Received: 14 July 2023 | Revised: 1 September 2023 | Accepted: 19 September 2023

DOI: 10.1002/ijc.34753

RESEARCH ARTICLE

Cancer Therapy and Prevention

IJC INTERNATIONAL JOURNAL of CANCER

Differences in time to patient access to innovative cancer medicines in six European countries

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Funding information
European Fair Pricing Network

Abstract

Patients across Europe face inequity regarding access to anticancer medicines. While access is typically evaluated through reimbursement status or sales data, patients can receive first access through early access programs (EAPs) or off-label use. This study aims to assess the time to patient access at the hospital level, considering different indications and countries. (Pre-)registered access to six innovative medicines (Olaparib, Niraparib, Ipilimumab, Osimeritinib, Nivolumab and Ibritunib) was measured using a cross-sectional survey. First patient access to medicines and indications were collected using the hospital databases. Nineteen hospitals from Hungary, Italy, the Netherlands, Belgium, Switzerland and France participated. Analysis showed that some hospitals achieved patient access before national reimbursement, primarily through EAPs. The average time from EMA-approval to patient access for these medicines was 2.1 years (Range: −0.9-7.1 years). Hospitals in Italy and France had faster access compared to Hungary and Belgium. Variation was also found within countries, with specialized hospitals ($\bar{x}$: −0.9 years; SD: 2.0) more likely to provide patient access prior to national reimbursement than general hospitals ($\bar{x}$: 0.4 years; SD: 2.9). Contextual differences were observed, with EAPs or off-label use being more prevalent in Switzerland than Hungary. Recent EMA-approved indications and drug combinations reached patients at a later stage. Substantial variation in patient access time was observed between and within countries. Improving pricing and reimbursement timelines, fostering collaboration between national health authorities and market authorization holders, and implementing nationally harmonized, data-generating EAPs can enhance timely and equitable patient access to innovative cancer treatments in Europe.

KEYWORDS
access, early access programs, Europe, off-label use, oncology, reimbursement

Abbreviations: EAP, Early Access Program; EMA, European Medicine Agency; HTA, Health Technology Assessment; MAH, Market Authorization Holder; NHA, National Health Authority.

What's new?

The first point of patient access to innovative medicines in Europe often occurs via early access programs (EAPs) or off-label use. Consideration of these factors, however, is mostly neglected in patient access evaluations. This study explored patient access to oncology medicines at the hospital level, with consideration of time, indications and context. Significant heterogeneity in time to access was observed between countries and hospitals. Specialized hospitals were likely to expedite access prior to reimbursement, and some countries were more likely to grant access via EAPs or off-label use. The findings highlight opportunities to improve access to oncology medicines across Europe.

1 | INTRODUCTION

Ensuring patient access to innovative cancer medicines, while safeguarding public budgets, is a challenging dilemma.[1] Despite pharmaceutical therapies' potential to contribute to effective anticancer care, high prices and high impact on healthcare budgets provide a barrier to patients' access to care.[2] After the European market authorization, it takes on average 511 days for an anticancer treatment until a national reimbursement decision is reached in European countries.[3] Time to reimbursed access to innovative medicines varies from 100 days in Germany to 960 days in Estonia, demonstrating inequities on macro levels and causing patients to possibly lose unnecessarily life years.[3-5]

To gain market access across Europe, innovative medicines are submitted through European and national procedures by the Market Authorization Holder (MAH).[6] After the innovative medicine is authorized by the European Medicine Agency (EMA), the pricing and reimbursement of the medicine is assessed by the National Health Authorities (NHAs).[7] When timely access to innovative medicines is crucial for patients in high medical need and no authorized therapeutic alternatives are accessible, access is facilitated through early access programs (EAPs) or off-label use. These programs allow patients to receive promising new medicines outside the scope of clinical trials and bridge the gap in time between the EMA authorization and national pricing and reimbursement decisions.[8]

While "patient access to medication" has been analysed by others,[6,9] studies tend to focus on national reimbursement status[10-13] or sales data[3,5] when evaluating time to access to medicines. However, this approach leaves a gap in the analysis of access because in many countries, prescription and coverage runs through hospital budgets. In this study, actual patient access is in place when patients with a specific indication receive the most suitable (pharmaceutical) treatment without facing considerably high out-off-pocket expenses. This perspective on patient access is closer to the actual reality of patients because it includes access through national reimbursement as well as EAPs and off-label use (Table 1). Access in clinical trials is not considered as their eligibility criteria and other limitations restrict the general participation of patients.[14]

Hence, our study aims to assess actual patient access to innovative oncology medicines in European countries from a hospitals perspective. Time to access, differences per indication and context of first access (EAPs, off-label use or reimbursed access) were collected on hospital level. This gives us detailed insights into the variability of patient access across Europe and allows us to support EU- and national policy makers in their efforts to reduce inequities.

TABLE 1 Contexts of patient access.

Reimbursed access	Approved use for an authorized medicine that is included in the national reimbursement list and covered by (national) health insurance.[15]
Off- label use	Unapproved use for an otherwise authorized medicine (eg, unapproved indication, age group, dosage). Often, it is requested by a physician and its reimbursement depends on (national) health insurance.[16]
EAP (Early Access Program)	Unapproved use for an unauthorized or authorized medicine under strict conditions if no satisfactory authorized therapies are accessible for patients.[17] These programs are often coordinated and implemented at national level but initiated and often paid for by market authorization holder (industry).[15] Depending on the country, these programs have different names for example, Compassionate use program or cohort Autorisation Temporaire d'Utilization.

2 | METHODS

To measure actual patient access to the selected medicines and their indications, a mixed method study design was applied, combining a cross-sectional survey and semi-structured interviews.

We invited European hospitals providing cancer care to participate in this study through the network of Organisation of European Cancer Institutes (OECI). The aim was to include at least three hospitals per participating country, different levels of specialization (general hospitals and specialized cancer/university hospitals) and a geographic spread across countries. Included hospitals had to treat at least 60% of the indications of interest. Through purposive sampling, hospital pharmacists working in oncology and having access to the general hospital databases related to the patient delivery of medicines were approached.

Patient access to six innovative medicines and their indications were reviewed in this study: Olaparib, Niraparib, Osimeritinib, Ipilimumab, Nivolumab and Ibritunib (Data S1). Selection criteria included national patient volumes (>500 patients treated annually for all indications), price (>€20.000 per patient per year), estimated national budget impact (>€10.000.000 budget impact annually for all approved indications), high clinical relevance/added therapeutic value (ESMO-MCBS>3) and a variety in indications and therapeutic working mechanisms. A panel of senior researchers (Scientific Advisory Board of the European Fair Pricing Network) in oncology advised on the final selection of medicines.

The interviews and survey were performed from February 2021 to February 2022. A pilot study to assess the content validity of the survey and interview was conducted with four hospital pharmacists for 10 medicines. In order to establish the most effective structure and content of the survey, every item underwent evaluation through a cognitive interview during the pilot study with the hospital pharmacists. This evaluation considered factors such as relevance, representativeness, clarity and comprehensiveness of the items to assess patient access to medicines. The focus was directed towards identifying the specific types and details of medication-related data accessible to the hospital pharmacists, including information such as the type and timing of initial access, patient volume and pricing details. The final survey included 22 questions regarding six medicines. For each medicine, hospital pharmacists were asked to provide information on the general access at the hospital, indication-specific access, national reimbursement status and time and context of first delivery. Semi-structured interviews were conducted in parallel to the survey and to ensure understanding of the survey questions and correct interpretation. Moreover, topics like EAPs, off-label use, payment support for unreimbursed medicines were assessed to gain insights into the hospital-specific context of implementation and delivery.

To provide a detailed overview of actual patient access to the selected medicines and their indications, we analysed and presented the data at hospital level. Time to patient access was calculated as the difference between first EMA-approval and time of first delivery of the medicine to a patient. Furthermore, dates of national reimbursement, and context of first patient access (EAPs, off-label use and/or reimbursed access) were analysed.

3 | RESULTS

Hospital pharmacists from 19 hospitals in six countries (The Netherlands [n = 3], France [n = 1], Switzerland [n = 5], Belgium [n = 5], Italy [n = 2] and Hungary [n = 3] participated [Data S2]). The aim of three hospital inclusions per country was reached in four of the six countries. Even after limiting the selection of medicines, including hospitals was met with various challenges, such as the difficulty of identifying pharmacists with appropriate database access, the time-consuming nature of data retrieval considering that it was a task on top of the high work load of hospital pharmacists, reluctance among some participants to share data and insufficient details within certain databases regarding access to medicines.

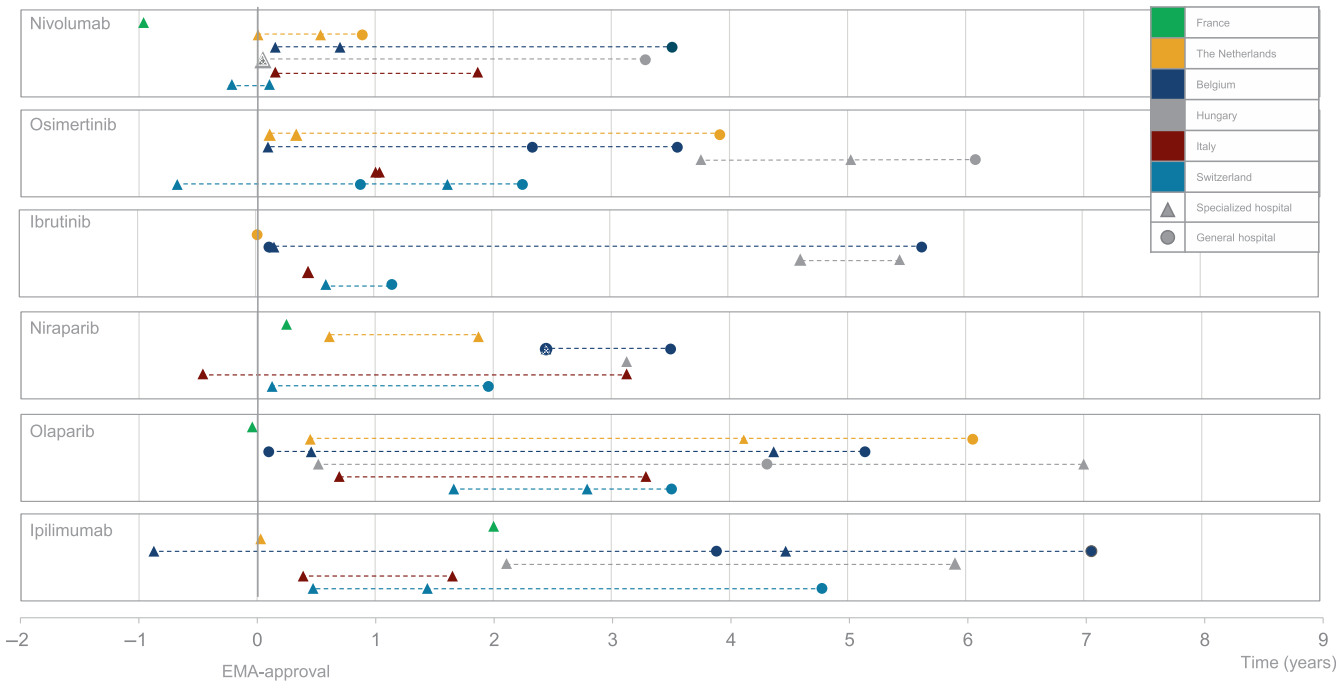

FIGURE 1 Time from EMA approval to actual first patient access per hospital and country. The "0" in the timeline shows when EMA approval was obtained. Each symbol (◯ or Δ) represents a general hospital (◯) or specialized hospital (Δ).They show the point of time when patient access was achieved. Each symbol (◯ or Δ) is equal to one observation in a hospital for a one of our selected medicines. Colors represent the country of the hospital. Note that in Switzerland, market auhtorisation is handeled by Swissmedic.

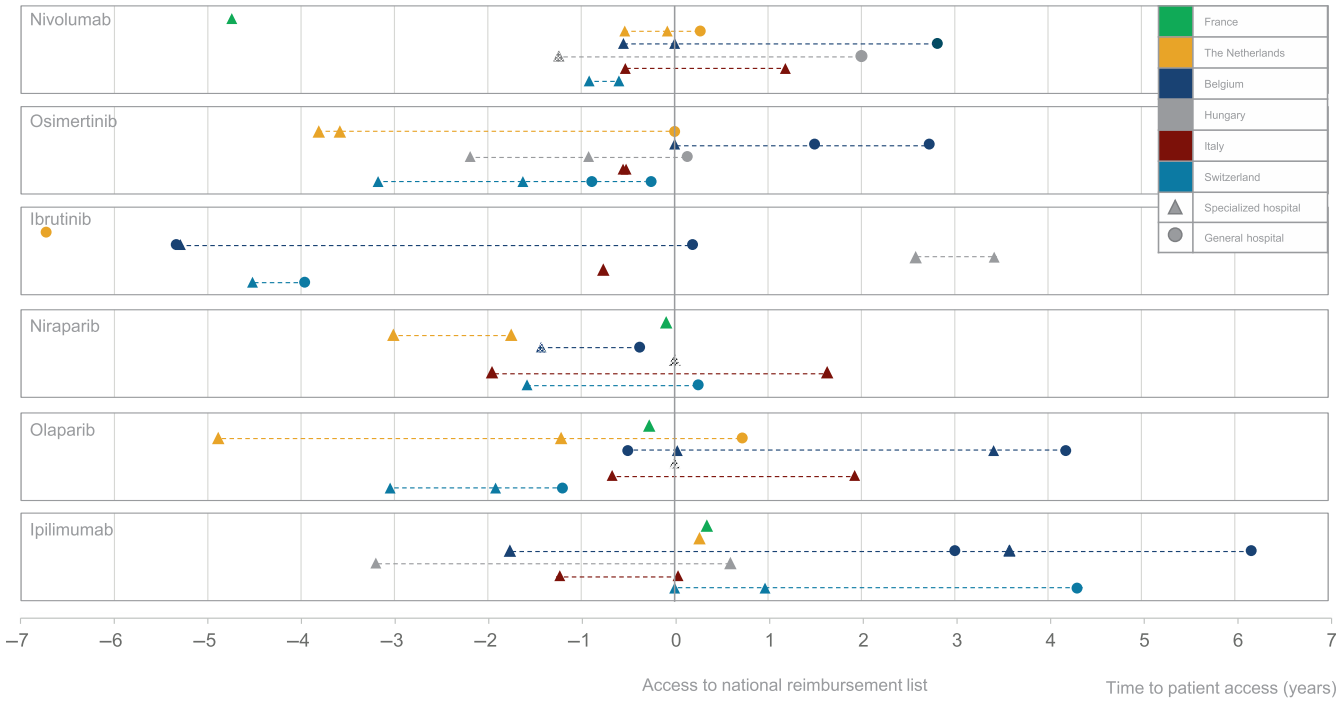

FIGURE 2 Time from national access to the reimbursement list to first actual patient access per hospital and country. The "0" in the timeline shows when national reimbursement was obtained (Data S3). Each symbol (◯ or Δ) represents a general hospital (◯) or specialized hospital (Δ). They show the point of time when patient access was achieved. Each symbol (◯ or Δ) is equal to one observation in a hospital for a one of our selected medicines. Colors represent the country of the hospital.

3.1 | Time between EMA approval, national reimbursement and actual patient access

Eighteen of participating hospitals from six countries were able to share in total 78 observations regarding the time of first medicine delivery of our selected medicines through their hospital databases (Data S3). The time to patient access was calculated using the date of EMA approval of the medicine (noted as "0" in the x-axis in Figure 1) or the date of national reimbursement (noted as "0" in the x-axis in Figure 2).

Regarding time between EMA approval and patient access (Figure 1), we found considerable variation between medicines, countries and hospitals. The average time from EMA-approval to patient access to our selected medicines was 2.1 years (Range: −0.9 to 7.1) in the participating hospitals. On average, time to patient access was the lengthiest in Hungary ($\bar{x}$: 3.7 years; SD: 2.2; observations: 14) and Belgium ($\bar{x}$: 2.5 years; SD: 2.1; observations: 20) followed by Switzerland ($\bar{x}$: 1.4 years; SD: 1.4; observations: 16) and the Netherlands ($\bar{x}$: 1.7 years; SD: 1.9; observations: 13). Nivolumab was the fasted accessible across the countries ($\bar{x}$: 0.7 years; SD: 1.2; observations: 14) and Olaparib was the slowest accessible ($\bar{x}$: 2.8 years; SD: 2.6; observations: 16). Note that Olaparib and Niraparib were not reimbursed in Hungary at the time of this study.

Regarding time between national reimbursement and patient access (Figure 2), we found that the average time of access to the selected medicines was −0.5 years (Range: −6.7 to 6.2 years). Patient access was faster in specialized hospitals ($\bar{x}$: −0.9 years, SD: 2.0; observations: 52) than in general hospitals ($\bar{x}$: 0.4 years, SD: 2.9; observations: 22). Access was on average earlier than national reimbursement in the Netherlands ($\bar{x}$: −1.9 years; SD: 2.2; observations: 13) and Switzerland ($\bar{x}$: −1.1 years; SD: 2.0; observations: 16). It was at or after the national reimbursement decision in Hungary ($\bar{x}$: 0.0 years; SD: 1.9; observations: 14) and Belgium ($\bar{x}$: 0.5 years; SD: 2.9; observations: 20).

Regarding time between EMA approval and national reimbursement status, high variability was found between medicines and countries. From our selected medicines, national reimbursed access was achieved faster in Italy ($\bar{x}$: 1.3 years; SD: 0.3) and France ($\bar{x}$: 1.1 years; SD: 1.3). Hungary ($\bar{x}$: 3.6 years; SD: 2.0) and the Netherlands ($\bar{x}$: 3.8 years; SD: 2.0) were slower to nationally reimburse the medicines.

3.2 | Context of first registered access

Seventeen hospitals from five countries were able to share in total 92 observations regarding the context of first accessibility of the selected medicines through their databases (Table 2).

First access of the selected medicines was more often realised through EAPs (43 out of 92 observations [47%]) than after national reimbursement (28 out of 92 observations [30%]) or through off-label use (7 out of 92 observations [8%]). EAPs and off-label use were more prevalent in Switzerland (17 out of 24 observations [71%]) and Italy (8 out of 11 observations [72%]) than in Belgium (12 out of 24 observations [50%]), the Netherlands (7 out of 16 observations [44%]) and

TABLE 2 Context of first accessibility of the medicines to the first patient in the first hospital per country per medicines.

Countries/ Medicines	Belgium				Hungary			Italy		Switzerland					Netherlands		
Type of hospitals	SP	SP	GEN	GEN	SP	SP	GEN	SP	SP	SP	SP	GEN	GEN	GEN	SP	SP	GEN
Olaparib																	
Niraparib																	
Nivolumab																	
Ipilimumab																	
Osimertinib																	
Ibrutinib							NA										

SP	Specialized hospital
GEN	General hospital
	First Access through early access program
	First Access through national reimbursement
	First Access through off-label use
	No access
	No context was given
NA	None of the indications of this medicine is treated in this hospital

TABLE 3 Accessibility to selected medicines and its indications.

Country	CH	CH	CH	CH	CH	IT	IT	HU	HU	HU	BE	BE	BE	BE	NL	NL	NL	FR
Type of hospital	GEN	SP	SP	GEN	GEN	SP	SP	SP	SP	GEN	GEN	SP	GEN	SP	GEN	SP	SP	SP
Olaparib																		
Accessibility																		
+ Breast cancer																		
+ Ovarian cancer																		
+ Adenocarcinoma of the pancreas																		
+ Prostate cancer																		
Niraparib																		
Accessibility																		
+ Ovarian cancer																		
Nivolumab																		
Accessibility																		
+ Melanoma																		
+ Melanoma (in combination with ipilimumab)																		
+ Non-small cell lung cancer																		
+ Renal carcinoma																		
+ Renal carcinoma (in combination ipilimumab)																		
+ Head and neck squamous cell carcinoma																		
Ipilimumab																		
Accessibility																		
+ Melanoma																		
+ Melanoma (in combination with Nivolumab)																		
+ Renal carcinoma (in combination Nivolumab)																		
Osimertinib																		
Accessibility																		
+ Non-small cell lung cancer																		
Ibrutinib																		
Accessibility																		
+ Mantle cell lymphoma																		
+ Chronic lymphocytic leukaemia (CLL)																		
+ Chronic lymphocytic leukaemia (CLL) (combo bendamustine and rituximab)																		
+ Chronic lymphocytic leukaemia (CLL) (combo obinutuzumab or rituximab)																		
+ Waldenström's macroglobulinaemia (combo rituximab)																		

GEN	General hospital		Medicines is accessible
SP	Specialized hospital		Medicine is not accessible
	None of the indications of this medicine is treated in this hospital		No context

Hungary (5 out of 17 observations [29%]). EAPs were more common in specialized hospitals (30 out of 41 observed [73%]) than general hospitals (12 out of 41 observed EAPs [29%]). Of the selected medicines, Nivolumab was the most accessible for the first time through in EAPs in 12 hospitals. Osimertinib was only accessible for the first time in through EAP in four hospitals and through reimbursed access in eight hospitals.

3.3 | Differences in access by indication

Eighteen hospitals were able to share details regarding the accessibility of the selected medicines according to indications. A full overview is presented in Table 3. All of the selected medicines were accessible in all countries in at least one hospital. This was not the case for all of the EMA-approved indications. Especially more recently approved indications were reported as 'not accessible'. Only one specialized hospital in Switzerland had all the selected medicines accessible for all selected indications. Across the countries, Niraparib was found to be the least accessible for ovarian cancer and Nivolumab the most accessible for non-small cell lung cancer. Olaparib was accessible for breast cancer and/or ovarian cancer in all hospitals except one general hospital in Belgium. Only in a specialized hospital in Switzerland, Olaparib was also accessible for prostate and pancreatic cancer. Combinations were less accessible than monotherapies. For example, Ibrutinib in combination with Bendamustine and Rituximab was only available to treat chronic lymphocytic leukemia in four hospitals. Ipilimumab and Nivolumab were both

accessible to patients in 14 hospitals and six countries. However, only in 11 hospitals they were accessible in combination to patients with melanoma and renal cancer.

4 | DISCUSSION

In this study, we report on patient access to innovative medicines in hospitals from Hungary, Italy, the Netherlands, Belgium, Switzerland and France. Considerable differences between hospitals, medicines and countries are found, despite the uniformity of EMA registration in the EU. Hospitals in Switzerland and the Netherlands that participated in this study generally reach faster patient access to the selected medicines compared to hospitals in Hungary and Belgium. Our analysis shows that a number of hospitals organize patient access before the national reimbursement decision, mostly in the context of EAPs. EAPs and off-label use are more prevalent in specialized hospitals compared to general hospitals, which translates into faster patient access. This is likely to be related with closer involvement in clinical research and/or centralization of services.

4.1 | The impact of the pricing and reimbursement process on actual patient access

Differences in access to medicines based on countries' healthcare systems are to be expected. However, the extend of the observed heterogeneity of access within and across countries is surprising. Underlying trends in the pricing and reimbursement system are likely to influence the time to access in our study. Delays in access for patients are likely to relate to the strategies of the MAH, in terms of the pricing and launch of their medicines, as well as the reimbursement processes of the NHA, in terms of national budget containment policies.

Pricing and launch strategies used to maximize profit for the MAH may result in delay and heterogeneity in patient access across Europe.[18,19] Since European countries engage in external reference pricing, the MAH uses strategic timing in their launch sequence to ensure that optimal prices dissimilate between coutries.[20] Consequently, the MAH also launches faster in bigger European pharmaceutical markets like Italy, France and the Netherlands.[21] These strategies may contribute to delayed patient access specifically in countries with a smaller market size (lower population/less profitable).[21] Especially when the evidence requirements of the NHA's are not (completely) met, the reimbursement process stops. Uncertainty about the clinical value of the treatment in combination with a high price might also create hurdles in the reimbursement process.[22-24] For medicines in high medical need, some countries allow the collection of additional safety and efficacy data during EAPs to meet these requirements.[22,25] To avoid strategic launching by the MAH, a mandatory submission deadline at EU level could be implemented. Early dialogues between the NHA and the MAH about expected endpoints from clinical development during the R&D process as well as more collaboration and information sharing regarding pricing and reimbursement decisions between NHA's could smooth the process to reimbursed access.

As there is no significant association between clinical benefit and (list) prices of oncology medicines in European countries, misalignment in pricing between the NHAs and the MAHs contributes to delay in patient access.[22,26,27] To protect healthcare budgets in the light of high price demands, NHAs have implemented budget containment strategies for expensive and high budget impact medicines in their pricing and reimbursement regulations.[28] According to an EU-directive, NHAs need to finalize their pricing and reimbursement decisions within 180 days.[29] However, the requested high prices of the innovative medicines in combination with budget containment policies often result in extended negotiation time.[30,31] For example in the Netherlands, the ministry can decide to temporarily put expensive medicines "on hold" based on specific criteria for national reimbursement to negotiate on an acceptable price with the pharmaceutical company.[32] All of our selected medicines were for at least one indication put "on hold" explaining the lengthy reimbursement time for our sample (x: 3.8 years; SD: 2.0).[29] This national example demonstrates that NHA's and MAHs sometimes fail to follow the EU-directive, amplifying the variation in actual patient access between countries.[29]

4.2 | Regional and hospital specific reasons that delay patient access to medicines

Organizational and strategic factors are likely to influence priorities at regional-, hospital- or physician level and hence add to the variation of access within countries.

At regional level, the fragmentation of decision-making may lead to divergent judgments and increase the risk of inequity in access within a country.[5,33] From our sample, this is likely to be most relevant for patient access in Italy and Switzerland, where healthcare decisions are regionally organized.[34] In Switzerland, cantons are in charge of issuing and implementing a large proportion of health-related legislation, including the reimbursement of medicines.[33,35] In Italy, a number of regional assessment steps follow the centralized authorization of inpatient medicines.[36] Moreover, the regions are the budget holders and responsible for the local provision of healthcare.[37] While the regional and fragmented organization of the healthcare system are used as an explanation when discussing our results with Swiss and Italian pricing and reimbursement experts, we do not observe a quantitatively higher variability of access in Italy and Switzerland compared to other countries in our sample.

At hospital- and physician level, the speed of guideline adaptation, budget decisions and other priorities also affect the local accessibility of treatment options. Hospital strategy influences access as well because hospitals may concentrate on certain tumour types, have to bear financial risks by dispensing the medicines or have to meet strict quality criteria formulated by health insurance companies. In our data,

TABLE 4 Recommendations.

- Implement a mandatory submission deadline at EU level at EMA registration, to avoid strategic launching by the MAH.
- Intensify collaboration and information sharing regarding P&R decisions between National Healthcare Agencies.
- Foster early dialogues regarding evidence requirements between the NHA and the MAH (early HTA) to increase the collection of early data and smoothen the pricing and reimbursement process
- Implement specific national P&R timelines and increase resources and capability at the NHAs to ensure that the EU directive of 180 days is met.
- Develop a transparent platform per country for physicians that report in which facilities innovative treatments are accessible through EAPs and off-label use to stimulate efficient referral agreements.
- Invest in and install structured programs to collect real world data through EAPs and use these for HTA and reimbursement decisions and price (re)negotiation
- Harmonize EAP regulations for medicines in high medical need to bridge the gap between EMA-approval and actual patient access across EU-countries

this is reflected for Ipilimumab, which is only accessible in one of the three Dutch hospitals due to strategic agreements between the organizations. Similarly, if treatment alternatives are available, for example in the case of Olaparib and Niraparib, hospitals make strategic priorities balancing clinical and economic considerations.[38] Some specialized treatments require training of staff, quality and safety measures and specialized treatment teams. Not every general hospital is able to fulfil these needs for adequate oncology care. Often, there are arrangements for referral policies to ensure access to every patient. Note that before participating, we verified that at least 60% of our indications of interest were treated in the hospitals. Moreover, if there is a lack of clarity on the positioning of a new medicine in a treatment pathway, physicians may be more reluctant to prescribe it.[39,40] In the presence of strong variation of access at regional and local level, clear and efficient referral agreements between the hospitals are especially important.[41]

4.3 | The benefits and risks of early access programs in patient access

Our results show that access before a national reimbursement decision is most frequently established in the context of EAPs and off-label use. EAPs are a valuable instrument to facilitate patient access when the standard reimbursement processes are slow to provide access due to the previously outlined reasons. In the current regulatory system, EAPs bridge the gap between closure of clinical trials or EMA-authorization and reimbursed access for medicines in high medical need. A good example is France, where the NHA finances EAPs and all of the selected medicines in this study were first accessible in the context of an EAP.[42] This is also reflected in the comparable quick average time to patient access of 0.3 years after EMA-authorization.

However, their unequal prevalence and implementation is also likely to be a major factor associated with variations in time to patient access.[43] Unequal implementation of EAPs exist due the MAHs' willingness to initiate the program and provide the medicines, the national criteria and regulations of NAHs', and the local policies of the hospitals.[43,44] Moreover, there are certain drawbacks associated with these programs. EAPs are usually initiated and paid by MAHs,[43] which are likely to prioritize attractive markets in terms of pharmaceutical revenue and regulatory transparency. Concerns exist that EAPs weaken the NHAs position during the pricing and reimbursement negotiations as physicians and patients get used to the treatments in EAPs and discontinuation of access to new patients should be avoided.[15]

EMA approval does not necessarily lead to a reimbursement status. A systemic evaluation of oncology drug approvals by the EMA in 2009 to 2013 showed that 57% (39/68) of drugs entered the market without evidence of improved overall survival or quality of life.[45] EAPs might also be organized for drugs with a low level of evidence. For example, Dostarlimab received conditional EMA-approval based on a phase I-II trial for patients with advanced or recurrent dMMR/MSI-H endometrial cancer and became accessible through an EAP in the Netherlands. Because the EAP has ended and the data is too immature, no reimbursement is granted and patient access is discontinued until further evidence is published.[46] Another important drawback are also safety concerns, as patient access before EMA-authorization is reported in multiple countries and could increase the safety risks for patients.

Access to innovative medicines with high medical need have to be timely accessible to patients. To achieve this, better regulation for EAPs at national, regional and local level is needed to harmonize access to these medicines within a country. While in the EU context, healthcare regulation lies mostly within the national competency, smaller EU markets would benefit from a greater harmonization of EAPs for medicines based on recommendations by the EMA. The use of real world data collected through the EAPs could provide additional clarity for health technology assessment, reimbursement decisions and price (re)negotiation.[22,25]

4.4 | Recommendations

Based on our research, the following recommendations would improve equity in actual patient access between and within European countries for medicines in high medical need (Table 4).

4.5 | Strengths and limitations

Our study has a number of limitations. First, the number of participating hospitals is limited, and findings can consequently not be generalized to the whole country (especially for Italy and France). Because of national or local quality and safety measures, difference

in accessibility between hospitals can also be based on well-considered policies and is not necessarily in the patients disadvantage. Second, depending on the detail of the general hospital databases, some hospitals could not provide information for all items (eg, details regarding indications). Third, even though perceived as correct by the hospital pharmacists, a degree of reporting error cannot be excluded. During cross-validation between the national reimbursement dates, the context and the time to first access some irregularities are observed. As the hospital pharmacists filled the survey in to their by best knowledge using the hospital database and further context was unknown, we chose to present the data as collected. Despite of these shortcomings, our results provide an insightful overview of the situation of cancer patients' access to innovative drugs across Europe. Our findings are not based on sales data or reimbursement data and this is the first study to report patient access acknowledging access through EAPs and off-label use. As our data is not nationally aggregated but displayed at hospital level, our findings reflect the local patient's perspective rather than a national perspective.

4.6 | Conclusion

High heterogeneity in patient access to new anticancer medicines are observed across hospitals in- and between European countries. Possible reasons for this variation could be the different launch and pricing strategies and budget containment policies, and varying regulations at national, hospital and physician level. By optimizing the pricing and reimbursement timeline, stimulating collaborations between the NHAs and MAHs, and bridging the gap to reimbursed access using nationally harmonized and data-generating EAPs, timely and equitable patient access to innovative cancer treatments across Europe could be improved.

AUTHOR CONTRIBUTIONS

The work reported in the paper has been performed by the authors, unless clearly specified in the text. Concept and planning of the work described (Julie M. Vancoppenolle, Nora Franzen, Simone N. Koole); acquisition, analysis and interpretation of the data (Julie M. Vancoppenolle, Nora Franzen); drafting and/or critical revision of the manuscript (Julie M. Vancoppenolle, Nora Franzen, Simone N. Koole, Valesca P. Retèl and Wim H. van Harten); and approved the final submitted version of the manuscript (Julie M. Vancoppenolle, Nora Franzen, Simone N. Koole, Valesca P. Retèl and Wim H. van Harten).

ACKNOWLEDGEMENT

We are sincerely grateful to all participating hospitals and hospital pharmacists, the European Fair Pricing Network and the Organization European Cancer Institutes.

FUNDING INFORMATION

This work was supported by the European Fair Pricing Network.

CONFLICT OF INTEREST STATEMENT

The authors have nothing to disclose for the work under consideration for publication. Prof. van Harten reported non restricted grants from Novartis, Intuitive Surgical and Agendia all ended over 3 years ago, Prof. Retèl reported non restricted grants from Intuitive and Agendia, all ended over 3 years ago, outside the submitted work. The other authors have nothing to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

ETHICS STATEMENT

The study protocol was approved by the Institutional Review Board of the Netherlands Cancer Institute and participants gave their consent to be included in this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Vancoppenolle JM, Franzen N, Koole SN, Retèl VP, van Harten WH. Differences in time to patient access to innovative cancer medicines in six European countries. *Int J Cancer*. 2023;1-9. doi:10.1002/ijc.34753