Addressing the sustainability of ATMPs in a European perspective to broaden an equal access to highly innovative therapies

#VITA[1] Working Group

In the last decades, the developments achieved in molecular and cellular biology and the progress achieved in the study of DNA have radically transformed the biomedical field in addressing the treatment of various genome-based diseases. In particular, in recent **years new genic, cellular and tissue engineering therapies** (the so-called **ATMP**, Advanced Therapy Medicinal Products) have emerged, presenting new opportunities for the treatment and prevention of a variety of diseases or for restoring, correcting or modifying compromised physiological functions in humans, including correcting mutations acquired on a genetic basis.

Their **characteristics** can be briefly summarized as follows, as they:

- **cure** (even otherwise fatal pathologies) **or** significantly **transform** the clinical history of the patient who has no therapeutic alternative, intervening directly on the causes of the disease;
- are **one-shot** therapies, that is, they are administered with a single treatment, unlike traditional drugs and protocols used for other pathologies, which provide for repeated and regular treatments, with an **evident temporal misalignment between current costs**, concentrated in the short term, **and future benefits**, spread over a longer time horizon**;**
- have **high investment costs**, because these are **personalized therapies with high complexity** (including production complexity), with a price that is between 1 million and 2 million euros per administration, but which **present significant future** benefits in clinical, therapeutic, social and economic terms for the health systems and the health of patients (direct, indirect and social costs avoided, recovery in productivity, higher tax revenues, etc.);
- are **administered only in qualified and specialized centers** and arise from extremely innovative and complex platforms.

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 the health service. 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 with which to finance them must therefore be tackled today so as not to arrive unprepared.

[1] To learn more about #VITA visit https://www.linkedin.com/company/vita-valore-ed-innovazione-delle-terapie-avanzate/

Nowadays, there are **14 Advanced Therapies already on the market in Europe**, for 17 indications. significant increase in such therapies is expected over the next decade: **by 2030, up to 60 new gene and cell therapies could be launched globally**, which could affect a total of approximately **350,000 patients**[2].

Therefore, the volume of resources necessary to access these therapies and the methods of payment and financing are the decisive challenge to deal with in order to allow the national health services to bear the cost and therefore to allow full access of these drugs for all eligible patients[4]**.**

The above is also confirmed in the context of the recently published ***Pharmaceutical Strategy for Europe***[5], where the European Commission recognizes Advanced Therapies as a **generational milestone** and highlights the **need for new pricing and reimbursement structures** that take into account the **benefits generated over time** from these therapies in the face of very high initial costs.

Again, in its White Book *"Shifting the paradigm for ATMPs: Adapting reimbursement and value frameworks to improve patient access in Europe"*[6], EFPIA (*European Federation of Pharmaceutical Industries and Associations*) proposes a series of recommendations aimed at accelerating the availability of Advanced Therapies and increasing their access to eligible patients, highlighting how this type of therapies needs **new and different payment and accounting methods**, which take into account the high initial costs and the wide and lasting benefits over time, both for the patient and for the national health system.

The time has therefore come to collectively build a future-proof innovation model that fosters the development of advanced therapies and access by all eligible patients.

With this respect, it is necessary to take into account the main aspect that suggests an economic and accounting evaluation of these different and innovative therapies compared to traditional drugs: the benefits that these therapies produce over time, both direct and indirect, have a characteristic of investment expenditure. The effectiveness of these therapies must be verified over a few years, when the more or less broad positive effects they have had on the treatment of the various pathologies and on the quality of life of the patients can be measured and estimated; therefore, **the considerable savings in direct and indirect costs that they allow can be measured**.

In this context, the **usual economic and accounting evaluation**, based on the estimate of the cost of drugs and traditional therapies (which are repeated and require an annual cycle of treatment) and on the criteria of economic competence typical of the financial statements, is **not suitable for Advanced Therapies** and for their particular technological and industrial characteristics highlighted above.

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[2] Estimating the Clinical Pipeline of Cell and Gene Therapies and Their Potential Economic Impact on the US Healthcare System - Casey Quinn, PhD, Colin Young, PhD, Jonathan Thomas, BSc, Mark Trusheim, MSc the MIT NEWDIGS FoCUS Writing Group, Center for Biomedical Innovation, MassachusettsInstitute of Technology, Cambridge, Massachusetts, USA. 2019 https://pubmed.ncbi.nlm.nih.gov/31198178/

[4] For these reasons, the **#VITA** working group, with the aim of finding solutions that allow fair and ready access to innovation by all potentially eligible patients, has developed a solution which, taking into account the aforementioned specificities of Advanced Therapies, introduce at-result multi-year payment systems (e.g. the cost of the drug is deferred over several years and the health service pays the individual instalments only if the therapy works), and also new accounting forms that provide for a treatment similar to that of amortization for capital expenditure. And in fact, in the current system, public budgets are blocked for the entire theoretical cost of therapy, and not for that expected on the basis of the results of clinical studies, with further constraints for health systems that cannot take full advantage of the opportunity offered by these innovative reimbursement agreements.
In the model proposed by **#VITA**, the undertaking of the expenditure commitment of each installment must take place in the financial years in which payments are expected to be arranged according to the contractual deadlines, exactly as it occurs for the investment expenditures, and not charging the budget with the full cost of the upfront therapy, as is the case of current expenditures.
This solution would allow the national health service on one hand to spend and account for only the real value of the benefit of these therapies (thus committing to the budget only the expenditure corresponding to the benefit obtained) and on the other to broaden the access to highly innovative therapies to the largest possible number of potentially eligible patients. This solution, however, to be implemented needs a change of the accountant providing that each installment is accounted in the year of competence, while EU accounting rules request that health cost must be accounted upfront - for the entire - in the year of administration of the drug.

[5] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52020DC0761&from=EN

[6] https://www.efpia.eu/media/636632/atmps-white-paper-cell-and-gene-therapies-related-market-access-issues.pdf

Continuing to treat ATMPs with an economic evaluation system that is not appropriate to the unique characteristics of these therapies may threaten patients' right to health as access to ATMPs is restricted for reasons of resource rationing. If we want innovative therapies, we need to think about a new system for dealing with healthcare spending. We need to abandon the idea of "ceilings" and think over the long term: moving from spending on silos to revenue for citizens' health.

In the last 30 years we have had many changes in the European accounting, made by EUROSTAT. In the 2008 NDA, the scope of investments was extended to include research and development (R&D) expenditure and expenditure on military defence systems.
Particularly, expenditure on large military defence systems is capitalised. The new SNA also records large military weapons - warships, ballistic missiles and tanks, etc. - as fixed capital. - as fixed capital (interestingly, single-use products such as ammunition, missiles, rockets and hand grenades are treated as military stocks).
As evidence of a continuous work of discussion and evaluation on possible updates in the System of National Accounts, several informal working groups promoted by the Eurostat Commission are active. Several issue papers have been requested by Eurostat from consulting firms[7].

The pandemic showed us that we should consider health expenditure as an investment, particularly when the therapies have not only immediate effects but also a lot of benefits on the long term, allowing the health system to save direct and indirect costs, as it is the case of ATMPs and to prepare our national systems to future challenges.

More in general, the Health & Life Sciences TF Policy Paper to the G20 states the need to priorities investment in appropriate prevention and treatment programs that reduce pressure on health and welfare. This implies the need to change the mindset from viewing healthcare as a cost to viewing it as an investment in order to enhance the use of technology to improve the prevention, prediction, early detection and treatment of disease. This needs to be underpinned by technology assessments that reflect the full humanistic, economic and social cost of the disease (or non-adoption of the technology). Economic evaluations of the health care delivery system, therefore, must be based on metrics that should be developed with a broader societal perspective to ensure the effectiveness of investments and cost drivers in the health care system.

Moreover, there are several mentions of efficiency within the broad context of post-COVID health systems strengthening. In particular, the recent report of the "Monti Commission" of WHO Europe proposes a shift in fiscal policies in favor of innovation and efficiency in the health system, recommending that:

- the way in which data on health expenditure is acquired should change so that there is a clearer distinction between current health expenditure on the one hand and so-called investments in disease prevention and improving the efficiency of care on the other;
- changes are made to the way in which health expenditure data is collected so that there is a clearer distinction between current health expenditure and investment. This will encourage countries to invest more in preventive services and is likely to support much needed innovation that improves the efficiency of care.

Within this scenario, it is clear that Advanced Therapies represent a radical change of the health pattern, moving from traditional medicine to the new frontier of personalized medicine, understood not only as a medicine based on the genetics of the person but as **a medicine that puts the person at the centre**. **This fundamental paradigm shift needs to be understood and shared by as many European countries and their main stakeholders as possible,** because Advanced Therapies are essential in the building process of the **European Health Union.**

The challenges posed by ATMPs can be the impetus for moving **from patient advocacy** in terms of patient protection and involvement, **to Institutional and Citizen Advocacy** in terms of circular participation of citizens and institutions. The goal is to create **widespread awareness of the ATMPs specific characteristics and the**

[7] In 2018, the informal working group promoted by Eurostat was established with the task of specifically assessing expenditure on intangible goods, see https://circabc.europa.eu/sd/a/725ae06f-0a27-426d-a1af-880859336184/Issue%20paper%20on%20accounting%20treatment%20of%20intangible%20assets%20.pdf

opportunities to make them accessible to all eligible patients, guaranteeing the sustainability of the various health systems, to sensitize European decision-makers to create common basis for adoption of specific and innovative solutions in line with the upcoming health innovations.

The #VITA coalition

#VITA (**V**alue and **I**nnovation of **A**dvanced **T**herapies) is a group of pharmaceutical companies specialized in the Advanced Therapies industry, with the scope of promoting the dissemination and enhancement of Advanced Therapies with the following purposes:

- To disseminate knowledge among the various stakeholders about the innovative value and therapeutic benefits of Advanced Therapies for patients and citizens;
- To ensure that the stakeholders themselves acquire objective data and facts regarding the opportunities and criticalities of Advanced Therapies in order to initiate a constructive dialogue to ensure prompt access innovation by patients and health care professionals.

In 2022, **#VITA** members are: Celgene – Bristol-Myers Squibb, Gilead Sciences,Pfizer, PTC e Roche.

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