The central focus of the BIO-DrIM project is the implementation of biomarker-driven strategies for personalizing immunosuppression (IS), with the aim of:

1. improving the long-term outcome in solid organ transplant patients,
2. decreasing adverse effects (graft toxicity, diabetes, cardiovascular events, opportunistic and community acquired infections, bone loss, and malignancies),
3. optimising the costs-benefit-ratio of chronic IS.

The mission of BIO-DrIM:

1. minimization of IS in a safe way,
2. shifting IS-therapies to individual and personalized strategies by identification of individual immune response profiles.

Why is this of importance?

1. for preventing the risk of over-immunosuppression (lowering the risk for infections and tumour development)
2. for reducing the organ toxicity of IS (lowering the risk for chronic allograft deterioration)
3. lowering the side effects of IS (risk for post-transplant diabetes, osteoporosis, hypertension, cardiovascular diseases…).

The biomarkers-guided management of IS is an ambitious program because it requires:

- multiple and cross platform tests,
- high quality standardization,
- multicenter clinical validation and the international network.

All these requirements are met in the BIO-DrIM project that involves academic partners, Big Pharmas and SMEs that are joining their efforts for accomplishing a methodical and clinical validation of biomarkers for guiding IS.

The BIO-DrIM project includes 5 innovative investigator-driven biomarker clinical trials with more than thousand patients.

**STUDY 1:** First IS withdrawal study in long-term liver transplant patients based on the presence of a molecular tolerance signature (personalized withdrawal). About 25-40% of liver transplant patients after year 3-5 post transplantation develop operational tolerance. However, in the majority (60-75%), standard immunosuppression has to be re-introduced because weaning failed and rejection and graft deterioration occurred. The biomarkers developed and validated by the BIO-DrIM consortium will be important and useful tools for improving the stratification of patients or for the monitoring of successful weaning.

**STUDY 2:** France prospective randomized double-blind, multicentre parallel controlled study of CNI weaning in selected long-term kidney transplant patients. This novel trial selects highly stable long-term kidney transplant patients for personalised IS withdrawal. The major focus is to demonstrate the improvement of renal function and to show a low incidence of acute and chronic rejection, graft lost, anti HLA antibodies and de novo proteinuria. Ancillary studies are the assessment of low and high immunological risk biomarkers (DNA chip, Phenotypes).

**STUDY 3:** Using Biomarkers of Tolerance to guide immunosuppression weaning in kidney transplant recipients. This pilot-trial study uses the cross-validated set of 14 molecular biomarkers, which are genes indicating “tolerance” after long-term kidney transplantation. The aim is to show safety and feasibility of IS minimization in patients “who score tolerant” by molecular biomarker signatures.

**STUDY 4:** Perioperative Biomarker-based stratification into low/high responder after kidney transplantation. The Study CELLIMIN (Prospective donor-specific Cellular alloresponse assessment for Immunosuppression Minimization in de novo renal transplantation) is an international multicentre open label randomized non-inferiority Phase II clinical trial for selection of low anti-donor T-cell responders using the IFN-γ ELISPOT assay as biomarker for patient stratification before transplantation to safely receive long-term drug minimization based on IS (tacrolimus) monotherapy. The perioperative stratification of patients into low/high-responders will demonstrate the clinical utility of the IFN-γ ELISPOT (Enzyme-Linked ImmunoSpot).

**STUDY 5:** Shifting kidney transplant patients to low-responders suitable for early IS minimization. Using a novel induction protocol, the increased incidence of tolerance signature will be demonstrated and the safety of a very early (day 3 after transplantation) low-dose IS will be validated. This trial has a precise plan for biomarker analysis.

In addition to the clinical trials, there are other innovative research activities:

- implementation of new biomarker candidates for personalized IS,
- *in vitro and in vivo studies* (mouse/rat transplant models) to analyse the mechanisms of success or failure of IS minimization strategies. In particular, the consortium is focussing on regulatory pathways.
- providing health-economic data in terms of cost/benefit ratio and the usefulness of biomarker guided IS minimization strategies for personalized IS.

For more details please visit our website at [www.biodrim.eu](http://www.biodrim.eu)
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