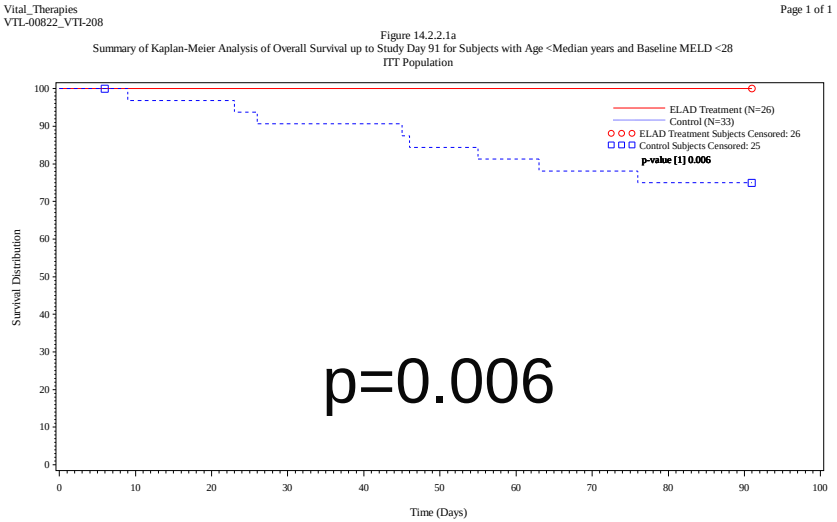
- MELD <28
  - ITT Total N=120 ELAD: N=51 Control: N=69
  - HR: 0.575 (1.74) p=0.077
  - Proportion survivors (91d): ELAD: 80.4% Control: 65.2% p=0.068
  - PP Total N=116 ELAD: N=48 Control: N=68
  - HR: 0.538 (1.86) p=0.059
  - Proportion survivors (91d): ELAD: 81.3% Control: 66.2% p=0.074
- Age <median (46.9 years)
  - ITT Total N=101 ELAD: N=43 Control: N=58
  - HR: 0.634 (1.58) p=0.167
  - Proportion survivors (91d): ELAD: 81.4% Control: 67.2% p=0.112
  - PP Total N=94 ELAD: N=38 Control: N=56
  - HR: p=0.
  - Proportion survivors (91d): ELAD: 84.2% Control: 67.9% p=0.074

Key Conclusions (5) Data Summary Combined Key Sub Groups

- MELD <28, Age <46.9

  ITT Total N=59 ELAD: N=26 Control: N=33

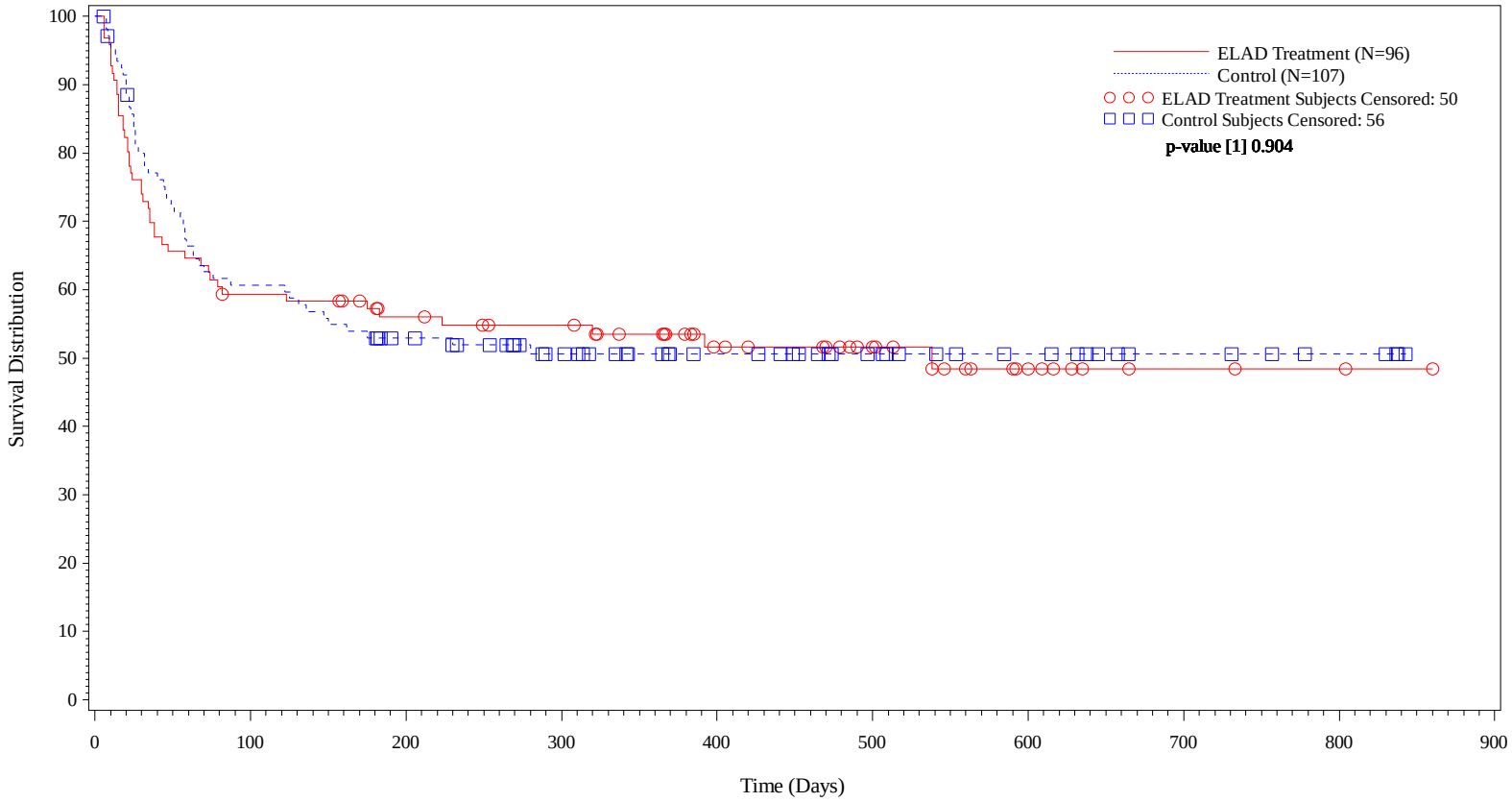




Overall Analysis

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

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

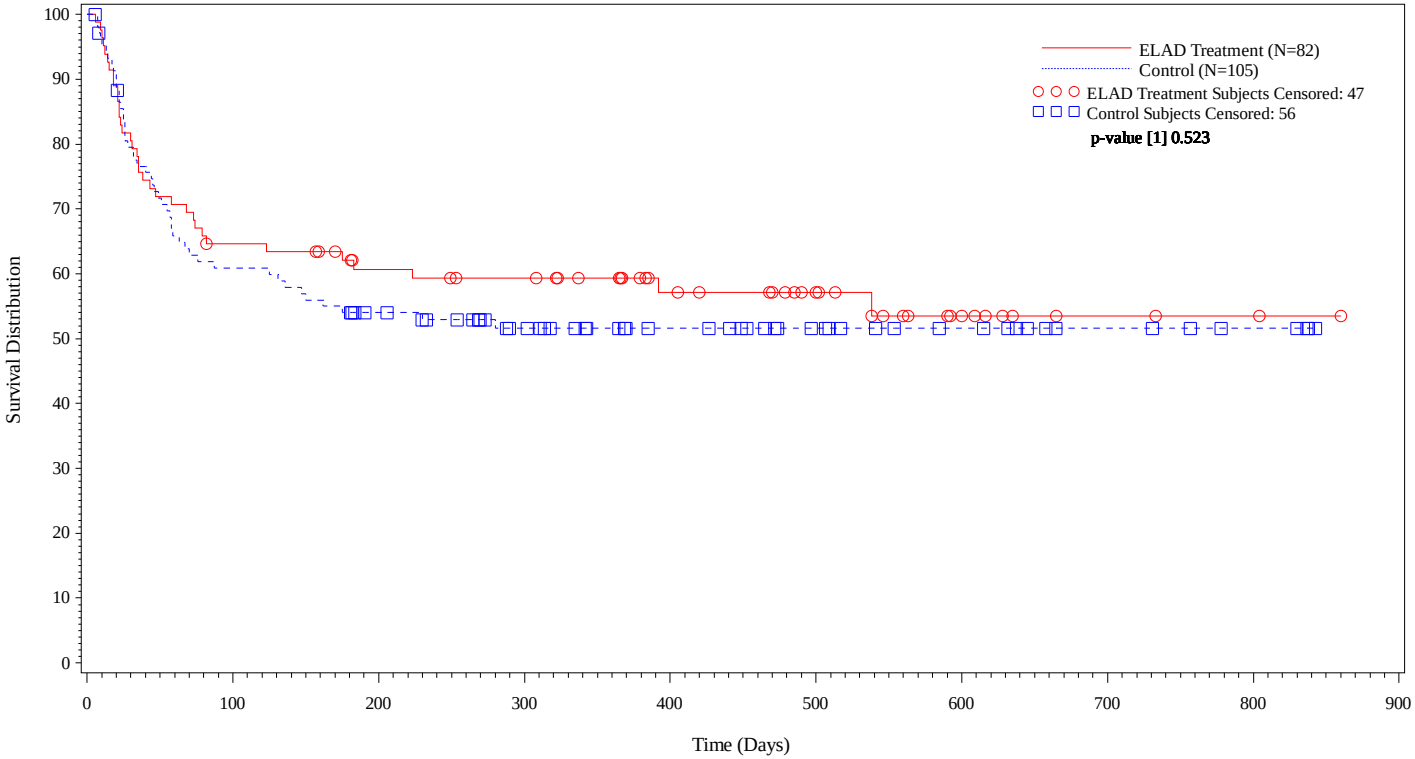
Survival Estimates	ELAD Treatment (N=96)		Control (N=107)
Number (%) of Subjects who Died	46 (47.9)		51 (47.7)
Number (%) of Subjects Censored	50 (52.1)		56 (52.3)
Censored reason: Still Alive	49 (51.0)		53 (49.5)
Censored reason: Lost to Follow-Up	1 (1.0)		3 (2.8)
Min, Max (days)	6, 860		6, 843
Min, Max for Non-Censored Subjects (days)	6, 538		7, 280
Percentiles [95% CI] (days) [1]			
25^{th}	30 [18, 47]		45 [26, 59]
Median	538 [79, -]		NA
75^{th}	NA		NA
Hazard Ratio [95% CI]		1.027 [0.689, 1.530]	
p-value [2]		0.904	

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] Kaplan-Meier product limit estimates
[2] p-value obtained from log-rank test, stratified by randomization strata.

Table 14.2.1a

Primary Endpoint
Overall Survival, PP population, including VTI-208E

Figure 14.2.1c
Summary of Kaplan-Meier Analysis of Overall Survival
PP 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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Table 14.2.1c

Primary Endpoint
Overall Survival, PP population, including VTI-208E

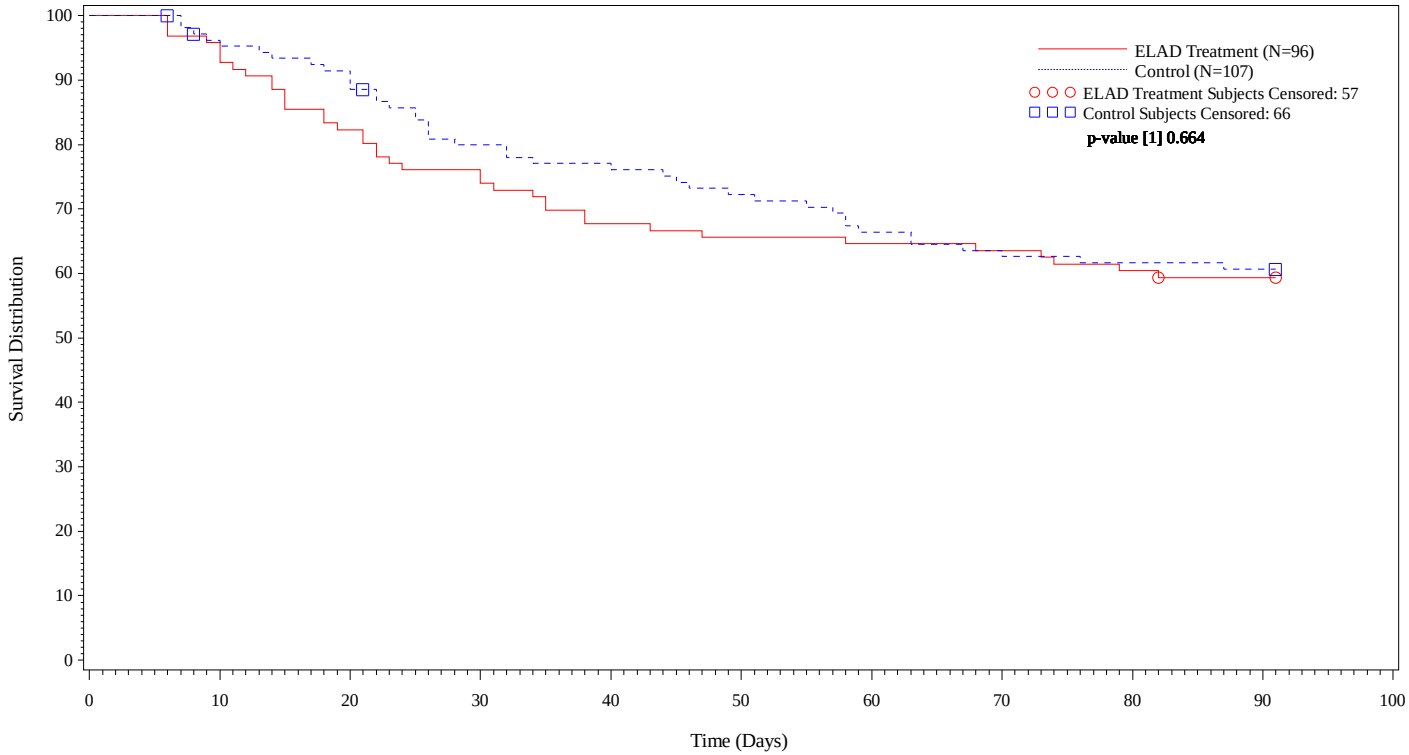
Survival Estimates	ELAD Treatment (N=82)		Control (N=105)
Number (%) of Subjects who Died	35 (42.7)		49 (46.7)
Number (%) of Subjects Censored	47 (57.3)		56 (53.3)
Censored reason: Still Alive	46 (56.1)		53 (50.5)
Censored reason: Lost to Follow-Up	1 (1.2)		3 (2.9)
Min, Max (days)	6, 860		6, 843
Min, Max for Non-Censored Subjects (days)	6, 538		7, 280
Percentiles [95% CI] (days) [1]			
25^{th}	38 [22, 82]		44 [25, 58]
Median	NA		NA
75^{th}	NA		NA
Hazard Ratio [95% CI]		0.871 [0.564, 1.345]	
p-value [2]		0.523	

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] Kaplan-Meier product limit estimates
[2] p-value obtained from log-rank test, stratified by randomization strata.

Table 14.2.1c

Primary Endpoint – Sensitivity Analysis
Overall Survival, ITT population, up to study day 91

Figure 14.2.2a
Summary of Kaplan-Meier Analysis of Overall Survival up to Study Day 91
ITT Population



Overall Survival up to Study Day 91 excludes data from follow-up Protocol VTI-208E that is after Study Day 91.
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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Table 14.2.2a

Primary Endpoint – Sensitivity Analysis
Overall Survival, ITT population, up to study day 91

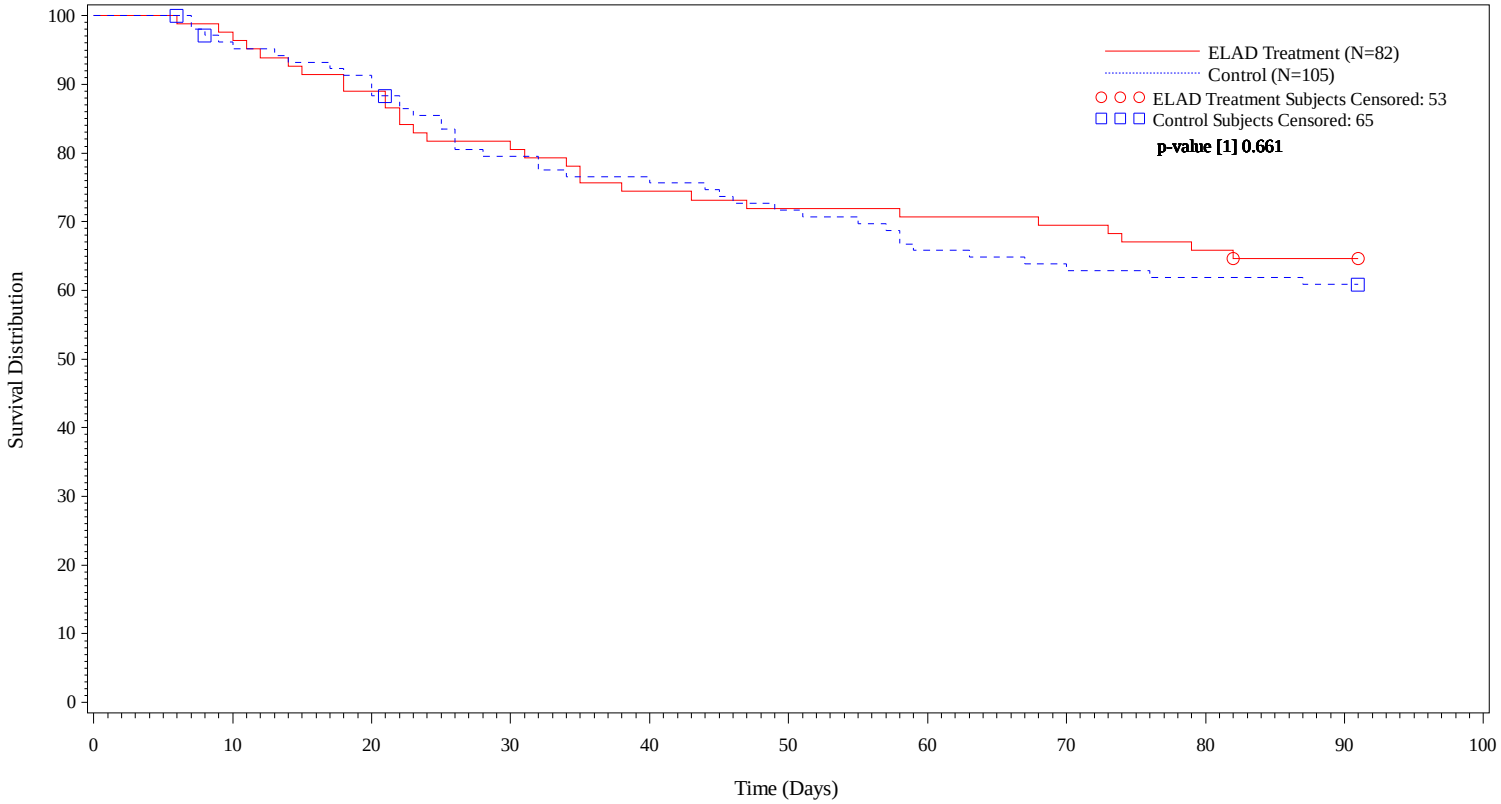
Survival Estimates	ELAD Treatment (N=96)		Control (N=107)
Number (%) of Subjects who Died	39 (40.6)		41 (38.3)
Number (%) of Subjects Censored	57 (59.4)		66 (61.7)
Censored reason: Still Alive	56 (58.3)		63 (58.9)
Censored reason: Lost to Follow-Up	1 (1.0)		3 (2.8)
Min, Max (days)	6, 91		6, 91
Min, Max for Non-Censored Subjects (days)	6, 82		7, 87
Percentiles [95% CI] (days) [1] 25th	30 [18, 47]		45 [26, 59]
Median	NA		NA
75th	NA		NA
Hazard Ratio [95% CI]		1.100 [0.709, 1.706]	
p-value [2]		0.664	

Overall Survival up to Study Day 91excludes data from follow-up Protocol VTI-208E that is after Study Day 91.
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, stratified by randomization strata.

Table 14.2.2a

Primary Endpoint – Sensitivity Analysis
Overall Survival, PP population, up to study day 91

Figure 14.2.2c
Summary of Kaplan-Meier Analysis of Overall Survival up to Study Day 91
PP Population



Overall Survival up to Study Day 91 excludes data from follow-up Protocol VTI-208E that is after Study Day 91.
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[1] p-value obtained from log-rank test, stratified by randomization strata.

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Table 14.2.2c

Primary Endpoint – Sensitivity Analysis
Overall Survival, PP population, up to study day 91

Survival Estimates	ELAD Treatment (N=82)		Control (N=105)
Number (%) of Subjects who Died	29 (35.4)		40 (38.1)
Number (%) of Subjects Censored	53 (64.6)		65 (61.9)
Censored reason: Still Alive	52 (63.4)		62 (59.0)
Censored reason: Lost to Follow-Up	1 (1.2)		3 (2.9)
Min, Max (days)	6, 91		6, 91
Min, Max for Non-Censored Subjects (days)	6, 82		7, 87
Percentiles [95% CI] (days) [1] 25th	38 [22, 82]		44 [25, 58]
Median	NA		NA
75th	NA		NA
Hazard Ratio [95% CI]		0.897 [0.556, 1.447]	
p-value [2]		0.661	

Overall Survival up to Study Day 91 excludes data from follow-up Protocol VTI-208E that is after Study Day 91.
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, stratified by randomization strata.

Table 14.2.2c

Secondary Endpoint: Proportion of Survivors at d28/91

ITT Population

Characteristic	ELAD Treatment (N=96)		Control (N=107)	Total (N=203)
Study Day 28 Number (%) of Subjects who Died	23 (24.0)		21 (19.6)	44 (21.7)
Number (%) of Subjects Still Alive	73 (76.0)		86 (80.4)	159 (78.3)
p-value [1]		0.455		
p-value [2]		0.443		
Study Day 91 Number (%) of Subjects who Died	39 (40.6)		41 (38.3)	80 (39.4)
Number (%) of Subjects Still Alive	57 (59.4)		66 (61.7)	123 (60.6)
p-value [1]		0.737		
p-value [2]		0.737		

PP Population

Characteristic	ELAD Treatment (N=82)		Control (N=105)	Total (N=187)
Study Day 28 Number (%) of Subjects who Died	15 (18.3)		21 (20.0)	36 (19.3)
Number (%) of Subjects Still Alive	67 (81.7)		84 (80.0)	151 (80.7)
p-value [1]		0.769		
p-value [2]		0.782		
Study Day 91 Number (%) of Subjects who Died	29 (35.4)		40 (38.1)	69 (36.9)
Number (%) of Subjects Still Alive	53 (64.6)		65 (61.9)	118 (63.1)
p-value [1]		0.701		
p-value [2]		0.705		

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

Table 14.2.4.1a

Table 14.2.4.1c

Demographics ITT Population

Baseline Demographics: ITT Population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)
Age (years)			
n	96	107	203
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)

Table 14.1.2a

Baseline Demographics: ITT Population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)
Height (cm) [1]			
n	84	97	181
Mean (SD)	171.2 (10.61)	174.5 (11.00)	173.0 (10.92)
Median	170.0	174.0	173.0
Min, Max	144, 200	150, 201	144, 201
Weight (kg) [1]			
n	84	99	183
Mean (SD)	80.74 (21.601)	85.60 (20.048)	83.37 (20.859)
Median	74.00	82.00	80.00
Min, Max	48.0, 160.0	41.0, 162.1	41.0, 162.1

Note: Percentages are based on the number of subjects randomized within each treatment group.
[1] From Screening visit.

Table 14.1.2a

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				
n	96	107	203	
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				
n	96	107	203	
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				
n	96	107	203	
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				
n	96	107	203	
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)	

Table 14.1.3.1a

Baseline Disease Characteristics: ITT population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)	p-value [1]
Baseline Maddrey Discriminant Function (MDF) score				
n	96	107	203	
Mean (SD)	73.4 (27.67)	72.6 (23.36)	73.0 (25.43)	0.833
Median	66.5	70.0	69.0	
Min, Max	33, 157	32, 140	32, 157	
Prothrombin Time/PT (seconds) at Baseline				
n	96	107	203	
Mean (SD)	22.25 (5.600)	22.54 (5.050)	22.40 (5.306)	0.699
Median	21.05	21.70	21.50	
Min, Max	13.1, 35.9	12.7, 38.5	12.7, 38.5	
Laboratory Control PT (seconds) at Baseline				
n	96	107	203	
Mean (SD)	11.99 (1.368)	12.02 (1.338)	12.00 (1.349)	0.897
Median	11.50	11.50	11.50	
Min, Max	10.0, 15.5	10.0, 15.0	10.0, 15.5	
Total Bilirubin (mg/dL) at Baseline				
Mean (SD)	26.20 (9.687)	24.18 (8.423)	25.14 (9.077)	0.114
Median	25.80	25.00	25.70	
Min, Max	9.3, 56.8	8.6, 44.6	8.6, 56.8	

Table 14.1.3.1a

Baseline Disease Characteristics: ITT population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)	p-value [1]
On renal replacement therapy (hemodialysis, CVVHD, CVVH, peritoneal, etc) at randomization, n (%)				0.290
Yes	1 (1.0)	0	1 (0.5)	
No	95 (99.0)	107 (100)	202 (99.5)	
On vasopressors at Baseline, n (%)				0.992
Yes	18 (18.8)	20 (18.7)	38 (18.7)	
No	78 (81.3)	87 (81.3)	165 (81.3)	
On ventilator / intubated at Baseline, n (%)				0.082
Yes	8 (8.3)	3 (2.8)	11 (5.4)	
No	88 (91.7)	104 (97.2)	192 (94.6)	
Time since last alcohol consumption (prior to date of current hospital admission)				
n	96	106	202	
Mean (SD)	19.8 (14.15)	19.3 (16.18)	19.5 (15.21)	0.806
Median	16.0	14.0	14.5	
Min, Max	3, 69	3, 94	3, 94	
Category, n (%):				0.820
0-7 days	15 (15.6)	22 (20.6)	37 (18.2)	
8-14 days	31 (32.3)	33 (30.8)	64 (31.5)	
15 days-1 month	32 (33.3)	32 (29.9)	64 (31.5)	
>1 month	18 (18.8)	19 (17.8)	37 (18.2)	
n	96	107	203	
Mean (SD)	10.0 (6.10)	9.4 (7.78)	9.7 (7.02)	0.514
Median	9.0	7.0	8.0	
Min, Max	2, 30	1, 61	1, 61	

Table 14.1.3.1a

Note: CVVHD = Continuous Venovenous Hemodialysis; CVVH = Continuous Venovenous Hemofiltration

[1] P-value for treatment difference of proportions based on Pearson chi-square test; p-value for treatment difference of means based on one-way ANOVA.

Baseline Disease Characteristics: ITT population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)	p-value [1]
Medical treatments at Baseline, n (%):				
Steroids	44 (45.8)	53 (49.5)	97 (47.8)	0.598
Pentoxifylline	33 (34.4)	34 (31.8)	67 (33.0)	0.694
N-acetyl-cysteine	5 (5.2)	5 (4.7)	10 (4.9)	0.860

Table 14.1.3.1a

Baseline Liver Disease Characteristics: ITT Population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)	p-value [1]
Basis for diagnosing subject with acute alcohol-related liver failure, n (%) [2]				
Confirmation by liver biopsy	15 (15.6)	13 (12.1)	28 (13.8)	0.473
Presence of hepatomegaly	72 (75.0)	81 (75.7)	153 (75.4)	0.908
Medical history of EtOH abuse	96 (100)	107 (100)	203 (100)	
AST>ALT, both levels less than 500 U/L	87 (90.6)	100 (93.5)	187 (92.1)	0.455
Leukocytosis	59 (61.5)	53 (49.5)	112 (55.2)	0.088
Other	8 (8.3)	13 (12.1)	21 (10.3)	0.373
Hepatic Encephalopathy, n (%)				0.346
0 (None)	52 (54.2)	52 (48.6)	104 (51.2)	
1 (Grade I) / 2 (Grade II)	38 (39.6)	39 (36.4)	77 (37.9)	
3 (Grade III) / 4 (Grade IV)	3 (3.1)	8 (7.5)	11 (5.4)	
Subject sedated?				
Yes	3 (3.1)	6 (5.6)	9 (4.4)	
No	91 (94.8)	100 (93.5)	191 (94.1)	
Ascites, n (%) [3]				0.943
Yes	57 (59.4)	63 (58.9)	120 (59.1)	
No	39 (40.6)	44 (41.1)	83 (40.9)	

Table 14.1.3.2a

Baseline Liver Disease Characteristics: ITT Population

Characteristic	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)	p-value [1]
Liver Size (cm) Liver size determined by Ultrasound, n (%)				
Yes	82 (85.4)	92 (86.0)	174 (85.7)	
No	14 (14.6)	15 (14.0)	29 (14.3)	
n	82	92	174	
Mean (SD)	19.10 (4.772)	19.33 (3.913)	19.22 (4.327)	0.737
Median	19.15	19.95	19.55	
Min, Max	10.0, 29.0	10.6, 27.3	10.0, 29.0	
Liver Volume (cc) Liver volume determined by CT scan, n (%)				
Yes	23 (24.0)	23 (21.5)	46 (22.7)	
No	73 (76.0)	84 (78.5)	157 (77.3)	
n	23	23	46	
Mean (SD)	2983.6 (1583.68)	3922.2 (1768.40)	3452.9 (1726.32)	0.065
Median	2812.0	3965.0	3264.5	
Min, Max	1228, 8095	1322, 9663	1228, 9663	
White Blood Cell Count (10^9/L) at Baseline				
n	96	107	203	
Mean (SD)	15.36 (7.989)	14.44 (8.129)	14.88 (8.056)	0.422
Median	13.80	13.40	13.70	
Min, Max	3.4, 39.8	3.5, 59.0	3.4, 59.0	
Total Bilirubin (mg/dL) at Baseline, n (%)				0.318
≥8.0 to <12.0	4 (4.2)	8 (7.5)	12 (5.9)	
≥12.0	92 (95.8)	99 (92.5)	191 (94.1)	
Does not have extensive cirrhosis, n (%)				
Yes	0	0	0	
No	96 (100)	107 (100)	203 (100)	

Table 14.1.3.2a

[1] P-value for treatment difference of proportions based on Pearson/Mantel-Haenszel chi-square test; p-value for treatment difference of means based on one-way ANOVA.
[2] Subjects may have more than one basis for diagnosis.
[3] Based on screening physical exam CRF.

Baseline Clinical Characteristics: ITT Population

Body System (parameter, unit)	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)
Liver (bilirubin, mg/dL), n (%)			
≥6.0 to <12.0	4 (4.2)	8 (7.5)	12 (5.9)
≥12.0	92 (95.8)	99 (92.5)	191 (94.1)
Kidney (creatinine, mg/dL), n (%)			
<1.2	68 (70.8)	82 (76.6)	150 (73.9)
≥1.2 to <2.0	19 (19.8)	22 (20.6)	41 (20.2)
≥2.0 to <3.5	6 (6.3)	3 (2.8)	9 (4.4)
≥3.5 to <5.0	0	0	0
≥5.0	2 (2.1)	0	2 (1.0)
Cerebral (HE Grade), n (%)			
0 (None)	52 (54.2)	52 (48.6)	104 (51.2)
1 (Grade I)	27 (28.1)	29 (27.1)	56 (27.6)
2 (Grade II)	11 (11.5)	10 (9.3)	21 (10.3)
3 (Grade III)	3 (3.1)	7 (6.5)	10 (4.9)
4 (Grade IV)	0	1 (0.9)	1 (0.5)
Subject sedated?			
Yes	3 (3.1)	6 (5.6)	9 (4.4)
No	91 (94.8)	100 (93.5)	191 (94.1)

Table 14.1.3.3a

Baseline Clinical Characteristics: ITT Population

Body System (parameter, unit)	ELAD Treatment (N=96)	Control (N=107)	Total (N=203)
Coagulation (INR), n (%)			
<1.1	1 (1.0)	0	1 (0.5)
≥1.1 to <1.25	3 (3.1)	4 (3.7)	7 (3.4)
≥1.25 to <1.5	6 (6.3)	7 (6.5)	13 (6.4)
≥1.5 to <2.5	66 (68.8)	73 (68.2)	139 (68.5)
≥2.5	19 (19.8)	23 (21.5)	42 (20.7)
Circulation (MAP, mmHg), n (%)			
≥70.0	69 (71.9)	74 (69.2)	143 (70.4)
<70.0	4 (4.2)	7 (6.5)	11 (5.4)
Vasopressin Use [1]	2 (2.1)	1 (0.9)	3 (1.5)
Lungs – Pulse Oximetry and FiO2, n (%) Pulse Oximetry (%)			
n	94	104	198
Mean (SD)	96.5 (2.54)	96.6 (2.38)	96.6 (2.45)
Median	97.0	97.0	97.0
Min, Max	88, 100	90, 100	88, 100
FiO2 (%)			
n	91	103	194
Mean (SD)	22.2 (3.69)	23.1 (9.95)	22.7 (7.67)
Median	21.0	21.0	21.0
Min, Max	21, 44	21, 100	21, 100

Table 14.1.3.3a

Note: HE = Hepatic Encephalopathy; INR = International Normalization Ratio; MAP = Mean Arterial Pressure

[1] Subjects who used vasopressin or terlipressin for hypotension

Safety Analysis

Summary of Treatment Emergent Adverse Events: Safety Population

Characteristic	ELAD Treatment (N=95)	Control (N=108)	Total (N=203)
Number (%) of Subjects Reporting Any TEAE	95 (100)	107 (99.1)	202 (99.5)
Number of TEAEs	2046	1619	3665
Number (%) of Subjects Reporting Any TESAE	73 (76.8)	75 (69.4)	148 (72.9)
Number of TESAEs	156	168	324

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.

Table 14.3.1.1b

Summary of Treatment Emergent Adverse Events: Safety Population

Characteristic	ELAD Treatment (N=95)	Control (N=108)	Total (N=203)
Number (%) of Subjects Reporting Any TEAE	95 (100)	107 (99.1)	202 (99.5)
Number of TEAEs	2046	1619	3665
Number (%) of Subjects Reporting Any TESAE	73 (76.8)	75 (69.4)	148 (72.9)
Number of TESAEs	156	168	324
Subjects with TEAEs by Highest Severity [1], n (%)			
Mild	2 (2.1)	9 (8.3)	11 (5.4)
Moderate	25 (26.3)	35 (32.4)	60 (29.6)
Severe	68 (71.6)	63 (58.3)	131 (64.5)
Subjects with TESAEs by Highest Severity [1], n (%)			
Mild	2 (2.1)	4 (3.7)	6 (3.0)
Moderate	15 (15.8)	14 (13.0)	29 (14.3)
Severe	56 (58.9)	57 (52.8)	113 (55.7)
Number (%) of Subjects Reporting at Least 1 ELAD-Related [2] TEAE	75 (78.9)	1 (0.9)	76 (37.4)
Related to ELAD Biologic	10 (10.5)	0	10 (4.9)
Related to ELAD Device	32 (33.7)	0	32 (15.8)
Related to ELAD Procedure	38 (40.0)	1 (0.9)	39 (19.2)
Unknown	17 (17.9)	0	17 (8.4)
Number (%) of Subjects Reporting at Least 1 ELAD-Related [2] TESAE	20 (21.1)	N/A	20 (9.9)
Related to ELAD Biologic	0	N/A	0
Related to ELAD Device	7 (7.4)	N/A	7 (3.4)
Related to ELAD Procedure	10 (10.5)	N/A	10 (4.9)
Unknown	4 (4.2)	N/A	4 (2.0)
Number (%) of Subjects with Any TEAE Leading to Premature Discontinuation of ELAD Treatment	27 (28.4)	N/A	27 (13.3)
Number (%) of Subjects with Any TESAE Leading to Premature Discontinuation of ELAD Treatment	13 (13.7)	N/A	13 (6.4)

Table 14.3.1.1b

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

Characteristic	ELAD Treatment (N=95)	Control (N=108)	Total (N=203)
Number of TESAEs	156	168	324
TESAEs by Severity, n (%)			
Mild	6 (3.8)	12 (7.1)	18 (5.6)
Moderate	52 (33.3)	48 (28.6)	100 (30.9)
Severe	98 (62.8)	108 (64.3)	206 (63.6)
TESAEs by ELAD Relationship, n (%)			
Not Related	129 (82.7)	168 (100.0)	297 (91.7)
Possibly Related	18 (11.5)	N/A	18 (5.6)
Probably Related	1 (0.6)	N/A	1 (0.3)
Related	8 (5.1)	N/A	8 (2.5)
TESAEs by Type of ELAD Relationship, n(%) [1]			
Related to ELAD Device	9 (5.8)	N/A	9 (2.8)
Related to ELAD Biologic	0 (0.0)	N/A	0 (0.0)
Related to ELAD Procedure	13 (8.3)	N/A	13 (4.0)
Unknown	5 (3.2)	N/A	5 (1.5)
Number (%) of TESAEs Leading to Premature Discontinuation of ELAD Treatment	14 (9.0)	N/A	14 (4.3)

Table 14.3.1.1.1b

Subjects with at least one TEAE by System Organ Class / Preferred Term: Descending Order

Preferred Term	ELAD Treatment (N=95) n (%)	Control (N=108) n (%)	Total (N=203) n (%)
Subjects Reporting at Least One TEAE	95 (100)	107 (99.1)	202 (99.5)
Ascites	37 (38.9)	38 (35.2)	75 (36.9)
Hepatic encephalopathy	42 (44.2)	33 (30.6)	75 (36.9)
Anaemia	46 (48.4)	19 (17.6)	65 (32.0)
Oedema peripheral	32 (33.7)	33 (30.6)	65 (32.0)
Renal failure acute	27 (28.4)	31 (28.7)	58 (28.6)
Abdominal pain	28 (29.5)	26 (24.1)	54 (26.6)
Hypokalaemia	22 (23.2)	30 (27.8)	52 (25.6)
Hypotension	31 (32.6)	19 (17.6)	50 (24.6)
Thrombocytopenia	35 (36.8)	12 (11.1)	47 (23.2)
Coagulopathy	31 (32.6)	13 (12.0)	44 (21.7)
Dyspnoea	21 (22.1)	21 (19.4)	42 (20.7)
Nausea	15 (15.8)	23 (21.3)	38 (18.7)
Pruritus	19 (20.0)	19 (17.6)	38 (18.7)
Diarrhoea	19 (20.0)	18 (16.7)	37 (18.2)
Hypophosphataemia	23 (24.2)	14 (13.0)	37 (18.2)
Pyrexia	25 (26.3)	12 (11.1)	37 (18.2)
Hypomagnesaemia	21 (22.1)	14 (13.0)	35 (17.2)
Hepatorenal syndrome	14 (14.7)	19 (17.6)	33 (16.3)
Metabolic acidosis	18 (18.9)	13 (12.0)	31 (15.3)
Pneumonia	15 (15.8)	16 (14.8)	31 (15.3)
Urinary tract infection	14 (14.7)	17 (15.7)	31 (15.3)
Vomiting	14 (14.7)	17 (15.7)	31 (15.3)

Table 14.3.1.2b

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

Subjects with at least one TEAE by System Organ Class / Preferred Term: Descending Order

Preferred Term	ELAD Treatment (N=95) n (%)	Control (N=108) n (%)	Total (N=203) n (%)
Subjects Reporting at Least One TEAE	95 (100)	107 (99.1)	202 (99.5)
Anxiety	21 (22.1)	9 (8.3)	30 (14.8)
Constipation	19 (20.0)	10 (9.3)	29 (14.3)
Hyperglycaemia	19 (20.0)	10 (9.3)	29 (14.3)
Insomnia	14 (14.7)	15 (13.9)	29 (14.3)
Leukocytosis	14 (14.7)	15 (13.9)	29 (14.3)
Hepatic failure	15 (15.8)	13 (12.0)	28 (13.8)
Tachycardia	17 (17.9)	10 (9.3)	27 (13.3)
Bacteraemia	17 (17.9)	9 (8.3)	26 (12.8)
Pleural effusion	12 (12.6)	14 (13.0)	26 (12.8)
Asterixis	9 (9.5)	16 (14.8)	25 (12.3)
Hyponatraemia	9 (9.5)	16 (14.8)	25 (12.3)
Abdominal distension	16 (16.8)	8 (7.4)	24 (11.8)
Agitation	16 (16.8)	8 (7.4)	24 (11.8)
Tremor	14 (14.7)	10 (9.3)	24 (11.8)
Back pain	9 (9.5)	13 (12.0)	22 (10.8)
Gastrointestinal haemorrhage	11 (11.6)	10 (9.3)	21 (10.3)
Hypocalcaemia	18 (18.9)	3 (2.8)	21 (10.3)
Oedema	9 (9.5)	12 (11.1)	21 (10.3)
Atelectasis	14 (14.7)	6 (5.6)	20 (9.9)
Multi-organ failure	9 (9.5)	10 (9.3)	19 (9.4)
Sepsis	10 (10.5)	9 (8.3)	19 (9.4)
Asthenia	6 (6.3)	12 (11.1)	18 (8.9)
Cardiac murmur	10 (10.5)	8 (7.4)	18 (8.9)
Headache	11 (11.6)	7 (6.5)	18 (8.9)
Rash	7 (7.4)	11 (10.2)	18 (8.9)
Confusional state	13 (13.7)	4 (3.7)	17 (8.4)
Epistaxis	11 (11.6)	6 (5.6)	17 (8.4)

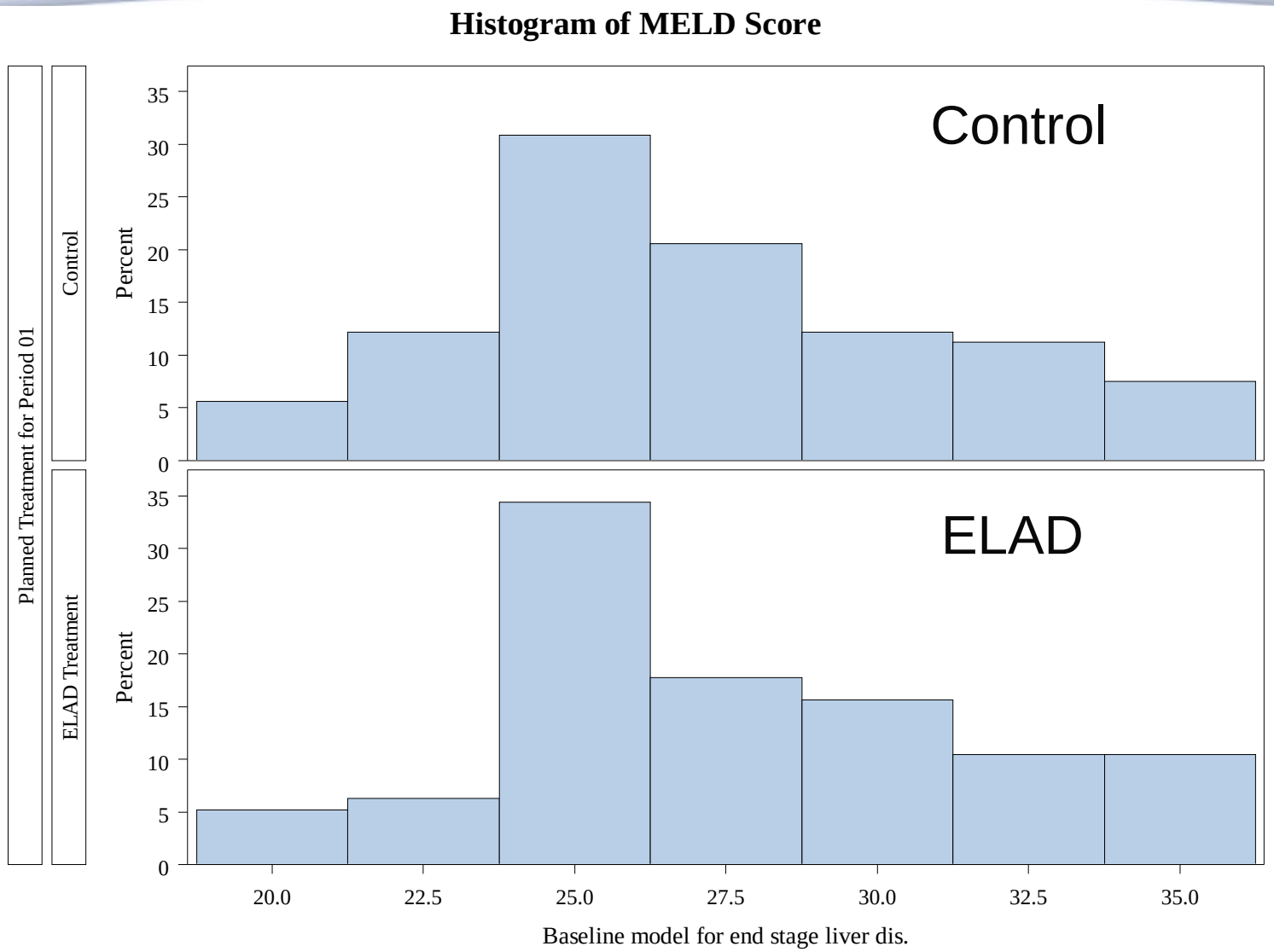
Subjects with at least one TEAE by System Organ Class / Preferred Term: Descending Order (used t14.3.1.3b)

Preferred Term	ELAD Treatment (N=95) n (%)	Control (N=108) n (%)	Total (N=203) n (%)
Subjects Reporting at Least One TEAE	95 (100)	107 (99.1)	202 (99.5)
Dehydration	7 (7.4)	6 (5.6)	13 (6.4)
Ecchymosis	7 (7.4)	6 (5.6)	13 (6.4)
Excoriation	9 (9.5)	4 (3.7)	13 (6.4)
Fall	8 (8.4)	5 (4.6)	13 (6.4)
Haemorrhoids	5 (5.3)	8 (7.4)	13 (6.4)
Hyperkalaemia	9 (9.5)	4 (3.7)	13 (6.4)
Hypernatraemia	8 (8.4)	5 (4.6)	13 (6.4)
Pulmonary oedema	8 (8.4)	5 (4.6)	13 (6.4)
Tachypnoea	7 (7.4)	6 (5.6)	13 (6.4)
Acute respiratory failure	8 (8.4)	4 (3.7)	12 (5.9)
Candidiasis	9 (9.5)	3 (2.8)	12 (5.9)
Portal hypertensive gastropathy	3 (3.2)	9 (8.3)	12 (5.9)
Septic shock	7 (7.4)	5 (4.6)	12 (5.9)
Catheter site haemorrhage	8 (8.4)	3 (2.8)	11 (5.4)
Hypoglycaemia	6 (6.3)	5 (4.6)	11 (5.4)
Hypovolaemia	6 (6.3)	5 (4.6)	11 (5.4)
Malnutrition	6 (6.3)	5 (4.6)	11 (5.4)
Pain in extremity	7 (7.4)	4 (3.7)	11 (5.4)
Acute respiratory distress syndrome	6 (6.3)	4 (3.7)	10 (4.9)
Arthralgia	7 (7.4)	3 (2.8)	10 (4.9)
Breath sounds abnormal	6 (6.3)	4 (3.7)	10 (4.9)
Clostridial infection	4 (4.2)	6 (5.6)	10 (4.9)
Disseminated intravascular coagulation	9 (9.5)	1 (0.9)	10 (4.9)

Ta[illegible] At each level of summation (overall, preferred term), subjects reporting more than one adverse event are counted only once. The descending order of incidence of TEAEs was based on the Total column.

Subgroup MELD

Distribution of Baseline MELD Scores



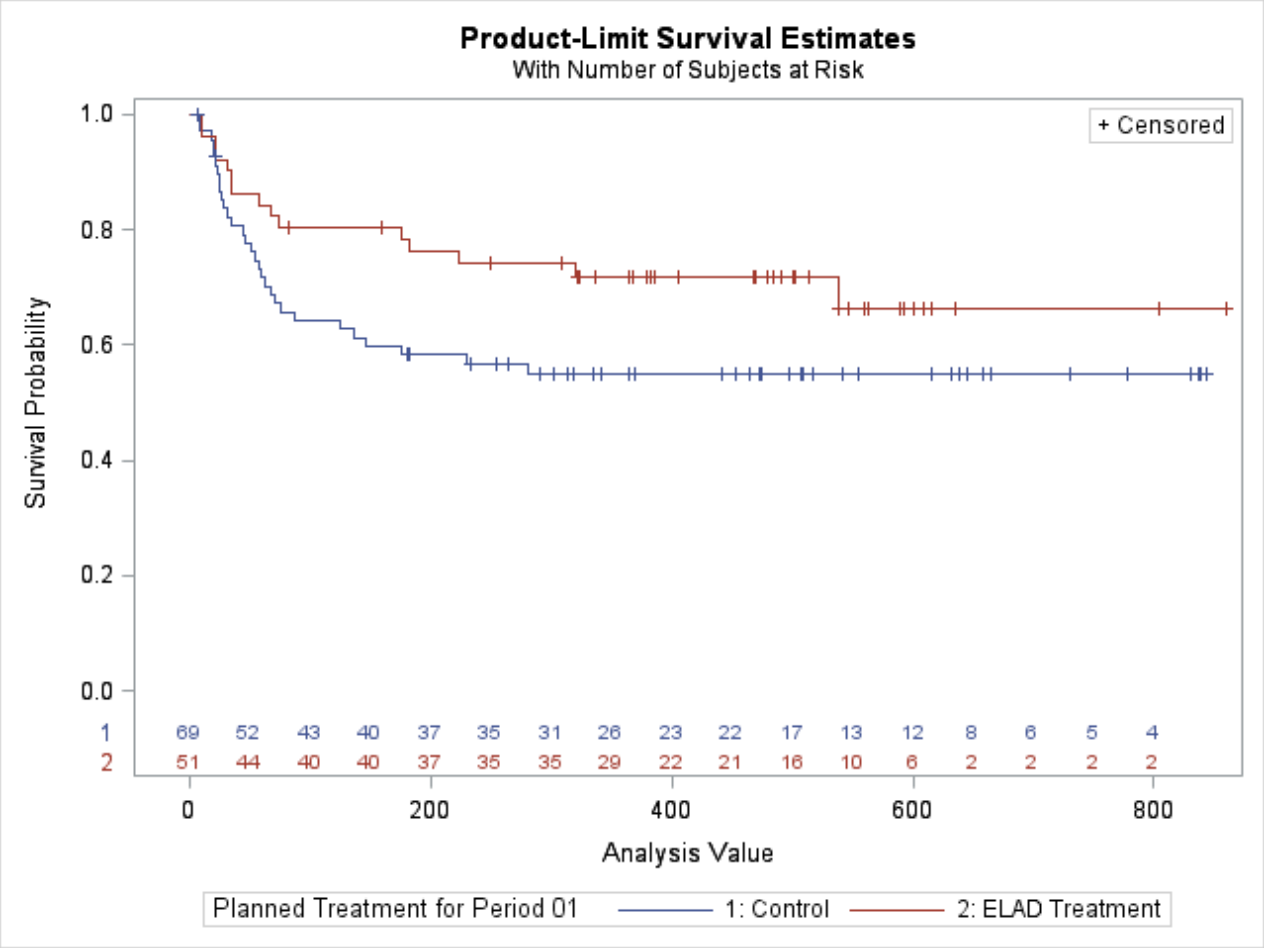
Subgroup Analyses: Overall Survival incl. VTI-208E: ITT

By MELD (< 28 vs ≥ 28)

	MELD Score <28				MELD Score ≥28		
Survival Estimates	ELAD Treatment (N=51)		Control (N=69)		ELAD Treatment (N=45)		Control (N=38)
Number (%) of Subjects who Died	15 (29.4)		30 (43.5)		31 (68.9)		21 (55.3)
Number (%) of Subjects Censored	36 (70.6)		39 (56.5)		14 (31.1)		17 (44.7)
Censored reason: Still Alive	35 (68.6)		37 (53.6)		14 (31.1)		16 (42.1)
Censored reason: Lost to Follow-Up	1 (2.0)		2 (2.9)		0		1 (2.6)
Min, Max (days)	10, 860		6, 843		6, 733		7, 757
Min, Max for Non-Censored Subjects (days)	10, 538		8, 280		6, 392		7, 162
Percentiles [95% CI] (days) [1] 25th	223 [35, -]		55 [26, 87]		15 [11, 21]		26 [13, 58]
Median	NA		NA		38 [21, 82]		131 [44, -]
75th	NA		NA		NA		NA
Hazard Ratio [95% CI]		0.575 [0.309, 1.070]				1.503 [0.863, 2.619]	
p-value [2]		0.077				0.146	

Table 14.2.6.3a

Subgroup Analyses: Overall Survival incl. VTI-208E: ITT Subjects with MELD < 28



Subgroup Analyses: Overall Survival incl. VTI-208E: PP

By MELD (< 28 vs ≥ 28)

Survival Estimates	MELD Score <28		MELD Score ≥28	
	ELAD Treatment (N=48)	Control (N=68)	ELAD Treatment (N=34)	Control (N=37)
Number (%) of Subjects who Died	13 (27.1)	29 (42.6)	22 (64.7)	20 (54.1)
Number (%) of Subjects Censored	35 (72.9)	39 (57.4)	12 (35.3)	17 (45.9)
Censored reason: Still Alive	34 (70.8)	37 (54.4)	12 (35.3)	16 (43.2)
Censored reason: Lost to Follow-Up	1 (2.1)	2 (2.9)	0	1 (2.7)
Min, Max (days)	10, 860	6, 843	6, 733	7, 757
Min, Max for Non-Censored Subjects (days)	10, 538	8, 280	6, 392	7, 162
Percentiles [95% CI] (days) [1]				
25th	223 [35, -]	55 [26, 125]	21 [12, 34]	26 [13, 49]
Median	NA	NA	60 [23, 392]	150 [40, -]
75th	NA	NA	NA	NA
Hazard Ratio [95% CI]	0.538 [0.280, 1.036]		1.296 [0.707, 2.376]	
p-value [2]	0.059		0.400	

Secondary Endpoints (MELD < 28 N = 120, ITT)

	Censor	ELAD	Control	Overall
Day 28	0	4 (7.8%)	11 (15.9%)	15 (12.5%)
Day 28	1	47 (92.2%)	58 (84.1%)	105 (87.5%)
Day 28: Chisq		0.1848		
Day 28: CMH		0.1850		
Day 91	0	10 (19.6%)	24 (34.8%)	34 (28.3%)
Day 91	1	41 (80.4%)	45 (65.2%)	86 (71.7%)
Day 91: Chisq		0.0682		
Day 91: CMH		0.0701		

Secondary Endpoints (MELD < 28 N = 116, PP)

	Censor	ELAD	Control	Overall
Day 28	0	3 (6.3%)	11 (16.2%)	14 (12.1%)
Day 28	1	45 (93.8%)	57 (83.8%)	102 (87.9%)
Day 28: Chisq		0.1060		
Day 28: CMH		0.1051		
Day 91	0	9 (18.8%)	23 (33.8%)	32 (27.6%)
Day 91	1	39 (81.3%)	45 (66.2%)	84 (72.4%)
Day 91: Chisq		0.0736		
Day 91: CMH		0.0750		

Demographics (1) MELD < 28

Characteristic	ELAD Treatment (N=51)	Control (N=69)	Total (N=120)
Randomization Stratum, n (%)			
Subject has AILD that is classified as severe Acute Alcoholic Hepatitis	47 (92.2)	64 (92.8)	111 (92.5)
Subject has AILD that is not classified as severe Acute Alcoholic Hepatitis	4 (7.8)	5 (7.2)	9 (7.5)
Age (years)			
n	51	69	120
Mean (SD)	45.6 (8.36)	45.8 (10.70)	45.7 (9.74)
Median	46.0	47.0	47.0
Min, Max	28, 59	26, 67	26, 67
Age Category, n (%)			
18-35 years	6 (11.8)	17 (24.6)	23 (19.2)
36-50 years	27 (52.9)	28 (40.6)	55 (45.8)
≥51 years	18 (35.3)	24 (34.8)	42 (35.0)
Sex, n (%)			
Male	25 (49.0)	40 (58.0)	65 (54.2)
Female	26 (51.0)	29 (42.0)	55 (45.8)
Ethnicity, n (%)			
Hispanic or Latino	6 (11.8)	9 (13.0)	15 (12.5)
Not Hispanic or Latino	45 (88.2)	60 (87.0)	105 (87.5)
Race, n (%)			
White	44 (86.3)	60 (87.0)	104 (86.7)
Black or African American	5 (9.8)	4 (5.8)	9 (7.5)
Asian	0	1 (1.4)	1 (0.8)
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	0	1 (1.4)	1 (0.8)
Other	2 (3.9)	3 (4.3)	5 (4.2)

Demographics (2) MELD < 28

Characteristic	ELAD Treatment (N=51)	Control (N=69)	Total (N=120)
Height (cm) [1]			
n	45	64	109
Mean (SD)	170.1 (11.84)	173.4 (10.54)	172.0 (11.16)
Median	170.0	173.0	172.0
Min, Max	144, 200	150, 193	144, 200
Weight (kg) [1]			
n	45	62	107
Mean (SD)	76.32 (21.518)	85.96 (20.740)	81.90 (21.508)
Median	69.00	81.50	78.50
Min, Max	48.0, 160.0	52.6, 162.1	48.0, 162.1

Liver disease characteristics (1) MELD < 28

Characteristic	ELAD Treatment (N=51)	Control (N=69)	Total (N=120)	p-value [1]
Medical treatments at Baseline, n (%):				
Steroids	24 (47.1)	39 (56.5)	63 (52.5)	0.305
Pentoxifylline	17 (33.3)	21 (30.4)	38 (31.7)	0.736
N-acetyl-cysteine	2 (3.9)	3 (4.3)	5 (4.2)	0.908
Baseline Model for Endstage Liver Disease (MELD) score				
n	51	69	120	
Mean (SD)	24.5 (1.87)	24.7 (1.94)	24.6 (1.91)	0.464
Median	25.0	25.0	25.0	
Min, Max	20, 27	20, 27	20, 27	
Category, n (%):				-
MELD Score <28	51 (100)	69 (100)	120 (100)	
MELD Score ≥28	0	0	0	
Serum Creatinine (mg/dL) at Baseline				
n	51	69	120	
Mean (SD)	0.74 (0.246)	0.75 (0.268)	0.75 (0.258)	0.924
Median	0.77	0.71	0.75	
Min, Max	0.3, 1.3	0.1, 1.4	0.1, 1.4	
Total Bilirubin (mg/dL) at Baseline				
n	51	69	120	
Mean (SD)	23.00 (7.925)	22.10 (7.759)	22.48 (7.810)	0.533
Median	23.50	22.30	22.95	
Min, Max	9.4, 52.6	8.6, 37.9	8.6, 52.6	
INR at Baseline				
n	51	69	120	
Mean (SD)	1.78 (0.331)	1.83 (0.359)	1.81 (0.347)	0.426
Median	1.70	1.80	1.80	
Min, Max	1.0, 2.5	1.2, 2.7	1.0, 2.7	

Liver disease characteristics (2) MELD < 28

Characteristic	ELAD Treatment (N=51)	Control (N=69)	Total (N=120)	p-value [1]
Subject had dialysis at least twice in the past week, n (%)				
Yes	0	0	0	
No	51 (100)	69 (100)	120 (100)	
Baseline Maddrey Discriminant Function (MDF) score				
n	51	69	120	
Mean (SD)	59.5 (13.97)	61.8 (18.00)	60.8 (16.39)	0.463
Median	58.0	59.0	58.0	
Min, Max	33, 92	32, 140	32, 140	
Prothrombin Time/PT (seconds) at Baseline				
n	51	69	120	
Mean (SD)	19.96 (3.394)	20.50 (4.313)	20.27 (3.942)	0.456
Median	19.50	20.50	20.40	
Min, Max	13.1, 28.0	12.7, 38.5	12.7, 38.5	
Laboratory Control PT (seconds) at Baseline				
n	51	69	120	
Mean (SD)	12.02 (1.409)	11.91 (1.312)	11.96 (1.349)	0.679
Median	11.50	11.30	11.35	
Min, Max	10.0, 15.5	10.0, 15.0	10.0, 15.5	
Total Bilirubin (mg/dL) at Baseline				
n	51	69	120	
Mean (SD)	23.00 (7.925)	22.27 (7.976)	22.58 (7.929)	0.617
Median	23.50	22.30	22.95	
Min, Max	9.4, 52.6	8.6, 39.6	8.6, 52.6	

Liver disease characteristics (3) MELD < 28

Characteristic	ELAD Treatment (N=51)	Control (N=69)	Total (N=120)	p-value [1]
On renal replacement therapy (hemodialysis, CVVHD, CVVH, peritoneal, etc) at randomization, n (%)				-
Yes	0	0	0	
No	51 (100)	69 (100)	120 (100)	
On vasopressors at Baseline, n (%)				0.404
Yes	3 (5.9)	7 (10.1)	10 (8.3)	
No	48 (94.1)	62 (89.9)	110 (91.7)	
On ventilator / intubated at Baseline, n (%)				0.038
Yes	5 (9.8)	1 (1.4)	6 (5.0)	
No	46 (90.2)	68 (98.6)	114 (95.0)	
Time since last alcohol consumption (prior to date of current hospital admission) (days)				
n	51	69	120	
Mean (SD)	17.7 (13.68)	16.9 (14.88)	17.3 (14.33)	0.760
Median	12.0	12.0	12.0	
Min, Max	3, 69	4, 94	3, 94	
Category, n (%):				0.455
0-7 days	14 (27.5)	16 (23.2)	30 (25.0)	
8-14 days	13 (25.5)	27 (39.1)	40 (33.3)	
15 days-1 month	16 (31.4)	16 (23.2)	32 (26.7)	
>1 month	8 (15.7)	10 (14.5)	18 (15.0)	
Time from hospital admission to randomization (days)				
n	51	69	120	
Mean (SD)	8.3 (5.79)	7.8 (4.87)	8.0 (5.27)	0.594
Median	6.0	7.0	6.5	
Min, Max	2, 27	1, 25	1, 27	

Safety Summary MELD < 28 (N = 120)

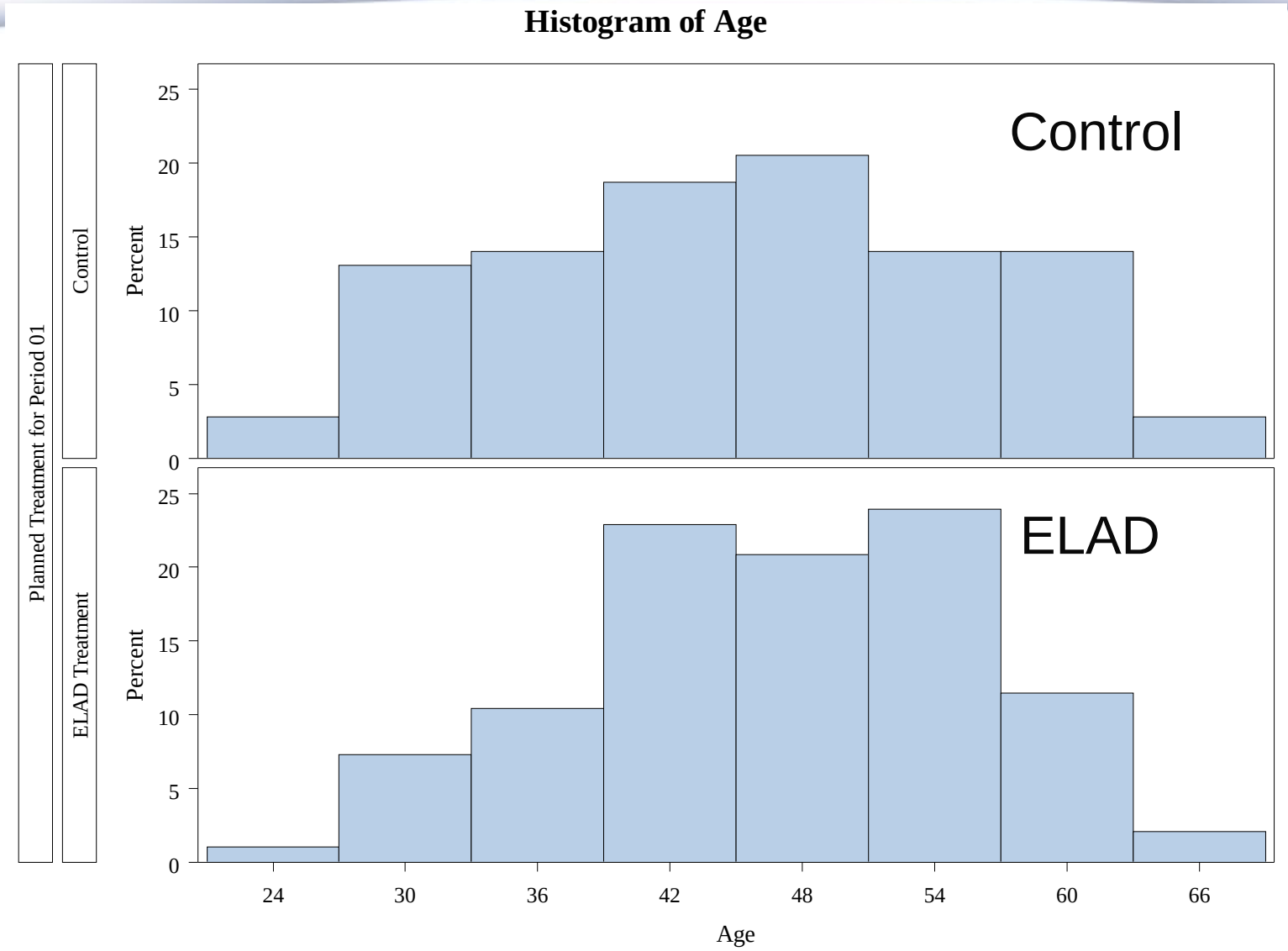
Characteristic	ELAD Treatment (N=52)	Control (N=68)	Total (N=120)
Number (%) of Subjects Reporting Any TEAE	52 (100)	68 (100)	120 (100)
Number of TEAEs	938	984	1922
Number (%) of Subjects Reporting Any TESAE	37 (71.2)	43 (63.2)	80 (66.7)
Number of TESAEs	69	101	170
Subjects with TEAEs by Highest Severity [1], n (%)			
Mild	1 (1.9)	8 (11.8)	9 (7.5)
Moderate	19 (36.5)	22 (32.4)	41 (34.2)
Severe	32 (61.5)	38 (55.9)	70 (58.3)
Subjects with TESAEs by Highest Severity [1], n (%)			
Mild	1 (1.9)	3 (4.4)	4 (3.3)
Moderate	12 (23.1)	7 (10.3)	19 (15.8)
Severe	24 (46.2)	33 (48.5)	57 (47.5)
Number (%) of Subjects Reporting at Least 1 ELAD-Related [2] TEAE	39 (75.0)	0	39 (32.5)
Related to ELAD Biologic	4 (7.7)	0	4 (3.3)
Related to ELAD Device	19 (36.5)	0	19 (15.8)
Related to ELAD Procedure	19 (36.5)	0	19 (15.8)
Unknown	10 (19.2)	0	10 (8.3)

Safety Summary MELD < 28 (N = 120)

Characteristic	ELAD Treatment (N=52)	Control (N=68)	Total (N=120)
Number (%) of Subjects Reporting at Least 1 ELAD-Related [2] TESAE	11 (21.2)	N/A	11 (9.2)
Related to ELAD Biologic	0	N/A	0
Related to ELAD Device	3 (5.8)	N/A	3 (2.5)
Related to ELAD Procedure	6 (11.5)	N/A	6 (5.0)
Unknown	2 (3.8)	N/A	2 (1.7)
Number (%) of Subjects with Any TEAE Leading to Premature Discontinuation of ELAD Treatment	10 (19.2)	N/A	10 (8.3)
Number (%) of Subjects with Any TESAE Leading to Premature Discontinuation of ELAD Treatment	5 (9.6)	N/A	5 (4.2)

Sub Group Age

Distribution of Baseline Age



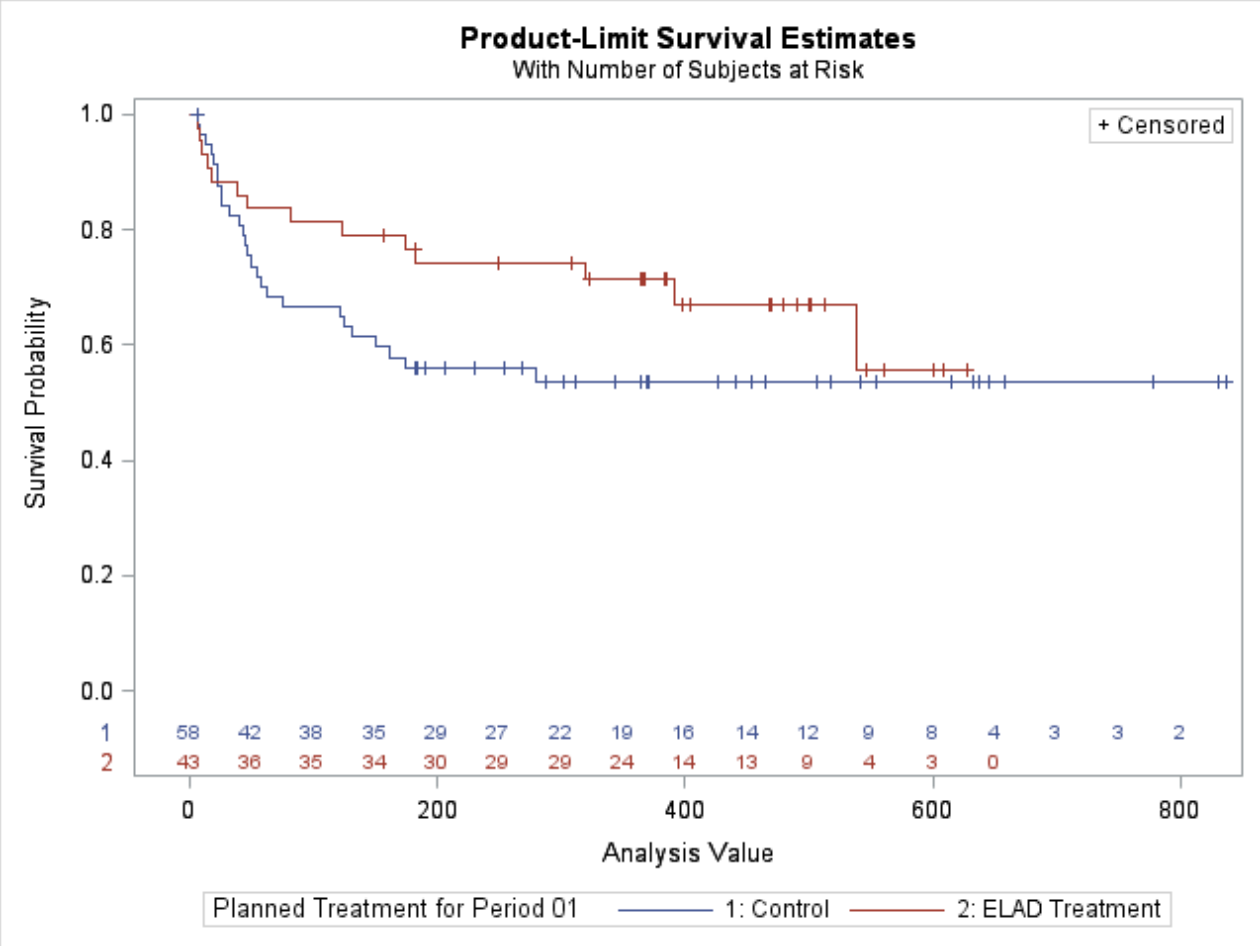
Subgroup Analyses: Overall Survival incl. VTI-208E: ITT

By Age

	Age < Median Years				Age ≥ Median Years		
Survival Estimates	ELAD Treatment (N=43)		Control (N=58)		ELAD Treatment (N=53)		Control (N=49)
Number (%) of Subjects who Died	14 (32.6)		26 (44.8)		32 (60.4)		25 (51.0)
Number (%) of Subjects Censored	29 (67.4)		32 (55.2)		21 (39.6)		24 (49.0)
Censored reason: Still Alive	29 (67.4)		31 (53.4)		20 (37.7)		22 (44.9)
Censored reason: Lost to Follow-Up	0		1 (1.7)		1 (1.9)		2 (4.1)
Min, Max (days)	6, 628		6, 837		6, 860		7, 843
Min, Max for Non-Censored Subjects (days)	6, 538		7, 280		6, 223		7, 230
Percentiles [95% CI] (days) [1]							
25th	183 [18, -]		49 [26, 125]		21 [14, 30]		28 [20, 59]
Median	NA		NA		58 [30, -]		147 [58, -]
75th	NA		NA		NA		NA
Hazard Ratio [95% CI]		0.634 [0.331, 1.217]				1.347 [0.798, 2.275]	
p-value [2]		0.167				0.261	

Table 14.2.6.1a

Subgroup Analyses: Overall Survival incl. VTI-208E: ITT Subjects < median age (46.9 yrs)



Secondary Endpoints (< median age N = 101, ITT)

	Censor	ELAD	Control	Overall
Day 28	0	5 (11.6%)	9 (15.5%)	14 (13.9%)
Day 28	1	38 (88.4%)	49 (84.5%)	87 (86.1%)
Day 28: Chisq		0.5759		
Day 28: CMH		0.6107		
Day 91	0	8 (18.6%)	19 (32.8%)	27 (26.7%)
Day 91	1	35 (81.4%)	39 (67.2%)	74 (73.3%)
Day 91: Chisq		0.1120		
Day 91: CMH		0.1134		

Subgroup Analyses: Overall Survival incl. VTI-208E: PP

By Age

Survival Estimates	Age < Median Years		Age ≥ Median Years	
	ELAD Treatment (N=38)	Control (N=56)	ELAD Treatment (N=44)	Control (N=49)
Number (%) of Subjects who Died	11 (28.9)	24 (42.9)	24 (54.5)	25 (51.0)
Number (%) of Subjects Censored	27 (71.1)	32 (57.1)	20 (45.5)	24 (49.0)
Censored reason: Still Alive	27 (71.1)	31 (55.4)	19 (43.2)	22 (44.9)
Censored reason: Lost to Follow-Up	0	1 (1.8)	1 (2.3)	2 (4.1)
Min, Max (days)	9, 628	6, 837	6, 860	7, 843
Min, Max for Non-Censored Subjects (days)	9, 538	7, 280	6, 223	7, 230
Percentiles [95% CI] (days) [1]				
25th	392 [38, -]	46 [26, 131]	24 [14, 35]	28 [20, 59]
Median	NA	NA	77 [34, -]	147 [58, -]
75th	NA	NA	NA	NA
Hazard Ratio [95% CI]	0.578 [0.283, 1.182]		1.106 [0.632, 1.937]	
p-value [2]	0.128		0.724	

Secondary Endpoints (< median age N = 94, PP)

	Censor	ELAD	Control	Overall
Day 28	0	3 (7.9%)	9 (16.1%)	12 (12.8%)
Day 28	1	35 (92.1%)	47 (83.9%)	82 (87.2%)
Day 28: Chisq		0.2437		
Day 28: CMH		0.2672		
Day 91	0	6 (15.8%)	18 (32.1%)	24 (25.5%)
Day 91	1	32 (84.2%)	38 (67.9%)	70 (74.5%)
Day 91: Chisq		0.0744		
Day 91: CMH		0.0766		

Liver disease characteristics (1) < median Age

Characteristic	ELAD Treatment (N=43)	Control (N=58)	Total (N=101)	p-value [1]
Medical treatments at Baseline, n (%):				
Steroids	20 (46.5)	27 (46.6)	47 (46.5)	0.997
Pentoxifylline	14 (32.6)	27 (46.6)	41 (40.6)	0.157
N-acetyl-cysteine	3 (7.0)	3 (5.2)	6 (5.9)	0.704
Baseline Model for Endstage Liver Disease (MELD) score				
n	43	58	101	
Mean (SD)	27.0 (3.27)	27.8 (3.84)	27.5 (3.61)	0.306
Median	27.0	27.0	27.0	
Min, Max	20, 35	20, 35	20, 35	
Category, n (%):				0.719
MELD Score <28	26 (60.5)	33 (56.9)	59 (58.4)	
MELD Score ≥28	17 (39.5)	25 (43.1)	42 (41.6)	
Serum Creatinine (mg/dL) at Baseline				
n	43	58	101	
Mean (SD)	0.92 (0.560)	0.94 (0.582)	0.93 (0.570)	0.855
Median	0.84	0.80	0.80	
Min, Max	0.3, 3.2	0.1, 3.2	0.1, 3.2	
Total Bilirubin (mg/dL) at Baseline				
n	43	58	101	
Mean (SD)	24.78 (7.965)	23.83 (9.423)	24.23 (8.802)	0.594
Median	24.40	22.80	23.90	
Min, Max	10.5, 56.8	8.6, 44.6	8.6, 56.8	
INR at Baseline				
n	43	58	101	
Mean (SD)	2.01 (0.487)	2.17 (0.461)	2.10 (0.477)	0.090
Median	1.90	2.13	2.00	
Min, Max	1.2, 3.3	1.3, 3.2	1.2, 3.3	

Liver disease characteristics (2) < median Age

Characteristic	ELAD Treatment (N=43)	Control (N=58)	Total (N=101)	p-value [1]
Subject had dialysis at least twice in the past week, n (%)				
Yes	0	0	0	
No	43 (100)	58 (100)	101 (100)	
Baseline Maddrey Discriminant Function (MDF) score				
n	43	58	101	
Mean (SD)	71.3 (23.08)	77.3 (22.18)	74.8 (22.65)	0.189
Median	67.0	76.0	72.0	
Min, Max	33, 127	32, 127	32, 127	
Prothrombin Time/PT (seconds) at Baseline				
n	43	58	101	
Mean (SD)	22.22 (4.809)	23.79 (4.442)	23.12 (4.644)	0.094
Median	21.60	23.45	22.50	
Min, Max	13.6, 34.1	14.0, 33.3	13.6, 34.1	
Laboratory Control PT (seconds) at Baseline				
n	43	58	101	
Mean (SD)	12.10 (1.518)	12.17 (1.315)	12.14 (1.398)	0.806
Median	11.50	11.80	11.70	
Min, Max	10.4, 15.5	10.4, 15.0	10.4, 15.5	
Total Bilirubin (mg/dL) at Baseline				
n	43	58	101	
Mean (SD)	24.76 (7.986)	23.86 (9.409)	24.24 (8.801)	0.614
Median	24.40	22.80	23.90	
Min, Max	10.5, 56.8	8.6, 44.6	8.6, 56.8	

Liver disease characteristics (3) < median Age

Characteristic	ELAD Treatment (N=43)	Control (N=58)	Total (N=101)	p-value [1]
On renal replacement therapy (hemodialysis, CVVHD, CVVH, peritoneal, etc) at randomization, n (%)				-
Yes	0	0	0	
No	43 (100)	58 (100)	101 (100)	
On vasopressors at Baseline, n (%)				0.318
Yes	5 (11.6)	11 (19.0)	16 (15.8)	
No	38 (88.4)	47 (81.0)	85 (84.2)	
On ventilator / intubated at Baseline, n (%)				0.017
Yes	6 (14.0)	1 (1.7)	7 (6.9)	
No	37 (86.0)	57 (98.3)	94 (93.1)	
Time since last alcohol consumption (prior to date of current hospital admission) (days)				
n	43	57	100	
Mean (SD)	17.8 (12.71)	18.9 (16.69)	18.4 (15.05)	0.700
Median	15.0	14.0	14.0	
Min, Max	4, 69	3, 94	3, 94	
Category, n (%):				0.757
0-7 days	7 (16.3)	13 (22.4)	20 (19.8)	
8-14 days	14 (32.6)	17 (29.3)	31 (30.7)	
15 days-1 month	16 (37.2)	17 (29.3)	33 (32.7)	
>1 month	6 (14.0)	10 (17.2)	16 (15.8)	
Time from hospital admission to randomization (days)				
n	43	58	101	
Mean (SD)	9.2 (5.66)	9.7 (9.09)	9.5 (7.78)	0.766
Median	8.0	7.0	7.0	
Min, Max	2, 27	2, 61	2, 61	

Demographics (1) < median Age

Characteristic	ELAD Treatment (N=43)	Control (N=58)	Total (N=101)
Randomization Stratum, n (%)			
Subject has AILD that is classified as severe Acute Alcoholic Hepatitis	42 (97.7)	55 (94.8)	97 (96.0)
Subject has AILD that is not classified as severe Acute Alcoholic Hepatitis	1 (2.3)	3 (5.2)	4 (4.0)
Age (years)			
n	43	58	101
Mean (SD)	38.2 (5.55)	36.6 (5.93)	37.3 (5.80)
Median	39.0	37.0	39.0
Min, Max	25, 46	25, 46	25, 46
Age Category, n (%)			
18-35 years	12 (27.9)	25 (43.1)	37 (36.6)
36-50 years	31 (72.1)	33 (56.9)	64 (63.4)
≥51 years	0	0	0
Sex, n (%)			
Male	22 (51.2)	33 (56.9)	55 (54.5)
Female	21 (48.8)	25 (43.1)	46 (45.5)
Ethnicity, n (%)			
Hispanic or Latino	10 (23.3)	7 (12.1)	17 (16.8)
Not Hispanic or Latino	33 (76.7)	51 (87.9)	84 (83.2)
Race, n (%)			
White	38 (88.4)	50 (86.2)	88 (87.1)
Black or African American	3 (7.0)	3 (5.2)	6 (5.9)
Asian	0	2 (3.4)	2 (2.0)
Native Hawaiian or Other Pacific Islander	0	0	0
American Indian or Alaska Native	0	1 (1.7)	1 (1.0)
Other	2 (4.7)	2 (3.4)	4 (4.0)

Demographics (2) < median Age

Characteristic	ELAD Treatment (N=51)	Control (N=69)	Total (N=120)
Height (cm) [1]			
n	45	64	109
Mean (SD)	170.1 (11.84)	173.4 (10.54)	172.0 (11.16)
Median	170.0	173.0	172.0
Min, Max	144, 200	150, 193	144, 200
Weight (kg) [1]			
n	45	62	107
Mean (SD)	76.32 (21.518)	85.96 (20.740)	81.90 (21.508)
Median	69.00	81.50	78.50
Min, Max	48.0, 160.0	52.6, 162.1	48.0, 162.1

Safety Summary age < median (N = 101)

Characteristic	ELAD Treatment (N=43)	Control (N=58)	Total (N=101)
Number (%) of Subjects Reporting Any TEAE	43 (100)	57 (98.3)	100 (99.0)
Number of TEAEs	837	830	1667
Number (%) of Subjects Reporting Any TESAE	29 (67.4)	37 (63.8)	66 (65.3)
Number of TESAEs	65	83	148
Subjects with TEAEs by Highest Severity [1], n (%)			
Mild	1 (2.3)	6 (10.3)	7 (6.9)
Moderate	17 (39.5)	21 (36.2)	38 (37.6)
Severe	25 (58.1)	30 (51.7)	55 (54.5)
Subjects with TESAEs by Highest Severity [1], n (%)			
Mild	0	1 (1.7)	1 (1.0)
Moderate	9 (20.9)	8 (13.8)	17 (16.8)
Severe	20 (46.5)	28 (48.3)	48 (47.5)
Number (%) of Subjects Reporting at Least 1 ELAD-Related [2] TEAE	30 (69.8)	0	30 (29.7)
Related to ELAD Biologic	2 (4.7)	0	2 (2.0)
Related to ELAD Device	11 (25.6)	0	11 (10.9)
Related to ELAD Procedure	15 (34.9)	0	15 (14.9)
Unknown	9 (20.9)	0	9 (8.9)
Number (%) of Subjects Reporting at Least 1 ELAD-Related [2] TESAE	9 (20.9)	N/A	9 (8.9)
Related to ELAD Biologic	0	N/A	0
Related to ELAD Device	2 (4.7)	N/A	2 (2.0)
Related to ELAD Procedure	4 (9.3)	N/A	4 (4.0)
Unknown	3 (7.0)	N/A	3 (3.0)
Number (%) of Subjects with Any TEAE Leading to Premature Discontinuation of ELAD Treatment	9 (20.9)	N/A	9 (8.9)
Number (%) of Subjects with Any TESAE Leading to Premature Discontinuation of ELAD Treatment			

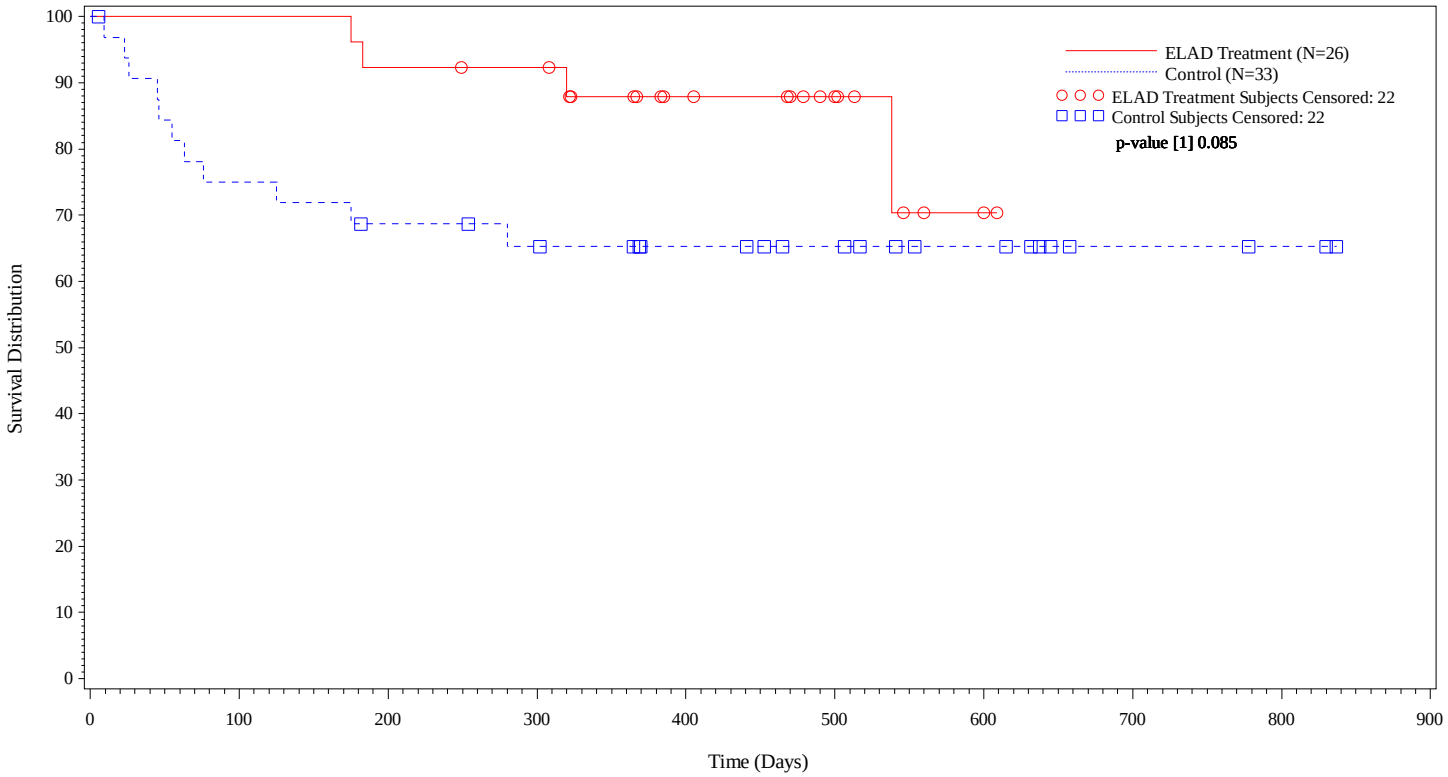
MELD < 28 and Age < median

Primary Endpoint
Overall Survival, ITT population, including VTI-208E through 7/30/15
Age < median years (46.9 yrs) *and* Baseline MELD <28

Survival Estimates	ELAD Treatment (N=26)		Control (N=33)
Number (%) of Subjects who Died	4 (15.4)		11 (33.3)
Number (%) of Subjects Censored	22 (84.6)		22 (66.7)
Censored reason: Still Alive	22 (84.6)		21 (63.6)
Censored reason: Lost to Follow-Up	0		1 (3.0)
Min, Max (days)	175, 609		6, 837
Min, Max for Non-Censored Subjects (days)	175, 538		9, 280
Percentiles [95% CI] (days) [1]			
25th	538 [183, -]		101 [26, -]
Median	NA		NA
75th	NA		NA
Hazard Ratio [95% CI]		0.374 [0.118, 1.184]	
p-value [2]		0.085	

Primary Endpoint
Overall Survival, ITT population, including VTI-208E through 7/30/15
Age < median years (46.9yrs) *and* Baseline MELD <28

Figure 14.2.1.1a
Summary of Kaplan-Meier Analysis of Overall Survival for Subjects with Age <Median years and Baseline MELD <28
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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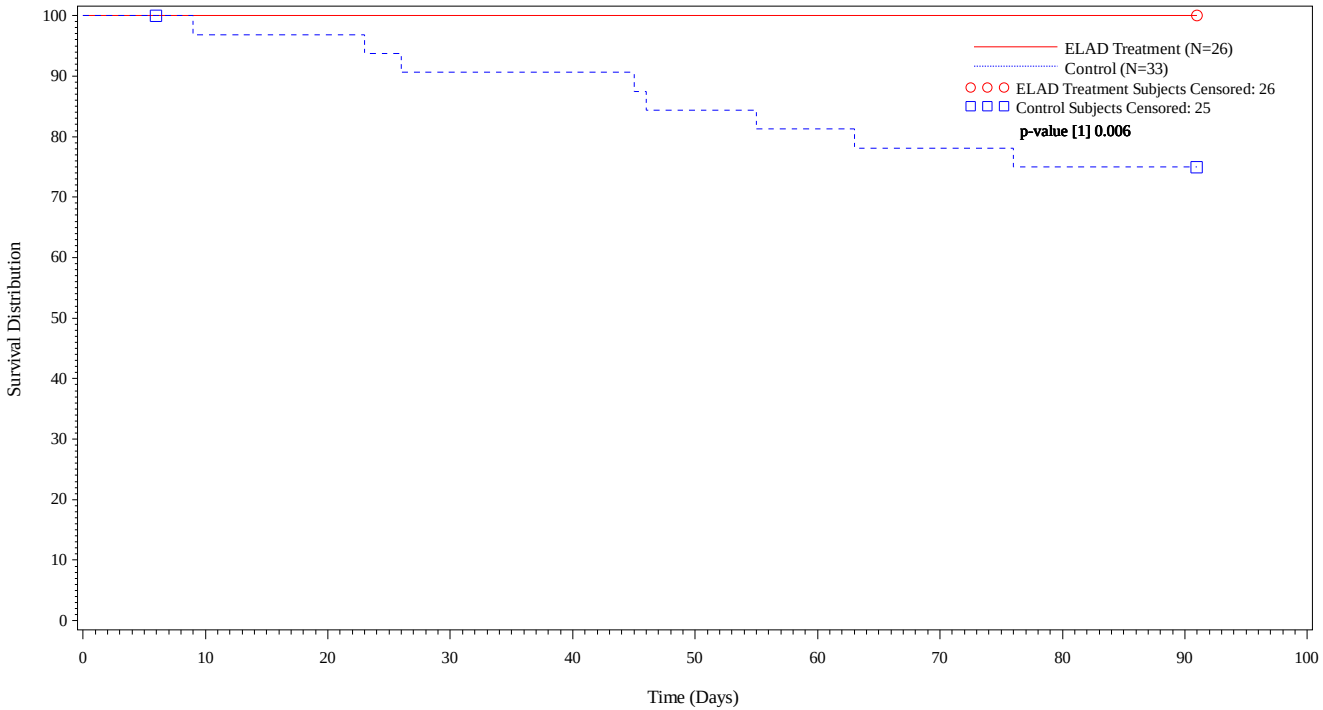
Primary Endpoint
Overall Survival, ITT population, up to Study Day 91
Age < median years (46.9 yrs) *and* Baseline MELD <28

Survival Estimates	ELAD Treatment (N=26)	Control (N=33)
Number (%) of Subjects who Died	0	8 (24.2)
Number (%) of Subjects Censored	26 (100)	25 (75.8)
Censored reason: Still Alive	26 (100)	24 (72.7)
Censored reason: Lost to Follow-Up	0	1 (3.0)
Min, Max (days)	91, 91	6, 91
Min, Max for Non-Censored Subjects (days)	-, -	9, 76
Percentiles [95% CI] (days) [1]		
25th	NA	NA
Median	NA	NA
75th	NA	NA
Hazard Ratio [95% CI]	0.000 [0.000, -]	
p-value [2]	0.006	

Primary Endpoint
Overall Survival, ITT population, up to Study Day 91
Age < median years (46.9 yrs) *and* Baseline MELD <28

Figure 14.2.2.1a
Summary of Kaplan-Meier Analysis of Overall Survival up to Study Day 91 for Subjects with Age <Median years and Baseline MELD <28
ITT Population



Overall Survival up to Study Day 91 excludes data from follow-up Protocol VTI-208E that is after Study Day 91.
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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