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Securing Equitable Patient Access to Advanced Therapies across Europe

Panelists:

- **MEP Tomislav Sokol**, Group of the European People's Party (Christian Democrats), co-chair of the MEPs Interest

Group "European Patients' Rights and Cross-border Healthcare" and member of the TRANSFORM MEP Interest Group

- **Mariano Votta**, Director - Active Citizenship Network
- **Mauro Maré**, Professor of Public Economics - University of Tuscia and LUISS University
- **Paschalia Koufokotsiou,** Policy officer - European Commission, DG SANTE - Unit D1: medical products, quality, safety, innovation
- **Sarah Garner**, PhD, Senior Policy Advisor Access to Medicines and Health Products - World Health Organization (WHO) Regional Office for Europe
- **Giorgio Alleva**, Professor of Statistics - Sapienza University of Rome; Former president - ISTAT (Italian National Institute of Statistics)
- **Androulla Eleftheriou**, Executive Director - Thalassemia International Federation; Director – Cyprus WHO Collaborating Centre of the Cyprus Ministry of Health
- **Jasna Karačić**, PhD, President - Croatian association for the promotion of patient's rights; Head of Health Diplomacy Unit - International Council of The Patient Ombudsman; Health attaché during the Croatian Presidency of the Council of the European Union

Discussion – Key Points

<u>Mep Tomislav Sokol</u>

- Healthcare unfortunately is not a priority of the Brussels bubble because it is considered as a national issue but COVID taught us that's not.
- Consensus and political will are needed to follow up on this project.
- Regulatory framework: Commission's proposal that new pharmaceutical legislation will be in place in March 2023. According to Sokol they can't do that without the industrial sector.
- There are two points of view: the regulatory and the financial. Financial is represented by Horizon Europe, and beating cancer is considered a political priority.
- We need financial instruments to fund research and regulatory instruments to enable the market launch of these therapies and then access for patients.
- We need to work with industry by providing incentives and investment in research and innovation.
- We also need to extend the period of innovativeness of products compared to the past.
- Still, we need a European database and interoperable systems to communicate data between member states.
- The single European system failed, and more transparency is needed at national level, and the transparency directive should be updated in this regard.
- Data protection and privacy are important but it's necessary an interoperable system to make possible the use of data which is fundamental for the development of ATMPs.
- Reimbursement is a national issue but at the European level is possible to ask for more transparency, and a new directive about that should be pretended.

- Regarding access one issue is the fact that not all the states pay the same price, and this is a problem above all for drugs for rare diseases and we can't have in Europe patients of first or second class.
- More collaboration between member states as was foreseen for Covid vaccines to guarantee patients' rights.

Mariano Votta

- Introduced the discussion, stressing the opportunities and challenges linked with the Advanced Therapies Medicinal Products (ATMPs) in the post-market dimension, with a strong focus on **sustainability of ATMPs**.
- In particular:
- The discussion around ATMPs is on reimbursement in terms of potentially eligible population as opposed to budget constraints: a narrative that inevitably undermines **patients'** fair **access to such therapies** for reasons mostly related to cost containment.
- ACN believe that the relevance of these innovative therapies places them at the center of the discussion on health and health policy choices for the future and the sustainability of each National Health System (NHS) across Europe. This will pose very delicate problems of choice and rationing in terms of access to treatment for patients, which could result in the treatment of fewer patients than eligible and therefore potentially treatable.
- A solution in terms of identifying the resources necessary to finance them must therefore be tackled today so as not to arrive unprepared tomorrow.
- Traditional reimbursement and budgeting schemes are unable to amortize the value of ATMPs, whose costs and benefits are not aligned.
- 43 associations across Europe signed ATMPs call to action.

Mauro Maré

- An increasing significant share of health expenditure has clear investment characteristics (multi-year benefits).
- Distinction between current and capital expenditure is not an easy task, economists have been debating this issue since decades.
- Current if *'the economic utility of goods and services ends within the same annual budget process (year)*".
- Capital when '*the economic effect lasts more than one year*' (multiannual).
- Investment expenditures identify 'all expenditures that directly or indirectly affect the formation of national, physical and human capital.
- Considerable increase of number of ATMPs: by 2030, up to 60 new genetic and cells therapies and 350.000 patients potentially eligible.
- A huge cost is a key challenge for national public budgets and healthcare systems.
- But in some years, it will emerge a considerable demand for these therapies.
- The sensitive issue for hard choice and rationing: who (and how) will define patients' access? who is going to be treated? implications and effect on health systems.
- ATMPs are potentially "curative" (many drugs slow the course of a disease, but do not cure it).
- They concern 'limited' populations and are generally considered to be orphan drugs.
- In many cases there are no comparators to set up non-inferiority studies or to test superiority.
- Require a single administration, while clinical and economic benefits spread over time.
- However, there is a potential for 'uncertainty' about how long the effects and outcomes will persist.
- They are *one-shot*, patient-specific; there is only a single treatment.
- They show high investment costs but also many benefits in clinical terms for patients.

- Provide patients with a perspective of a long-lasting recovery.
- ATMPs do not mitigate symptoms but act directly on the cause of illness.
- Have a high timing asymmetry between the emergence of costs – which are almost all upfront – and that of benefits.
- Produce direct and indirect benefits over time: (health care savings, expenditure reduction, the increase in life expectancy, increased productivity, higher tax revenues....).
- The decision on which therapy is worthy of funding should be based on an estimate of the overall economic effects on the health system and the health of citizens.
- Not only by considering the frontal and immediate costs, but also the long-term value to society.
- Costs are concentrated in the single initial year when the financial requirement arises; benefits are instead multi-annual.
- The usual economic valuation, based on the estimation of the cost of traditional therapies (drugs) and on the accrual basis of the public budget (financial statements), is not very suitable for advanced therapies and their particular technological and industrial characteristics.
- A new budget economic approach is required.
- Sars-CoV-2 pandemic 'comes to our aid': the health of EU citizens is crucial for economic, social, and financial sustainability.
- The trade-off between health and the economy, in reality, is not the case at all: without good health conditions, economies will not recover again.
- After Sars-CoV-2, the value of human life and good health for growth potential is evident: vaccines solve, permanently, epidemic; in the same way, ATMP permanently treats different pathologies.
- The flow of (direct and indirect) benefits for many years and cost savings (lower consumption of drugs and facilities, lower costs for the family, etc.).
- Current budgetary procedures are based on the principle of economic accrual (expenditure commitments, not cash budget).
- The budgetary rules provide that the total cost of medicine (therapy) is fully accounted for in the budget of the first year, based on defined expenditure commitments.
- This expenditure can also be settled and paid in subsequent years, but its total amount must be charged in the year in which the accounting obligation arises. This is an important barrier for the application of any annuity payment models, that would allow the national health system to spread the cost of the advanced therapies over time, along with the benefits (outcome-based) (hence, to pay for value).
- Need to build a budget accountancy scheme compatible with annuity payment models, able to align ATMP payments to the benefits of the therapy.
- The decision of which therapy is worthy of funding must be based not only on frontal and immediate costs, but also on the long-term value to society, with an estimate of the overall economic effects on the health system and citizens' health.
- A broad revision of the public accounting criteria is probably needed, to be used in the appraisal procedure of public expenditure.
- Some skepticism by the Eu Commission to partially allow investments within the framework of national public budget.
- Not easy to estimate and some risks of forms of *creative accounting.*
- New accounting approach in the Eu public finances is needed.
- Technological development have made clear that a rethinking of the concept of capital is needed (statistical and national accounting).
- Traditional approach: the notion of capital is only referred to the economic (physical) dimension
- Innovative approach: capital is a broader concept, we need also to include human, social and natural capital (environment, health conditions, etc.).
- The chance of NEGU is therefore critical to rebuild an adequate stock of net capital, especially in the domain of health, environment, and social sustainability.

- The time has come to review and update the current accounting conventions in a serious way, considering that some of the current expenditure is necessary to increase a nation's capital stock and economic assets.
- The accounting criteria are the result of a compromise and are an accounting convention.
- It can and must be updated when technological conditions evolve, the degree of social development changes, and the common feeling of Nations and Peoples of the Community.

Paschalia Koufokotsiou

- There are many post-market obligations and the payers and health care system and reimbursement want to see the cost-effectiveness of these products, the issue is how to see real-world evidence data, regarding ATMPs they seem never enough. Comparability among the real-world data e and the data of the trial (a combination).
- There is a commitment of Commission to revise the incentives for the development of innovative therapies.
- Post-market: therapies must be effective to reimburse the treatments. But often there is not enough evidence.
- Clinical trials are often insufficient due to poor quality and incomplete data. A change of approach to randomized and combined clinical trials is needed.
- The revision of the pharmaceutical legislation must be the starting point. The Commission wants to review incentives and include advanced therapies, but reliable data are needed to understand the impact of ATMPs.
- Enhance the role of academies and implement pilot projects.

Sarah Garner

- In this area, there is a collaboration among the private and the public-sector and this is a success.
- These products are very disruptive, and the challenges are the costs and the regulatory aspects.
- Compliment to the creator of the proposal which is a good solution to deal with the budget issue.
- The WHO must play its part.
- We need to increase transparency in cost management and train as many staff as possible on the subject.
- We need shared roadmaps and platforms, and more public-private interactions.

Giorgio Alleva

- If it were allowed, however, the cost of these therapies could be amortized over the years in relation to the savings generated over time. In particular, they could be indicated in the State budget in several years and not all in the year of expenditure.
- Doing so would significantly increase the financial sustainability of these costs by the public sector over time, and this would promote greater and more equitable use of ATMPs in the population, without putting public finances at risk.
- A totally innovative approach, which would have the characteristic of a 'win win' formula: advantageous both for the patient, who would benefit from highly innovative and effective treatments, and for the National Health Service, which could amortise the cost of the therapy over the years.
- Innovation in the compilation of the accounts can be introduced by modifying the regulation or updating its interpretation. To achieve these results requires courage and a strong conviction on the part of the European Parliament.

- The current accounting conventions have always been updated periodically according to the evolution of the scientific and political-institutional debate.
- The revisions of the national accounting system introduced since the 1990s by the international community (UN and EU) have always concerned a progressive enlargement of the perimeter of investments, classifying as such expenses previously considered current, thus recognizing the increase in the stock of a nation's capital.
- Therefore, decisive for the future of a country and its economic sustainability - and that for this reason, Advanced Therapies expenditures can be considered, at least in part, as investment expenditures. After all, with the 2010 ESA revision, military expenditure was also reclassified from current expenditure to investment expenditure.
- Over time, the component of intangible investments has grown steadily in both corporate and public accounts. The inclusion of tangible and intangible assets in the definition of gross fixed investments in national and community accounts shows an expansion of the narrow vision of investments as a mere increase in physical and technological capital. The capitalization of expenses for the purchase of software, expenses for scientific research, or military expenses were innovations introduced with a new regulation (ESA 2008 and ESA 2010).
- An intangible asset is by definition an asset without physical substance. They cannot be held in the hand or tagged with an inventory system" (EPSAS, 2018). ATMPs are genetic material but also customized 'algorithms' and 'transfection' to people suffering from specific pathologies. Are they tangible or intangible assets? In any case, whether they can be considered tangible assets or intangible assets: they are products of production processes with a relevant research component. The first requirement to be able to consider ATMs as investment assets is met.
- After transfection in the body, ATMPs continue to function over time; that is, they maintain their curative action.
- One possibility that should be tested is that of a recognition of the R&D cost component. In fact, it would be a question of taking the road that led to the capitalization of R&D expenses in the defence sector, recognising a collective value. An agreement between ATMP manufacturers could at least overcome the issue of competition within the sector and give greater strength to a negotiation with the PA.
- From the 2010 ESA Regulation emerge clearly the evidence of the consideration of future economic benefits as an estimate of the increase in the value of the capital stock deriving from intangible assets (the case of creative works in order to increase the baggage of knowledge, including human knowledge). Unless this increase of value can be reasonably estimated, the value of benefits is calculated, by convention, as the sum of costs to produce them. The part that don't provide benefits to the owner is not classified as an activity but is recorded as intermediate consumption. The estimate of the net economic benefits deriving from ATMT will therefore benefit from the vast literature on methods for estimating the effects of investments in health care on the well-being of the population and on the income produced.
- A formal proposal to modify a European Regulation in the compilation of the accounts can come from Parliament or the European Council (for example, but not necessarily from the Eurostat Commission) and enter the agenda of the Working Party on Statistics, composed of the Presidents of the national institutes of EU statistics (INS). This body discusses and

amends the proposal internally and, if approved, it is then negotiated with the European Parliament and the European Council.

- Updates in the interpretation take place through a Eurostat opinion on a proposal from one or more Member States through the NSIs. In this case, the innovations in the classification of expenses can be introduced in a short time.
- Updating the Regulations is a long process, as they must pass through working groups, and they can include intermediate phases with satellite accounts and experiments. They certainly need a political push from the Council and/or the European Parliament.
- The opponent of the change is the usual conservatism, personally I don't think it will be the national accountants, the keepers of the rules, to promote a new classification of expenses for ATMPs. It can only succeed thanks to a proposal from Parliament, representing European citizens and their needs for health and equal rights.

Jasna Karačić

- In Croatia they have public health but they are not rich enough to provide ATMPs to patients.
- It's not only a problem related to the money or funding but it's also a health literacy problem, which means that patients don't know well which possibility of treatment they have. Right to information. This implies inequality in access to care.
- Who will decide which disease will have priority related to budget? it is difficult to justify the use of funds: the question could be "why spending 2 billion € for one person so he can move a finger and 0 € for another one?". The answer is that these therapies are transformative and new ones are coming and they will be increasingly effective. They must be equally accessible in each country of the European Union.
- The future presidency should be committed in changing payment model to guarantee access to ATMPs.

Q&A

Mr Sylvain GIRAUD, Head of Unit at DG SANTE D2: Medical products: quality, safety, innovation - European Commission

- One issue is the fact that there are uncertainties related to the effectiveness (clinical effectiveness) of these therapies.
- Another is the actual level of the price how much of that is related to costs.
- The concerns of payers and healthcare systems are not related only to budget but above all to public health in general.

Dariusz Adamczewski, Head of Healthcare Policy, Government Affairs & Market Access at Johnson & Johnson

- More clinical evidences are needed in order to solve further doubts about innovative therapies.
- Innovative payment models are needed too.
- Another issue is the ensuring of access to genetic tests.
- The second issue is the optimize of cross border healthcare avoiding barriers for patients that need to move to get therapies.
- Availability to collaborate in order to find good solutions.

Conclusion and Next Steps (Mariano Votta)

- First, to give a better and better account of the treatment expectations and access difficulties of patients in their own countries;
- For example, to encourage Parliamentarians in our home country to take inspiration to create in their own Parliament an aggregation of Parliamentarians as there is in Europe, as in the European Parliament there is TRANSFORM, in the Italian Parliament there is the Interest Group "Sustainable Innovation in Healthcare" as very well described by its promoter, the Italian Parliamentary Daniela Manca.
- Promoting multi-stakeholder alliances and launching appeals like ours that gathered more than 40 associations among global/European/national civic & patients' organizations that I still thank.
- From today's meeting, as civil society stakeholders & patient associations, we take home first of all an increased awareness that all potentially eligible patients have the right to access care in particular ATMPs, and that national health budget constraints cannot be a barrier to patients to have access to advances therapies. How to leverage this message?
- We will continue our efforts to identify and carve out those spaces for participation and dialogue in which to bring the demands of patients potentially eligible for the new ATMPs and the proposal discussed today. I point out that in Italy, one of the last acts of the past government was that of October 3 when the General Secretariat of the Ministry of Health issued an act of guidance on how civil society, i.e., associations, companies, and organizations involved in health issues, can participate in the Ministry's decision-making processes.
- About the issue discussed today, individual patient associations could assign the ethics committees at the National Drug Agencies, as we will try to do in Italy where we are within the National Ethics Committee for clinical trials related to ATMPs at the Italian Drug Agency, established by Decree February 1, 2022, of the Minister of Health; in Europe, we will try to do with The Committee for Advanced Therapies (CAT) at EMA, which of course we had invited for today.
- Also at the European level, as an ideal next step of this meeting, I am pleased to announce that we will dedicate to the topic of advanced therapies the 17th European Patients' Rights Day, whose European celebrations are scheduled here in the European Parliament next April 26, 2023.

This document has been drafted by Maddalena D'Urso, a member of the ACN staff.