# 1642TiP - ENSURE: Dendritic cell therapy (MesoPher) in combination with extended-pleurectomy/decortication after chemotherapy in subjects with resectable mesothelioma, a feasibility study

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## Background

Malignant pleural mesothelioma (MPM) is an uncommon but aggressive neoplasm with low survival rates. For patients with **early stage - resectable MPM** the role of radical surgery remains controversial and **multimodal treatment** might improve patients' prognosis. **Dendritic cell therapy (DCT)** with Mesopher proved to be safe and yielded promising results in patients with MPM, with single agent radiological activity[1,2], representing the rationale for a combined **(neo)adjuvant** approach with **extended pleurectomy/decortication (eP/D)** surgery.

## Trial Design

Open label, single center (Erasmus MC), feasibility study.
**Study start date**: January 2022
**Total study duration**: approx. 24 months

- **Sixteen** adult patients diagnosed with **resectable epithelioid MPM** will be enrolled following first-line chemotherapy.
- Before standard-of-care chemotherapy, a leukapheresis will be performed from which monocytes will be isolated and used for further differentiation into DCs. Hereafter, the DC will be loaded with allogeneic MPM tumor cell line lysate (**Pheralys**) and maturated using the Jonuleit cytokine cocktail [**Figure 1**].
- The subsequently formulated drug product (**Mesopher**) will be re-injected 4 weeks after completing chemotherapy, 2 times every other week. Four weeks after the first injection with DCT, patients will undergo eP/D surgery followed by three bi-weekly injections with DCT, starting 4 weeks after surgery. In total, **five DC vaccinations** will be administered. If there is a surplus, a 6th and 7th vaccination at 3 and six motnhs after the last vaccination can be considered [**Figure 2**].
- **Tumor material** will be collected before starting neo-adjuvant DCT and at time of surgery.

## Study Objectives

**Primary objective**
To assess whether (neo)-adjuvant DCT with Mesopher is **feasible** in resectable epithelioid MPM patients after first-line chemotherapy.

**Secondary objectives**
Safety, efficacy (as measured by progression free and overall survival).

**Exploratory objective**
Determine the **anti-tumor immune response** induced by (neo)adjuvant DCT. Tumor-specific immune activation will be investigated on both tumor material and peripheral blood samples prior and post DCT by flow cytometry, imaging mass cytometry, and T-cell receptor (TCR) repertoire analysis.

**Figure 1.** Mesopher production process.

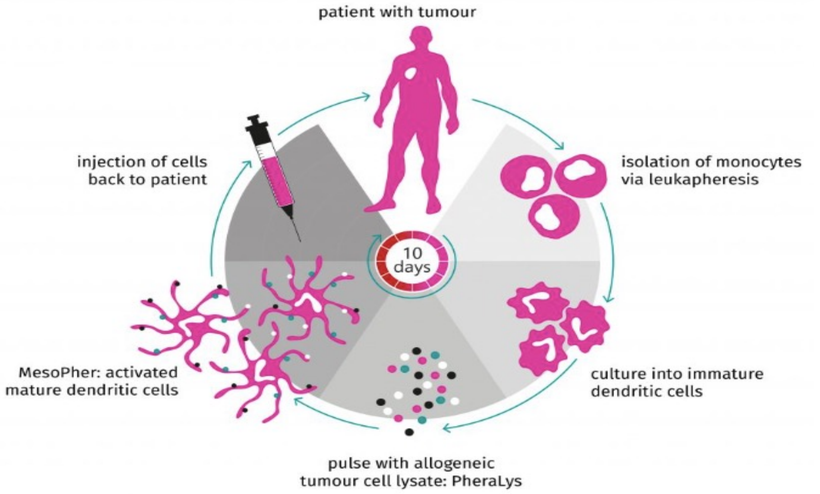
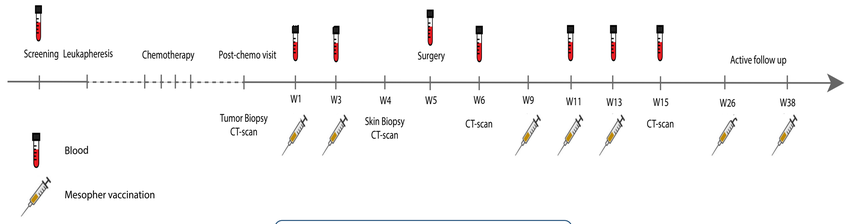



**Figure 2.** Study procedures and timeline.




## Study Information

**Status**: Recruiting at the Erasmus MC, Rotterdam, NL
**EudraCT number**: 2021-000496-37
**Lead Investigator**: Prof. Joachim G.J.V. Aerts
**ClinicalTrials.gov Identifier**: NCT05304208

## References

[1]Aerts JGJV, et al. Autologous Dendritic Cells Pulsed with Allogeneic Tumor Cell Lysate in Mesothelioma: From Mouse to Human. Clin Cancer Res. 2018 Feb 15;24(4):766-776.
[2] Belderbos RA, et al. A multicenter, randomized, phase II/III study of dendritic cells loaded with allogeneic tumor cell lysate (MesoPher) in subjects with mesothelioma as maintenance therapy after chemotherapy: DENdritic cell Immunotherapy for Mesothelioma (DENIM) trial. Transl Lung Cancer Res. 2019 Jun;8(3):280-285.

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*The first and presenting author has no conflicts of interest to declare.*

## Key Eligibility Criteria

**Inclusion criteria**
- ✓ Histologically confirmed diagnosis of **epithelioid MPM**.
- ✓ **Resectable disease** defined by stage cT1-3, N0-1, M0 (I to IIIA)
- ✓ Eligibility for **2 to 4 cycles** of platinum-based chemotherapy.
- ✓ Fit to undergo a **P/D** with optional removal of hemidiaphragm and pericardium.
- ✓ **Tumor tissue available** after completing chemotherapy and before starting treatment with DCT.
- ✓ Adequate bone-marrow, renal, and liver function.
- ✓ ECOG performance status of 0 or 1.

**Exclusion criteria**
- ✓ Clinical or radiological invasion of mediastinal structures and widespread chest wall invasion (stage T4). Involvement of N2 nodes. **Stage IV** (metastatic disease).
- ✓ Any **different histology** from the epithelioid MPM.
- ✓ Unavailability of **tumor tissue** after completing chemotherapy.
- ✓ Use of >10 mg of prednisolone or equivalent/day (or other immunosuppressive agents)
- ✓ **Prior treatment** of any kind for MPM.
- ✓ Any previous malignancy.
- ✓ Major surgical procedure in the last month.