# Detailed PICOS and criteria used in the SLRs and TLR

*Table 1. PICOS criteria used in the non-clinical SLR*

| Element | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Participants | Adult females with EpCAM+ ovarian cancer with malignant ascites<br>Adults (males or females) with EpCAM+ epithelial cancers of any origin with malignant ascites, including but not limited to:<br>Breast<br>Cholangiocarcinoma<br>Colon<br>Endometrium<br>Fallopian tube<br>Gastric<br>Liver<br>Lung<br>Melanoma<br>Oesophageal<br>Pancreas<br>Primary peritoneal<br>Rectal<br>Urothelial<br>Uterine<br><br>Note that these are the primary populations of interest, although the broader population of epithelial cancer (of any EpCAM status, including unclear) with malignant ascites will be tagged during screening as a surrogate for the population of interest in the case of limited evidence retrieval for EpCAM+ patients<br><br>Studies in mixed epithelial cancer types are included | Patients with non-malignant ascites, malignant ascites with EpCAM-negative tumours or malignant ascites due to non-epithelial cancers<br>Paediatric patients |
| Intervention<br>Comparator | Economic evaluations:<br>Catumaxomab*<br>Paracentesis<br>Paracentesis + catumaxomab*<br>Paracentesis + other<br>Catheter drainage (any type, and including PleurX™/PeritX™, Bonano suprapubic etc.)<br>Cost/HRU and HSUV/HRQoL:<br>No restrictions | - |
| Outcomes | Economic evaluations:<br>Summary costs and health outcomes (e.g. QALYs, LYG)<br>ICER/ICUR<br>Model summary and structure, including model type, perspective, time horizon, discounting, cycle length<br>Assumptions underpinning model structures<br>Sources of key model inputs<br>Cost/HRU:<br>Direct costs<br>Medical costs (e.g. medications, staff, hospitalisations) | Drug costs |

| Element | Inclusion criteria | Exclusion criteria |
|---|---|---|
| | Non-medical/out-of-pocket costs (e.g. travel, childcare)<br>Indirect costs (work/school absenteeism or presenteeism, productivity loss)<br>Cost drivers<br>Healthcare resource use (e.g. length of hospitalisation/ICU stay, number of medical visits, number and frequency of hospitalisations)<br>Workplace/productivity measures<br>HSUV/HRQoL:<br>HSUVs for relevant health states for patients and caregivers derived using:<br>Direct elicitation (e.g. SG, TTO, VAS)<br>Generic, using preference-based instruments (e.g. EQ-5D, SF-6D, HUI2 and HUI3, AQoL)<br>Any EORTC-QLQ HRQoL tools<br>Mapping algorithms allowing data from disease-specific/generic measures to be mapped to preference-based HSUVs<br>Disutilities or decrements for relevant health states | |
| Study Design | Economic evaluations:<br>Cost-effectiveness analyses<br>Cost-utility analyses<br>Cost-benefit analyses<br>Cost-minimisation analyses<br>Cost-consequence analyses<br>Cost-comparison analysis<br>Budget impact analyses<br>Cost/HRU:<br>Interventional clinical studies (RCTs or non-RCTs, including single arm studies)<br>Economic evaluations reporting original cost/HRU data<br>Cost of illness studies<br>Cost-consequence studies<br>Real-world evidence (e.g. database studies collecting cost data, surveys)<br>HSUV/HRQoL:<br>Economic evaluations reporting original HSUV/HRQoL data<br>HSUV elicitation studies<br>Interventional clinical studies (RCTs and non-RCTs)<br>Real-world evidence (e.g. epidemiological studies, cohorts, cross-sectional studies, patient surveys, registry data and case series) | Systematic reviews*<br>Commentaries<br>Letters<br>Review/editorials<br>Animal/*in vitro* studies<br>Case studies<br>Studies with <30 patients<br>Conference abstracts pre-2022 |
| Subgroups | Ovarian cancer<br>Non-ovarian cancer<br>Pooled (any cancer) | - |
| Geography | No restriction.<br>UK, England, Scotland, Wales, N. Ireland, Ireland, Europe (EU-4 (France, Germany, Italy, Spain) and other European countries) are of primary interest | - |
| Language | Non-English language studies will be tagged during screening | - |
| Date | No restriction | - |

* At present, catumaxomab is the only licensed treatment for rMA

*Table 2. PICOS criteria used in the clinical SLR*

| Element | Inclusion criteria | Exclusion criteria |
|---|---|---|
| **Participants** | • Adult females with EpCAM+ ovarian cancer with malignant ascites<br>• Adults (males or females) with EpCAM+ epithelial cancers of any origin with malignant ascites, including but not limited to:<br>▪ Breast<br>▪ Cholangiocarcinoma<br>▪ Colon<br>▪ Endometrium<br>▪ Fallopian tube<br>▪ Gastric<br>▪ Liver<br>▪ Lung<br>▪ Melanoma<br>▪ Oesophageal<br>▪ Pancreas<br>▪ Primary peritoneal<br>▪ Rectal<br>▪ Urothelial<br>▪ Uterine<br><br>Note that these are the primary populations of interest, although the broader population of epithelial cancer (of any EpCAM status, including unclear) with malignant ascites will be tagged during screening as a surrogate for the population of interest in the case of limited evidence retrieval for EpCAM+ patients.<br><br>Studies in mixed epithelial cancer types are included. | • Patients with non-malignant ascites, malignant ascites with EpCAM-negative tumours or malignant ascites due to non-epithelial cancers<br>• Paediatric patients |
| **Intervention** | • Catumaxomab*<br>• Paracentesis<br>• Paracentesis + catumaxomab*<br>• Paracentesis + other<br>• Catheter drainage (any type, and including PleurX™/PeritX™, Bonanno suprapubic etc.) | • Alternative therapies or naturopathic interventions |
| **Comparator** | Any | - |
| **Outcomes** | **<u>Efficacy:</u>**<br>• Overall survival (OS)/mortality<br>• Puncture-free survival (PuFS)<br>• Progression-free survival (PFS)<br>• Time to progression (TTP)<br>• Time to next puncture (TTPu)/drainage/treatment/ paracentesis<br>• Number of punctures<br>• Ascites volume<br><br>**<u>Safety:</u>**<br>• Any adverse event (AE)<br>• Any grade ≥3 AEs<br>• Any serious AEs<br>• Treatment-related AEs<br>• Treatment-related serious AEs<br>• Discontinuation due to AEs<br>• Death due to AEs<br>• Cytokine-release syndrome (CRS) | - |

| Element | Inclusion criteria | Exclusion criteria |
|---|---|---|
| | • Specific ascites- or CRS-related AEs, including:<br>▪ Bloating<br>▪ Chills<br>▪ Diarrhea<br>▪ Dizziness<br>▪ Fatigue<br>▪ Fever<br>▪ Headache<br>▪ Hypotension<br>▪ Joint or muscle pain<br>▪ Nausea/vomiting<br>▪ Swelling in the stomach or legs<br>▪ Rash<br>▪ Shortness of breath<br>▪ Tachycardia<br>▪ Weight gain<br><br>**HRQoL:**<br>• Disease-specific quality-of-life tools:<br>▪ EORTC-QLQ-OV28<br>▪ FACIT-AI<br>▪ QOL-Ovarian Cancer Scale<br>• Generic quality-of-life tools:<br>▪ EORTC-QLQ-C30<br>▪ EORTC-QLQ-C15-PAL<br>▪ Any other relevant EORTC scales<br>▪ EQ-5D, EQ-5D VAS | |
| **Study Design** | Randomised controlled trials, including *post-hoc* analyses | • Phase 1 studies<br>• Observational studies<br>• Systematic reviews*<br>• Commentaries<br>• Letters<br>• Reviews/editorials<br>• Animal/*in vitro* studies<br>• Case studies<br>• Case series<br>• Single arm studies<br>• Conference abstracts pre-2022 |
| **Subgroups** | • Ovarian cancer<br>• Non-ovarian cancer | - |
| **Geography** | No restriction.<br>*UK, England, Scotland, Wales, N. Ireland, Ireland, Europe (EU-4 (France, Germany, Italy, Spain) and other European countries) are of primary interest* | - |
| **Language** | Non-English language studies will be tagged during screening | - |
| **Date** | No restriction | - |

* At present, catumaxomab is the only licensed treatment for rMA

*Table 3. PICOS criteria applied in the targeted literature review*

| Element | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Participants | • Adults (males or females) with EpCAM+ epithelial cancers with malignant ascites<br>• Adult females with EpCAM+ ovarian cancer with malignant ascites<br><br>Note that these are the primary populations of interest, although the broader population of epithelial cancer (of any EpCAM status, including unclear) with malignant ascites will be tagged during screening as a surrogate for the population of interest in the case of limited evidence retrieval for EpCAM+ patients | • Patients with non-malignant ascites, malignant ascites with EpCAM-negative tumours or malignant ascites due to non-epithelial cancers<br>• Paediatric patients |
| Intervention<br>Comparator | No restriction (ideally any or no treatment i.e. an unselected population) | - |
| Outcomes | <u>Effectiveness:</u><br>• Overall survival (OS)/mortality<br>• Puncture-free survival (PuFS)<br>• Progression-free survival (PFS)<br>• Time to progression (TTP)<br>• Time to next puncture/drainage/treatment/ paracentesis (TTPu)<br>• <u>Safety:</u><br>• Any AE<br>• Any grade ≥3 AEs<br>• Any serious AEs<br>• Discontinuation due to AEs<br>• Death due to AEs<br>• Cytokine-release syndrome (CRS)<br><u>HRQoL:</u><br>• Disease-specific quality-of-life tools:<br>• EORTC-QLQ-OV28<br>• FACIT-AI<br>• QOL-Ovarian Cancer Scale<br>• Generic quality-of-life tools:<br>• EORTC-QLQ-C30<br>• EORTC-QLQ-C15-PAL<br>• Any other relevant EORTC scales<br>• EQ-5D, EQ-5D VAS<br><u>Patient experience</u><br><u>Treatment patterns:</u><br>• Frequency of treatment use<br>• Increase/decrease in usage over time | - |
| Study Design | • Observational studies (real-world evidence), either prospective or retrospective<br>• SLRs of real-world evidence | • RCTs<br>• Commentaries<br>• Letters<br>• Review/editorials<br>• Animal/*in vitro* studies<br>• Conference abstracts pre-2022<br>• Economic studies (e.g. CEA, CUA, BIA)<br>• Pharmacokinetic studies<br>• Non-randomised interventional studies<br>• Sample size limits of <30, <50 or <100 patients may be |

| Element | Inclusion criteria | Exclusion criteria |
|---|---|---|
| | | applied to prioritise the studies |
| Subgroups | • Ovarian cancer<br>• Non-ovarian cancer<br>• Pooled (any cancer) | |
| Geography | No restriction<br>*UK, England, Scotland, Wales, N. Ireland, Ireland, Europe (EU-4 (France, Germany, Italy, Spain) and other European countries) are of primary interest, and geography restrictions may be applied during screening to identify a priority dataset* | - |
| Language | Only English language records are of interest | - |
| Date | No restriction, although data may be prioritised by date to help manage the size of the included study pool | - |

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