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LAGOON (OP-115): A non-interventional study of melphalan flufenamide (melflufen) in combination with dexamethasone in patients with relapsed and/or refractory multiple myeloma (RRMM) in Spain according to the approved label

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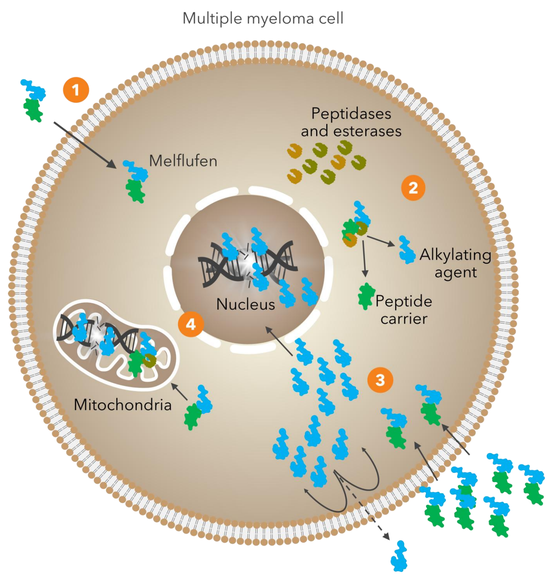
BACKGROUND

- Melphalan flufenamide (also known as melflufen) is a lipophilic alkylating peptide-drug conjugate that utilizes increased peptidase and esterase expression to rapidly release hydrophilic cytotoxic alkylating agents inside tumor cells (**Figure 1**).[1-6]
- Melflufen is EMA approved, in combination with dexamethasone, for treatment of adult patients with RRMM who have received at least 3 prior lines of therapy and who are refractory to a proteasome Inhibitor (PI), an immunomodulatory drug (IMiD) and an anti-CD38 monoclonal antibody.[7]
  - For patients with prior autologous stem cell transplantation (ASCT), the time to progression should be at least 36 months from transplantation.[7]

Figure 1. Melflufen: A peptide-drug conjugate (PDC)



1. Lipophilic entry
Melflufen is highly lipophilic and diffuses quickly and passively through the cell membrane, without the need of transporter proteins.[1,2]

2. Rapid hydrolyzation
Melflufen utilizes the overexpression of peptidases and esterases inside tumor cells and is rapidly hydrolyzed to release cytotoxic hydrophilic alkylating agents.[3,4]

3. Gradient-driven influx & accumulation
The rapid hydrolysis of melflufen creates a concentration gradient that drives further influx of melflufen into the cell, resulting in an intracellular peak of alkylating agents.[4,5]

4. Nuclear damage and apoptosis
Alkylating metabolites of melflufen cause irreversible nuclear and mitochondrial damage by breaking DNA strands which induces apoptosis.[5,6]

DNA, deoxyribonucleic acid; Melflufen, melphalan flufenamide.

- After the completion of the large melflufen studies (pivotal phase 2 study HORIZON and confirmatory phase 3 study OCEAN),[8,9] other new drugs have become available and updated guidelines have been adopted.[10]
  - Therefore, it is important to study the effectiveness and safety of melflufen in the current treatment landscape. In addition, real world evidence (RWE) studies are important since the therapeutic potential of new drugs in pivotal clinical trials often are overestimated, because the trial eligibility criteria select a patient population that is non-representative.[11]

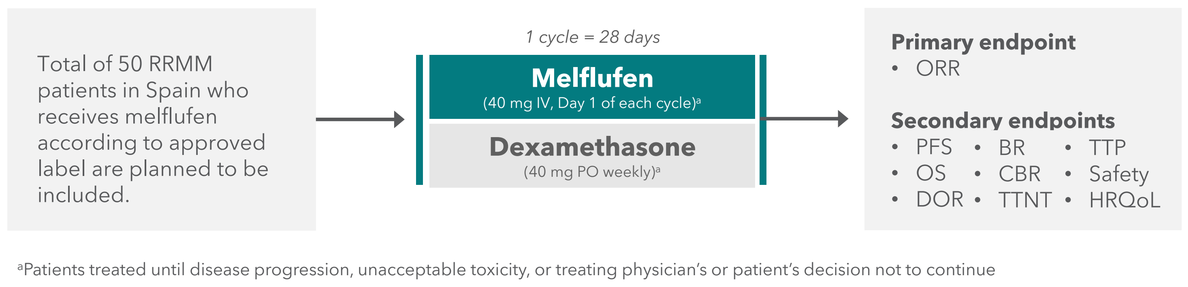
OBJECTIVE

- LAGOON (OP-115) is a non-interventional study (NIS) and aims to observe the effectiveness of melflufen in combination with dexamethasone, used in accordance with the approved label, to treat RRMM in standard clinical practice.
- The patients in this observational study will receive the same treatment and undergo the same diagnostic procedures as they would have if they were not included in the study.

METHODS

- LAGOON is a prospective observational study in Spain enrolling 50 adult patients in who receive melflufen plus dexamethasone as 4th or later-line treatment, per the approved label, by their treating physician prior to enrollment (**Figure 2**).
  - Retrospective inclusion is allowed within a maximum time of 6 weeks after treatment start if no efficacy assessment occurred.
  - Patients will receive melflufen 40 mg intravenously on day 1 and dexamethasone 40 mg on days 1, 8, 15, and 22 of each 28-day cycle until disease progression, unacceptable toxicity, or physician determines it is not in patient's best interest to continue treatment.
  - The primary endpoint is overall response rate (ORR) per the International Myeloma Working Group Uniform Response Criteria.
  - Secondary endpoints include best response, duration of response (DOR), clinical benefit rate (CBR), time to next treatment (TTNT), time to progression (TTP), progression-free survival (PFS), overall survival (OS), incidence and severity of adverse events, and quality of life (EORTC QLQ-C30).

Figure 2. LAGOON (OP-115): Non-interventional study in Spain



[a]Patients treated until disease progression, unacceptable toxicity, or treating physician's or patient's decision not to continue

BR, best response (sCR, CR, VGPR, PR MR, SD, and PD); CBR, clinical benefit rate (proportion of patients with ≥ MR [sCR, CR, VGPR, PR or MR]) as best response); DOR, duration of response (time from first confirmed response of ≥ PR to confirmed disease progression, or death); HRQoL, health-related quality of life (EORTC QLQ-C30); IV, intravenous; melflufen, melphalan flufenamide; ORR, overall response rate (proportion of patients with ≥PR [sCR, CR, VGPR or PR] as best response); OS, overall survival (time from start of melflufen administration to death); PO, orally; PFS, progression-free survival (time from start of melflufen administration to confirmed disease progression or death); RRMM, relapsed/refractory multiple myeloma; TTNT, time to next treatment (time from start of melflufen administration to initiation of first subsequent MM therapy); TTP, time to progression (time from start of melflufen administration to confirmed disease progression).

ELIGIBILITY CRITERIA

Inclusion criteria

- The patient fulfils basic eligibility criteria as described in the observational plan (including organ function and fertility status)
- Be at least 18 years of age.
- Ability to provide signed and dated informed consent.
- Decision for treatment with the combination therapy melflufen and dexamethasone is made before inclusion in the study.

Exclusion criteria

- Patients who are currently participating in any interventional clinical study (unless the patient only remains in survival follow-up).
- Any assessment of effectiveness of ongoing melflufen treatment has been performed.
- Previous treatment with melflufen, or ongoing treatment with melflufen has been longer than 6 weeks

STUDY STATUS

The study will include 50 patients at approximately 25 sites in Spain. The study is ongoing and open for enrollment. The study is ongoing and has enrolled 9 patients to date.

FUNDING SOURCE

The study is funded by Oncopeptides

REGISTRATION

The study is registered at Spanish Clinical Trials Register (reec.aemps.es) at 0069-2025-OBS

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DISCLOSURES

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For more information about this study on Spanish Clinical Trials Register (0069-2025-OBS), click the link or scan the QR code:

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