Strengthening the European Ecosystem for Equitable Patient Access to Advanced Therapy Medicinal Products

Policy paper

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The complete speakers' list, with short biographies and photos, is available on the ACN website.[1].

[1] https://www.activecitizenship.net/multimedia/files/insight/2024-07-04-VITA_4July2024_speakers_list.pdf

Commissioned by

Cittadinanzattiva-Active Citizenship Network carried out an independent analysis. The initiative is unconditionally supported by #VITA - Value and Innovation for Advanced Therapies.

About #VITA - Value and Innovation of Advanced Therapy Medicinal Products[2]

#VITA - Value and Innovation of Advanced Therapy Medicinal Products, is an umbrella group of pharmaceutical companies - coordinated by LS CUBE Global Law Firm - specialising in the Advanced Therapy Medicinal Product sector.

#VITA is formed of: Bristol-Myers Squibb, Gilead, Johnson & Johnson, Novartis, Pfizer, PTC Therapeutics, Roche and Vertex.

#VITA aims to promote the use and development of Advanced Therapy Medicinal Products with the underlying purposes:

• to transparently disseminate knowledge and know how to stakeholders of the value and therapeutic benefits of Advanced Therapy Medicinal Products for patients and citizens;

• To ensure those stakeholders acquire objective data and facts on the pros and cons of Advanced Therapy Medicinal Products in order to initiate a constructive dialogue between patients and healthcare providers to prompt access to innovation.

About Cittadinanzattiva-Active Citizenship Network

Cittadinanzattiva[3] is an organization, independent of political affiliation, trade unions, private companies and public institutions.

It was founded in Italy in 1978. Its core mission is to promote citizens' activism for the protection of rights, the common good and support the underprivileged and under-represented in Italy and across the EU.

Its mission refers to article 118 of the Italian Constitution[4], which recognizes the autonomous initiative of citizens, individuals and associates to carry out activities of common interest and based on the principle of subsidiarity, provides for the obligation of institutions to favour active citizens.

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[2] https://coalizionevita.it/

[3] https://www.cittadinanzattiva.it/

[4] https://www.senato.it/istituzione/la-costituzione/parte-ii/titolo-v/articolo-118

Cittadinanzattiva considers citizens a fundamental resource for democracy who play an active role in society and should have the opportunity to participate in everyday policy making.

As the European interface of Cittadinanzattiva, Active Citizenship Network[5] operates under the umbrella of Cittadinanzattiva's mission.

ACN aims to better protect citizens' rights in collaboration with partners from across the EU and non-EU countries[6].

It is active both at the member state and European level in the promotion of civic activism and participation in public policies.

Why Cittadinanzattiva-Active Citizenship Network and ATMPs

Since 2022, Active Citizenship Network has focused on ATMPs, as part of its ongoing commitment to advocate for patients' rights and access to healthcare.

At a national level Cittadinanzattiva, it is an official member of the National Ethics Committee for clinical trials on advanced therapies[7] at AIFA – the Italian Medicines Agency. It is the only official member that represents both the civic and patient perspective.

At an EU level Active Citizenship Network works to facilitate discussion and exchange of knowledge among stakeholders.

Under its mission to protect and advocate for the enforcement of rights, Cittadinanzattiva-Active Citizenship Network ultimate goal is to ensure the right to access to care, including to advanced therapies, is recognised. It is for this reason that Cittadinanzattiva-Active Citizenship Network has decided to collaborate with the #VITA consortium.

Disclaimer:

Independent, external experts have contributed to this report via their participation in a stakeholder roundtable discussion on July 4th 2024. Input from these interactions was analysed by the authors and formed the backbone of this report. The external experts did not co-author this report and therefore did not necessarily agree with every element and/or recommendation contained herein.

[5] https://www.activecitizenship.net/

[6] https://www.activecitizenship.net/our-network.html

[7] https://www.aifa.gov.it/documents/20142/1807486/DM-02-03-2022_nomina_componenti_CE_terapie_avanzate.pdf

Preface

Advanced Therapy Medicinal Products (or 'ATMPs') are biological medicinal products that are classified into four main groups: gene therapy medicinal products, somatic cell-based medicinal products, tissue-engineered products and combined advanced therapy medicinal products.

The development of ATMPs brings new opportunities for the treatment and prevention of a variety of medicinal conditions (genetic, oncological and chronic diseases) with no alternative treatment options or for re-establishing, correcting or modifying physical impairments in humans, including by correcting genetically-acquired mutations. From a clinical standpoint, unlike conventional medicinal products, ATMPs consist of genetic material or cells or tissues or combinations thereof.

Evaluation of expenditure on ATMPs: from national to European multi-stakeholder debate

Access to advanced therapies is extremely complicated. It is precisely for this reason that Cittadinanzattiva-Active Citizenship Network is motivated to find solutions and or least to explore new ways to enable greater patients access to them.

In this regard, an interdisciplinary group of Italian professionals has put forward a proposal with a European scope , drawn up on the basis of the findings of a scientific study entitled *'Evaluation of expenditure on advanced therapy medicinal products',*[8] carried out by the Alta Scuola di Economia e Management dei Sistemi Sanitari (ALTEMS) of the Università Cattolica del Sacro Cuore[9] in collaboration with LS CUBE[10] and with the unconditional contribution of #VITA (Value and Innovation for Advanced Therapies).

Initially, this proposal was presented to interlocutors - institutional and non-institutional - in Italy[11], even receiving an encouraging endorsement from the new Italian Health Minister Orazio Schillaci in January 2023[12].

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[8] https://www.lscube.it/wp-content/uploads/2023/12/VITA_ENG_ottobre_mod.pdf

[9]For details on the Working Group, by whom it was funded, since when it has been working on the issue: https://altems.unicatt.it/altems-master-e-corsi-master/altems-health-economics-la-valutazione-della-spesa-per-le-terapie-avanzate

[10] https://www.lscube.it/

[11]As an example, the following documents, all in Italian, can be consulted: https://www.senato.it/application/xmanager/projects/leg18/attachments/documento_evento_procedura_commissione/files/000/311/601/_VITA_-_Nota_sulle_ATMP.pdf; https://www.sanita24.ilsole24ore.com/art/medicina-e-ricerca/2023-12-14/terapie-avanzate-serve-nuovo-sistema-finanziamento-pubblico-zaffini-obiettivo-e-fondo-ad-hoc-ma-ora-incassiamo-ordine-giorno-120127.php?uuid=AFSWPF3B; https://altems.unicatt.it/altems-locandina%20valutazione%20spesa%20terapie%20avanzate.pdf.

[12] **FARMACI: SCHILLACI, 'NUOVO QUADRO NORMATIVO PER RIMBORSO TERAPIEINNOVATIVE'** = 'With a special discussion panel'. Rome, 17 Jan 2023. (Adnkronos Salute) - The subject of advanced therapies 'on the one hand presents extremely high absolute costs and on the other the ability to decisively and very quickly affect the natural history of

Formulating the Policy Paper

After positive feedback on the Italian level, the #VITA consortium decided to present its proposal at the European level. And so began the collaboration between #VITA and Active Citizenship Network - the European branch of Cittadinanzattiva. This partnership has led to further publications at a European level (videos[13], interviews[14], articles[15]) and to the presentation of the #VITA proposal through different initiatives listed below:

1) Two events organised at the European Parliament, the first in the presence of the European Commission, the second in the presence of two Interest Groups of MEPs (MEPs Interest Group "European Patients' Rights & Cross-Border Healthcare; TRANSFORM MEP Interest Group) and with the significant underlining of the European Commissioner for Health (see below point 3 for more details).
2) Endorsement by 43 patient associations[16], from 12 EU countries[17].

pathologies with a high mortality rate and health impact by avoiding prolonged treatment over time. These aspects make the costs of these therapies more of an investment, a capital expenditure than a current expense. It is therefore a question of defining a new specific regulatory framework for the reimbursement of these therapies by the SSN that provides on the one hand for the possibility of a payback period and on the other a 'pay for performance' reimbursement scheme'. This was announced by the Italian Minister of Health, Orazio Schillaci, during his speech in the Health and Labour Commission of the Senate in the continuation of the communications on the policies of his ministry. "In order to define a hypothesis of this new framework, I reiterate the advisability of activating a special round table that would include, in addition to the competent general directorates of the Ministry of Health, expert representatives of our Aifa, of the Mef, technicians from the State Accounting Department, and other competent external bodies and research institutes that have taken an interest in the matter," Schillaci concluded. (Frm/Adnkronos Salute) ISSN 2465 – 1222. 17-GEN-23 18:21NNNN.

[13] https://www.youtube.com/watch?v=tI6Wnzt7bDI

[14] https://www.healtheuropa.com/the-value-of-investing-in-advanced-therapy-medicinal-products/120290/

[15] https://www.activecitizenship.net/insights/1103-advanced-therapies-time-to-consider-them-an-investment-instead-of-a-cost.html?highlight=WyJhdG1wcyJd

[16] ATMPs revolution: empowering leaders of EU civic and patients' advocacy: https://www.activecitizenship.net/events/407-24-may-2022-ATMPs-revolution-empowering-leaders-of-eu-civic-and-patients-advocacy.html?highlight=WyJhdG1wcyJd

[17] Call to action "ATMPs revolution & the respect of the patients' right to access to care" launched by Active Citizenship Network in 2022 with the endorsement of 43 Patient Advocacy Groups (PAGs) from 12 countries: https://www.activecitizenship.net/insights/406-advanced-therapies-medicinal-products-revolution-the-respect-of-the-patients-right-to-access-to-care-a-call-to-action.html?highlight=WyJhdG1wcyJd

3) How to provide eligible patients with faster and wider access to ATMPs, where experts speak out.

On 26 April 2023, Active Citizenship Network organized an event at the European Parliament in Brussels to celebrate the 17th European Patients' Rights Day. An event entirely dedicated to access to treatment for Advanced Therapy Medicinal Products.

On the occasion, the EU Health Commissioner Stella Kyriakides stated that "*ATMPs give hope to patients where therapeutic options are currently lacking or non-existent, and they must be able to reach patients sooner. Our priority is always to put patients' interest first*"[18].

A year later, on 4 July 2024, ACN organized a high-profile pan-European closed-door meeting[19] along the broad theme of ATMPs under its commitment to the topic.

The aim was to establish how to provide eligible patients with faster and broader access to care. Key questions related to the direction experts felt we should move and how the newly elected European institutions could act in order to make the right to care and access to innovative treatments, such as ATMPs, enforceable.

The backbone of the discussion was a scientific study - conducted by ALTEMS, in collaboration with LS CUBE and #VITA which includes a concrete proposal that aims to recalibrate public spending to view ATMPs as an investment, not as an expense.

During the session, the proposal was outlined by one of its co-authors, Prof. Mauro Marè, Professor of Public Economics at University of Tuscia and LUISS University (Italy) with his speech entitled "*Evaluation of expenditure on advanced therapy medicinal products*"[20].

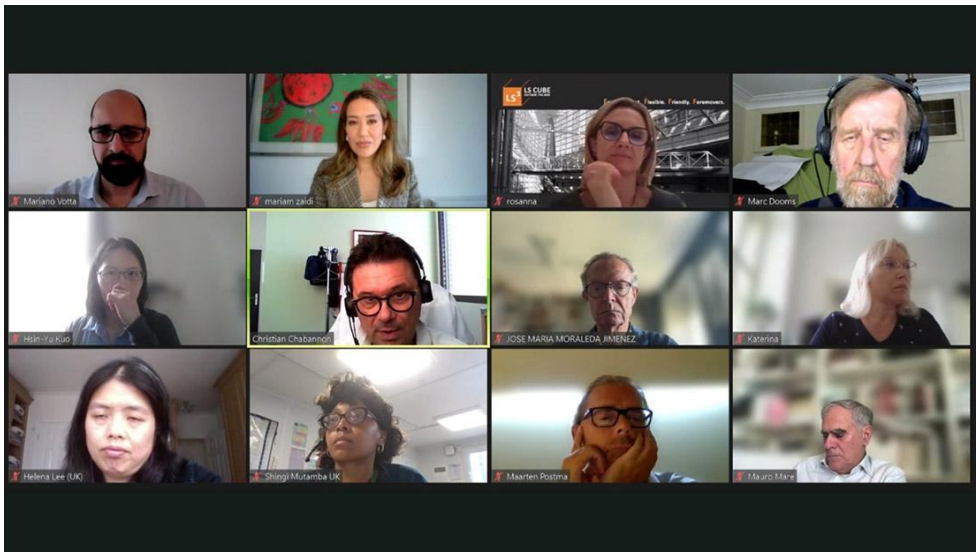
The meeting – titled "*Strengthening the European ecosystem for equitable patient access to Advanced Therapy Medicinal Products (ATMPs)*[21]" provided interesting insights from independent experts across 7 countries: Belgium, Czech Republic, France, Italy, Netherlands, Spain, UK.

[18] https://www.youtube.com/watch?v=-BpxcyJ21IU

[19] https://www.activecitizenship.net/events/1218-4-july-2024-strengthening-the-european-ecosystem-for-equitable-patient-access-to-advanced-therapy-medicinal-products-ATMPs.html

[20] His presentation, titled "*The Economics of Advanced Therapy Products: Reasons for a New Accounting and Economic Approach*" is available for the download in the ACN website: https://www.activecitizenship.net/multimedia/files/insight/2024-07-04-Mauro_Mare_ATMP_22_July.pdf

[21] https://www.activecitizenship.net/insights/1221-how-to-provide-eligible-patients-with-faster-and-wider-access-to-advanced-therapy-medicinal-products-ATMPs-experts-speak.html



Methodology

The selection of experts took place after careful consultation and evaluation of the sector's literature, institutional accreditation, participation in recent public events on the subject, and were also based on the suggestion of PAGs from several countries related to ACN. A closed-door meeting, conducted under Chatham House rules was held, in order to encourage an open debate.

The event was recorded for internal purposes only to allow the editorial team to document suggestions that emerged.

Findings and key messages of closed-door meeting:

All potential, eligible patients have the right to have access to Advanced Therapy Medicinal Products. National health budget constraints cannot be a barrier to this.

Today, traditional reimbursement and budgeting schemes are unable to amortise the value of the Advanced Therapy Medicinal Products (ATMPs), whose costs and benefits are not aligned.

These types of therapies need new and different payment and accounting methods, which consider the high initial costs and the large and lasting benefits over time, both for the patients and the national health systems. It is time for an institutional mindset change to classify Advanced Therapy Medicinal Product expenditure as an investment and not a cost which is possible if a decision is taken to review – from Eurostat downwards – the economic/financial classifications of healthcare expenditure currently in force.

Given the expected approval of 60 new ATMPs by 2030, affecting around 500,000 patients, there is an urgent need to address funding and sustainability. These therapies, costing between 1 and 3

million euros per administration, raise critical issues for health policy and service sustainability, potentially limiting patient access.

To address these challenges, the already mentioned study "*Evaluation of expenditure on advanced therapy medicinal products*" proposes an Annuity Payment Model. This model spreads the cost over multiple years and links payments to treatment outcomes. If a therapy proves ineffective, future payments cease, sharing the financial risk between the NHS and manufacturers. This approach requires consistent accounting methods to align costs with payment timelines, ensuring financial sustainability and allowing resources to be allocated to other medical needs.

In particular, the study "*Evaluation of expenditure on advanced therapy medicinal products*" outlines the economic and clinical distinctions between ATMPs and conventional medicines, highlighting their unique characteristics and economic implications for health systems:

1. One-Shot Therapies: ATMPs are often administered as a single treatment, unlike conventional treatments requiring ongoing administration.
2. Cost and Benefit Mis-alignment: ATMPs incur high initial costs but provide long-term benefits for some patients.
3. High Investment and Benefits: Despite significant upfront costs, ATMPs may offer substantial clinical, therapeutic, social, and economic advantages.
4. New Therapeutic Solutions: ATMPs provide potential cures for previously untreatable conditions.
5. Direct Disease Action: They act directly on the disease causes.
6. Complex Preparation: The preparation process is lengthy and more complex than that for conventional medicines.
7. Biological Origin: Produced from patients' own cells, engineered in specialized manufacturing sites. As the patient is the origin of biological material, they must be granted the rights under the new EU Substances of Human Origin (SoHO) Regulation[22].
8. Specialized Administration: Only administrable in specialized centers.
9. Ongoing Maintenance: Continuous maintenance and innovation are required.
10. Additional Benefits: They improve occupational productivity, psychological, interpersonal, and social aspects, and might offer financial savings for the NHS if the treatment is successful.
11. Healthcare System Impact: Their use involves hospital resources and a shared responsibility between the pharmaceutical industry and health services.

[22] https://health.ec.europa.eu/blood-tissues-cells-and-organs/overview/new-eu-rules-substances-human-origin_en

Conclusions from closed-door meeting: Points of strength and barriers to be removed

During the online meeting on ATMPs on July 4, 2024, our diverse group of experts evaluated the validity of the proposal and offered useful insight around the management of ATMPs, based on their own experiences.

From the discussion, observations emerged that highlight and underline the need for innovative financial models, regulatory frameworks, and the unique economic and clinical nature of advanced therapies.

- ATMPS are heterogeneous in nature. Some of them are derived from human cells or tissues and raise specific questions. Others are derived from other living categories, such as viruses, and raise different issues, both in terms of development and access. As the number of ATMPS increases, there is a need to address different blocks of issues, including very different infrastructures - both at the manufacturing and delivery stages - to facilitate patient access to these different categories of products. It is therefore a huge complexity for each product and process, which have also a dynamic component, that quickly changes over time. So much so that each individual ATMPS may have a unique pathway from the laboratory to the clinic.
- So far, only products made by the for-profit sector have been able to reach the EU market. The problem relates to very high costs - which could be reduced to a more reasonable or negotiable profit - and sometimes lack of manufacturing capacity for marketing authorization holders.
- Main challenges for access could be addressed by academic and non-profit sectors in different ways.
- Once the product has been manufactured, approved, and is commercially available, a huge number of problems remain to be solved. Such as gathering specialized human resources in hospitals, in blood banks, in other health care sectors that would allow the supply chain to be mastered for a significant number of patients and allow the capabilities of clinical departments to manage potential complications.
- Based on the above point, it is crucial to train healthcare workers with very specific skills.
- Establishment of national, regional and cross-border networks dedicated to ATMPs to ensure patients have access to ATMPs and make sure that good candidates for these treatments get them in time to experience the highest possible clinical benefit.

- Not all ATMPS provide a definitive cure so it is necessary to build tools to measure actual benefits enjoyed by patients, which do not always translate into a cure.
- It is not certain, that a drug qualifies as an ATMP, will provide a definitive cure for 100% of patients. Sometimes a fraction of these patients' relapse. However, it is fair to say that patients enjoy a period of time without further treatment. So, this is more about quality of life than cure.
- It would be good to build tools to measure the actual benefits that patients enjoy, even if it is not always a definitive cure. For this reason, it would also be necessary to give a more rigorous definition of what different therapies are as well as the definition of concrete parameters for the identification of eligible patients, according to European standardised criteria.
- Establishing an EU register for each ATMP to collect measurable benefits that ATMPS brings to real life, to measure the goals that are achieved by the patient, but also any adverse reactions and the impact in the patient's life. The register should be open for medical professionals and patients.
- It is necessary to consider the complexity of regulatory pathways, which differ between member states and geographic locations. Most ATMPS are regulated at the European level, following a centralized procedure, but the less known part involves ATMPS that are prepared on a non-routine basis. These are regulated at the Member State level and include hospital exemptions, for indications which are not covered by SmPC (Summary of Product Characteristics), and other aspects such as naming, patient use or compassionate use. Whether and how these pathways are used to produce ATMPS without central authorization is largely unknown to the broader community (although the national regulatory authorities are aware), and even for this reason, the actual cost for this type of non-routine ATMPS use is often unknown and could vary widely.
- For national health systems ATMPs represent a potential investment, although at the moment the discussion is based on an experimental economic model and not on concrete data. It is necessary to invest in research and knowledge, infrastructure, specialised networks, etc.
- From a medical and social point of view, the first objective must be to treat patients. Timely access is the most important aspect, especially for patients suffering from very rare diseases, for whom the time factor is decisive. It is also extremely important to investigate on

prognostic factors that define successful outcomes in order to appropriately select patients who will benefit from ATMP treatments.

- Sharing data on the cost-effectiveness of ATMP treatments and the conclusions of cost-effectiveness assessments will aid the discussion about the availability of ATMPs in individual EU countries. This data should be accessible to patients and care payers.
- Funding ATMPs is crucial for the availability of care. Sharing prices across EU countries, or jointly negotiating prices, would greatly help in ensuring equal access to treatment.
- Other methods should be considered to make these particular medicinal products more accessible, such as academic and public research and manufacturing methods to complement private production.

Further considerations – the political dimension

The online closed-door discussion was also an opportunity to reflect on the direction to be taken by newly elected members of European institutions and how they could act on ATMPs. The difficult socio-political environment at a global and European level, does not make it easy to force the issue for eligible patients.

For this reason, it is more important than ever to facilitate the exchange of information and knowledge between those involved in the field of ATMPs. We must promote synergetic actions and have courage to experiment with solutions that are capable of exploiting the potential of advanced therapies for a large number of European citizens while respecting the budget constraints that healthcare has long been paying for in almost all of Europe.

This Policy Paper has been drafted thanks to the unconditional support of #VITA – Value and Innovation of Advanced Therapies (Bristol-Myers Squibb, Gilead, Johnson & Johnson, Novartis, Pfizer, PTC Therapeutics, Roche e Vertex), coordinated by LS CUBE Global Law Firm