

# IMPLEMENTATION AND OPTIMIZATION OF A SOMATIC CELL THERAPY MEDICINAL PRODUCT CIRCUIT BY CLINICAL PHARMACISTS

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## Background

Somatic Cell Therapy Medicinal Product (sCTMP) is classed as Advanced Therapy Medicinal Products (ATMPs). Darvadstrocel consists of expanded human allogeneic mesenchymal adult stem cells and is indicated for the treatment of complex perianal fistulas in adult patients with luminal Crohn's disease when fistulas have shown an inadequate response to at least one conventional or biologic therapy.

## Objective

- ✓ Implementation and optimization of the sCTMP circuit by the pharmacists, in the hospital setting, as pharmacist oversight and handling are required in order to assure the quality, efficacy, and safety for the intended use.

## Design

The accurate handling and administration of sCTMP is crucial to the effectiveness of the treatment. Thus, the pharmacists:

- Ensure correct ordering, reception, and storage of darvadstrocel.
- Handle darvadstrocel in the operating room, next to the surgeon.
  - ✓ carefully invert the vial several times until a homogeneous cell suspension is obtained, avoiding bubble formation.
  - ✓ push air into the vial to avoid vacuum and air bubbles from forming and gently aspirate all contents.
  - ✓ ensure that needles no thinner than 22G are used throughout the process to avoid cell disruption.
  - ✓ ensure that darvadstrocel is injected immediately after resuspension to prevent cell re-sedimentation.



Figure 1. The pharmacists handled darvadstrocel in the operating room.

- Evaluate cell concentration and viability ensuring compliance with the certificate of conformity.

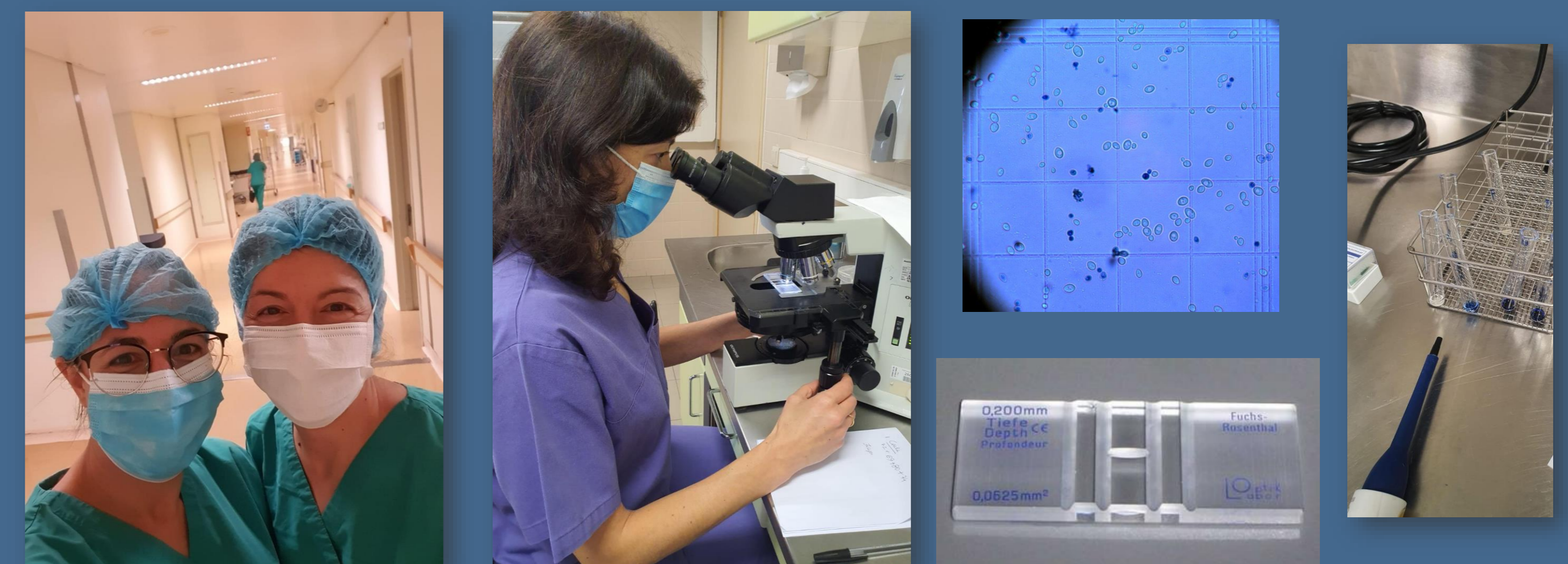


Figure 2. Evaluation of cell concentration and viability with the trypan blue exclusion test.

- The effectiveness of darvadstrocel was evaluated by the proportion of patients who remain in clinical remission, with closure of all treated external openings that were draining at baseline despite gentle finger compression and absence of pain.

## Results

Table 1. Assessment of clinical remission at 26, 43 and 52 weeks.

Pharmacist intervention	Remission 26 weeks	Pain	Remission 43 weeks	Pain	Remission 52 weeks	Pain	Remission
<b>Yes</b> n=5	Yes	No	Yes	No	-	-	<b>60.0%</b>
	Yes	No	Yes	No	-	-	
	No	No	Partial	No	-	-	
	Yes	No	Yes	No	-	-	
<b>No</b> n=6	Partial	No	-	No	-	-	<b>33.3%</b>
	No	Yes	-	-	No	Yes	
	No	Yes	-	-	No	Yes	
	No	Yes	-	-	No	Yes	
	Partial	No	-	-	Yes	No	
Yes	No	-	-	Yes	No		
No	No	-	-	No	No		

All the analyzed darvadstrocel vials were in conformity with the certificate's specifications.

- ✓ Appearance: white to yellowish homogeneous suspension containing a sediment, which is readily dispersed on shaking.
- ✓ Volume: 6 mL/vial
- ✓ Cell concentration: 4-6 M/mL
- ✓ Cell viability: ≥ 85%

## Conclusions

The implementation of the sCTMP circuit was successful and accepted by the multidisciplinary team. The optimization of the circuit of darvadstrocel by the pharmacists assured quality, efficacy and safety of the sCTMP use.