Implantation of the alfapump System for Peritoneal Ascites Drainage Through Urinary Bladder Evacuation

sequanamedical

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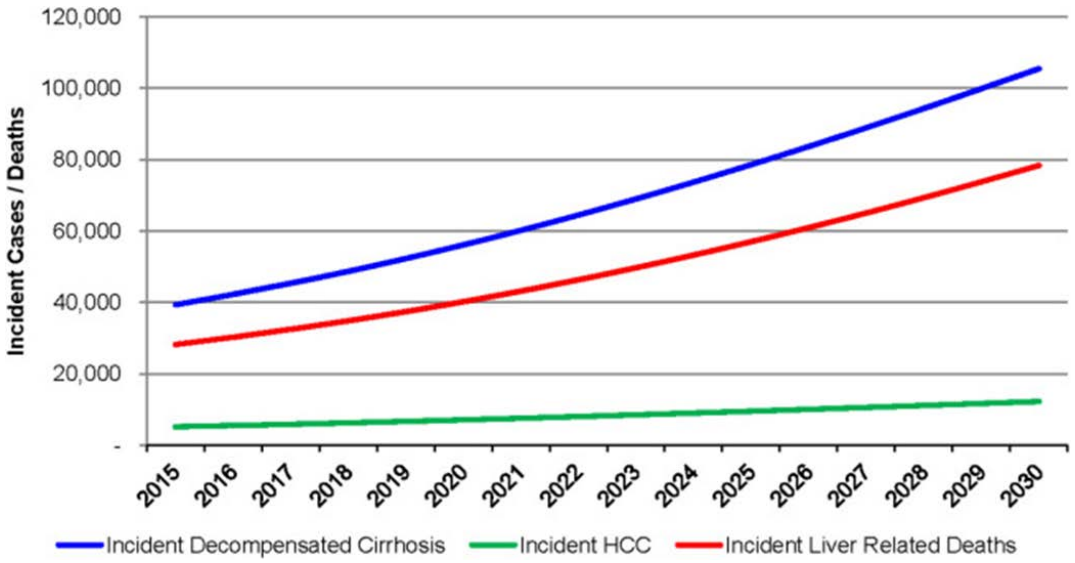
NASH is a Growing Incidence Driver of Liver Cirrhosis in the United States

Healthy Liver

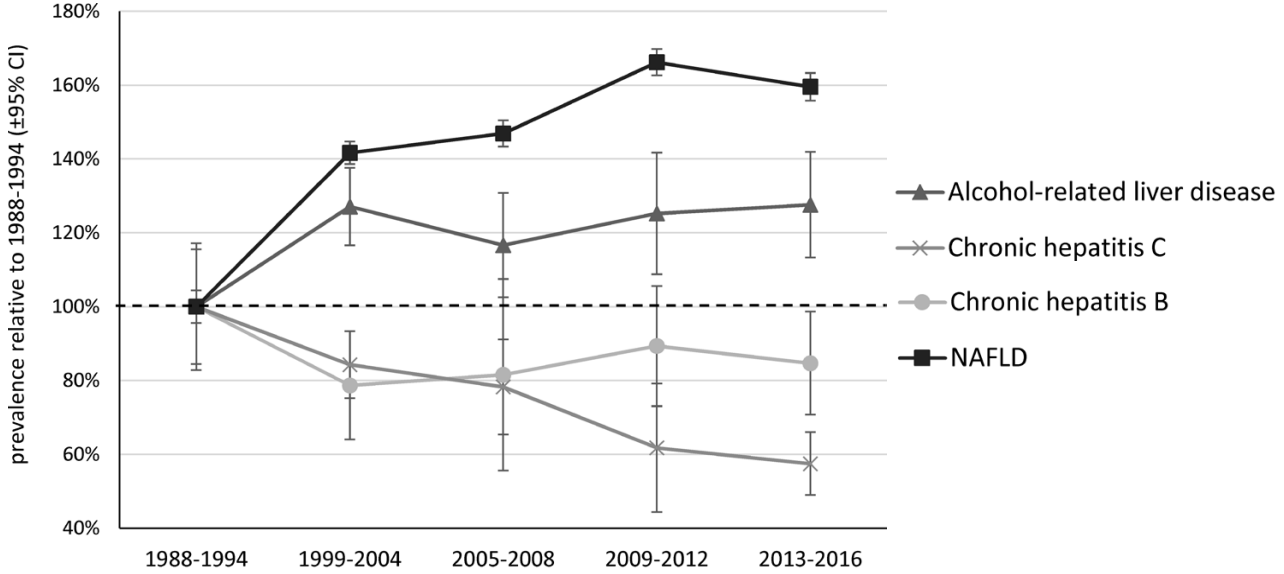
Progressive scarring; Obstructed blood flow;
Fluid leakage (ascites) and risk of variceal bleeding

Cirrhotic Liver

The Prevalence of Decompensated Cirrhosis is Expected to Increase by 180% from 2015 to 2030.[1]



Nonalcoholic Fatty Liver Disease is the Fastest Growing Cause of Liver Cirrhosis in the United States.[2]

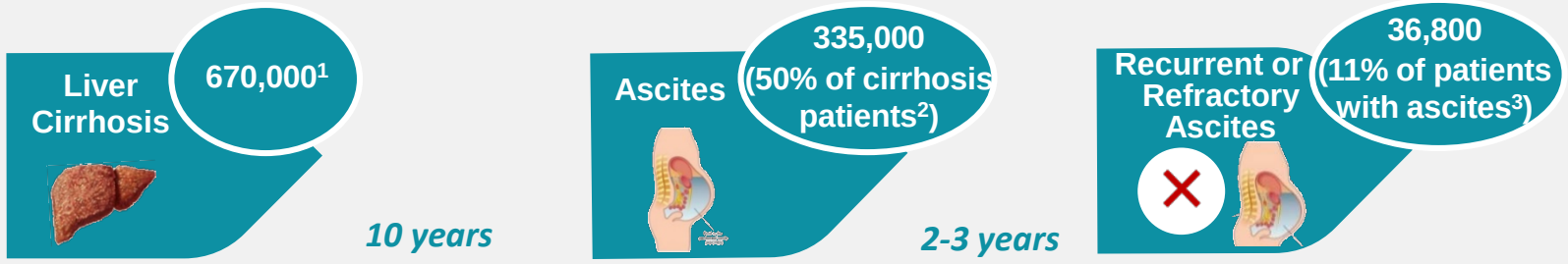


No effective therapies for NASH expected on the market in the near future
Search for alternative approaches that improve quality of life

Source 1: Estes et al., Hepatology, 2018
Source 2: Younossi, Z. M., et al., Gut, 2020

Recurrent or Refractory Ascites due to Liver Cirrhosis

Estimated prevalence of patients with recurrent or refractory ascites from liver cirrhosis

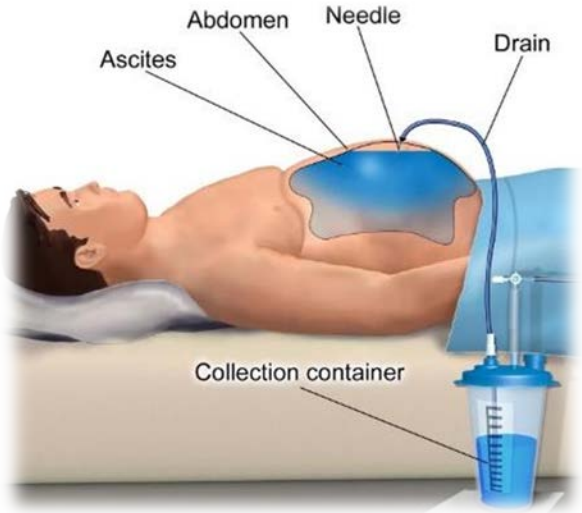


Liver cirrhosis	Ascites	Recurrent or Refractory Ascites
Caused by: ▪ Viral infections (Hep. B & C) ▪ Alcoholic Liver Disease (ALD) ▪ NASH	▪ Abnormal buildup of fluid in the abdomen (more than 25 mL of fluid in the peritoneal cavity)	▪ Unresponsive to low sodium diet and high-dose diuretic treatment ▪ Recurs rapidly after paracentesis
▪ Patients with cirrhosis suffer from immune dysfunction, increasing their risk for bacterial infections[3]	▪ Associated with poor quality of life, increased risk of infection, renal failure, hernia, malnutrition, muscle wasting and increased mortality[4]	▪ Associated with increased mortality: 2 year survival rate for patients with refractory ascites is approximately 25%[4]

Source 1: Scaglione et al., Journal of Clinical Gastroenterology, 2015, projected for US population growth to 2018
Source 2: Runyon, Hepatology, 2009.
Source 3: Adebayo et al., Am. J. Gastroenterol. 2018.
Source 4: Khungar et al., Glinical Gastroenterology and Hepatology, 2011

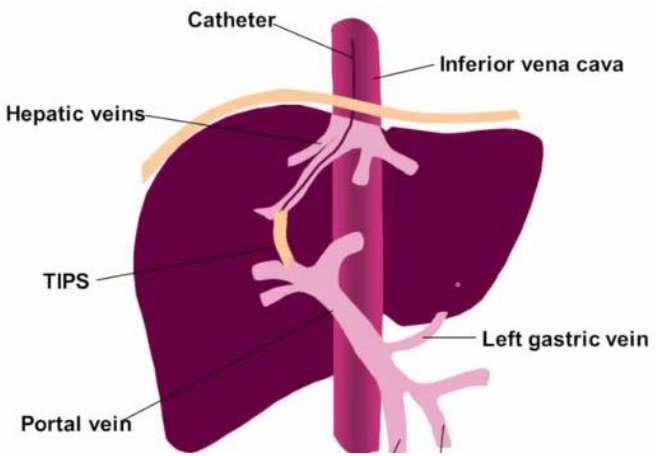
Severe limitations of existing therapies

Large Volume Paracentesis (LVP)



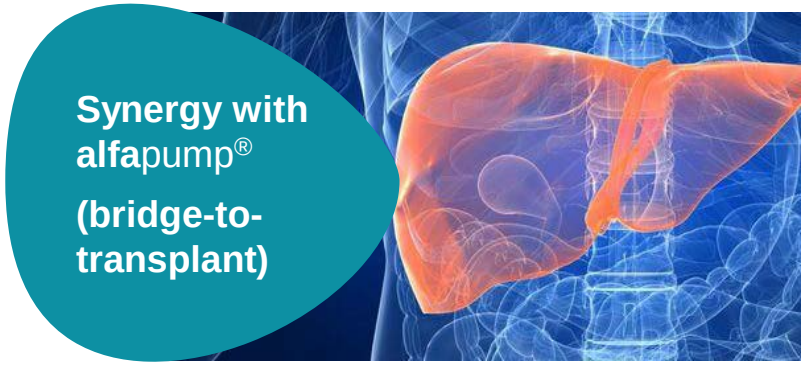
- Patients with refractory ascites require frequent visits for LVP.
  - Associated with malnutrition and increased complications.
  - Complications include bleeding, infections and circulatory dysfunction.
  - Frequent visits associated with increased risk of infections and other complications.

Transjugular Intrahepatic Portosystemic Shunt (TIPS)



- TIPS is only available to a very narrow population. Examples of contraindications include:
  - Rapidly progressing liver failure;
  - Pulmonary arterial hypertension;
  - Age;
  - Heart Failure.

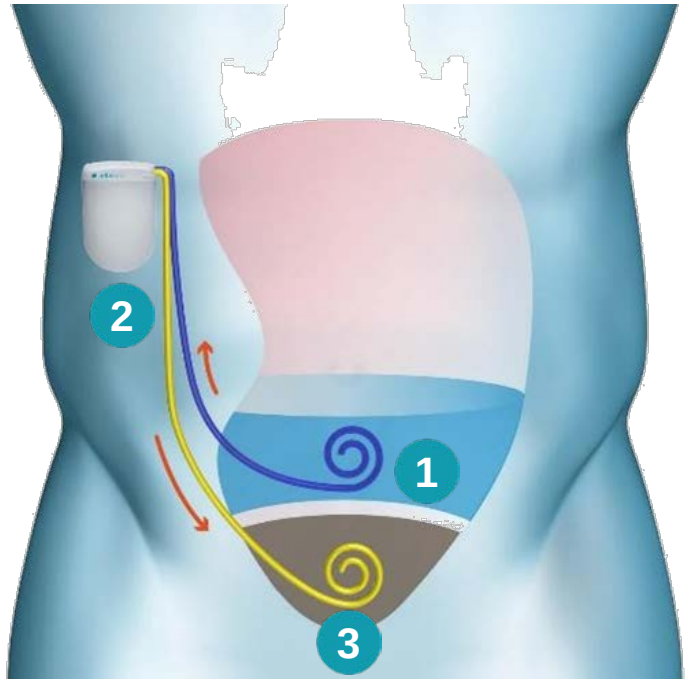
Liver Transplant

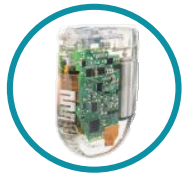


- Availability of Liver Transplant is limited.
- Many patients with refractory ascites do not receive a liver transplant because they:
  - Do not qualify for transplantation; or
  - Are not considered a priority on the liver transplantation list.

alfapump®

Fully implanted, automatic, wireless charged system for the long-term treatment of recurrent or refractory ascites





alfapump®

SmartCharger

Programmer

The fully subcutaneous alfapump system has three implanted components:

1. **Peritoneal Catheter**
2. **Pump Device**
3. **Bladder Catheter**

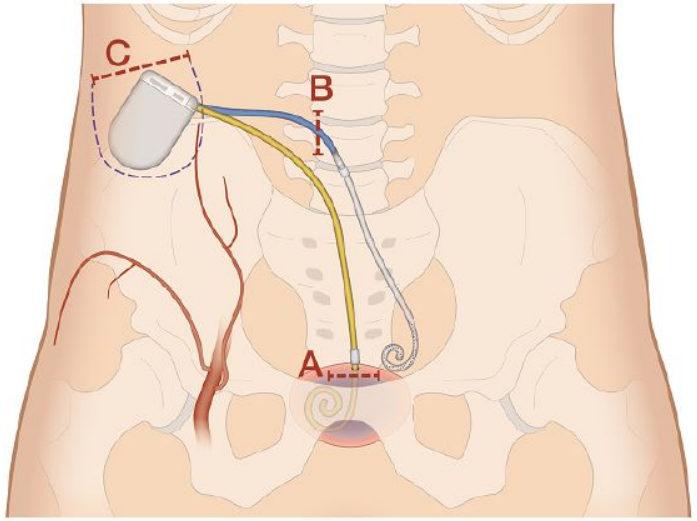
Key actions performed by a fully implanted pump system:

- A Automatic and continuous removal of ascites from peritoneal cavity
- B Ascites is pumped into bladder (daytime only)
- C Ascites leaves the body through normal urination
- D Wireless charging and communication for monitoring

alfapump was designated a Breakthrough Device by the FDA in January 2019.

alfapump® System Implant Procedure

The alfapump system is implanted using a minimally invasive procedure



Typical procedure time: 60-90 minutes

ummary of implant procedure steps:

Percutaneous peritoneal catheter placement and drainage of ascitic fluid:

- Insertion with needle & guidewire through ~1cm incision with purse-string placement;
- Insertion with 18F introducer, using 10F and 14F dilators;
- Partial drainage of ascites and closure of purse-strings.

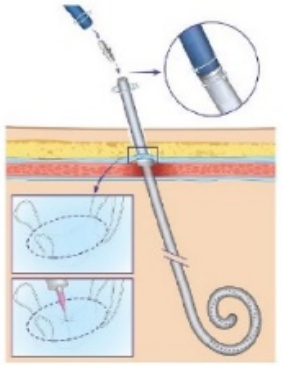
Percutaneous bladder catheter placement:

- Similar to placement of peritoneal cather, but without purse-string sutures.

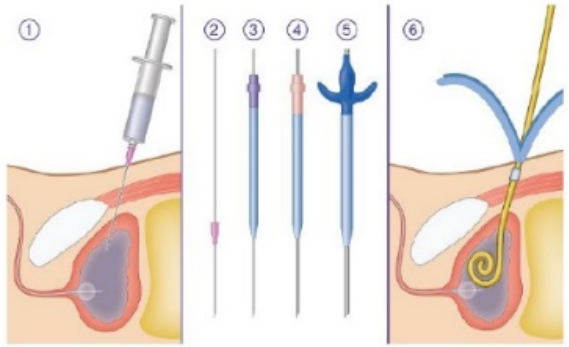
Pump pocket creation:

- 5-6cm incision at mid-clavicular line, below the costal border;
- Blunt dissection to create pocket.

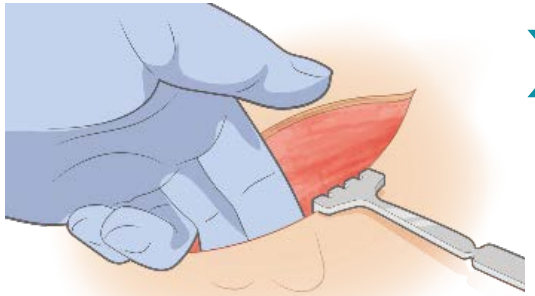
Peritoneal Catheter Placement (B)



Bladder Catheter Placement (A)

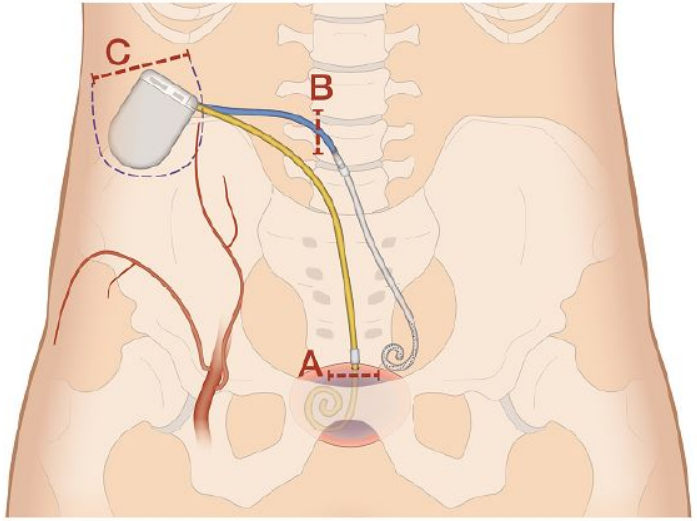


Pump Pocket Creation (C)



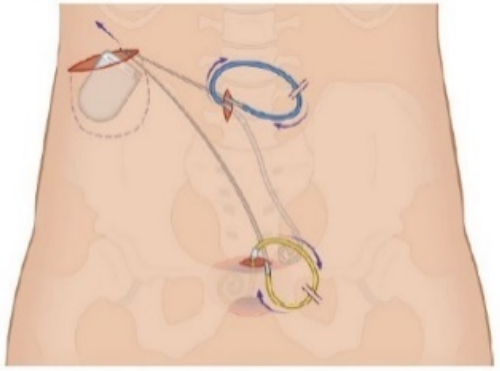
alfapump® System Implant Procedure (cont.)

The alfapump system is implanted using a minimally invasive procedure

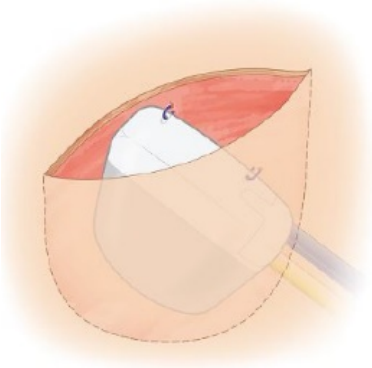


- Tunneling of both peritoneal and bladder catheter to the pump pocket.
- Preparation of the Pump and Smart Charger:
  - Waking the alfapump;
  - Priming and testing of the alfapump using normal saline.
- Place pump, connect catheters:
  - Use pump as guide to trim catheters to length;
  - Attach catheters to locking cap, connect with pump and test again;
  - Place pump into pocket, and test again.
- Fixate pump, close incisions:
  - Subcutaneous sutures through pump fixation holes, deep into pocket;
  - Multi-layer, water-tight closure.

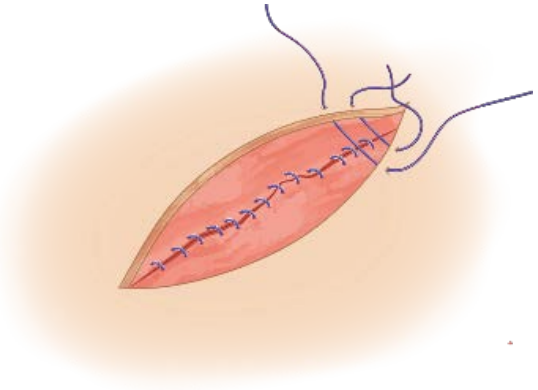
Catheter Tunnelling



Pump Connection & Fixation

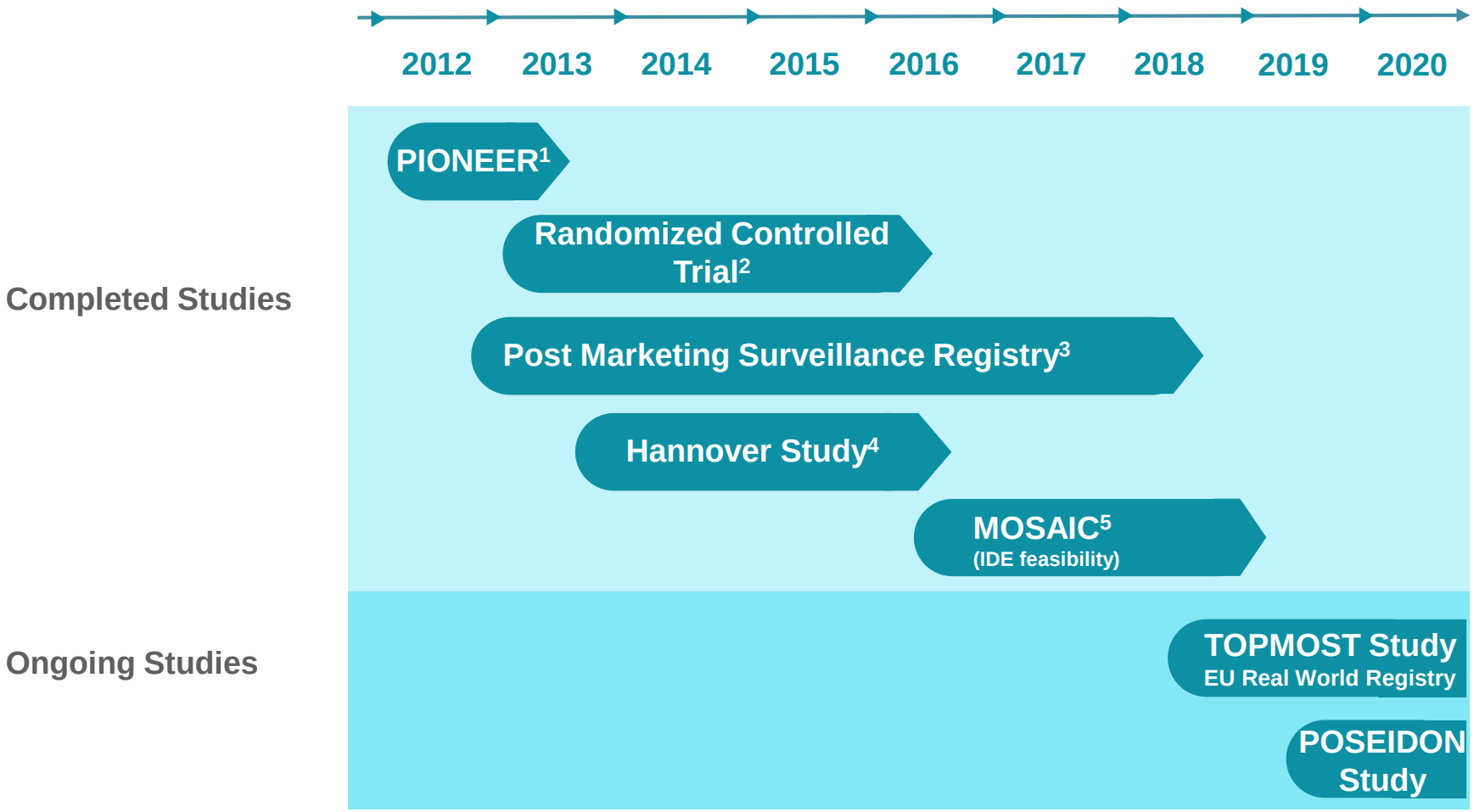


Close Incisions



Validated Clinical Performance

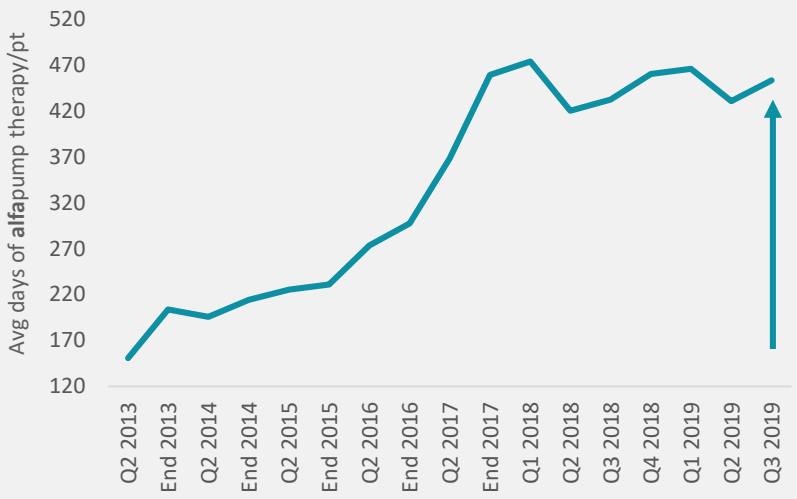
Over 700 implants and included in EASL guidelines for decompensated liver cirrhosis



Source 1: Bellot et al. Journal of Hepatology 2013
Source 2: Bureau et al. Journal of Hepatology, 2017
Source 3: Stirnimann et al. Alimentary Pharmacology and Therapeutics, 2017
Source 4: Solbach et al. Eu J of Gastroenterology and Hepatology, 2018
Source 5: Wong et al. Liver Transplantation, 2020

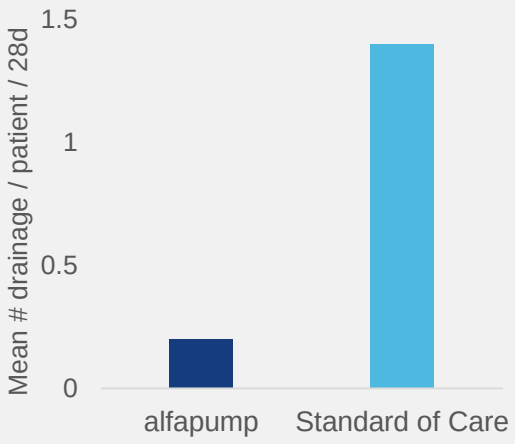
Strong Clinical Validation

Clear increase in clinical outcomes



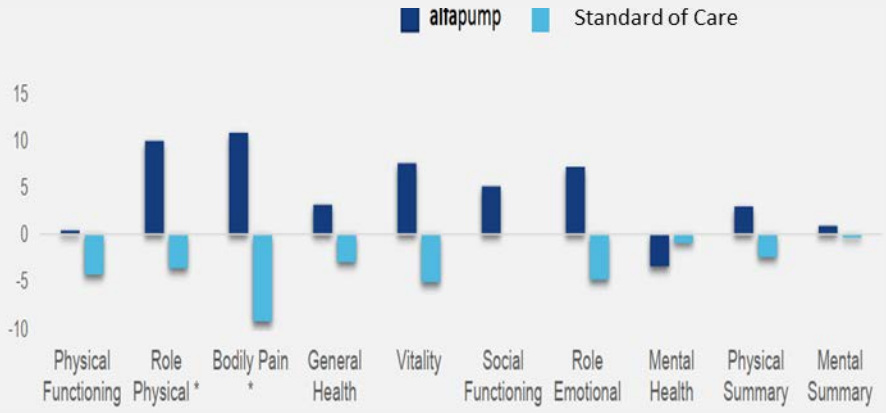
Sequana Medical data

Drastically reduced need for drainage



Stirnimann et al.[1]

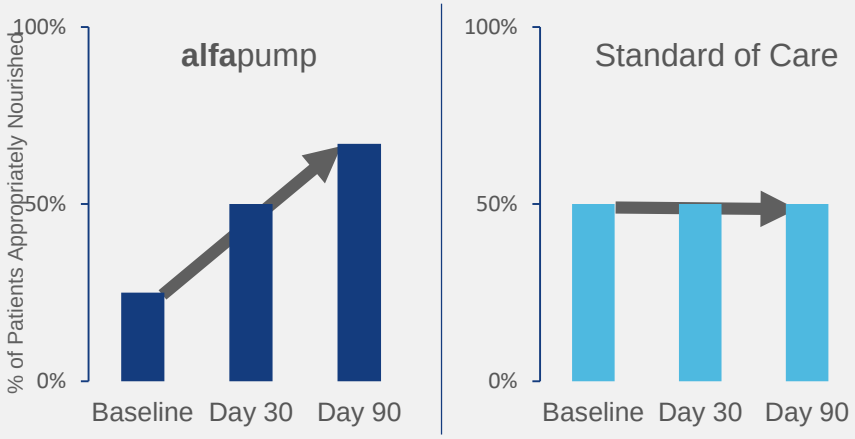
Improved quality of life



Stirnimann et al.[1]

** p<0.05 data from SF-36 Quality of Life Questionnaire*

Improved nutrition



Stirnimann et al.[1]

Source 1: Stirnimann et al. Alimentary Pharmacology and Therapeutics, 2017

MOSAIC – North American IDE Feasibility Study
Significant reduction in need for LVP and increase in QoL

Overview

- Patients with liver recurrent or refractory ascites not eligible for TIPS (N=30)
- 29 of 30 implants used interventional radiology implantation

- Prospective multicenter, open-label, uncontrolled, single-arm feasibility study
- US and Canada (6 centres)
- Primary and secondary endpoint evaluation at 3 months, safety follow-up at 12 and 24 months

- Primary objective: safety of **alfa**pump®
- Secondary objectives: requirement for LVP, nutritional status and QoL, device function

Trial Results

- Significant reduction in number of LVPs

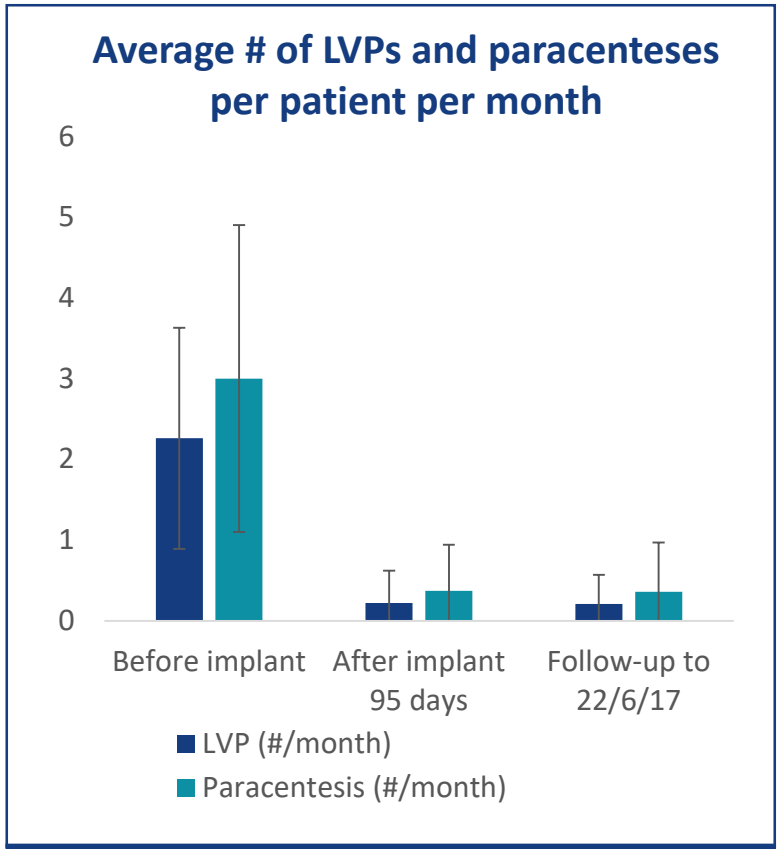
- Clinically relevant and statistically significant improvement in QoL

- Mean overall survival estimated at 15 months (greater than expected in a population of patients with refractory ascites)

- Reinterventions, explants and adverse events related to acute kidney injury and infection were concerns

- The MOSAIC manuscript has been accepted and published in Liver Transplantation

- Initial results: poster presentation at AASLD 2017 and 2018



91% reduction in average number of required LVP per patient per month: from 2.47 at baseline to 0.22 after 3 months

Wong et al. Liver Transplantation, 2020

Post-marketing surveillance registry (PMSR)
Real-world data confirms RCT Results

Overview

- 100 “real world” patients.
- Patients selected based on contraindication for TIPS.

- Prospective multicenter, open-label, observational study.
- Ten European referral centers.
- Follow-up for at least 12 months with maximum of 24 hours.

- Objective: Safety and efficacy of the **alfa**pump®. LVP frequency, hepatic decompensations, infections, death, adverse device events and liver transplants.

Data from first 56 patients in registry

- Significant reduction in number of LVPs by over 90%.
- Most LVP events were due to clogging or pump programming issues.

- Mean actuarial survival was 12.8 months (consistent with that of patients undergoing LVP).
- Re-intervention procedures were mostly simple, rapidly performed and associated with a good outcome.

- “Preliminary results of a new version of the peritoneal catheter show a markedly decreased rate of catheter related complications.”

- Data from all 100 patients under review – submitted for publication.

Source: Stirnimann et al. Alimentary Pharmacology and Therapeutics, 2017

POSEIDON: North American Pivotal Study (Ongoing)

Trial Design:

- A multicenter, single arm within subject crossover design pivotal IDE study.
- Enrollment: Up to 60 enrolled patients and up to 30 additional roll-in patients across 15 North American centers.

Inclusion Criteria

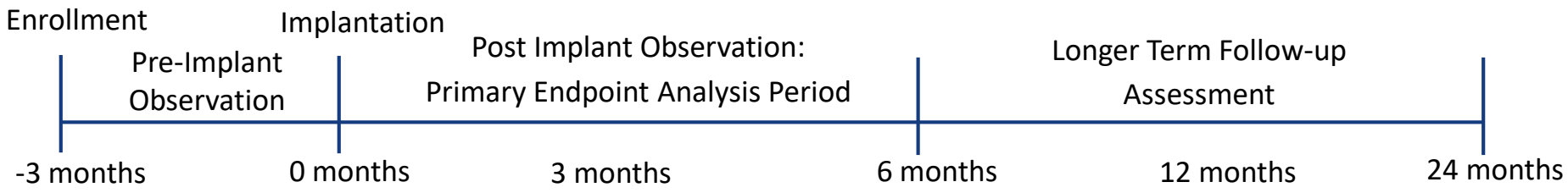
- Patients >18 years with cirrhosis with refractory or recurrent ascites.
- Not a candidate for TIPS.
- Life expectance of at least 6 months following pump implant.

Primary Effectiveness Endpoints:

- Per-patient ratio of post-implant to pre-implant monthly therapeutic paracenteses (removal of ≥ 1.5 L ascites).
- Proportion of patients with at least 50% reduction in number of therapeutic paracenteses from pre-implant to post-implant.

Primary Safety Endpoints:

- Combined rate of open surgical reintervention due to pump system related AEs or to restore pump functionality, or pump explant due to system related AE, or pump system related death up to 6 months post-implant.



The principal purpose of the study is to test whether alfapump improves health outcomes of appropriately selected patients.

Conclusions

There are limited treatment options for patients with recurrent or refractory ascites from liver cirrhosis.

alfapump provides patients with a long-term solution for ascites management.

alfapump reduces the need for hospital visits for therapeutic paracentesis, and the associated risks.

alfapump provides clinically relevant and statistically significant improvement to patient quality of life.

Current ICD-10-PCS codes do not uniquely identify an implantation procedure that implants:

- A programmable, wirelessly rechargeable pump system;
- That actively measures and pumps ascitic fluid from the peritoneal cavity to the bladder.

More specific coding is needed for accurate reporting and outcome-tracking for this novel system.

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