NIHR | Innovation Observatory

Newcastle University

# Health Technology Briefing
# August 2023

# Mirvetuximab soravtansine for advanced, epithelial ovarian, fallopian tube, or primary peritoneal cancer with high folate receptor-alpha expression

| Company/Developer | ImmunoGen Inc |
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☒ New Active Substance ☐ Significant Licence Extension (SLE)

| NIHRIO ID: 29274 | NICE TSID: Not available | UKPS ID: Not available |
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## Licensing and Market Availability Plans

Currently in a phase III clinical trial.

## Summary

Mirvetuximab soravtansine is in clinical development for the treatment of adults with advanced, platinum-resistant, high-grade epithelial ovarian cancer, primary peritoneal cancer and fallopian tube cancer with high folate receptor-alpha expression. Epithelial ovarian cancer means the cancer started in the surface layer covering the ovary. The main symptoms are frequent swollen or bloated tummy, pain or tenderness in the stomach, loss of appetite and an urgent need to urinate. Symptoms can go unnoticed, so the cancer can be diagnosed when the disease is advanced and challenging to treat. Most patients have the cancer removed surgically and receive chemotherapy, which usually includes platinum-based drugs. However, the disease often recurs, and platinum-based chemotherapy drugs may be less effective. If the cancer recurs within 6 months of the previous treatment, and platinum-based chemotherapy does not work, the disease is called “platinum-resistant”.

Mirvetuximab soravtansine is administered by intravenous infusion and works in two stages. First, it recognises a receptor on the cancer cells, attaches itself to the cancer cell and then enters it. When it is inside the cancer cell, the drug releases a toxic substance that kills the cancer cell and other nearby cancer cells. If licensed, this drug would provide an additional optimal treatment option to women with ovarian cancer when other treatments have stopped working.

## Proposed Indication

Females aged 18 years and older with advanced, platinum-resistant, high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancer with folate receptor-alpha (FRα) expression.[2,3]

## Technology

### Description

Mirvetuximab soravtansine (Elahere) is an antibody drug conjugate consisting of the monoclonal antibody M9346A against folate receptor 1 (FOLR1) conjugated, via the disulphide containing cleavable linker sulfo-SPDB, to the cytotoxic maytansinoid DM4, with potential antineoplastic activity. The anti-FOLR1 monoclonal antibody moiety of mirvetuximab soravtansine targets and binds to the cell surface antigen FOLR1. After antibody-antigen interaction and internalization, the antibody drug conjugate releases DM4, which binds to tubulin and disrupts microtubule assembly/disassembly dynamics, thereby inhibiting cell division and cell growth of FOLR1-expressing tumour cells. FOLR1, a member of the folate receptor family is overexpressed on a variety of epithelial derived cancer cells. The sulfo-SPDB linker prevents cleavage in the bloodstream and may improve this agent's efficacy in multidrug resistant tumour cells.[4]

Mirvetuximab soravtansine is in clinical development for the treatment of FRα positive, platinum-resistant, high-grade epithelial ovarian, primary peritoneal or fallopian tube cancer in women.[5] In the phase III clinical trial (NCT04209855), mirvetuximab soravtansine is administered as an intravenous (IV) infusion at 6mg/kg calculated using adjusted ideal body weight on day 1 of a 21-day cycle.[6]

### Key Innovation

Despite advances in surgical techniques and chemotherapeutic agents, mortality rates for epithelial ovarian cancer have overall survival 5-year survival rates of 45% and prognosis worsens in women with platinum-resistant cancer where response rates to existing nonplatinum-based chemotherapy are around 10-30%. A lack of curative therapeutics and a low response rate to existing therapies indicates a need for the development of innovative therapies.[7] Mirvetuximab has shown promising single-agent clinical activity.[8] If licenced, mirvetuximab soravtansine will offer an additional treatment option for platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal patients who currently have few effective therapies available.

### Regulatory & Development Status

Mirvetuximab soravtansine does not currently have marketing authorisation in the EU/UK for any indication.

Mirvetuximab soravtansine is currently in phase II or III clinical development for:[9]

- Endometrial cancer
- Fallopian tube cancer
- Ovarian cancer
- Primary peritoneal cancer

Mirvetuximab soravtansine has the following regulatory designations/awards:[10,11]

- Orphan designation in the EU on 19 March 2015 (EU/3/15/1458) for the treatment of ovarian cancer.
- FDA accelerated approval on 14 November 2022 for FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer.

## Patient Group

### Disease Area and Clinical Need

Epithelial ovarian cancers start in the cells covering the ovaries and are the most common type of ovarian cancer. Primary peritoneal cancer and fallopian tube cancer are similar to epithelial ovarian cancer and are treated in the same way. Primary peritoneal cancer is a rare cancer of the peritoneum and fallopian tube cancer starts in the fallopian tubes which connect the ovaries to the womb.[12] Women who experience recurrence within 6 months following an initial response to platinum based chemotherapy (carboplatin) are characterised as having platinum-resistant ovarian cancer.[7] In comparison to non-cancerous tissues, FRα, is overexpressed in cells impacted by epithelial ovarian carcinoma. Frα also has the unique ability to internalise large molecules which makes FRα ideally situated antibody-drug conjugate (ADC)-based therapeutic approaches.[13] Factors that can increase the risk of ovarian cancer includes age - most ovarian cancers develop after menopause - obesity, a family history of ovarian cancer, hereditary conditions (e.g., BRCA1 and BRCA2 mutations), fertility treatment, smoking and diet.[14] Signs and symptoms of ovarian, fallopian tube, or peritoneal cancer include pain or swelling in the abdomen, sudden or frequent urge to urinate, trouble eating or feeling full, lump in the pelvic area and gastrointestinal problems, such as gas, bloating, or constipation.[15]

In females in the UK, ovarian cancer is the 6th most common cancer, with around 7,500 new cases every year. Ovarian cancer accounts for 4% of all new cancer cases in females in the UK. Incidence rates for ovarian cancer are projected to rise by 5% in the UK between 2023 and 2025 and 2038-2040. Around 81.2% of women in England diagnosed with ovarian cancer aged 15-44 survive their disease for ten years or more, compared with more than a fifth (21.5%) of women diagnosed aged 75-99 (2013-2017).[16] In England in 2021-2022, there were 47,590 finished consultant episodes (FCEs), and 44,233 hospital admissions with a primary diagnosis of malignant neoplasm of ovary and fallopian tube and primary peritoneal (ICD-10 code C56, C57, C48), resulting in 61,352 FCE bed days.[17]

### Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommended options relating to the treatment of adult patients with platinum-resistant, epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have received one to three prior systemic treatment regimens include:

- Pegylated liposomal doxorubicin hydrochloride as a monotherapy for the treatment of advanced ovarian cancer in women who have failed a first-line platinum-based chemotherapy regimen.[19]

## Clinical Trial Information

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| Trial | **MIRASOL**, NCT04209855, EudraCT 2019-003509-80; A Randomized, Open-label, Phase 3 Study of Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers With High Folate Receptor-Alpha Expression<br>**Phase III** – Active, not recruiting<br>**Location(s):** 10 EU countries, UK, USA, Canada and other countries<br>**Primary completion date:** Sep 2023 |
| Trial Design | Randomised, parallel assignment, open-label |

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| Population | N=453 (actual); platinum resistant, high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancer positive for FRα expression who have received 1-3 prior systemic treatments; aged 18 years and over. |
| Intervention(s) | Mirvetuximab soravtansine at 6 mg/kg adjusted to ideal body weight and administered on day one of every three week cycle |
| Comparator(s) | Paclitaxel, topotecan and pegylated liposomal doxorubicin |
| Outcome(s) | Primary outcome: Progression-free survival (PFS) [Time frame: Up to 2 years]<br><br>See trial record for full list of other outcomes |
| Results (efficacy) | With a data cut off from March 6, 2023, 227 patients were randomised to the intervention arm of mirvetuximab (MIRV); 226 to the comparator arm. Median follow-up was 13.1 months. Baseline characteristics were well balanced across arms; 14% of patients had one, 39% two, and 47% three prior lines of therapy; 62% received prior bevacizumab; and 55% received prior PARPi therapy. The study met its primary and key secondary endpoints with statistically significant results in progression free survival (by investigator, INV), overall response rate (INV), and overall survival. In the bevacizumab-pretreated subset (n=281), progression-free survival hazard ratio was 0.64 (0.492, 0.842) and overall survival hazard ratio was 0.74 (0.535, 1.036); in the bevacizumab-naïve subset (n=172), progression-free survival hazard ratio was 0.66 (0.459, 0.942) and overall survival hazard ratio was 0.51 (0.306, 0.860).[5] |
| Results (safety) | The adverse event profile of mirvetuximab (MIRV) was consistent with prior reports: predominantly low-grade ocular (MIRV vs comparator all grade 56% vs 9%; grade 3+ 14% vs 0%) and gastrointestinal events (MIRV vs comparator all grade 70% vs 66%; grade 3+ 13% vs 15%). Compared with the comparator, MIRV was associated with lower rates of grade 3+ treatment-emergent AEs (42% vs 54%), serious AEs (24% vs 33%), and discontinuations due to TEAEs (9% vs 16%). Fourteen percent of patients on the MIRV arm remained on study drug vs 3% on the comparator arm.[5] |

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| Trial | **SORAYA, NCT04296890, EudraCT 2020-000179-19;** A Phase 3, Single Arm Study of Mirvetuximab Soravtansine in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers With High Folate Receptor-Alpha Expression<br>**Phase III –** completed<br>**Location(s):** 8 EU countries, USA, Australia and Israel<br>**Actual study completion date:** November 2022 |
| Trial Design | Single group assignment, open-label |
| Population | N=106 (actual); platinum-resistant, advanced high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptor-alpha expression; aged 18 years and older. |

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| Intervention(s) | Mirvetuximab soravtansine at 6mg/kg adjusted ideal body weight administered on day 1 of every 3-week cycle |
| Comparator(s) | No comparator |
| Outcome(s) | Primary outcome: Objective Response Rate (ORR) [Time frame: Up to 2 years]<br><br>See trial record for full list of other outcomes |
| Results (efficacy) | One hundred six patients were enrolled; 105 were evaluable for efficacy. All patients had received prior bevacizumab, 51% had three prior lines of therapy, and 48% received a prior poly ADP-ribose polymerase inhibitor. Median follow-up was 13.4 months. Objective response rate (ORR) was 32.4% (95% CI, 23.6 to 42.2), including five complete and 29 partial responses. The median duration of response was 6.9 months (95% CI, 5.6 to 9.7). In patients with one to two priors, the ORR by investigator was 35.3% (95% CI, 22.4 to 49.9) and in patients with three priors was 30.2% (95% CI, 18.3 to 44.3). The ORR by investigator was 38.0% (95% CI, 24.7 to 52.8) in patients with prior poly ADP-ribose polymerase inhibitor exposure and 27.5% (95% CI, 15.9 to 41.7) in those without.[20] |
| Results (safety) | The most common treatment-related adverse events (all grade and grade 3-4) were blurred vision (41% and 6%), keratopathy (29% and 9%), and nausea (29% and 0%). Treatment-related adverse events led to dose delays, reductions, and discontinuations in 33%, 20%, and 9% of patients, respectively.[20] |

## Estimated Cost

The cost of mirvetuximab soravtansine is not yet known.

## Relevant Guidance

### NICE Guidance

- NICE technology appraisal in development. Alpelisib with olaparib for treating BRCA wild-type platinum-refractory or -resistant ovarian, fallopian tube or primary peritoneal cancer after 1 to 3 previous treatments TS ID 11830 (GID-TA11251). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Cediranib with olaparib for treating recurrent platinum-resistant ovarian, fallopian tube or primary peritoneal cancer after 3 therapies [ID1639]. (GID-TA10607). Expected date of issue to be confirmed.
- NICE technology appraisal. Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer (TA389). April 2016
- NICE technology appraisal. Guidance on the use of paclitaxel in the treatment of ovarian cancer (TA55). January 2003.
- NICE clinical guideline. Ovarian cancer: recognition and initial management (CG122). April 2011.
- NICE quality standard. Ovarian Cancer (QS18). May 2012.
- NICE interventional procedures guidance. Maximal cytoreductive surgery for advanced ovarian cancer (IPG757). April 2023.

### NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Complex Gynaecology – Specialist Gynaecological Cancers. E10/S/f.

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a. NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

### Other Guidance

- National Comprehensive Cancer Network. Ovarian Cancer, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. February 2021.[21]
- Spanish Society of Medical Oncology. SEOM clinical guideline in ovarian cancer (2020). January 2021.[22]
- Scottish Intercollegiate Guidelines Network. SIGN 135 - Management of epithelial ovarian cancer. October 2018.[23]
- British Gynaecological Cancer Society. British Gynaecological Cancer Society (BGCS) Epithelial Ovarian / Fallopian Tube / Primary Peritoneal Cancer Guidelines: Recommendations for Practice. 2017.[24]

## Additional Information

ImmunoGen Inc did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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