5th Guildford Advanced Pain & Symptom Management Course

The management of ascites

Marinos Pericleous
Objectives

• Overview of management of ascites due to liver cirrhosis & malignancy

• Evidence-based approach for the patient with
  – Small/Moderate volume ascites
  – Large volume ascites
  – Spontaneous Bacterial Peritonitis

• Locoregional and peer-reviewed guidelines

• Other therapies e.g. intraperitoneal treatments and pleurX drains
Ascites

• 75% due to cirrhosis
• 25% other causes
• The aetiology is multifactorial
• Mortality is 40% in first and 50% in second year in cirrhotics
• Management is complex
GUIDELINES

Guidelines on the management of ascites in cirrhosis

K P Moore, G P Aithal

Clinical Practice Guidelines

EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis

European Association for the Study of the Liver

PRACTICE GUIDELINE

Management of Adult Patients with Ascites Due to Cirrhosis: Update 2012

Bruce A. Runyon
X marks the spot

• Prompt assessment ABC
• Assess for signs of Chronic liver disease
• Assess for hepatic decompensation
• Confirm presence of shifting dullness
EASL Grading of ascites

<table>
<thead>
<tr>
<th>Grade of ascites</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 ascites</td>
<td>Mild ascites only detectable by ultrasound</td>
</tr>
<tr>
<td>Grade 2 ascites</td>
<td>Moderate ascites evident by moderate symmetrical</td>
</tr>
<tr>
<td></td>
<td>distension of abdomen</td>
</tr>
<tr>
<td>Grade 3 ascites</td>
<td>Large or gross ascites with marked abdominal</td>
</tr>
<tr>
<td></td>
<td>distension</td>
</tr>
</tbody>
</table>
Perform an ascitic tap for inpatients and outpatients with clinically apparent new-onset ascites
The samples for the lab

- Fluid albumin with paired serum albumin for serum-ascites albumin gradient (SAAG)
- Superior than total protein. But send total protein as well
- SAAG is ≥1.1 g/dL (11g/L) = portal hypertension
- 97% accuracy\(^1\)
- Maintains sensitivity despite IV fluids and diuretics\(^2\)
- Light’s criteria not used for ascites
- Ascitic total protein

The samples for the lab (2)
SAAG

Table 1  Serum ascites-albumin gradient (SA-AG)

<table>
<thead>
<tr>
<th>SA-AG ≥11 g/l</th>
<th>SA-AG &lt; 11 g/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>Tuberculosis</td>
</tr>
</tbody>
</table>
The samples for the lab (3)

- A polymorphonuclear cell count of >250 strongly predicts the presence of SBP\(^1\)
- Failure of the first line of defense?
- Failure of peritoneal macrophages, to kill invading bacteria

The samples for the lab (4)

- Inoculation of blood culture bottles at the bedside, increases successful culture of causative organisms 50→80% \(^1,2\)
- True for PMNs>250
- To be taken before antibiotics

• Fluid albumin with paired serum albumin for serum-ascites albumin gradient (SAAG)
• Ascitic total protein
• Ascitic sample in universal container for microscopy
• Blood cultures for all and inoculated at bedside
Other samples

• **Lactate dehydrogenase**, and **glucose** (1o Vs 2o bacterial peritonitis; sensitivity 100% and specificity of 45%\(^1\))

• **CEA** (>5 ng/mL) and ascitic fluid **alkaline phosphatase** (>240 units/L) for gut perforation; sensitivity 92% and specificity 88%\(^2\)

• **Cytology**
• **Fluid culture for mycobcateria**
• **Amylase**
• NOT **CA125**

Management of Ascites
Diet/Fluid Restriction

• Education around low-salt diet and fluid intake
• Salt restriction:
  • 88 mmol = 2000 mg per day; AASLD
  • 80-120 mmol = 4.6- 6.9g of salt/day; EASL
  • 90 mmol = 5.2g/day; BSG
• Fluid restriction is not necessary unless serum sodium is less than 125 mmol/L (AASLD)
• Do not fluid restrict if Sodium levels are normal (EASL)
• Fluid restrict is rarely effective in hypervolaemic hyponatraemia and no data for hypertonic saline (EASL)
## Management of ascites

### Sodium/Diuretics/Fluid restriction

<table>
<thead>
<tr>
<th>Serum Sodium mmol/L</th>
<th>Serum Creatinine μmol/L</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>126-135</td>
<td>Normal</td>
<td>Continue diuretics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not fluid restrict</td>
</tr>
<tr>
<td>121-125</td>
<td>Normal</td>
<td>Stop diuretics or observe closely</td>
</tr>
<tr>
<td>121-125</td>
<td>&gt;120</td>
<td>Stop diuretics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Volume expansion</td>
</tr>
<tr>
<td>≤120</td>
<td>Regardless</td>
<td>Stop diuretics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Volume expansion</td>
</tr>
</tbody>
</table>

Management of Ascites

Diuretics

• Hyperactivation of RAS
• First line should be Aldosterone antagonists (effect is slow)
• **AASLD**: Spironolactone 100mg (max 400mg) +/- Frusemide 40mg (max 160mg)\(^1,2\)
• **EASL/BSG**: First episode of Moderate ascites: only Spironolactone (Target 400mg). Add loop diuretics in non-responders or in recurrent ascites
• Increased dose every 3-5 days (AASLD) (every 7 days EASL)
• Maintain ratio
• Amiloride or Triamterene in gynaecomastia. Not much evidence for Eplerenone

---

Management of Ascites
Diuretics (2)

• Diuresis: no greater than 0.5 kg/day in patients without peripheral oedema and 1 kg/day in those with peripheral oedema

• Stop diuretics in severe hyponatremia (<120 mmol/L), hyperkalaemia (>6 mmol/L) progressive renal failure, worsening hepatic encephalopathy incapacitating muscle cramps and gynaecomastia

• Stop Frusemide in severe hypokalaemia
Management of Ascites: Other drugs

- Blood Pressure in cirrhotics
  - vasopressin
  - angiotensin
  - aldosterone
- Inhibition leads to low BP and impaired renal perfusion. Linked to reduced survival in cirrhotic patients with ascites
- Beta blockers e.g. Propranolol shown to reduce survival
- NSAIDs reduce urinary sodium excretion and promote azotaemia in cirrhotic patients

• ACE inhibitors should be avoided
• ARB2 inhibitors should be avoided
• NSAIDs should be avoided
• The use of beta blockers should be carefully evaluated in each case
• Abstinence from alcohol
Tense ascites

• Initial large volume paracentesis is safe
• Safe at 5L without circulatory support\textsuperscript{1}
• Then sodium restriction and
• Oral diuretics

Tense ascites (2)

- Initial large volume paracentesis is safe
- Single session
- **AASLD**: Safe at 5L without circulatory support\(^1\)
- **EASL**: Give albumin even if <5L drained due to concerns over other plasma expanders
- **BSG**: Give other plasma expanders but not albumin in <5L drained
- Then sodium restriction and oral diuretics
- Larger volume removal may lead to post-paracentesis circulatory dysfunction (PPCD)
  - rapid re-accumulation of ascites
  - 20% of these patients develop HRS
  - Portal pressure increases
  - shortened survival.

Tense ascites (3)

**Albumin Infusion in Patients Undergoing Large-Volume Paracentesis: A Meta-Analysis of Randomized Trials**

Mauro Bernardi, Paolo Caraceni, Roberta J. Navickis, and Mahlon M. Wilkes

- 1225 patients
- Meta-analysis of 17 RCTs
- 5.5-15.9 liters removed
- Albumin is superior than other plasma expanders for higher volumes removed
- Statistical significance in reduction of complications (compared to no treatment and other expanders) and mortality
• No requirement for albumin cover if < 5L to be drained (AASLD). Cover with Albumin (EASL). Cover with other plasma expanders (BSG).

• For higher volumes, albumin should be given at a dose of 6-8g/L of ascitic fluid removed (ASSLD) (8g/L EASL/BSG).

• **BSG**: give the volume expansion once paracentesis is complete
Refractory ascites

- Serial therapeutic paracenteses is the first line treatment (AASLD), in those who do not excrete urinary Sodium >30mmol/day (EASL)
- Referral for liver transplantation should be expedited if they meet criteria (AASLD, EASL, BSG)
- TIPSS should be considered (AASLD, EASL, BSG)
Spontaneous Bacterial Peritonitis (SBP)

- Occurs in the absence of contiguous source of infection or inflammation
- Bacterial translocation has been implicated\(^1\)
- Also impaired opsonisation\(^2\)
- Commonest isolates: *Escherichia coli*, *Klebsiella pneumoniae*, and *Streptococcal pneumoniae*

1. Miguel-Ángel Llamas, María-Ángeles Aller, Domingo Marquina, María-Paz Nava, Jaime Arias, Bacterial Translocation to Mesenteric Lymph Nodes Increases in Chronic Portal Hypertensive Rats
2. Runyon B. Patients with deficient ascitic fluid opsonic activity are predisposed to spontaneous bacterial peritonitis
Spontaneous Bacterial Peritonitis (SBP) (2)

• In the absence of recent beta-lactam antibiotic exposure, start empiric antibiotic therapy, e.g., an intravenous third-generation cephalosporin, preferably cefotaxime 2 g every 8 hours

• In recent beta-lactam antibiotic exposure, follow local protocols

• Give Cephalosporins when you suspect SBP even when PMNs<250

1. Miguel-Ángel Llamas, María-Ángeles Aller, Domingo Marquina, María-Paz Nava, Jaime Arias, Bacterial Translocation to Mesenteric Lymph Nodes Increases in Chronic Portal Hypertensive Rats
2. Runyon B. Patients with deficient ascitic fluid opsonic activity are predisposed to spontaneous bacterial peritonitis
Spontaneous Bacterial Peritonitis (SBP) (3)

- 90% successfully treated with antibiotics
- Perform a **follow-up paracentesis in 48 hours** to assess response to treatment (AASLD, EASL)
- When PMNs > 250 and
  - Creatinine > 1 mg/dL and urea nitrogen > 30 mg/dL OR
  - Bilirubin > 4 mg/dL
- 1.5g albumin per kg body weight within 6 hours of detection and 1.0g/kg on day 3 (reduced mortality)\(^1\)

Management of Ascites

Bleeding Prophylaxis (1)

• Ascitic taps and Large Volume Paracentesis are safe
• <1% complications
• Commonly abdominal wall haematomas
• <1/1000 haemoperitonium or bowel perforation
• Inaccuracy of routine blood tests for coagulation
• Costs of giving blood products to every patient

Hypothesis:
- puncture of a superficial abdominal wall vein
- puncture of mesenteric varices
- mesenteric variceal rupture precipitated by sudden release of abdominal wall
Severe haemorrhage following abdominal paracentesis for ascites in patients with liver disease

I. PACHE & M. BILODEAU
Service d’hépatologie, Centre hospitalier de l’Université de Montréal, Hôpital Saint-Luc, Montréal, Québec, Canada

Accepted for publication 20 December 2004
Management of ascites

Bleeding Prophylaxis (2)

• Largest series
• 4729 abdominal Large Volume Paracenteses
• 9 patients bled
• All bleeders had high MELD and CPSs
• All but one bleeders had impaired renal function
• 71% abnormal PT
• Severe haemorrhage after abdominal paracentesis is a rare (0.19%)
• Death following this complication in 0.02%
• Haemorrhagic complications do not necessarily occur in the setting of severe thrombocytopenia and/or prolonged coagulation time
Performance Standards for Therapeutic Abdominal Paracentesis

Catherine M. Grabau, Sharon F. Crago, Linda K. Hoff, Julie A. Simon, Cheryl A. Melton, Beverly J. Ott, and Patrick S. Kamath
Management of ascites
Bleeding Prophylaxis (3)

• 1100 Large Volume Paracenteses
• 513 patients had cirrhosis
• Lowest platelet count 19x10⁹ /L (54% <50,000)
• Highest INR 8.7 (75% >1.5 and 26.5% >2.0)
• No prophylactic blood products
• Reported no haemorrhagic complications
• Routine prophylactic use of fresh frozen plasma or platelets before paracentesis is not recommended (AASLD, EASL)
• BSG: no recommendation but LVP not contraindicated in patients with prolonged PT or thrombocytopaenia
• Caution in severe coagulopathy
• Caution in DIC
Long term SBP prophylaxis

• Recurrence of SBP; 69% in one year
• Norfloxacin 400 mg/day PO (or trimethoprim/sulfamethoxazole) (AASLD)
• Norfloxacin 400 mg/day PO for ascitic fluid protein < 15g/L (EASL)
• or alternatives
Other specific guidance

- Patients with Child-Pugh C cirrhosis due to alcohol should abstain
- Baclofen can be given to reduce alcohol craving
- Avoid the use of Vaptans for hyponatraemia
- Oral Midodrine should be considered
- Umbilical hernias: treat electively after resolution of ascites (or perioperative TIPSS) or during/after OLTx
- Hepatic Hydrothorax: Reduce dietary sodium and diuretics. TIPS is second line. Chest drains are contraindicated
- Avoid PEGs in patients with cirrhosis and ascites
Other specific guidance

• Bed rest is not recommended (also BSG)
• Vaptans may be considered in patients with severe hypervolemic hyponatremia (<125 mmol/L).

Management of ascites due to liver cirrhosis; Learning points

- Assess patient ABC etc
- Assess fluid status
- Stop nephrotoxins, NSAIDs/ACEI/ARB2
- Always perform an ascitic tap LIF or RIF preferred
- Samples for:
  - Ascitic albumin
  - Total protein
  - PMNs
  - +/- Amylase, Cytology
  - Fluid in blood culture bottles and inoculate at bedside
- Calculate SAAG
  - >11 g/L (or 1.1 g/dL) = portal hypertension likely
- Diuretics for Grade 1 -2 ascites
- Large Volume Paracentesis for Grade 3 ascites
Management of ascites due to liver cirrhosis; Learning points (2)

Grade 1-2 Ascites

- Salt restriction (dietician support)
- Poor evidence for fluid restriction
- Start diuretics: Spironolactone 100mg (max 400mg) +/- Frusemide 40mg (max 160mg)
- Diuresis: 0.5 kg/day (no peripheral oedema) and 1 kg/day (peripheral oedema)
- Stop diuretics if serum Na ≤125mmol/L
- Plasma expansion if Na ≤125mmol/L and renal impairment (Creatinine > 120μmol/L)
Management of ascites due to liver cirrhosis; Learning points (3)

Grade 3/Refractory Ascites

- Large Volume Paracentesis is the treatment of choice
- Failure to give volume expansion may lead to post-paracentesis circulatory dysfunction with impairment of renal function and electrolyte disturbances
- Plasma expansion regardless of fluid drained is the safest approach: 100 ml of 20% albumin/2L ascites.
- FFP, platelets are not recommended
- Stop diuretics and restart 1-2 days later
Management of SBP; Learning Points

- PMNs >250 = SBP → Treat immediately with antibiotics
- If SBP < 250 but strong clinical suspicion → treat immediately with antibiotics
- There are no sufficient data on the role of total paracentesis in the management of SBP but...
- DO NOT put drains in people who are septic, have renal failure or generally unwell (includes SBP)
- follow-up paracentesis in 48 hours to assess response to treatment
- Give albumin on Day 1 and Day 3
- Consider long-term SBP prophylaxis with Norfloxacin
Management of ascites due to malignancy
Considerations

• The pathophysiology of ascites in those with massive hepatic metastases and without peritoneal deposits may be similar in some respects to that in cirrhotic liver disease\(^1\).
• Mechanisms and the homeostatic environment are different in other patients with malignancy
• Commonest: ovarian, breast and GI malignancy
• The principle of "minimal disturbance" should guide management

Published guidelines

The development of clinical guidelines on paracentesis for ascites related to malignancy

J Stephenson Derriford Hospital and St. Luke’s Hospice, Plymouth and J Gilbert Exeter and District Hospice and Royal Devon and Exeter Hospital, Exeter

- 26 patients (51 procedures)
- Framework of 12 points
- No need for US if G3 Ascites
- Spironolactone up to 400mg sometimes in conjunction to Furosemide
- No IV fluids (unless dehydration or AKI). HAS not mentioned
- Remove after 6 hours (or when drainage stops)
- Overnight stay
- No guidance on bleeding diathesis, volume removed, screening bloods, types of fluid (in AKI/dehydration)
Published guidelines (2)

Management of Ascites in Ovarian Cancer Patients

Scientific Impact Paper No. 45
November 2014
Review

Malignant ascites: Systematic review and guideline for treatment

Gerhild Becker⁶⁺*, Daniel Galandi¹⁺⁺, Hubert E. Blum⁶⁺⁺⁺

⁶Department of Internal Medicine II, University Hospital of Freiburg, Hugstetter Str. 55, D-79106 Freiburg, Germany
⁺Department of Internal Medicine, HELIOS Hospital, Jossistraße 12, D-79822 Titisee-Neustadt, Germany
⁺⁺German Cochrane Centre, University Hospital of Freiburg, Department for Medical Statistics, Stefan-Meier-Str. 26, D-79104 Freiburg, Germany
Summary of recommendation

• Systematic Review 1966-2005
• 3 main sections
  • Symptomatic management by paracentesis
    – 3 case series, 2 prospective uncontrolled trials
    – 502 patients
    – Hypotension avoided by 5% Dextrose infusion
    – Safe without fluid replacement (up to 5L)
    – No consensus on duration of drain in-situ (30mins-90 mins-6h-12-24h)
  • Management with diuresis
    – 3 cohort studies, 1 non-randomised open trial, 1 case report
    – successful in approximately 43%
    – Effective in serum-ascites albumin gradient >1.1 g/dl and hepatic metastases
    – Ascites due to peritoneal carcinomatosis or chylous ascites did not respond
    – Response cannot be predicted (renin/aldosterone ratio?)
    – Type and dose of diuretic not evaluated
  • Management by peritoneovenous shunts
    – See next section
Locoregional guidance for malignant ascites

Paracentesis for Malignant Ascites Procedure

St Joseph’s Mercy Hospice

Guidelines for the Management of Malignant Ascites

Northern Health and Social Care Trust

This is an official Northern Trust policy and should not be edited in any way

Palliative Management of Malignant Ascites Guidance

Mercy Hospice Auckland

Management of Malignant Ascites

Guidelines for the Management of Malignant Ascites

St Peters Hospice, Bristol

The Management of Malignant Ascites in Gynaecological Oncology

Classification: Policy and Clinical Guideline
Lead Author: Wai Pheng Chan (Jackie) Gynae Oncology Specialist Nurse
Additional authors: Dr Dina Kasir (Consultant Radiologist)
Authors Division: Gynaecology – Oncology Department
Unique ID: Gyn2(06)
Issue number: 3
expiry Date: June 2017

LCA Acute Oncology Clinical Guidelines

September 2013
<table>
<thead>
<tr>
<th>Summary from local guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Need for US</strong></td>
</tr>
<tr>
<td>INR&gt;1.4-1.5</td>
</tr>
<tr>
<td>Na&lt;126</td>
</tr>
<tr>
<td>Albumin &lt;20</td>
</tr>
<tr>
<td><strong>Trial of diuretics</strong></td>
</tr>
<tr>
<td>Spironolactone</td>
</tr>
<tr>
<td><strong>Amount</strong></td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
</tr>
<tr>
<td><strong>Other fluids</strong></td>
</tr>
<tr>
<td><strong>Drain in situ</strong></td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td><strong>PleurX</strong></td>
</tr>
</tbody>
</table>
Skin-tunnelled indwelling (pleurX\textsuperscript{TM}) catheters (1)

- **Tapping et al (2012)\textsuperscript{1}**
  - 28 patients; single centre
  - Mean patency 113 days (Range: 5-365 days)
  - 86% fully functional until death/resolution of ascites
  - Advice: 500 ml (one standard vacuum bottle)/12 h.
  - Complications are rare: leak (10%), localised infection (10%) (no systemic infection), incisional hernia
- **Rosenberg et al (2004)\textsuperscript{2}**
  - 40 patients (40 pleurX) Vs. 67 patients (392 paracenteses); single centre
  - 67% fully functional until death/resolution of ascites (27.5% lost to F/U)
  - Same complication rate 7.5% For pleurX: infection (n = 1), leakage (n = 1) and loculations (n = 1)
- **Courtney et al (2008)\textsuperscript{3}**
  - 34 patients; multicentre
  - 85% fully functional until death/resolution of ascites
  - Complication rates, leakage (n = 7), dizziness/weakness (n = 5), peritonitis (n = 1), localised infection (n = 1), pain (n = 1), death due to presumed PE (n = 1)

---

Skin-tunnelled indwelling (pleurX™) catheters (2)

- **Mullan et al (2011)**\(^1\)
  - 50 patients (52 pleurX drains); single centre
  - Complications: peritonitis (n = 1), lymphangitis (n = 1), occlusion/loculations (n = 3), ascitic leakage (n = 1), displacement (n = 1) and pain (n = 1);

- **Richard et al (2001)**\(^2\)
  - 10 patients
  - Complications: occlusion/loculations (n = 1), displacement (n = 1)
  - Mean patency 70 days (Range: 1-100 days)

- **Saiz-Mendiguren et al (2010)**\(^3\)
  - 10 patients
  - Median patency 52 days (Range: 13-113 days)
  - Mean fluid drained 1 litre/2-10 days

---

Skin-tunneled indwelling (pleurX™) catheters (3) OVERALL

- Near 100% technical success of catheter insertion
- Great success rates with nurse practitioners or interventional radiologists
- Patency rates: 52-113 days
- Generally indicated when prognosis >3/12
- Limitations: All studies are retrospective and no RCTs, Means Vs. Median, Volume of fluid drained?
The PleurX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites

NICE medical technology guidance [MTG9]  Published date: March 2012
NICE medical technology guidance [MTG9]; March 2012 (2)

• Estimated **cost saving of £679** per patient when compared with inpatient large-volume paracentesis.

• The Committee concluded that the PleurX peritoneal catheter drainage system is a **clinically safe and effective palliative** therapy for the management of **treatment-resistant, recurrent malignant ascites**, which has the potential to improve quality of life and is cost saving when compared with inpatient large-volume paracentesis.

• Some local guidelines don’t recommend it
Other treatments
The alfaPump system

1. During charging data are transferred from alfaPump to Smart Charger.
2. alfaPump data transferred via phone network to data specialists.
3. alfaPump data specialists analyse data. Reports sent as often as requested.
4. Fewer follow-up visits, latest data always available, save time and resources.

Smart Charger with DirectLink Technology
The handheld Smart Charger is used by the patient to charge the alfaPump wirelessly through the skin. During charging the Smart Charger collects and records pump activity. The Smart Charger contains a GSM chip which transfers pump data to Sequana Medical servers for analysis.

Catheters and Surgical Kit
Implantable grade silicone catheters are utilised to collect ascites from the peritoneal cavity and transport it to the bladder. The bladder catheter features a pigtal design that rests inside the bladder. Dacron cuffs facilitate tissue in-growth and help secure the catheters after implantation. A tunneler to facilitate catheter tunnelling is provided, as well as additional catheter extensions and connectors to adjust the length of catheters when required.
Each alfaPump system is delivered with a surgical kit containing the required introducer, guidewire and dilators, so there is no need to stock additional accessories for implanting at the hospital.

alfaPump Programmer
Physicians use the notebook and integrated software to download pump data and to change settings. Unique FlowControl software enables quick and easy adaption of patient-specific pumping programs.

Phase 3; NCT01528410
Intraperitoneal tumor necrosis factor-alpha

- Early 1990; small case series; 29 patients\(^1\)
- Intraperitoneal recombinant human tumour necrosis factor alpha (rhTNF-alpha) with mixed results
- 1996; RCT; 18 patients\(^2\)
- Not effective in preventing recurrence

Intraperitoneal Anti-angiogenesis

- 1997; Phase I/II trial with batimastat
  - Good results but terminated; bowel obstruction
- 2008; phase II trial with Sunitinib (NCT00796861); terminated due to poor recruitment
- 2011; phase II trial with Aflibercept (NCT00396591); effective and reduces interval between paracenteses
- 2010-15; phase II trial with Bevacizumab (NCT01200121); Completed; a/w results

Catumaxomab; (Removab®, Neovii Biotech GmbH, Graefelfing, Germany)

- Monoclonal antibody
- 2010; Phase 2/3 trial (C + P) Vs. (P) alone. 258 patients (NCT00836654)¹
- Ovarian, gastric, breast, pancreas, colon, and endometrial malignancies
- Improved survival and delayed need for further drainage
- 2009; European Union approval for the intraperitoneal treatment of patients with malignant ascites²

Others
All pending...

• Autologous Mesenchymal Stem Cell Transplantation in Cirrhosis Patients With Refractory Ascites (NCT01854125)

• Anti-oxidized macrophage migration inhibitory factor (oxMIF) (IP) Vs. (IV + IP) (NCT02540356)

• Intraperitoneal Docetaxel for malignant ascites (NCT02779608)
• Cirrhotic & non-cirrhotic
• SBP in palliative care
• HRS in palliative care
• Establish need for USS
• Electrolytes
• Fluid replacement including HAS
• Diuresis and monitoring
• Bleeding diathesis
• Duration of drains to stay in situ
• Overnight stay?
• Consolidate knowledge around PleurX drains. Who can do them?
• Escalation: TIPSS, IP VEGF inhibitors
Summary

- Classification of ascites; aetiology, biochemistry
- Can dictate treatments and outcomes
- National and international guidance for cirrhotic ascites
- Locoregional variation in guidance for malignant ascites
- There is evidence and NICE advice for pleurX drains and IP monoclonal antibodies have been approved
  - community based
  - principle of “minimal disturbance”
  - Often nurse led/delivered; more training required
  - Often reliance on carers
  - access to services e.g. poorer mobility
  - poorer prognosis. Limited accessibility to trials? Industry?
  - historical and anecdotal evidence
Objectives

• Overview of management of ascites due to cirrhosis & other causes
• Evidence-based approach for the patient with
  – Small/Moderate volume ascites
  – Large volume ascites
  – Spontaneous Bacterial Peritonitis
• Locoregional and peer-reviewed guidelines
The end