

# Management of refractory ascites and the role of the alfapump

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# alfapump<sup>®</sup> System vs Large Volume Paracentesis in the Treatment of Refractory Ascites: A Multicentre Randomised Controlled Study

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UK (2), France (2), Spain, Austria, Italy,

# RCT Study Overview

## Design

- Multicentre, open, randomised, and controlled trial in 7 European centres
- 60 patients  $\geq 18$  years with refractory ascites, randomised to either treatment with **alfapump** system (AP) or Standard of Care (SoC) with evacuation large volume paracentesis

## Primary Objective (6 months)

- Paracentesis-free survival
  - Defined as time to first large volume therapeutic paracentesis (LVP)  $\geq 5$  litres

## Secondary Objectives (6 months)

- Cirrhosis-related complications
- Nutrition
- Survival
- Quality of life
- Need for repeat paracentesis

# Baseline Demographics

	AP N=27	SoC N=31	P-value†	Sub-study N=17	Not in Sub-study N=41	P-value†
Age (years), mean (SD)	61.1 (8.5)	62.6 (8.4)	0.537	62.6 (7.4)	61.6 (8.9)	0.592
Gender (male), n (%)	21 (77.8%)	25 (80.6%)	1	13 (76.5%)	33 (80.5%)	0.733
BMI (kg/m <sup>2</sup> ), mean (SD)	27.7 (4.8)	27.3 (5.7)	0.596	26.4 (4.6)	28.0 (5.5)	0.406
MELD Score, mean (SD)	12.2 (2.5)	11.3 (3.9)	0.121	12.7 (3.9)	11.4 (3.0)	0.442
Child-Pugh score, mean (SD)	8.2 (1.1)	8.4 (1.1)	0.78	8.1 (1.3)	8.4 (1.0)	0.197
Child Pugh Class, n (%)						
B	22 (81.5%)	24 (77.4%)	0.855	14/16 (87.5%)	32/38 (84.2%)	0.756
C	3 (11.1%)	5 (16.1%)		2/16 (12.5%)	6/38 (15.8%)	
Etiology of Liver Cirrhosis, n (%)						
Alcohol	20 (74.1%)	21 (67.7%)	0.773	10 (58.8%)	31 (75.6%)	0.221
Non-alcohol	7 (25.9%)	10 (32.3%)		7 (41.2%)	10 (24.4%)	
Time since start of paracentesis treatment (years), median (Q1, Q3)	1.1 (1, 2)	1.0 (1, 2)	0.397	1.1 (0.7, 1.7)	1.0 (0.6, 2.1)	0.868
History prior to enrolment						
Renal failure, n	<b>11 (40.7%)</b>	<b>6 (19.4%)</b>	<b>0.163</b>	<b>9 (52.9%)</b>	<b>9 (22.0%)</b>	<b>0.020</b>
Hepatorenal syndrome, n	3 (11.1%)	4 (12.9%)	1.000	3 (17.7%)	5 (12.2%)	0.681
Hepatic encephalopathy, n	8 (29.6%)	9 (29.0%)	0.784	6 (35.3%)	12 (29.3%)	0.652
Spontaneous bacterial peritonitis, n	7 (25.9%)	7 (22.6%)	0.764	4 (23.5%)	10 (24.4%)	0.944
Urinary infection, n	1 (3.7%)	3 (9.7%)	0.617	0 (0%)	4 (9.8%)	0.310
Variceal haemorrhage, n	11 (40.7%)	6 (19.4%)	0.090	6 (35.3%)	11 (26.8%)	0.540
Hospitalized in previous 3 months, n (%)*	14 (52%)	21 (68%)	0.285	16 (94.1%)	19 (46.3%)	<0.001

\*all overnight hospitalizations in both groups due to liver disease including those for paracenteses, spontaneous bacterial peritonitis, and TIPS and transplant evaluations

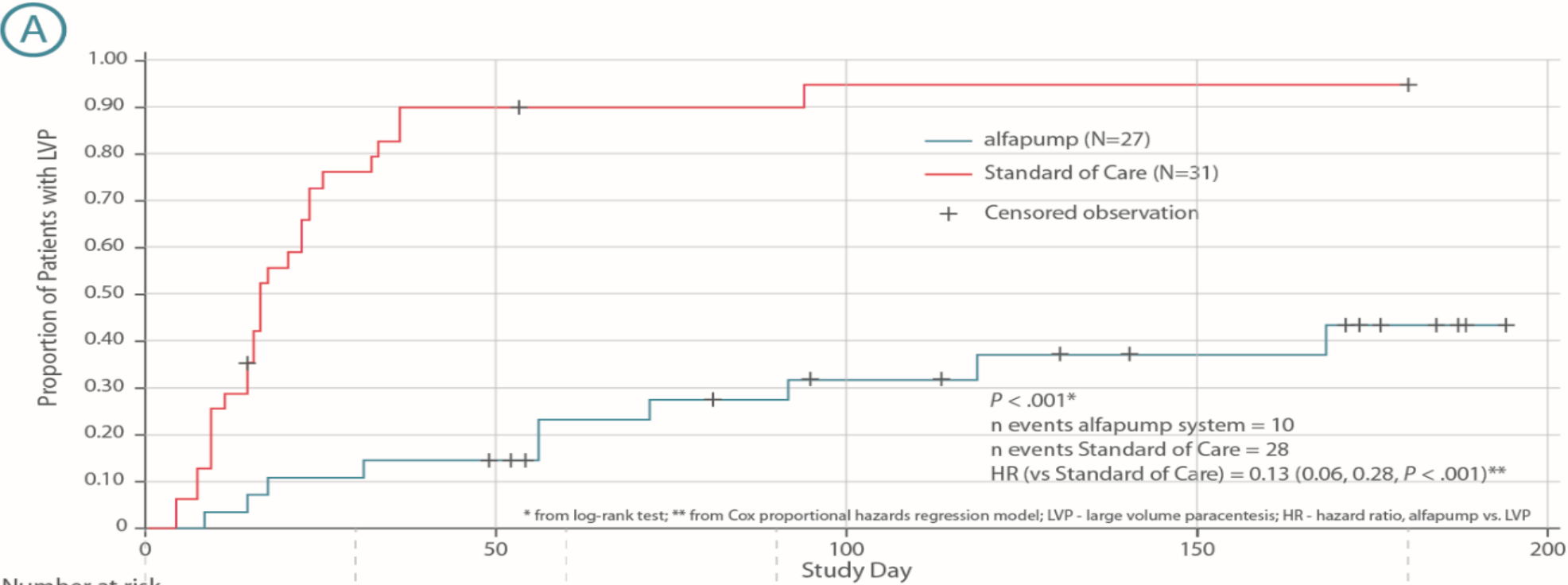
\*\*investigator or patient choice

AP, alfapump system; SoC, Standard of Care; SD, standard deviation; TIPS, transjugular intrahepatic portosystemic shunt

†All p-values Chi-Square test except Mann-Whitney U (Age, BMI, MELD, Child-Pugh score, time since start of paracentesis, and time on study)

# alfapump Significantly Increases Time to First LVP

Kaplan-Meier Plot of Time to First LVP



Number at risk

Day	0	30	60	90	180
AP	27	27	24	22	12
SoC	31	30	29	27	12

Median time to LVP was 15 days in SoC group versus >6 months in the alfapump group ( $p < 0.001$ )

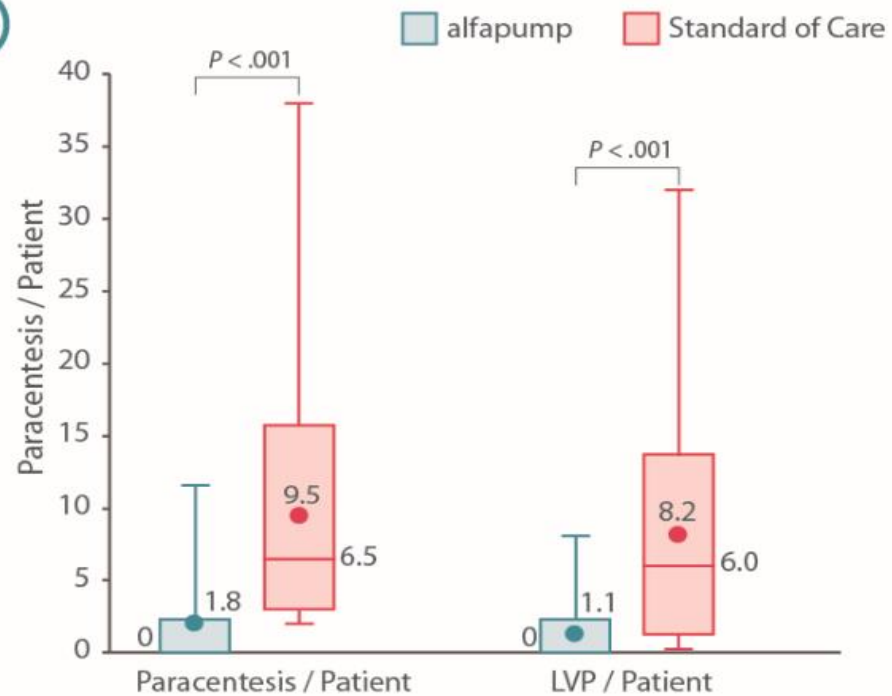


But....No difference was noted in survival

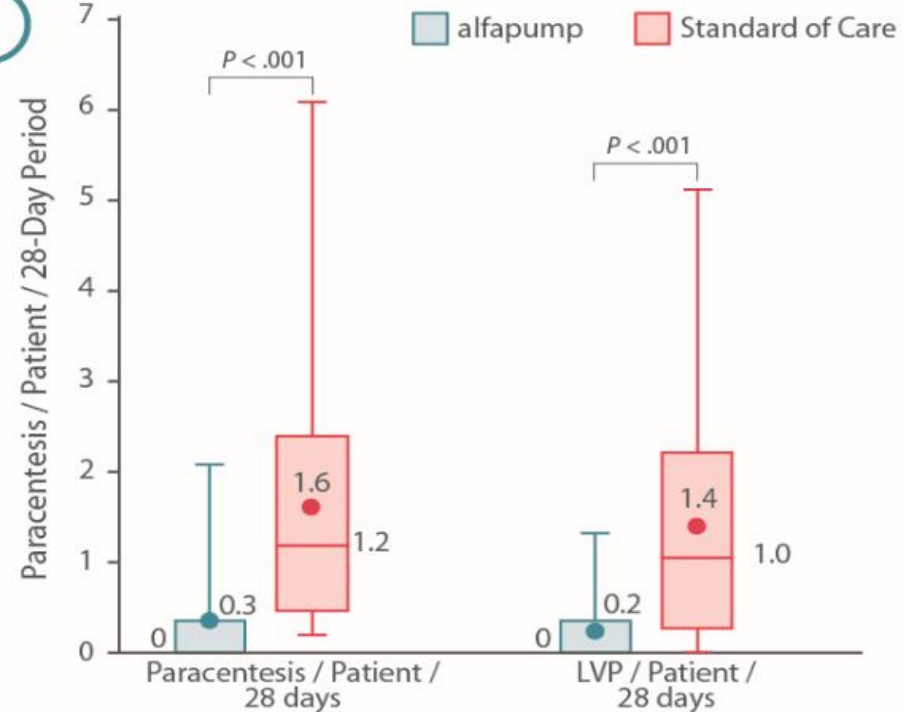
# alfapump Significantly Reduces Need for Paracentesis

## Median Number of Paracentesis

(B)



(C)



Median number of LVPs per month is **reduced** from 1.0 in SoC group to ZERO in alfapump group



# Nutritional Parameters

Parameter		Baseline		Day 30		Day 90	
		AP	SoC	AP	SoC	AP	SoC
<b>Royal Free Hospital General Assessment, n (%)</b>							
Adequately Nourished		2 (25.0)	4 (50.0)	4 (50.0)	4 (50.0)	4 (66.7)	3 (50.0)
Moderately Malnourished		5 (62.5)	2 (25.0)	4 (50.0)	2 (25.0)	2 (33.3)	1 (16.7)
Severely Malnourished		1 (12.5)	2 (25.0)	0 (0)	2 (25.0)	0 (0)	2 (33.3)
P-Value*		-		0.099		0.090	
<b>BMI (kg/m<sup>2</sup>)</b>	N			7	8	6	7
	Adjusted change <sup>1</sup>	-	-	1.237	-0.145	1.992	-0.650
	P-Value	-		0.056		<0.001	
<b>TSF (mm)</b>	N			7	8	6	6
	Adjusted change <sup>1</sup>	-	-	0.466	-0.432	1.898	-0.848
	P-Value	-		0.137		0.003	
<b>MAMC (cm)</b>	N			7	8	6	6
	Adjusted change <sup>1</sup>	-	-	0.89	-0.24	1.80	0.16
	P-Value	-		0.010		0.008	
<b>Hand-grip (kg)</b>	N			7	8	6	6
	Adjusted change <sup>1</sup>	-	-	2.44	0.84	4.03	-1.69
	P-Value	-		0.447		0.044	

\*Nourishment data were on an ordinal scale, whereby the three categories were ordered. These data were analyzed by the Cochran-Mantel-Haenszel procedure, in which the one- and three-month data were stratified by their baseline category. For the analysis, the three ordered categories were assumed to be equally spaced.

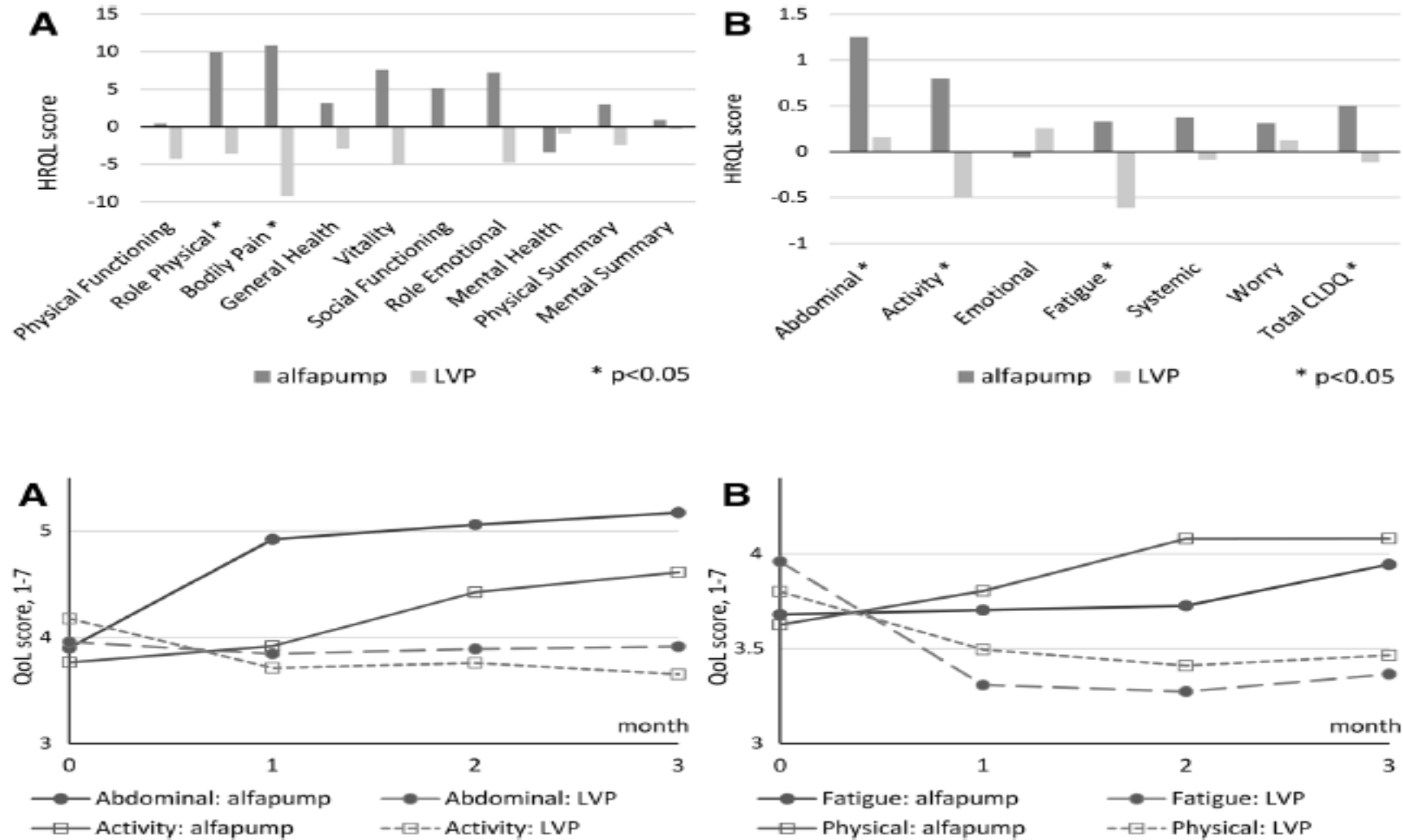
<sup>1</sup> Mean change from baseline adjusted for the baseline mean by an analysis of covariance

AP, alfapump system; SoC, Standard of Care; BMI, body mass index, TSF, tricipital skin fold thickness;

MAMC, mid arm muscle circumference



## Patients with refractory ascites treated with alfapump® system have better health-related quality of life as compared to those treated with large volume paracentesis: the results of a multicenter randomized controlled study





# Re-interventions

Issue	Time to re-intervention (days)*	Intervention	Anesthesia / Type	Outcome
<b>alfapump</b>				
Lack of communication pump and charger	94	Pump exchange	General / Open	FR
<b>Bladder catheter (BC)</b>				
Kinked	5	BC repositioned and pump exchange <sup>†</sup>	General / Laparoscopy	FR
Dislocated	20	BC exchange	Local / Laparoscopy	FR
Dislocated	113	BC exchange	Local / Interventional radiology	FR
<b>Peritoneal catheter (PC)</b>				
Disconnected	6	PC and BC repositioned and pump exchange <sup>†</sup>	Local / Open	FR
Dislocated and occluded	177	PC and pump exchange <sup>†</sup>	General / Open	FR
<b>alfapump system (AP)</b>				
SBP / cellulitis / UTI	8	System explant	Unknown	FR
Pocket hematoma / abscess	50	System explant	General / Laparoscopy	FR
UTI /pocket abscess / wound dehiscence /	79	System explant	General / Laparoscopy	FR

FR, fully recovered; UTI, urinary tract infection; SBP, spontaneous bacterial peritonitis; BC, bladder catheter; PC, peritoneal catheter

\*prophylactic pump exchanges performed at time of catheter re-interventions due to failure of a patency test or a potential issue with pump function

<sup>†</sup>after implantation

# Summary

- AP is an exciting new tool for the management of refractory ascites
- AP successfully reduces the need for paracentesis and results in improvement in QoL and Nutritional Parameters
- Latest NICE guidance refers to 'special arrangements' but does not limit use to research alone
- **The main areas that require improvement**
  - **Re-intervention: Improvement in Device design**
  - **AKI: Need for Albumin replacement as in LVP**
  - **Assessment of cost-effectiveness**

# Q: Is there an appetite for a Cost-Effectiveness evaluation study and inclusion of QUALY?

Seek funding stream e.g. HTA for trial of LVP vs. ALFA Pump

- Cost effectiveness based on cost of repeat LVP (£700-800/visit) vs. total care for ALFA pump
- Follow-up over 12 months