EE688

The Clinical, Humanistic and Economic Burden of the Management of Patients with Recurrent Malignant Ascites in the UK and Europe

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1. Introduction

Background: Recurrent malignant ascites (rMA) is the persistent re-accumulation of tumour-cell-positive peritoneal fluid in patients with advanced-stage cancer who are refractory to systemic therapies.[1,2] rMA is most common in metastatic cases of ovarian (≤40%), pancreatic (≤21%) and gastric cancer (≤18%), but can also develop in patients with other cancer types.[3-6] Patients with metastases to the peritoneum or liver are at greatest risk of developing rMA.[3,5] Patients with malignant ascites experience severe physical discomfort and a range of symptoms that are both painful and emotionally distressing.[7] These symptoms are consistent irrespective of primary cancer type and include a range of gastrointestinal (GI) symptoms (abdominal swelling and pain, loss of appetite, nausea and vomiting, constipation, and heartburn), dyspnoea (breathlessness), loss of mobility and extreme fatigue.[8–10] Additionally, the development of rMA is a marker of poor prognosis, indicating systemic therapy resistance and progressive disease.[1,2,5] Consequently, patients with rMA are typically approaching the end of life, with a median overall survival (mOS) of approximately 6-7 months post-diagnosis.[3] The current management of patients with rMA consists solely of palliative care, which focuses on symptomatic relief to maintain or improve health-related quality of life (HRQoL).[1,11,12]

Objectives: This study aimed to characterise the current clinical, humanistic, and economic burden associated with rMA management strategies in the UK and Europe.

2. Methods

- **Systematic literature reviews (SLRs)** followed guidance from Cochrane and the CRD and were reported using PRISMA guidelines (all searches to 27 March 2025). There were no restrictions on geography, language or date. PICOS are summarised in **Table 1**. Sources were:
  - **Clinical SLR:** Embase® (Ovid), MEDLINE® (Ovid), 2 clinical trial registries, 5 conferences, 16 HTA agencies, CENTRAL, CDSR, CRD (including: DARE, HTA database and NHS-EED) and the bibliographies of included studies.
  - **Non-clinical SLR:** Embase® (Ovid), MEDLINE® (Ovid), 2 clinical trial registries, 5 conferences, 16 HTA agencies, the bibliographies of included studies, EconLit (Ovid) and others.
- **Targeted literature reviews (TLR):** RWE studies were sought from the same databases as the SLRs and complemented with hand-searches. Outcomes included effectiveness, safety, HRQoL, patient experience and treatment patterns, and there were no restrictions on interventions or comparators. Prospective or retrospective observational studies and SLRs were included.

A list of all references cited in this poster are available here:

[a] Full details of the PICOS and criteria used in the SLRs and TLR via the QR code provided.

Table 1: PICOS criteria applied in clinical and non-clinical SLRs[a]

Element	Inclusion criteria	Exclusion criteria
Participants	• Adults with EpCAM+ epithelial cancers of any origin with MA including but not limited to: breast; cholangiocarcinoma; colon; endometrium; fallopian tube; gastric; liver; lung; melanoma; oesophageal; ovarian, pancreas; primary peritoneal; rectal; urothelial; uterine	• Patients with non-malignant ascites, EpCAM-negative or non-epithelial cancers • Paediatric patients
Intervention	• Catumaxomab; paracentesis; paracentesis + catumaxomab; paracentesis + other; catheter drainage (any) • **Non-clinical SLR:** no restrictions for cost/HRU and HSUV/HRQoL studies	• Alternative therapies/naturopathic interventions
Comparator	• Any	• N/A
Outcomes	**Clinical SLR:** • Efficacy: OS/mortality; PuFS; PFS; TTP; TTPu; number of punctures; ascites volume. • Safety: Any AE; any grade ≥3 AEs; any SAEs; TRAEs; TRSAEs; discontinuation due to AEs; death due to AEs; CRS; specific ascites- or CRS-related AEs • Disease-specific and generic HRQoL tools and relevant EORTC scales. **Non-clinical SLR:** • Economic evaluations; costs/HRU; HSUV/HRQoL	• Non-clinical SLR: drug costs
Study Design	**Clinical SLR:** • RCTs, including post-hoc analyses. **Non-clinical SLR:** • Economic evaluations: CEAs; CUAs; cost-benefit analyses; cost-minimisation analyses; cost-consequence analyses; cost-comparison analysis; budget-impact analyses. • Cost/HRU/HSUV/HRQoL: Interventional clinical studies; original cost/HRU data; original HSUV/HRQoL data; HSUV elicitation studies; cost of illness studies; cost-consequence studies; RWE.	• Systematic reviews; commentaries; letters; reviews/editorials; animal/in vitro studies; case studies; conference abstracts pre-2022 • Clinical SLR: Phase I studies; observational studies; case series; single arm studies • Non-clinical SLR: studies with <30 patients

3. Results

Clinical SLR:
- Of 17 studies which met all eligibility criteria, **5 studies (published 1995–2016)** were relevant to the UK and Europe; 3 were multinational studies,[13–15] 1 study was conducted in Germany[16] and 1 in Italy.[17]

Non-clinical SLR:
- Of 38 studies which met all eligibility criteria, 18 studies were relevant to the UK and Europe:
  - **6 economic evaluations** (4 in the UK,[18–21] 1 in Germany[22], and 1 in the Netherlands[23]).
  - **16 with cost/HRU data** (2 multinational study,[4,24] 8 in the UK,[18–28] 4 in Germany,[22,29–31] 1 in Italy,[32] and 1 in Poland[33]).
  - **3 with HSUV/HRQoL data** (1 multinational study,[24] 1 in the Netherlands[23] and 1 in Poland[33]).

TLR (RWE):
- 74 studies met all eligibility criteria, of which 27 were prioritised (studies were deprioritised if they reported a small number of outcomes, few relevant results and/or smaller sample sizes). Sixteen of 27 prioritised studies were relevant to the UK (n=7)[3,20,26,27,34–36] and Europe (3 multinational,[4,37–38] 2 studies in Germany,[30,39] and 1 in each of Belgium,[40] Denmark,[41] Finland[42] and Poland[43]). Targeted hand-searches identified clinical guidelines[11] and data on the frequency of recurrence.[45]

Patients with rMA have heavy symptomatic burden and reduced HRQoL

Symptomatic burden in patients with rMA was reported by 6 RWE studies (**Table 2**).[3,38,39,41–43] Patients' also reported **limited mobility**, **sleep disorders** and **psychological distress**.[39]

A multinational RCT reported baseline data for HRQoL (EORTC QLQ C30) in patients with rMA (N=258).[15] The **mean global HRQoL score was 41.1 (SD 18.2),** substantially lower than published scores for other populations with metastatic cancer (**Figure 1**).[15,44]

Figure 1: Mean global HRQoL scores in patients with metastatic cancer with or without rMA[15,44]

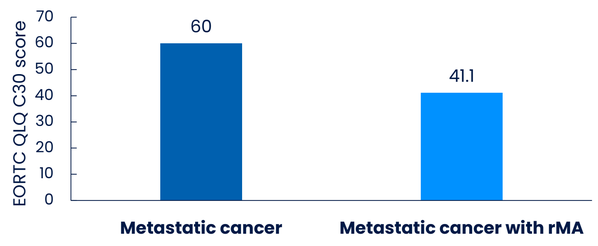


Table 2: Symptoms of MA [3,38,39,41–43]

Symptom (Studies, N)	Patients, %
Abdominal discomfort (3)	79–94
Abdominal swelling (3)	35–93
Abdominal pain (3)	30–82
Loss of appetite (2)	17–71
Fatigue (2)	17–68
Dyspnoea (6)	11–65
Early satiety (2)	6–65
Anorexia (2)	36–60
Pain (2)	19–60
Nausea (5)	11–54
Peripheral oedema (4)	3–53
Constipation (2)	7–51
Vomiting (5)	6–25
Obstipation (2)	2–11
Heartburn (2)	1–4

Current treatments for rMA provide only temporary symptomatic relief

RWE studies (N=3) reported **serial paracentesis (PCT) (ultrasound-guided abdominal puncture followed by drainage of ascitic fluid) as the primary treatment modality,** used in up to ~90% of patients with rMA (2007-2015).[3,4,34] UK treatment guidelines (2022) recommend serial PCT, followed by a permanent **indwelling peritoneal catheter (IPC) for patients who have received ≥2 prior PCT procedures.**[11] Following surgical placement, an IPC allows outpatient drainage, usually with the assistance of a district nurse.[11,21] In the UK, the IPC PeritX® (previously PleurX®) received recommendation from NICE in 2012.[21]

Patients with rMA no longer respond to systemic anti-cancer therapy, and drainage of ascitic fluid is a strictly palliative treatment.[1,3] Median OS following an initial PCT and a final PCT has been estimated at **~200 days and ~100 days, respectively (N=1).**[27] Median OS post-placement of an IPC is **≤77 days** (N=3).[20,41,42]

In rMA, the persistent accumulation of ascitic fluid necessitates serial PCT in a hospital or hospice setting, with a mean of 2 PCT procedures (range 1–7) per patient.[3] The rate of recurrence can increase as a patient nears the end-of-life, increasing the frequency of PCT (**Figure 2**).[45]

Symptomatic relief following drainage of ascitic fluid either by PCT or an IPC is effective and immediate, but wanes over time as ascitic fluid re-accumulates (**Figure 3**).[38]

Figure 2: PCT events in the final year of life[45]

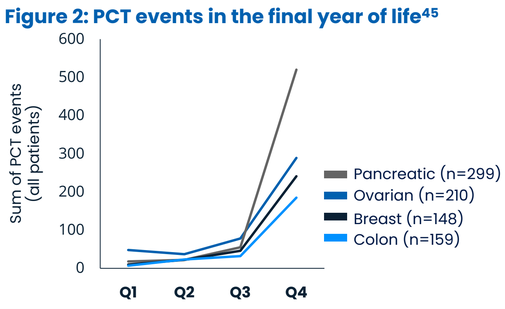
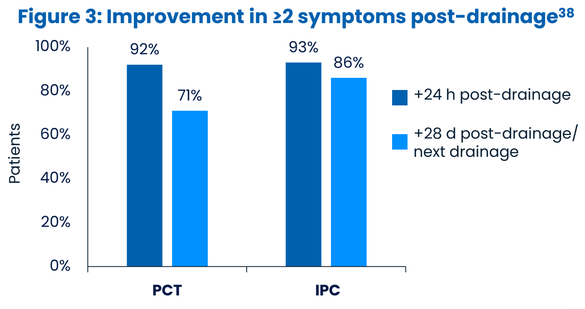


Figure 3: Improvement in ≥2 symptoms post-drainage[38]



Repeated hospital visits and treatment complications create additive burden

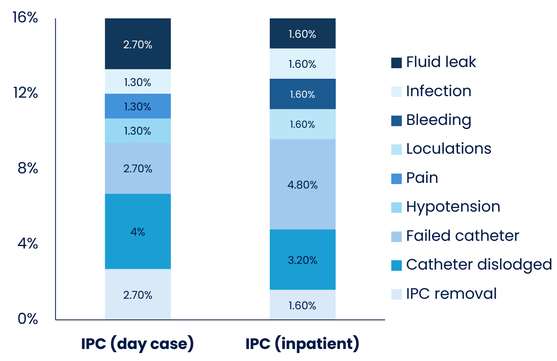
Repeated hospital visits for serial PCT negatively impact the HRQoL of patients who may be only months away from death.[3,24,35,39] IPCs allow drainage at home, but patients may be unwilling or unable to use them without assistance.[11,27,35] The **incidence of complications is also higher for IPCs compared with PCT** (**Table 3**). A direct comparison between day-case and inpatient settings for IPC surgical placement reported a complication rate of ~16% in either setting (**Figure 4**).[18]

Table 3. Complications following PCT or IPC placement

Treatment	PCT		IPC		
Setting / AE, %	Any[38]	Day-case [27,42]	Any[38]	Day-case [26,42]	Inpatient [20,31,36,40,41]
Fluid leak	≤13	2.0–3.2	≤15	8.0–22.2	1.0–9.8
Hypotension	≤8	2	≤10	0	1
Pain	≤2	0.6–3.0	≤7	8	2–3.9
Infection (any)	NR	NR	NR	8	1.0–10.7
Peritonitis	1.3	0	NR	3–4	1.9
Cellulitis	NR	0.4	4.3	5.8	3.9
Bleeding	1.3	0.2–1.0	NR	NR	NR
IPC malfunction	NA	NA	NR	1	3.3–14

Data for ref. 38 were collected from hospice (39%), acute hospital (49%) and day-case settings (12%).

Figure 4: Complications following IPC placement (day-case [N=75] or inpatient [N=63])[18]



Delaying symptomatic recurrence of MA helps preserves HRQoL in patients with terminal cancer

Decreasing the frequency of PCT is key for patients with rMA, who may have only months left to live.[3,24,35,39] The clinical SLR identified 3 relevant RCTs in which the efficacy and safety of combining a pharmacological agent with PCT was compared directly with PCT alone.[13,15,16] The interval between PCT events was assessed as **puncture-free survival (PuFS),** the time to next therapeutic puncture or death, and **time to next puncture (TTPu).**[13,15,16]

Efficacy. PuFS and TTPu were significantly extended by combining PCT with either aflibercept (a VEGF inhibitor), or catumaxomab (a trifunctional anti-EpCAM mAb).[13,15] The addition of either catumaxomab or the VEGF inhibitor bevacizumab to PCT also extended mOS (**Table 4**).[13,15]

Safety. As expected, there is an increase in the frequency of AEs when drug-based therapy is added to PCT (**Table 5**), and discontinuation rates due to AEs ranged from ~6% (catumaxomab + PCT) to 17% (aflibercept + PCT).[13,15,16,46]

Table 4: Efficacy data from 3 RCTs of novel treatments[a] for rMA

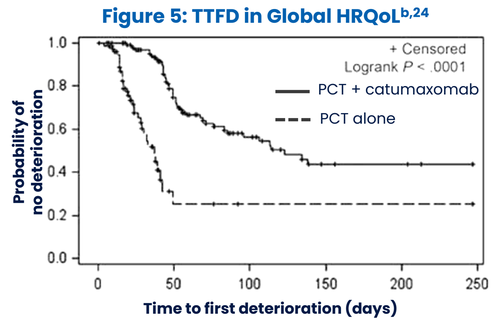
Study details	Treatments	mPuFS, days	mTTPu, days	mOS, days
Gotlieb 2012[9] Multinational. N=55	PCT + aflibercept vs. PCT + pbo	42 vs. 18 HR: 0.348 (0.187–0.648); **P=0.0008**	39 vs. 18 HR: 0.298 (0.154–0.578); **P=0.0002**	90 vs. 112 HR: 1.02 (0.56–1.86); P=0.9329
Heiss 2010[11] Multinational. N=258	PCT + catumaxomab vs. PCT	46 vs. 11 HR: 0.254 (0.185–0.350); **P≤0.0001**	77 vs. 13 HR: 0.169 (0.114–0.251); **P<0.0001**	72 vs. 68 HR: 0.723 (0.498–1.048); P=0.0846
Jordan 2016[12] Germany. N=49	PCT + bevacizumab vs. PCT + pbo	14.0 vs. 10.5 HR: 0.74 (0.40–1.37); P=0.16	19.0 vs. 17.5	64.0 vs. 31.5 HR: 0.73 (0.40–1.37); P=0.31

HRQoL. HRQoL as assessed using EORTC-QLQ-C30 was reported in 1 of 3 RCTs.[24] Patients who received catumaxomab + PCT benefitted from a significant delay in the time to first deterioration in Global HRQoL compared with patients who received PCT alone (p<0.0001, **Figure 5**).[24]

Table 5: AE data from 3 RCTs of treatments for rMA

Treatments	Any SAE, %	Discontinuations, %
PCT+aflibercept vs. PCT+pbo[13]	90 vs. 72	17 vs. 20
PCT+catumaxomab vs. PCT[15,46]	Non-ovarian cancer: 68.8 vs. 31.8	Non-ovarian cancer: 7.8 vs. NA
	Ovarian cancer: 47.5 vs. 15.9	Ovarian cancer: 6.3 vs. NA
PCT+bevacizumab vs. PCT+pbo[16]	51.5 vs. 68.8	9.1 vs. 0

Figure 5: TTFD in Global HRQoL[b,24]



[a] At present, catumaxomab is the only licensed treatment for rMA.
[b] EORTC QLQ-C30 Global HRQoL scale; Numbers in parentheses are 95% confidence-intervals

Costs of current management are driven by procedures and hospitalisations

Total costs for PCT were driven by hospitalisation and length of stay (LoS) in hospital (~3 days).[19,20] Day-case PCT gave substantial cost-savings.[19–22] IPC costs were mainly driven by the expense of the initial surgical procedure itself, whether in an inpatient or day-case setting, followed by 'at-home drainage kits' and the provision of home care (**Table 6**).[18,20–22]

Table 6: Direct costs associated with PCT or IPCs for the drainage of MA

Study details	PCT total medical costs	IPC total medical costs
Siefen 2023. Germany. N=82 EUR, cost year 2020/2021[22]	Inpatient: €721.54 Outpatient: €60.02	€1,918.58 (incl. 3 home visits/wk)
ZIN 2013. Netherlands. N=NR. EUR, cost year NR[23]	€5,206	NA
Daga 2022. UK. N=NR GBP, cost year NR[18]	NA	Inpatient: £3,118.48 (inc. 2.5 d in hospital) Day-case: £1,268.02
Harding 2012. UK. N=31 GBP, cost year 2009/2010[19]	Inpatient: £1,473 (inc. 3 d in hospital) Day-case: £954	NA
Mullan 2015. UK. N=50 GBP, cost year NR[20]	£165.45 (excl. hospital stay) £1,409.45 (inc. 2.8 d in hospital)	£429.64 (excl. hospital stay) £837.64 (inc.1 d in hospital)
NICE 2022. UK. (MTG9 costing report) GBP, NHS reference costs 2019/2020 and PSSRU 2020[21]	£180.18 (excl. hospital stay) Calculated base case, inpatient: £3,659 Calculated base case, day-case: £1,668	£455.97 (excl. hospital stay) Drainage kits and home visits: £733.64 Calculated base case: £2,564

Additional medical costs are accrued due to the **management of treatment complications** (**Table 7**).[21] An IPC may need to be entirely replaced; it is estimated that an IPC may need to be reinserted in 4.0% to ~6.5% of patients.[19,20] One study of 34 patients reported that 6% of IPCs were removed due to complications (tumour infiltrations [3%] or non-resolving cellulitis [3%]).[26]

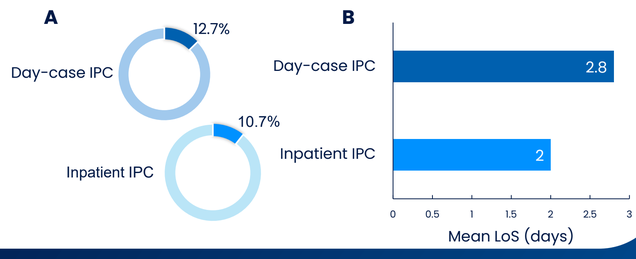
HCRU due to management of PCT-related complications included the following estimates:
- Of 123 patients who received day-case PCT, 1.1% were hospitalised due to complications.[27]
- ~12% of 138 patients who received an IPC were re-hospitalised due to complications, with a mean LoS of 2.0–2.8 days (**Figure 6**).[18]

Table 7: Medical-costs of managing complications[21]

Complication	PCT	IPC
Infection	£153.11	£153.11
Catheter failure	£441.50	£441.50
Re-intervention	Not applicable	£823.75

Cost year: 2019/2020

Figure 6: Re-hospitalisation rate (A) and LoS (B) due to complications post-placement of an IPC[18]



4. Conclusions

The symptoms caused by repeated fluid accumulation in patients with rMA lead to significantly diminished HRQoL.[24,39] The current management of rMA consists of providing temporary symptomatic relief through fluid drainage. However, these interventions require frequent hospitalisation (PCT) and/or are associated with a high incidence of complications (IPCs).[11,18,38] As patients with rMA are nearing the end of life, palliative care should focus on minimising hospital visits to optimise care and improve the patient's HRQoL.[3,12,45] Evidence from randomised clinical trials indicates that combining pharmacological agents* with PCT can prolong PuFS and improve HRQoL compared with drainage alone.[13, 15–16,24] Although such agents* are not part of the current management of rMA, their implementation could lead to prolonged symptom relief, reduced hospitalisations and procedure-related complications, and ultimately help reduce the overall economic burden associated with rMA.[11, 13, 15–16,18–22, 24]

At present, catumaxomab is the only licensed treatment for rMA

AE, adverse event; CDSR, Cochrane Database of Systematic Reviews; CEA, cost-effectiveness analysis; CENTRAL, Cochrane Central Register of Controlled Trials; CRD, Centre for Reviews and Dissemination; CRS, cytokine release syndrome; CUA, cost-utility analysis; DARE, Database of Abstracts of Reviews of Effects; EORTC, European Organisation for Research and Treatment of Cancer; EpCAM, epithelial cell adhesion molecule; HRQoL, health-related quality of life; HCRU, healthcare resource utilisation; HSUV, health-state utility value; HTA, health-technology assessment; IPC, indwelling peritoneal catheter; MA, malignant ascites; NHS-EED, National Health Service Economic Evaluation Database; LoS, length of stay; OS, overall survival; pbo, placebo; PCT, paracentesis; PICOS, population-intervention-comparator-outcome-study design; PFS, progression-free survival; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; PuFS, puncture-free survival; RCT, randomised controlled trial; rMA, recurrent malignant ascites; RWE, real-world evidence; SAE, serious adverse event; SLR, systematic literature review; TRAE, treatment-related adverse event; TRSAE, treatment-related serious adverse event; TTP, time to progression; TTPu, time to next puncture.

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