A NOVEL IMMUNOTHERAPY FOR HEART FAILURE

CHALLENGE:
Heart failure (HF) is a leading cause of mortality. Inflammation is implicated in HF, yet clinical trials targeting pro-inflammatory cytokines in HF were unsuccessful, most likely due to redundant functions of individual cytokines rendering them non-ideal targets. Yet an urgent clinical need remains to identify and develop new and better therapies for HF.

INNOVATIVE SOLUTION:
We identified, via immunophenotyping at different stages of the disease, an association between the presence of T cells (the population of immune cells that mediates chronic and specific responses) and heart failure (HF), both in experimental models and in human HF patient biopsies. On the basis of this finding, we then utilized an FDA-approved drug, Abatacept, that interferes with T cell function by blocking T cell costimulation, to treat experimentally-induced HF. Treatment resulted in a block of progression of HF, in a manner 300% more efficient than current standard drugs (beta-blockers) targeting cardiac disease. The treatment was able to block disease even when administered late in the progression of disease (Kallikourdis et al, Nature Communications 2017).

APPLICABILITY, EFFICACY, CLINICAL DATA, LACK OF TOXICITY, EXPERT OPINIONS:
Treatment with costimulation inhibitors has the potential to become an effective therapy option for patients suffering from cardiac function insufficiency, as determined by echocardiography and/or MRI. The target, T cells, is present in the hearts of both major groups of HF patients (HFrEF and HFrEF).
Our treatment was tested using the gold-standard TAC mouse model of HF, which is the main accepted tool for developing new heart failure therapies. Our treatment was also efficacious when tested in alternative models of HF. Recent clinical data have reported 2 human patients successfully treated from tumor-therapy-induced HF using our method.

The first-in-class drug Abatacept (Orencia) by Bristol Myers Squibb (BMS), is currently FDA approved and in use for the treatment of Rheumatoid Arthritis and has an exemplary safety profile. This is likely to be shared by all molecules acting on the same mechanism.
The dosage in our studies matches that of the current FDA-approved use of the drug.
Based on the evaluation by a former global toxicology director in a major pharma, all the pre-clinical and phase I dossier filed by BMS for Abatacept use in Rheumatoid Arthritis can be used to support our project as the drug therapeutic window is the same.

Our method of using costimulation inhibitors was very recently hailed in an independent high-profile cardiological review as “world-altering for the treatment of Cardiovascular Disease” (Simons et al, 2019 Nat Rev Cardiol 2019).

COMMERCIAL OPPORTUNITY:
The estimated market size for the disease, applicable to our therapy, is approx. $1-2 bn/yr.
We aim to run a multicentric (Humanitas Hospitals being one of the centers) phase I/II study on a selected group of patients (around 200) with surrogate end-points to show efficacy and confirm safety on the heart failure application. All regulatory activities to support the entry into humans for this specific disease will be contracted out. The estimated cost is around € 2M.
The first-in-class drug will become generic within 2020, creating novel potential opportunities for an aggressive entry into the very sizeable HF market.
Our patent, covering the use of Abatacept as well as of the class of molecules with the same mechanism of function is available for licensing.

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