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Long-term Follow-up of Patients with Cirrhosis and Recurrent Ascites Treated with an Automatic Low Flow Ascites Pump (alfapump) in North America

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INTRODUCTION

- Ascites is the most common complication of decompensated cirrhosis and occurs in 10% of all cirrhotic patients
- Diuretic non-responsive recurrent ascites can be treated with repeat large volume paracentesis (LVPS), or the insertion of TIPS in the appropriate patients.
- Many patients with recurrent ascites are not suitable for TIPS. Attending for LVPs places a significant burden on the health care system
- The **A**utomated **L**ow **F**low **A**scites pump (**alfa**pump)(Sequana Medical AG) is a subcutaneous implantable rechargeable device that automatically transfers the ascitic fluid from the peritoneal cavity into the bladder, which is then discharged as urine
- The alfapump effectively carries out a continuous low-rate paracentesis for approximately 16 hrs per day and therefore keeps the ascites under control

AIM

• To assess the North American experience of long-term efficacy, safety and clinical outcome of patients who received an alfapump as a treatment for recurrent ascites.

MATERIALS & METHODS

- Prospective, open label, single arm multi-center study, with all patients receiving an alfapump
- Enrolled cirrhotic patients with recurrent large ascites, not suitable for TIPS, requiring LVP for symptom relief ≥ once/month for 3 months
- Diuretic & albumin use were not mandated but nonetheless given at PI's discretion
- Patients were monitored for ascites control, laboratory abnormalities, adverse events, quality of life (QoL), and survival
- Ascites control: evaluated by assessing LVP requirement after insertion of alfapump.
- QoL: Evaluated using CLDQ & Ascites-Q questionnaire, instruments used to measure quality of life in patients with ascites.

RESULTS

Figure 1: Study Schema

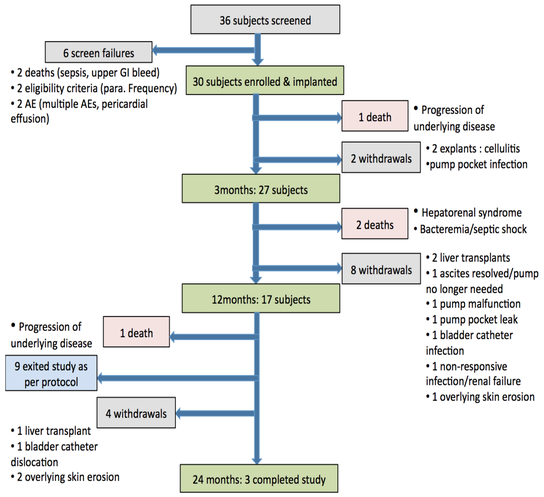


Table 1: Patient Demographics

	Parameter
n	30
Age (years)	63 (32-72)
M : F	17 : 13
Etiology of cirrhosis	
alcohol	9 (30%)
NASH	9 (30%)
viral hepatitis	3 (10%)
alcohol/viral	3 (10%)
alcohol/NASH	2 (6.7%)
cholestastic	2 (6.7%)
others	2 (6.7%)
Serum Na^+ (mmol/L)	134±5
Serum K^+ (mmol/L)	4.38±0.72
Serum creatinine (µmol/L)	93±23
Child-Pugh score at enrolment	7.87±0.90
MELD-Na score at enrolment	15.9±4.6

Figure 2: Change in LVP Requirement

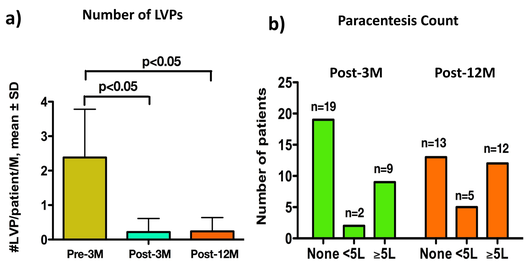


Table 2: Reasons for LVPs

Reason for LVP	3 months		12 months	
	# patients	# LVPs	# patients	# LVPs
Total	9	20	12	59
Pump malfunction	1	1	2	3
Pump pocket Fluid collection			1	2
Peritoneal catheter blocked	2	6	2	12
Bladder catheter dislocation	1	1	2	6
Bladder catheter occlusion			1	8
PI decision	1	2	3	4
Patient preference/request	1	1	1	1
Renal dysfunction	3	8	4	19
Urinary retention	1	1	1	2
Unknown			1	2

Figure 4: Changes in Quality of Life

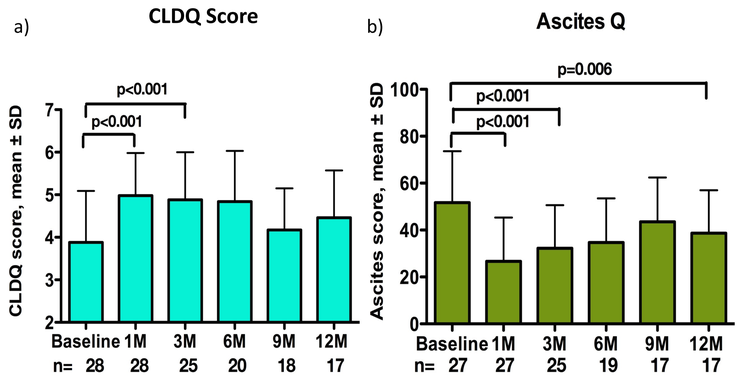


Table 3: Serious Adverse Events

a) Related to implantation, device or therapy

	3 months		12 months	
	# of events	# of patients n/30 (%)	# of events	# of patients
Total	12	10/30 (33.3%)	27	13/30 (43.3%)
Postoperative bleeding	1	1/30 (3.3%)	1	1/30 (3.3%)
Leakage of fluid into pump pocket	2	2/30 (6.7%)	2	2/30 (6.7%)
Wound dehiscence	1	1/30 (3.3%)	1	1/30 (3.3%)
Pump malfunction	2	2/30 (6.7%)	4	3/30 (10%)
Bladder catheter malfunction	1	1/30 (3.3%)	3	3/30 (10%)
Peritoneal catheter dislodgement	0	0	1	1/30 (3.3%)
Hematuria	1	1/30 (3.3%)	1	1/30 (3.3%)
Infection	3	3/30 (10.0%)	9	8/30 (26.7%)
Hyponatremia	1	1/30 (3.3%)	2	1/30 (3.3%)
Acute kidney injury	0	0	2	2/30 (6.7%)
Skin erosion over pump	0	0	1	1/30 (3.3%)

Many of the electrolyte & AKI SAE's not related to the alfapump therapy appeared to be related chronologically to diuretic therapy

Figure 3: Nutritional Status

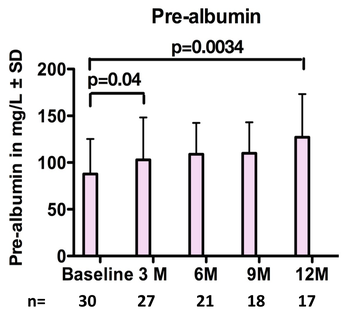
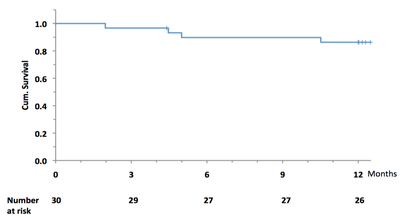


Figure 5: Survival



b) Unrelated to implantation, device or therapy

	3 months		12 months	
	# of events	# of patients n/30 (%)	# of events	# of patients
Total	25	9/30 (30.0%)	52	17/30 (56.7%)
Arm deep vein thrombosis	0	0	1	1/30 (3.3%)
Acute kidney injury	5	3/30 (10.0%)	9	7/30 (23.3%)
Anemia	2	2/30 (6.7%)	2	2/30 (6.7%)
Anasarca	0	0	1	1/30 (3.3%)
Bacterial infections	0	0	3	2/30 (6.7%)
Dehydration	1	1/30 (3.3%)	1	1/30 (3.3%)
Diabetic complications	2	2/30 (6.7%)	3	3/30 (10.0%)
Exacerbation of chronic abdominal pain	1	1/30 (3.3%)	1	1/30 (3.3%)
Gastroenteritis	1	1/30 (3.3%)	1	1/30 (3.3%)
GI Bleed	0	0	2	2/30 (6.7%)
Hepatic encephalopathy	0	0	2	2/30 (6.7%)
Hyperkalemia	1	1/30 (3.3%)	1	1/30 (3.3%)
Hyponatremia	7	4/30 (13.3%)	8	4/30 (13.3%)
Hypotension	0	0	1	1/30 (3.3%)
Hypovolemic shock	0	0	1	1/30 (3.3%)
Incarcerated umbilical hernia	0	0	2	2/30 (6.7%)
Incomplete bowel obstruction	0	0	1	1/30 (3.3%)
Pulmonary hypertension	0	0	1	1/30 (3.3%)
Ruptured umbilical hernia	0	0	2	2/30 (6.7%)
Septic shock	0	0	1	1/30 (3.3%)
UTI	2	2/30 (6.7%)	2	2/30 (6.7%)
Urinary retention	2	1/30 (3.3%)	2	1/30 (3.3%)
Worsening of Ascites	1	1/30 (3.3%)	3	1/30 (3.3%)

CONCLUSIONS

- In this North American study, the implantation of an alfapump is effective in removing ascites and reduces LVP requirement significantly
- Cirrhosis related complications seem no more frequent with alfapump in situ
- Renal dysfunction including electrolyte abnormalities and infections remain concerns.
- Patients had improved nutritional status and quality of life during follow-up
- Therefore, alfapump insertion can be a treatment for recurrent ascites, especially in patients who are not TIPS candidates
- Future directions with alfapump therapy will include i) reducing device issues with better pump and catheter designs, ii) eliminating concomitant diuretic use and adding albumin infusions, & iii) vigilant monitoring to reduce infections

DISCLOSURES

FW: Consultant for Mallinckrodt Pharmaceuticals; grant/research support from Sequana Medical AG, Mallinckrodt Pharmaceutical & Grifols.
FT: Consultant for Abbvie, Dova, Shionogi, Mallinckrodt, Vital Therapies; Research support from Sequana, Gilead, Mallinckrodt, Conatus
ZH: Becton-Dickinson; WL Gore and Associates; Boston Scientific; Bendit; Medtronic research support- Siemens, Sequana, Bluegrass Medical, Teclison
AS: President, Sanyal Biotechnologies, Stock options: Genfit, Akarna, Tiziana, Indalo, Durect, Exhalenz, Hemoshear, Consultant: Lilly, Pfizer, Novartis, Ardelyx, Salix, Hemoshear, Novo, Galectin, Intercept, Merck, Bristol Myers, Immuron, Gilead, Chemomab, Affimmune, Protalix, Nitto Denko, Cirius, Boehringer Ingelhie, Grants to institution: Gilead, Tobira, Allergan, Merck, Bristol Myers, Astra Zeneca, Immuron, Intercept, Novo Nordisk, Shire, Boehringer Ingelhiem, Cirius
JC: Sequana Medical AG employee
PK: Grant/research support from Sequana Medical AG

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