Presidenza del Consiglio dei Ministri

ON THE QUESTION OF THE USE OF ORGANS FROM ANTI-HCV-POSITIVE AND HCV-RNA-POSITIVE DONORS FOR TRANSPLANTATION IN ANTI-HCV-NEGATIVE PATIENTS

(Response to a query submitted to the National Bioethics Committee by the National Transplant Centre of the National Institute of Health)

12 July 2018

Introduction

On 6 April 2018, the Italian Committee for Bioethics received from the Director of the National Transplant Centre (NTC) of the National Institute of Health (NIH), Dr. Alessandro Nanni Costa, a request for an evaluation (Annex 1) on "the use of organs from anti-HCV-positive and HCV-RNA positive donors for transplantation in anti-HCV-negative patients"[1] The proposal to use these organs for transplantation (to date, heart, kidney and lung) would be justified "in light of the availability of new direct-acting antiviral drugs (DAA) for the treatment of hepatitis C".

In this regard:

A. on 20 November 2017, the Ethics Committee (EC) of the NIH issued a positive ethical opinion with regard to the question raised, in which it took note of the criteria defined by AIFA concerning the reimbursement of DAA drugs for the treatment of hepatitis C in patients transplanted in the aforementioned circumstances. Considering these criteria, as well as the "therapeutic revolution brought about by DAAs" and the scientific-clinical research conducted internationally involving the administration of DAA in anti-HCV-negative recipients from anti-HCV-positive and HCV-RNA-positive donors , the EC of the NIH argued its opinion basing it on the link between these premises and the informed consent issued in the given situation, with all necessary precautions and guarantee procedures (NIH protocol PRE-875/17, see Appendix). Furthermore, "a commitment to activate appropriate clinical studies even after the use of the drug" in the post-transplant phase was deemed necessary by the EC;

B. on 26 January 2018, the Italian Medicines Agency (AIFA), "having taken note of the NTC's proposals and the relative evaluations made by the Ethics Committee of the NIH", expressed its "willingness to undertake the necessary actions to redefine the criteria for the reimbursement of DAAs, in order to meet the needs of patients waiting for solid organ transplants ". However, AIFA subordinated its readiness to an ethical opinion expressed by the ICB, which, in the same note (Annex 2), "represented the need".

Response

As a premise to this response, the Italian Committee of Bioethics recalls that its expertise is limited solely to the evaluation of possible critical aspects of a bioethical nature, since the ICB is not a technical-scientific consultancy body for biomedical matters.

With regard to the query raised, the ICB expresses its approval for the following reasons:

1. according to the evaluations of the NTC, reported by its Director in the dedicated hearing, and according to what emerges from the scientific evidence and examination of the forwarded documentation, the comparison with the use

[1] HCV: Hepatitis C Virus (the presence of anti-HCV antibodies indicates that you have been exposed to the virus); RNA: ribonucleic acid, a molecule implicated in the expression of genes, in this case viral (the presence of HCV RNA in the patient's blood indicates an active infection and gives a measure of the detectable viral load or viremia).

of standard risk donors did not register "significant differences" in survival compared to organ transplantation from anti-HCV-positive and HCV-RNA-positive donors to anti-HCV-negative patients: “as now the organ is treated after transplantation" in an effective manner. Therefore, the current trend in international transplantation is towards treatment of the person who received the organ rather than the selection of donors;

2. the decisive criterion regarding the ethical nature of the practice is the acquisition of free, prior, fully informed and verified consent, resulting from a deliberative process evolving from the patient-doctor relationship; the consent should be easily withdrawn and should not entail any discrimination or penalization (apart from, of course, the non-access to organs from non-standard risk donors). Given the conditions set out in point (1) and without prejudice to the necessity for a clinical evaluation on a case-by-case basis, the elective ethical principle therefore remains respect for the recipient's autonomy and fundamental right to the enjoyment of the highest *attainable* standard of health[2]. In fact, there are not sufficient reasons to preclude patients from an option that guarantees their primary interest, namely improvement of their state of health (or at least from making an attempt to do so) in undoubtedly less time, which would compensate for, in his opinion, the residual risk linked to the transplantation of an organ donated by a non-standard risk donor;

3. in addition to offering benefit in terms of waiting times for individuals who want to join the organ allocation program from non-standard risk donors, it can also be argued that the use of these organs increases the chances of health and survival for all: the greater availability, in absolute numbers, of transplant organs, indirectly also favours the group on the waiting list that is in the worst condition (in urgent need of an organ and in clinical conditions that discourage non-standard risk organ transplantation). The benefit also extends to the group of those who freely decide not to opt in to the proposed transplant from non-standard risk donors: a greater number of organs from standard risk donors is in fact available for them. Accepting organs from non-standard risk donors positively combines the protection of personal interests with solidarity towards other sick people;

4. last but not least, it should be emphasized that the use of organs from anti-HCV-positive and HCV-RNA-positive donors involves a dual consent procedure by anti-HCV-negative recipients: the first taking place at registration on the waiting list and the second, usually deferred for many months, when the organ for transplantation has actually been found. The need to reiterate a request for treatment is a procedure already provided for in a variety of clinical practices with significant bioethical profiles, including some types of transplants, as the best guarantee of effective awareness and freedom of choice on the part of the person giving consent. In the case in question, the interval between the two subsequent consents allows for in-depth analysis, thus ensuring that it is a pondered decision based on extensive consultation of documentary materials, on data and scientific evidence, on the opinions of experts and individual

[2] See the Constitution of the World Health Organization (which came into force on 7 April 1948) and the Universal Declaration of Bioethics and Human Rights of UNESCO (adopted by acclamation on 19 October 2005 by the XXXIII Session of the General Conference of UNESCO).

thoughts shared by patients with those they consider as reference points. Moreover, the dual consent procedure also allows those who initially did give their consent the possibility to reconsider their choices.

On the basis of what has been briefly illustrated above, the ICB deems necessary that:

a. there should be a rapid initiation of the development of procedures, modalities and programmes in order to make possible the most widespread, clinically justified, use of organs from anti-HCV-positive and HCV-RNA-positive donors to anti-HCV-negative patients, throughout the country in a homogenous manner and, in particular, it considers it necessary for AIFA to establish the reimbursement of DAAs even for these indications;

b. the scientific-clinical guidelines on the subject should be promptly and constantly updated, also with regard to information counselling and patient decision support;

c. the National Transplantation Centre of the NIH should integrate the institutional website with a section on this subject, it should include scientific-clinical information that is accessible to patients and constantly updated in order to help ensure the opportunity for patients to express dynamic consent, i.e. based on knowledge gained gradually as well as on the results obtained.

d. studies on safety and long-term efficacy of this transplantation sector should be promoted and financed.

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The ICB discussed the text of the response in the plenary session on 18 May and 12 July 2018, on the latter date the response was voted and approved unanimously by those present.

In order to formulate this response, the ICB availed itself of hearings involving Dr. Alessandro Nanni Costa, Director of the National Transplant Centre, and Dr. Maria Cristina Morelli, Director of the Department of Organ Insufficiency and Transplantation of the Sant'Orsola Malpighi Polyclinic in Bologna.

The text was drawn up by Prof. Cinzia Caporale.

The following professors voted in favour: Salvatore Amato, Carlo Caltagirone, Stefano Canestrari, Cinzia Caporale, Carlo Casonato, Francesco D'Agostino, Bruno Dallapiccola, Lorenzo d'Avack, Mario De Curtis, Riccardo Di Segni, Silvio Garattini, Marianna Gensabella, Maurizio Mori, Assunta Morresi, Laura Palazzani, Lucio Romano, Luca Savarino, Monica Toraldo di Francia, Grazia Zuffa.

The following members, without the right to vote, Drs. Maurizio Benato, Amedeo Cesta and Carlo Petrini, also expressed their support.

The following professors, Luisella Battaglia, Antonio Da Re, Gian Paolo Donzelli, Mariapia Garavaglia, Tamar Pitch, Massimo Sargiacomo, Lucetta Scaraffia and, the consultative members, Dr. Carla Bernasconi and Dr. Anna Teresa Palamara were absent from the session and subsequently expressed their support.

Ministry of Health
National Institute of Health
National Transplant Centre

Prot. 891/CNT2018
6 April 2018

Prof. Lorenzo D'Avack
President Italian Committee for
Bioethics

RE: Request for an evaluation by the Italian Committee for Bioethics regarding the "*Proposal for the use of organs from anti-HCV-positive and HCV-RNA- positive donors for transplantation in anti-HCV- negative patients*".

I, the undersigned Dr. Alessandro Nanni Costa, Director of the National Transplant Centre of the National Institute of Health make a request to the Italian Bioethics Committee for an opinion on the proposed use for transplantation of organs from HCV-positive donors in HCV-negative subjects, in light of the availability of new direct-acting antiviral drugs (DAA) for treatment of hepatitis C.

With best regards.

Director of the National Transplant Centre
Dr. Alessandro Nanni Costa