B·DEBATE International Center for Scientific Debate BARCELONA

Vall d'Hebron Institut de Recerca VHIR

UNSOLVED PROBLEMS IN HEART REPAIR

PROGRAM

Wednesday, November, 28th, 2012

BASIC SCIENCE

Morning sessions (9:00-13:30)

1. In light of the present knowledge, which stem cell type(s) is/are likely the most useful for an effective repair of the damaged myocardium? Advantages and drawbacks for each cell type (autologous, allogeneic, embryonic, iPS). Chair: **Andre Terzic**
2. Is it scientifically proven that allogeneic cells transplanted by whatever means into the myocardium (with or without spilling to other tissues) are eliminated in a short time by the host immune system? If so, does this affect the characterization requirements for these cells vs autologous. Chair: **Dominique Charron**
3. What are the essential parameters for the in vitro characterization of cell type(s)? Chair: **Massimiliano Gnecchi**
4. What should be the goal of the cell therapy? Myocyte regeneration? Neo-vascularization? Prevention or amellioration of remodeling? Or a combination of both? Are these goals dependent on the cell type used? Should the goal determine the time of administration? Chair: **Georgina Ellison**

Coffee Break (by 10:30h)

5. The term "stem cells" has been used very losely in the field of myocardial cell therapy. Should the established criteria of stem cell therapy be limited to the therapeutic uses of bona fide stem cells or stem-progenitor cells, followed by the tissue of origin of the stem cells used? Chair: **Daniele Torella**
6. What is the intended mechanism of action of the therapeutic cells? Paracrine effect over cells at risk? Stimulation of the endogenous cardiac stem cells? Replenishment of the endogenous cardiac stem cell cohort? Direct contribution of the therapeutic cells to the regenerated/repaired myocardium? Chair: **Bernardo Nadal-Ginard**
7. What is the optimal time for the application of the therapeutic cells in the AMI animal model? In the acute phase before the development of the inflammatory reaction? In the post-acute phase when the inflammatory reaction has subsided? Is the time of intervention dependent on the type of cell used? Chair: **Stefan Janssens**
8. Tracking of the transplanted cells either autologous or allogeneic in experimental animals. How? When? In the case of allogenic cells what is an accepted proof that ALL transplanted cells have been eliminated from the host? Chair: **Bernardo Nadal-Ginard**

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BASIC SCIENCE

Afternoon sessions (15:00-18:00)

9. Dose and composition of the autologous and allogeneic cell therapy product. How to design tests which allow for a valid comparison of results among different animals and/or batches of cells? What is best, a pure or an heterogenous cell population? Chair: **Felipe Prosper**
10. Are the cells and the methodology used for AMI the same or different for the therapies intended for the treatment of heart failure? Chair: **Maria Josè Goumans**
11. How and when can tissue engineering help cell therapy? Chair: **Wolfram Zimmermann**
12. Objective criteria for the evaluation of myocardial regeneration in animal models: **Georgia Ellison**
13. Logistics of iPSC-derived cardiomyocytes: a) Can a line realistically be made for each patient? b) What is the likelihood of this overcoming immune rejection? c) Will each line need individual regulatory validation? Chair: Angel Raya
14. Should myocardial cell therapy be a one time event or should it be repeatable upon interval(s). What are these intervals? Should we use different routes of administration at the different intervals? Different criteria for AMI and HF? Chair: **Felipe Prosper**
15. What preclinical data should be necessary to obtain prior to the initiation of clinical studies? Should the required preclinical information be the same for cell-based therapies than for cell-free therapies? Chair: **Nabil Dib**
16. What safety data is required for hES or iPS technologies? Chair: **Andrew Baker**

Coffee Break (by 16:30h)

17. Should it be a requisite for the initiation of clinical trials to have an understanding of the mechanism of action of the experimental therapy? Chair: **Asterios Tsiftsoglou**
18. What are the most appropriate experimental models (amphibians, rodents, bigger animals) for the study of cell therapy, its mechanisms and efficacy? Should clinical trials be started based solely on data obtained in rodent animal models? Chair: **Keiichi Fukuda**
19. What is the most appropriate large animal model in which to test myocardial regenerative therapies? What kind of parameters should be obtained to assess treatment efficacy? Chair: **Manuel Galiñanes**
20. What kind of immunological investigations and in which model should be performed before clinical application? Chair: **Jordi Barquinero**
21. Is there any useful information gained in the test of the therapeutic cells for tissue distribution and onco/teratogenesis in immunodeficient mice models? Should the criteria be the same for the autologous and allogeneic therapies? Chair: **Felipe Prosper**
22. Should the preclinical data on tissue distribution, oncogenic potential, etc. be the same for autologous and allogeneic cell therapy? Chair: **Dominique Charron**

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UNSOLVED PROBLEMS IN HEART REPAIR

COSMOCAIXA . C/ ISAAC NEWTON, 26. BARCELONA

Thursday, November, 29th, 2012

CLINICAL STUDIES

Morning sessions (9:00-13:30)

1. What is the minimal and optimal set of preclinical information required before the start of clinical trials? Chair: **Anthony Mathur**
2. How to evaluate the results of clinical trials when the composition and dose of therapeutic agent is different for each patient? Chair: **Daniele Torella**
3. From a regulatory standpoint, what are the criteria the establish therapeutic equivalence of different cell populations and or different mixtures? Chair: **Bernardo Nadal-Ginard**
4. Criteria for patient selection. Does it depends on the cells used and/or the mode of administration? Chair: **Nabil Dib**

Coffee Break (by 10:30h)

5. What should be the sequence and the protocol of the first-in-man trails? Dosis scalation? Follow-up for how long? Chair: **Asterios Tsiftsoglou**
6. What type of primary end-points clinical studies should have? Chair: **Stefan Janssens**
7. What markers can be used ethically and practically to track cells implanted clinically? Chair: **Sian Harding**
8. Is it safe and desirable to undertake clinical studies without the demonstration of the mechanism involved? Chair: **Manuel Galiñanes**
9. Should the end-points for AMI and HF be the same? Should the end-points be the same independently of the mode of administration of the cells: intracoronary, intramyocardial by catheter or by surgery? Chair: **David García-Dorado**

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Thursday, November, 29th, 2012

CLINICAL STUDIES

Afternoon sessions (15:00-18:00)

10. What is the minimal follow-up time required to ascertain clinical effectiveness and evaluation of side effects of the therapy? Chair: **Antoni Bayés Genis**
11. Immunological implications of all regenerative therapies: a) Feasibility and safety of the use of allogeneic cells. b) What are the immunological consequences of applying allogeneic material? c) Are allogeneic cells, genetically modified or not, immunologically neutral? Chair: **Dominique Charron**
12. Use of MSC primarily to modulate immune and inflammatory responses: a) Is this a valid target per se? b) Could/should these cells be used in conjunction with others to dampen immune responses? Chair: **Dominique Charron**
13. Which is the best route of administration? Does it depend on the clinical condition to treat? Chair: **Antoni Bayés Genís, Santi Roura and Paloma Gastelurrutia**

Coffee Break (by 16:30h)

10. Should it always be randomised and blind to the patients? Chair: **Dominique Charron**
11. Should an international register for cell therapy patients be established? If so, by whom? Chair: **Daniele Torella**
12. What system(s) should be put in place to make comparable the results obtained by different groups using the same type of therapy and among the different types of cell therapy? Chair: **Keiichi Fukuda**
13. If these therapies become routine for millions of people, what will be the rate-limiting step for each strategy? Chair: **Sian Harding**

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COSMOCAIXA . C/ ISAAC NEWTON, 26. BARCELONA

Friday, November, 30th, 2012

ETHICS AND REGULATORY BODIES

Morning sessions (9:00-13:30)

1. What are the ethical implications of cell therapy? a) for the donor; b) for the recipient; c) the same for autologous and allogeneic therapies? Chair: **Asterios Tsiftsoglou**
2. What kind of information from animal models is required before seeking approval for clinical trials? Is it the same for autologous and allogeneic cell therapies? Chair: **Sol Ruiz and Sanne Jansen of Lorkees**

Coffee Break (by 10:30h)

1. Necessary conditions to safely perform clinical studies using cell therapy and therapies for the growth of cardiac tissue. Chair: **Bernardo Nadal-Ginard**
2. Should a standarized protocol be agreed upon by the regulatory agencies for the design of phase I/IIa clinical trial for new cell types and/or novel protocols? Chair: **Anthony Mathur**
3. Role of EMA vs. National Agencies Chair: **Sol Ruiz and Asterios Tsiftsoglou**

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