YONDELIS® (trabectedin)
YONDELIS - Extravasation

SUMMARY

- Extravasation of YONDELIS can occur, resulting in tissue necrosis requiring debridement.[1]
- Evidence of tissue necrosis can occur more than 1 week after the extravasation.[1]
- There is no specific antidote for extravasation of YONDELIS. Administer YONDELIS through a central venous line.[1]
- In a subset analysis of the phase 3 SAR-3007 study evaluating the efficacy, safety, and patient-reported outcomes of YONDELIS based on the first infusion site of care, infusion site extravasation occurred in 0/100 inpatients and 5/277 (2%) outpatients, with 2 of these events being reported as grade 3. Soft-tissue necrosis was reported in 0/100 inpatients and 4/277 (1%) outpatients, with all 4 events being grade 3.[2]
- As a vesicant, YONDELIS has the potential to cause necrosis, blistering, and pain when extravasation occurs, which may require surgical intervention, as evidenced by published reports.[3-11]
- Extravasation should be managed according to standard institutional practice.
- Management strategies described in published reports of YONDELIS extravasation include discontinuation of the infusion, surgical debridement/surgical lavage, and the use of topical/oral antibiotics, opioid/nonopioid analgesics, and hydrocolloid, silver hydrocolloid, hydrogel bandages, ice, and cortisone cream.[3-12]
- In a retrospective, pooled analysis of 19 phase 2 clinical studies evaluating the safety of YONDELIS administered via a central line, extravasation-related adverse events (AEs) were rare (6/1132 patients, 0.5%), with 3 of these events considered serious or treatment-limiting (grade 4).[13]
- Please refer to the DOSAGE AND ADMINISTRATION, WARNINGS AND PRECAUTIONS, PATIENT COUNSELING INFORMATION, and PATIENT INFORMATION sections of the full Prescribing Information.

CLINICAL DATA

To provide the most relevant information, the summary below is limited to a subset analysis of a phase 3 study, published reports, and a retrospective pooled analysis of 19 phase 2 studies describing extravasation associated with the use of YONDELIS.

Subset Analysis of Phase 3 Study (SAR-3007)

Jones et al (2019)[2] conducted a subset analysis of the phase 3 SAR-3007 study in patients with advanced liposarcoma (LPS) or leiomyosarcoma (LMS) to evaluate the efficacy, safety, and patient-reported outcomes of YONDELIS based on the first infusion site of care when administered in the inpatient vs outpatient setting. YONDELIS was administered as a 24-hour intravenous (IV) infusion via a central venous catheter. Infusion site extravasation occurred in 0/100 inpatients and 5/277 (2%) outpatients, with 2 of these events being reported as grade 3. Soft-tissue necrosis was reported in 0/100 inpatients and 4/277 (1%) outpatients, with all 4 events being grade 3.

Management of infusion site extravasation was reported for 1 patient who experienced grade 3 extravasation on day 2 after the fourth cycle, which then progressed to necrosis by day 12. The patient was hospitalized and treated with IV antibiotics, pain management, and surgical excision with debridement, and was discharged on day 20. YONDELIS was discontinued permanently due to the infusion site extravasation. The events of soft-tissue necrosis and infusion site extravasation resolved by day 110.

Published Reports of Extravasation with Necrosis

Several reports have described extravasation with necrosis in patients who received YONDELIS.[3-8, 10, 11] In the majority of reports, YONDELIS was administered via a central

venous access device (CVAD).[3-8, 10] In addition, administration of YONDELIS via a peripheral vein has been associated with a high risk of extravasation, and therefore should be avoided.[9, 12]

Potential contributing factors to extravasation of YONDELIS have been described, including failure to secure needle, body mass index >30, patients with large, fleshy chests, and inadequate education for the patient and healthcare team.[8] In one case, extravasation associated with an aging device was described.[4]

Reported Management Strategies

Management of YONDELIS extravasation in published reports has included discontinuation of the infusion and surgical debridement (with or without reconstruction) or surgical lavage.[3-8, 10, 11] Repeat surgical interventions were described in some cases.[5,7] The use of topical/oral antibiotics, opioid/nonopioid analgesics, and hydrocolloid, silver hydrocolloid, and hydrogel bandages was also reported.[5, 10] In a report of extravasation in 3 patients with ovarian cancer, the infusion was stopped and the vein was flushed with saline and dexamethasone 25 mg. Ice cubes were applied to the skin, and a cortisone cream was later applied twice daily for 10 days, resulting in resolution of all extravasation lesions in the next 3 weeks without sequelae.[9]

Reported Preventative Strategies

Strategies to minimize the risk of extravasation injury during YONDELIS therapy have also been proposed. These include proper patient selection, consideration of alternative intravenous (IV) lines for access, proper needle placement, and optimal security of the needle into a CVAD. In addition, patients should receive proper education to inform the healthcare team about CVAD malfunction and undergo rapid expert assessment.[3]

Extravasation Events from a Retrospective Pooled Analysis

Le Cesne et al (2012)[13] conducted a retrospective, pooled analysis of 19 phase 2 studies that included 1132 patients with advanced solid tumors who received YONDELIS IV via 1 of 3 schedules: 1.5 mg/m^2 as a 24-hour infusion every 3 weeks (Q3W), 1.3 mg/m^2 as a 3-hour infusion Q3W, or 0.58 mg/m^2 as a 3-hour infusion for 3 consecutive weeks every 4 weeks. Overall, a median of 3 YONDELIS cycles (range, 1-59) were administered over a median treatment duration of 9.4 weeks (range, 3.0-236.7). Extravasation-related AEs following injection were rare (6/1132 patients, 0.5%), with 3 of these events considered serious or treatment-limiting (grade 4). Information regarding the management of extravasation-related events was not reported.

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) was conducted on 04 May 2023.

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