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Case report

[Translated article] Possible severe gastrointestinal toxicity following the first cycle of mirvetuximab soravtansine in a patient with high-grade serous ovarian carcinoma

Posible toxicidad digestiva grave tras el primer ciclo de mirvetuximab soravtansina en una paciente con carcinoma de ovario seroso de alto grado

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Introduction

Ovarian cancer is the second deadliest gynaecological malignancy worldwide, and the leading cause of death from such malignancies in developed countries.[1]

Platinum-resistant ovarian cancer is associated with a poor prognosis. Standard treatment for platinum-resistant disease consists of chemotherapy as monotherapy, including paclitaxel, pegylated liposomal doxorubicin, or gemcitabine, or in combination with bevacizumab.[2]

Most ovarian cancers overexpress the folate receptor alpha (FRα), which is associated with poor prognosis and reduced response rates to chemotherapy. Mirvetuximab soravtansine (MS) is an antibody-drug conjugate comprising an FRα-targeting monoclonal antibody and the cytotoxic agent soravtansine, which inhibits tubulin polymerisation and induces cell apoptosis. Mirvetuximab soravtansine (MS) is indicated for use as monotherapy to treat adult patients with high-grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have platinum-resistant disease and FRα expression intensity greater than 75%, and who have received 1–3 prior lines of systemic therapy.[3]

The main adverse events (AEs) include ocular toxicity, pneumonitis, and peripheral neuropathy.[3]

We report a case of fatal gastrointestinal toxicity in a patient with recurrent ovarian cancer, following a single dose of MS.

Case description

A 70-year-old woman diagnosed in 2023 with high-grade serous tubo-ovarian-peritoneal carcinoma. She had stage IIIC disease (post-surgical FIGO IIIB) and harboured germline and somatic BRCA1 mutations. She received neoadjuvant treatment with carboplatin and paclitaxel for 3 cycles, followed by interval surgery with optimal cytoreduction and 3 further cycles of adjuvant therapy, completed in February 2024. Subsequently, maintenance therapy with olaparib was initiated.

After a platinum-free interval of 7 months, peritoneal disease progression was observed, and second-line therapy with carboplatin, liposomal doxorubicin, and bevacizumab was initiated in September 2024. She continued maintenance bevacizumab until biochemical progression, indicated by rising CA-125 levels, alongside clinical progression with the onset of colicky abdominal pain, which led to hospitalisation in May 2025. Radiological progression was confirmed, with partial small-bowel obstruction secondary to progression of peritoneal carcinomatosis. Effective symptomatic management was achieved, and the patient remained stable in terms of gastrointestinal symptoms after discharge.

On June 12, 2025, third-line therapy with MS was initiated at a dose of 6 mg/kg, based on adjusted ideal body weight (51.56 kg), following confirmation of positive FRα expression. Initial laboratory findings showed creatinine 2.36 mg/dL, white blood cell count 8.77/μL, and neutrophil count 5.81/μL.

On day 7 post-treatment (June 19), the patient presented to the emergency department with a 4- to 5-day history of watery diarrhoea, up to 10 bowel movements per day, without pathological findings, with slight improvement following loperamide administration. Laboratory findings showed creatinine 1.86 mg/dL, white blood cell count 15,660/μL, neutrophil count 12,630/μL, and C-reactive protein (CRP) 6 mg/dL. Stool culture and *Clostridioides difficile* toxin testing were ordered. Since no clear infectious cause was suspected, antibiotic therapy was not initiated, and the patient was discharged home with symptomatic management due to clinical stability.

Forty-eight hours later (June 21), the patient returned due to persistent grade 2 to 3 diarrhoea, weakness, anorexia, and overall

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deterioration. It was decided to admit her to hospital. Laboratory findings showed creatinine 1.81 mg/dL, white blood cell count 12,850/μL, neutrophil count 10,790/μL, procalcitonin (PCT) 2 ng/mL, and CRP 38.4 mg/dL. Supportive treatment was initiated with fluid therapy and empirical antibiotic therapy with piperacillin/tazobactam 4 g/6 h. Given the laboratory and clinical findings, methylprednisolone 40 mg/24 h was added.

On June 23, the stool culture was negative. Follow-up laboratory results showed creatinine 1.60 mg/dL, white blood cell count 14,140/μL, neutrophil count 11,490/μL, PCT 3.07 ng/mL, and CRP 27.10 mg/dL. The patient had severe abdominal pain that was not controlled with subcutaneous rescue doses of morphine chloride; therefore, a continuous infusion was initiated.

On June 24, an abdominopelvic CT scan showed signs of pancolitis, pneumoperitoneum due to intestinal perforation with an associated intra-abdominal collection, and left ureterohydronephrosis secondary to extrinsic compression of the proximal ureter. Laboratory results on June 24 showed worsening renal function with creatinine 2.42 mg/dL, as well as PCT 7.77 ng/mL, and CRP 37.3 mg/dL. Due to the increase in PCT, antibiotic therapy was escalated to meropenem 1 g/8 h.

Given the clinical situation and the patient's overall deterioration, surgical intervention was ruled out, and palliative sedation was initiated; the patient died on June 25, 2025.

Discussion

The safety of MS in the treatment of platinum-resistant ovarian cancer has been evaluated primarily in 4 clinical trials[4–7] that included a total of 682 patients. In the integrated safety analysis, the most common AEs were blurred vision (43%), nausea (41%), diarrhoea (39%), and fatigue (35%), most of which were grade 1 to grade 2. There were grade 3 or higher AEs in 48% of patients, primarily keratopathy and blurred vision (5% each). Severe gastrointestinal adverse effects were rare (nausea in 2% of patients, diarrhoea in 3%, and grade ≥3 abdominal pain in 4%).[8] Similarly, the PICCOLO trial[9] reported a mild-to-moderate gastrointestinal toxicity profile in patients with platinum-sensitive disease receiving third-line or later treatment, with no cases of intestinal perforation or severe colitis.

The EudraVigilance database has recorded 73 cases of MS-related gastrointestinal AEs, of which 21 were diarrhoea and 3 were intestinal perforation. A single fatal case of colitis and intestinal perforation has been reported (Autonomous Pharmacovigilance Centre identification number 20,250,021,581, corresponding to the clinical case described).[10]

The close temporal relationship between drug administration and the onset of severe diarrhoea is highly suggestive of drug-induced toxicity. The Naranjo algorithm score was 3, indicating a “possible” adverse drug reaction.

In patients with extensive peritoneal carcinomatosis and gastrointestinal fragility, the risk of perforation may be increased by multiple mechanisms, including direct epithelial damage, intestinal inflammation, and local hypoperfusion secondary to advanced tumour disease.

This case highlights the importance of actively monitoring the gastrointestinal safety profile of MS, particularly in patients with multiple lines of therapy and peritoneal involvement. The systematic reporting of new cases will allow for a more accurate characterisation of the drug's safety profile in real-world clinical practice.

CRediT authorship contribution statement

Carlota Rodríguez-Tenreiro Rodríguez: Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Data curation, Conceptualization. **Alicia Caso González:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Marina Muñoz Villasur:** Writing – review & editing, Investigation, Data curation. **Lucía Roncero Sánchez:** Writing – review & editing, Investigation, Data curation. **Ana Lozano Blázquez:** Writing – review & editing, Validation, Supervision.

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Conflicts of interest

None declared.

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