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RESEARCH ARTICLE

# Equity, barriers and cancer disparities: study of the Spanish Society of Medical Oncology on the access to oncologic drugs in the Spanish Regions

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**Abstract**
*Purpose* The Spanish Society of Medical Oncology (SEOM) has conducted a study on the access to oncologic drugs across the 17 Spanish Regions with the aim of identifying potential heterogeneities and making proposals for eliminating the barriers identified at the different levels.
*Methods* An Expert Panel made up of medical oncologists designed a survey on certain indications approved for 11 drugs in the approach of breast cancer, melanoma, lung cancer, prostate cancer and support treatment. This survey was sent to 144 National Health System (NHS) hospitals.
*Results* 77 hospitals answered the survey. The information modules analysed were: scope of the Commission that establishes binding decisions related to drug access; conditions, stages and periods of drug application, approval and administration processes; barriers to accessing drugs.
*Conclusions* The study shows variability in drug access. The SEOM makes proposals addressed to reducing the differences identified and homogenizing drug access conditions.

**Keywords** Antineoplastic agents · Heterogeneity · Barriers · Inequities · Spain

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## Introduction

Cancer represents one of the main health concerns. At the world level, 14 million of new cases were detected and 8.2 million of deaths were related to cancer in 2012 [1]. The prevision for the next 20 years is an incidence increase of around 70 % [2].

In Spain, despite the variability in the quality of epidemiological data between the different regions, due to the heterogeneity of the records used, an estimation of 241,284 new cases were detected in 2014 (145,813 in men and 95,471 in women), the most frequent tumour was colon and rectal cancer, followed by prostate, lung and breast cancer [3].

Although medical advances in the treatment, prevention measures and early diagnosis are significantly reducing mortality and improving life quality of patients with cancer [4], this disease is in Spain, the main cause of death in men and the second one in women, following cardiovascular disease [5].

The use of drugs in the National Health System requires a series of stages for them to become accessible to patients. In the European Union (EU), oncologic drugs undergo a centralised procedure, so that once authorised by the European Medicines Agency (EMA), authorisation for commercialization is valid in all the EU countries [6]. In Spain, subsequently to the approval by the Spanish Agency of Medicines and Medical Devices (AEMPS), pricing and reimbursement conditions are established, although in the case of some drugs the following stage is the elaboration of the so-called *Therapeutic Positioning Report* (*Informe de Posicionamiento Terapéutico—IPT)* aimed to establish the basis for the selective funding by consensus of health professionals and, if appropriate, for pricing and to act as a reference for any action related to the acquisition and promotion of a rational use [7]. The price, within the public health system, is established by the *Inter-Ministerial Commission for Medicines Pricing (Comisión Interministerial de Precios de los Medicamentos—CIPM)*. Afterwards, the Regions cover the pharmaceutical expense, as a part of their budget. The Regions' Health Departments, together with the bodies responsible for the regions' public health system management, have prescription information and monitoring systems, and promote initiatives for managing the use of drugs.

Patient access to oncological drugs varies widely between the main developed countries. In 2014, Spain stood out together with Japan and South Korea for the limited access to new drugs against cancer commercialised at the world level; they had only accessed half of the drugs commercialised during the period 2009–2013 [8].

A study reports that, due to the existence of different criteria in the decisions on the acquisition and use of innovative oncologic treatments in the different regions, a problem of equity arises in the access to therapeutic innovation for patients from different territories and even between different hospitals from the same region [9].

Within this context, and based on its commitment with the best healthcare delivery to cancer patients in equity conditions, the Spanish Society of Medical Oncology (SEOM) engaged in this study on the access to oncologic drugs in the Regions. The aim of the study is to analyse oncologic drugs traceability in terms of times and mechanisms of approval at different levels. The objectives are to study possible heterogeneities in patient access to different approved drug indications throughout the whole country, establish a solid starting point for solving potential inequities, and issue proposals for eliminating the barriers identified at the different levels (national, regional and hospital).

## Materials and methods

An electronic survey was designed aimed to analyse the standard process undergone by oncologic drugs from approval at the European level by the EMA to first prescription at hospitals in terms of required stages, their duration and the involved agents. A Panel of Experts was established for the elaboration of the survey, made up by medical oncologists affiliated to SEOM who, additionally, contributed to the validation of the survey through the conduction of a pre-test in 5 hospitals from different regions. The pre-test objectives were to validate the adequacy of the survey for collecting the appropriate information to carry out a quality analysis of drug access, and to analyse its simplicity to be completed by medical oncologists. It was considered that information would be obtained in many centres thanks to the collaboration of several oncologists (for being specialists in the different pathologies included), as well as of pharmacists from the Hospital Pharmacy Service.

The survey was uploaded to an online platform for facilitating its completion. An analysis of the state-of-the-art was carried out with the resulting data which allowed identifying areas of improvement and issuing proposals for eliminating the barriers identified. Another Panel of Experts reviewed and validated the conclusions of the study.

With the aim of analysing the different access conditions, the survey included the approved indications of 11 drugs for the treatment of breast cancer (pertuzumab, everolimus, nab-paclitaxel eribulina), melanoma (ipilimumab), prostate cancer (abiraterona, cabazitaxel), lung cancer EGFR + (gefitinib, erlotinib, afatinib), and support treatment (denosumab) (Table 1). The reason for selecting

**Table 1** Approved indications of the 11 analysed drugs in this study

| | |
|---|---|
| Breast cancer | |
| Pertuzumab | Combined with trastuzumab and docetaxel for the treatment of adult patients with HER2-positive locally recurrent unresectable or metastatic breast cancer, who have not received previous anti-HER2 or chemotherapy treatment for metastatic disease |
| Everolimus | Treatment of advanced breast cancer, with hormone receptor-positive, HER2/neu-negative, combined with exemestano, in postmenopausal women not suffering from a symptomatic visceral disease, after recurrence or progression to a non-steroidal aromatase inhibitor |
| Nab-paclitaxel | Indicated in monotherapy for the treatment of metastatic breast cancer in adult patients where first line treatment for metastatic disease has failed and where standard therapy with anthracycline is not indicated |
| Eribulina | Treatment of patients with locally advanced or metastatic breast cancer with progression after of, at least, two chemotherapy regimens for advanced disease. Previous therapy must have included anthracycline and taxane in adjuvant or metastatic framework, unless these treatments were not appropriate for the patients |
| Melanoma | |
| Ipilimumab | Treatment of advanced melanoma (unresectable or metastatic) in adults |
| Support treatment | |
| Denosumab | Prevention of elements related to skeleton (pathologic fracture, bone radiotherapy, spinal cord compression or bone surgery) in adults with solid tumour bone metastasis |
| Prostate cancer | |
| Abiraterona | Treatment of prostate metastatic cancer resistant to castration in adult men where disease has progressed during or after a docetaxel-based chemotherapy regimen |
| Cabazitaxel | Combined with prednisona or prednisolona it is indicated for the treatment of patients with metastatic hormone-resistant prostate cancer, previously treated with a docetaxel-containing therapy |
| Lung cancer EGFR + | |
| Gefitinib | Treatment of adult patients with locally advanced or metastatic non-microcytic lung cancer with activating mutations of EGFR-TK |
| Erlotinib | Non-microcytic lung cancer: first line treatment of patients with locally advanced or metastatic non-microcytic lung cancer with activating mutations of EGFR |
| Afatinib | Indicated as monotherapy in the treatment of adult patients with locally advanced or metastatic non-microcytic lung cancer with activating mutations of epidermal growth factor receptor (EGFR) not previously treated with a tyrosine-kinase inhibitor of EGFR |

those drugs and indications was based on both their innovative characteristics and the prevalence of target population. The period of time considered for the analysis was 2014.

Open questions were combined with multiple choice (multiple answer) questions and single answer questions.

Questions were grouped in six modules: centre's data, data on drugs for the treatment of breast cancer, data on drugs for the treatment of melanoma, data on drugs for support treatment, data on drugs for the treatment of lung cancer and data on drugs for the treatment of prostate cancer. The module on the centre collected information on its reference population, level of complexity, and information on the Commission where binding decisions related to drug access were taken: scope; number of members; participation of the Medical Oncology Department, the Hospital Pharmacy Department, the Medical Director and the Regional Health Service. The objective of this module was to determine, in the opinion of each centre, which of the different commissions determined finally the actual use conditions of each drug and the degree of information on its composition. The modules about drugs provided detailed information on the indication included in the questions, and the *IPT* if available. In this modules, information was collected about the date of application of the drug to the binding Commission for its use in the centre for that indication; the date of assessment of the drug for that indication by the binding Commission; the outcome, that is the approval/refusal of the use of the drug in the centre; in the case of approval, the conditions of use approved by the binding Commission; utilization criteria; the date of first prescription of the drug for that indication and the number of patients treated with the same drug for that indication in the year 2014. The objective of this module of questions was to analyse the differences between centres regarding the duration of each stage of the process from approval by EMA to first prescription, the process' transparency and the reasons—in the opinion of oncologists—for explaining use conditions other than the approved. The detail of the questions is included in Appendixes 1 and 2.

For the analysis of the time passed between the different stages required for accessing drugs within their correspondent indications, we considered the approval dates by

the EMA and *the Spanish Agency of Medicines and Medical Devices* (AEMPS), and the date where Pricing and Reimbursement Conditions (PRC) were established, these data were requested to pharmaceutical companies commercialising the drugs. The median of months passed from the date of PRC establishment to the drug's first prescription for the corresponding indication, as well as, the minimum and the maximum number of resultant months based on the answers from the centres participating from each region, were determined for each drug and indication. The analysis did not consider first prescription dates precedent to the date of PRC establishment. Likewise, the global median of months passed from the date of PRC establishment to the first prescription in the centre was analysed for each drug.

Access to the survey was available between April and July 2015, throughout which a monitoring of the completion process was carried out, as support for solving potential doubts; e-mail and telephone assistance on questions interpretation or technical problems was provided and a follow up of submission deadlines was done. Quality control was done by providing a summary of the answers to each centre for its review.

Furthermore, data on the region's consumption in 2014 were requested to the pharmaceutical companies commercialising the drugs subject of study. Once the required confidentiality agreements were signed, we had access to consumption data provided in different variables: units, sales and % of sales of each region compared to the national territory of the following drugs: pertuzumab, nab-paclitaxel, denosumab, ipilimumab, abiraterona, gefitinib, erlotinib and afatinib; data were standardised to 100,000 inhabitants.

## Results

A total of 144 national health system hospitals from the 17 regions were invited to participate in the survey, through e-mail and telephone contact. The survey was completed by 77 hospitals, which represent 53.5 % of the contacted centres. From the participant hospitals, 48.1 % presented level 3 of complexity, followed by 37.7 % of level 2 and 14.3 % of level 1. Concerning the reference population, 27.3 % of the participating centres covered an area of 300,001–500,000 inhabitants, 16.9 % an area of 250,001–300,000 inhabitants, 14.3 % an area of 500,001–700,000 inhabitants, 11.7 % an area of more than 700,001 inhabitants, 10.4 % an area of 200,001–250,000 inhabitants, 10.4 % an area of 150,000–200,000 inhabitants, 5.2 % an area of 100,0001–150,000 inhabitants, 2.6 % an area of <50,000 inhabitants and 1.3 % an area of 50,001-100,000 inhabitants.

*Analysis of the scope of the Commission who establishes binding decisions related to drug access* According to the answers from the participating centres, the most frequent scope was the own hospital (65.3 %), followed by the region (27.8 %). In 5.6 % of the centres Commissions with more than one scope existed.

*Analysis of the procedure of applying for drug use to the binding Commission* 22.1 % of the answers provided by the centres stated that the use of some of the 11 drugs-indications subject of analysis had not been requested to the binding Commission. The causes include: excessive delay; demotivation due to previous refusals of other drugs; expensive drugs require an individual report regardless of their inclusion in the hospital's guidelines; high impact drugs do not require application to the Pharmacotherapy Commission, although they are prescribed according to rigorous practice and based on therapy recommendation guidelines and IPT; drug access regulation is done at the regional level and do not require an application; the drug is not requested because the patient is referred to the reference centre; the drug is directly requested to the Hospital Pharmacy Service; low therapeutic benefit is detected; absence of candidate patients.

*Analysis of drug approval by the binding Commission* The dates of PRC establishment of the 11 drugs analysed in the study ranged from 2009 (corresponding to the most ancient) to June 2014 (corresponding to the most recent). 16.1 % of the answers provided by the centres reported that, to the date of completion of the survey, some of the 11 drugs-indication had not been approved yet for their use in the centre (10.2 % of answers) or were still pending of assessment (5.9 % of answers). From this 16.1, 12.3 % of answers reported the unavailability of procedures for accessing some of the drugs already approved by the Spanish Ministry of Health, Social Services and Equity (MSSSI) and 44.7 % reported the unavailability of mechanisms for referring patients to other centres so they could receive these drugs.

*Analysis of the average period from the date of PRC establishment to drug prescription* (Table 2) In relation with the drugs analysed for approaching breast cancer, the median of months from PRC establishment to first prescription date, ranged from 6 (pertuzumab) to 23 (nab-paclitaxel). For pertuzumab variability ranged from 2 (Navarra) to 7 months (Madrid; Aragón). For nab-paclitaxel variability ranged from 17 (Aragón) to 58 months (Castilla y León). For eribulina it ranged from 1 (Cantabria) to 16 months (Comunidad Valenciana). The date of PRC establishment for everolimus was not available, therefore, the analysis of this drug was done considering

**Table 2** Time from PRC establishment date to first prescription of the analysed drugs

| Regions | Total population (INE, 2014) | *C* | Pertuzumab | | | | Everolimus* | | | | Nab-paclitaxel | | | | Eribulina | | | | Ipilimumab | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* |
| Andalucía | 8.402.305 | 18 | 6 | 4 | 10 | 7 | 21 | 18 | 27 | 6 | 45 | 29 | 54 | 5 | 13 | 2 | 17 | 3 | 8 | 2 | 17 | 5 |
| Aragón | 1.325.385 | 7 | 7 | 7 | 7 | 1 | 3 | 3 | 3 | 1 | 17 | 17 | 17 | 1 | 13 | 13 | 13 | 1 | 10 | 10 | 10 | 1 |
| Asturias | 1.061.756 | 2 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | 27 | 27 | 27 | 1 |
| Baleares | 1.103.442 | 3 | 5 | 5 | 5 | 1 | 20 | 19 | 20 | 2 | 21 | 19 | 22 | 2 | 8 | 8 | 8 | 1 | 20 | 18 | 22 | 2 |
| C. de Madrid | 6.454.440 | 23 | 7 | 4 | 9 | 4 | 17 | 13 | 31 | 4 | 22 | 15 | 33 | 4 | 5 | 2 | 7 | 2 | 12 | 4 | 24 | 6 |
| C. La Mancha | 2.078.611 | 7 | – | – | – | – | 4 | 4 | 4 | 1 | 22 | 22 | 22 | 1 | – | – | – | – | 26 | 26 | 26 | 1 |
| C. Valenciana | 5.004.844 | 20 | 4 | 1 | 7 | 3 | 12 | 8 | 19 | 4 | 40 | 22 | 48 | 5 | 16 | 16 | 16 | 1 | 12 | 4 | 32 | 6 |
| Canarias | 2.104.815 | 4 | – | – | – | – | – | – | – | – | – | – | – | – | 14 | 14 | 14 | 1 | – | – | – | – |
| Cantabria | 588.656 | 2 | – | – | – | – | 25 | 25 | 25 | 1 | 26 | 26 | 26 | 1 | 1 | 1 | 1 | 1 | 10 | 10 | 10 | 1 |
| Castilla y León | 2.494.790 | 8 | 6 | 5 | 7 | 2 | 24 | 16 | 31 | 2 | 58 | 42 | 64 | 2 | 11 | 4 | 18 | 2 | 19 | 15 | 23 | 2 |
| Cataluña | 7.518.903 | 25 | 2,5 | 1 | 7 | 5 | 17 | 15 | 26 | 6 | 23 | 1 | 40 | 6 | 6 | 4 | 8 | 5 | 20 | 16 | 25 | 3 |
| Extremadura | 1.099.632 | 4 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Galicia | 2.748.695 | 9 | 5,5 | 1 | 10 | 2 | 32 | 32 | 32 | 1 | – | – | – | – | 15 | 15 | 15 | 1 | 20 | 20 | 20 | 1 |
| La Rioja | 319.002 | 1 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Navarra | 640.790 | 1 | 2 | 2 | 2 | 1 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| País Vasco | 2.188.985 | 6 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| R. de Murcia | 1.466.818 | 3 | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Global medianl (months) | – | – | 6 | | | | 18 | | | | 23 | | | | 12 | | | | 19 | | | |

| Regions | Denosumab | | | | Abiraterona | | | | Cabazitaxel | | | | Gefitinib | | | | Erlotinib | | | | Afatinib | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* |
| Andalucía | 24 | 23 | 30 | 3 | 5 | 3 | 11 | 3 | 7 | 6 | 35 | 3 | – | – | – | – | – | – | – | – | 9 | 7 | 10 | 2 |
| Aragón | 11 | 11 | 11 | 1 | – | – | – | – | 11 | 10 | 11 | 2 | – | – | – | – | – | – | – | – | – | – | – | – |
| Asturias | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Baleares | 9 | 5 | 13 | 2 | 22 | 16 | 25 | 2 | 24 | 22 | 28 | 3 | 11 | 10 | 52 | 3 | – | – | – | – | 6 | 5 | 6 | 2 |
| C. de Madrid | 9 | 4 | 13 | 4 | 31 | 18 | 40 | 5 | 5 | 3 | 21 | 3 | 27 | 3 | 32 | 4 | 19 | 19 | 19 | 1 | 5 | 2 | 10 | 5 |
| C. La Mancha | 17 | 11 | 23 | 2 | – | – | – | – | 44 | 44 | 44 | 1 | 5 | 5 | 5 | 1 | – | – | – | – | 9 | 9 | 9 | 1 |
| C. Valenciana | 3 | 1 | 28 | 5 | 6 | 2 | 9 | 4 | 16 | 2 | 22 | 6 | 14 | 3 | 39 | 4 | – | – | – | – | 11 | 10 | 11 | 2 |
| Canarias | 20 | 20 | 20 | 1 | 16 | 16 | 16 | 1 | 27 | 27 | 27 | 1 | 51 | 51 | 51 | 1 | – | – | – | – | – | – | – | – |
| Cantabria | 7 | 7 | 7 | 1 | 22 | 22 | 22 | 1 | 29 | 29 | 29 | 1 | 17 | 17 | 17 | 1 | 1 | 1 | 1 | 1 | 12 | 12 | 12 | 1 |
| Castilla y León | 15 | 4 | 26 | 2 | 28 | 28 | 28 | 1 | 32 | 32 | 32 | 1 | – | – | – | – | – | – | – | – | 10 | 10 | 10 | 1 |
| Cataluña | 3 | 1 | 9 | 5 | 20 | 1 | 38 | 6 | 18 | 6 | 36 | 7 | 16 | 1 | 35 | 6 | – | – | – | – | 8 | 4 | 10 | 5 |
| Extremadura | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Galicia | 5 | 5 | 5 | 1 | – | – | – | – | 2 | 2 | 2 | 1 | 17 | 17 | 17 | 1 | – | – | – | – | – | – | – | – |

**Table 2** continued

| Regions | Denosumab | | | | Abiraterona | | | | Cabazitaxel | | | | Gefitinib | | | | Erlotinib | | | | Afatinib | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* | Med. | Min. | Max. | *N* |
| La Rioja | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Navarra | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| País Vasco | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| R. de Murcia | – | – | – | – | – | – | – | – | 34 | 34 | 34 | 1 | – | – | – | – | – | – | – | – | – | – | – | – |
| Global medianl (months) | 9 | | | | 21 | | | | 21 | | | | 16 | | | | 10 | | | | 9 | | | |

Median of months, minimum and maximum period and number of answers by Regions

*C* number of centres invited to complete the survey; *Med* median, months; *Min* minimum period, months; *Max* maximum period, months; *N* answers

* Everolimus: time from AEMPS approval to first prescription has been considered

the date of approval by the AEMPS, so conclusions are not comparable to the rest of the drugs.

Concerning the median of months passed from notification of PRC by the MSSSI to first prescription of ipilimumab, the period ranged from 8 (Andalucía) to 27 months (Principado de Asturias). For denosumab, variability ranged from 3 (Comunidad Valenciana; Cataluña) to 24 months (Andalucía).

Concerning the drugs analysed for the treatment of prostate cancer, both showed a median period of 21 months. Individually, in abiraterona (for post-chemotherapy indication) variability ranged from 5 (Andalucía) to 31 months (Madrid) while in cabazitaxel, variability ranged from 2 (Galicia) to 44 months (Castilla la Mancha).

Concerning the drugs analysed for the treatment of lung cancer, variability in the median of months ranged from 9 (afatinib) to 16 months (gefitinib). When analysing each drug separately, a high variability was also observed among regions concerning the median of months from PRC establishment to prescription in each centre. Thus, for gefitinib variability ranged from 5 (Castilla la Mancha) to 51 months (Canarias), for erlotinib it ranged from 1 (Cantabria) to 19 months (Madrid) and for afatinib it ranged from 5 (Madrid) to 12 months (Cantabria).

*Analysis of the stages' duration from drug approval by EMA to first prescription (median and ranges)* (The analysis did not consider first prescription dates precedent to the date of PRC establishment for avoiding considering drug prescription previous to commercialisation in Spain, such as compassionate drug use in research). According to the information provided by the centres on the date of drugs' first prescription, the median of months from approval date by the EMA/AEMPS to first prescription was 24 months, with 212 answers received, the minimum period reported in the survey was lower than 1 month (1 answer) and the maximum 74 months (1 answer).

Concerning the period of months from approval by AEMPS to the date of publication of the IPT, if appropriate, a median of 24 months was registered.

*Transversal analysis of drug approval condition.* From the total of answers provided with relation to drug approval, 54.2 % reported that some of the 11 drugs were approved with the same conditions established in the Data Sheet or in the IPT (if available). From the other 45.8, 21.7 % reported that they accessed to some of the 11 drugs analysed with different conditions than the ones established in Data Sheet/IPT, and 16.1 % reported that some of the 11 drugs had not been approved or were pending of approval (Fig. 1).

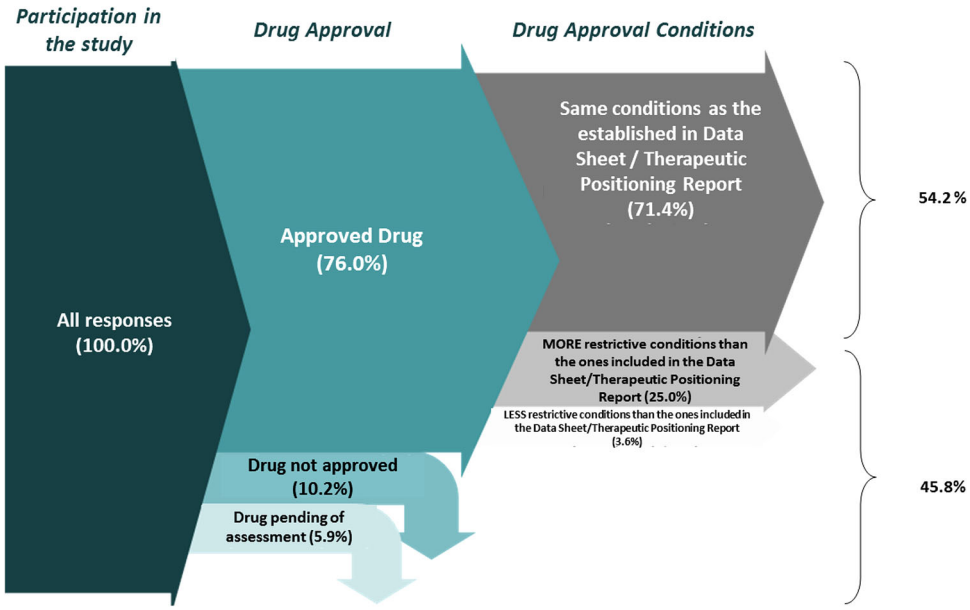


**Fig. 1** Centres responses distribution at different stages of the drugs approval and access process since their request to the binding Pharmacy and Therapy Commission (% of total responses)

*Identification of barriers in drug access* 37.8 % of answers reported the existence of barriers or limitations to accessing some of the drugs subject of study. The most frequent barriers reported by the centres were the application of more restrictive criteria than the established in the Data Sheet and IPT and the existence of a Regional Commission of Harmonization, due to the delay this could involve in the approval process. Detailed information on the main barriers identified is included in Table 3.

*Consumption results by drugs and by Regions* Significant differences were observed in the consumption profile of the same drug in the different Regions, which did not depend on demographic characteristics and were difficult to explain only by clinical variability. Detailed information on the results is included in Appendix 3.

## Discussion

SEOM, referent society for Medical Oncology in Spain, from its commitment with the specialty and the promotion of the best cancer care delivery, decided to boost the elaboration of this study on patient access to oncologic drugs. SEOM considers that the identification of potential inequities and the proposal of improvements contributing to ensure the access to drugs in equal conditions throughout the national territory is a major priority. All this without prejudice of the measures trending to rationalize prescription and use of drugs and health products taken by the regions in the course of their responsibilities, as established in the modification of Article 88.1 of December 2014 of Law 29/2006 on guaranties and rational use of drugs and health products. SEOM denounced before the Ombudsman, in April 2014, the delays in the introduction of new drugs and territorial inequities in drug access [10]. The Spanish Society of Hospital Pharmacy has also shown its concern to this regard and has declared in favour of promoting a rapid access to oncologic drugs for patients with clinical benefit, and of promoting equity in the access to health resources [11].

At the European level, this concern has been reported in recent studies showing that the access to oncologic drugs in the European Union is significantly different in the member states, and there is a need of carrying out initiatives focused in ensuring equal access to patients in the whole European Union [12].

The main limitations identified in the study are the margin of error due to the lack of completion of the whole survey by the centres invited to participate and the limited number of answers received for some of the items, which has not allowed comparisons and conclusions. Nevertheless, drug consumption patterns provided by pharmaceutical laboratories represent the whole Spanish population and the centres having answered the survey represent oncologic care delivery to half of the Spanish population.

Although the study has focused only in 11 drugs, and the answers obtained represent slightly more than 50 % of the centres, obtained data show three major concerns related to patients' accessibility to the oncologic drugs analysed. The detail of the participation per Region is included in Appendix 4.

The first one is the long time passed between drug approval by EMA and Pricing and Reimbursement

**Table 3** Main access barriers identified by participant centres

| Scope | Barrier identified |
|---|---|
| Barriers related to the existence of regional Commissions | Drug to be approved by the Regional Harmonization Commission |
| | Drug use is authorised by a Regional Sub-commission. |
| | Drug is pending of assessment by the Regional Pharmacy Commission |
| Barriers related to budgetary issues | High price of the drug and lack of hospital budget |
| | Implantation of debt ceiling systems |
| | Approval of drugs with the same indication and lower price |
| Barriers related to the centres' specific procedures of application/approval and use | Need of a justification report for each patient |
| | Drug not included in the centre's Pharmacotherapy Guidelines |
| | Use of the drug in exceptional conditions |
| | Compulsory referral of patients to the reference centre |
| | Following to the medical oncologist report, the Hospital Pharmacy Service elaborates another report and authorisation is requested to Medical Director |
| | Drug assessment in a Special Commission for high economic impact drugs |
| | Delay in the application to the Commission where binding decisions related to drug access are taken |
| | Delays in the approval process |
| | Drug has been approved in conditions which are more restrictive than the ones in the Data Sheet and Therapeutic Positioning Report |

Conditions establishment in Spain, which is a "sine qua non" condition for prescription.

The second one is variability between Regions and between different centres from the same Region, concerning the time from Pricing and Reimbursement Conditions establishment to first prescription. Based on the received answers, drugs showing higher medians of time from Pricing and Reimbursement Conditions establishment to first prescription are nab-paclitaxel (23 months), abiraterona (21 months), cabazitaxel (21 months) e ipilimumab (19 months). Analysis of months passed from approval by EMA to first prescription shows that period ranges from a period lower than 1 month to 74 months, with a median of 24 months.

The third concern identified is variability between Regions and between centres from the same Region, concerning the scope of the assessment Commissions where binding decisions related to drug access are taken as well as the lack of information and homogeneity in the criteria for modifying prescription conditions within the mentioned Commissions. 37.8 % of participants identified access barriers, mainly associated to the high number of assessment commissions and to the need of elaborating a specific report for each patient despite the previous establishment of prescription conditions by a commission, which are often more restrictive than the ones approved by EMA. This arbitrariness involves that in 45.8 % of the centres drugs are either approved in conditions which are more restrictive than the ones in the Data Sheet/IPT or not approved, which clearly conditions variability in the access, and makes final prescription conditions heterogeneous and more restrictive in general.

Variability in the decision to include new drugs by Hospital Commissions in Spain has also been subject of other studies [13]. SEOM considers it is relevant that, despite the existence of common documents such as the EMA approval conditions or the IPT, it is at the hospital level where binding decisions related to drug access are more often taken (65.3 %), which causes heterogeneity in each centre's services portfolio and a vulnerability situation both for patients and doctors, as they cannot access drugs in already approved conditions in our country. Furthermore, we consider it is a priority to analyse the potential impact of these facts on patients' health outcomes depending on the identified access differences. Therefore, we defend that, in harmony with the criteria established for drug funding, final use conditions must arise from a national consensus and be compulsory. It is important to remind that the National Government has exclusive authority for determining which drugs are fundable as well as the funding conditions. Roya-Decree-law 16/2012, of the 20th of April, on urgent measures for ensuring sustainability of the National Health System and improving the quality and safety of services provided, established that: "Regions will not be allowed to establish, unilaterally, specific singular reserves of prescription, provision and funding of drugs or health products".

On the other hand, the survey conclusions are consistent with the striking differences between Regions identified

from the analysis of drug consumption per capita and per Region according to the data provided by the pharmaceutical industry.

As a result of the study, we have also identified a lack of transparency and accessibility to the information related to the different stages and periods undergone by a drug from the EMA approval to the moment it is available for patients in the different Regions. European studies show a lack of accessibility to the information related to drug assessment procedure and decision-making on Pricing and Reimbursement Conditions [14], and alert on the potential consequences on patients health [15]. SEOM calls for a higher transparency and accessibility to information on the status of drugs throughout the assessment process by the different national, regional or local commissions.

SEOM declares also its concern on the lack of identification of a common pattern that explains the variability identified for the 11 analysed drugs between centres from the same region and between different regions, and the implications for patients, considering that the analysis was done on indications already approved in our country. Considering that final decision is independently taken at each hospital and that decision criteria are not clearly defined, SEOM considers there is a need of developing and implementing clinical guidelines that support professionals' prescription decision, and contribute to decrease heterogeneity in the access to oncologic drugs, considering an appropriate independent management of each patient.

In this situation and with the aim of making drugs and technologies that provide the best effectiveness and efficacy outcomes equally available for patients in the whole national health system, SEOM considers there is a need of implementing initiatives focused in: reducing the identified differences and homogenizing access conditions, demanding that these conditions are the ones approved by the AEMPS or in their absence, the ones proposed by IPT; reducing the existent delay from European drug approval and prescription to patients; eliminating regional and hospital barriers that make the actual access to the approved drugs difficult and increasing transparency in the access to information related to drug accessibility. SEOM also recommends the promotion of a national cancer register that includes variables agreed by consensus, allowing future measurements of health outcomes and analysis of treatment effectiveness as the best way of contributing to public health system's sustainability in real equity conditions.

## Conclusions

This study shows the existence of a number of binding commissions without common criteria that determine drug use conditions for indications already approved by EMA, AEMS and with PRC. The study shows, as well, variability in the composition of these commissions, in the decision-making and conclusions process.

The present heterogeneity in drug access and the variability of prescription criteria directly affects patients, as their access to certain drugs depends on the region and the centre.

Thus, SEOM considers that the approval's conditions for each drug should be equal, independently from Region or hospital. Therefore, equity in drug access is imperative for patients care and should not be linked to each Region budget. SEOM also commits to work with health authorities in implementing oncology diseases management strategies looking for reducing disparities between regions and hospitals.

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**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Research involving human participants and/or animals** For this type of study formal consent is not required. This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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## Appendix 1. Descriptive centre's details

1. **Please select your province (REQUIRED)**
2. **Please select your hospital level**
3. **Please select the number of inhabitants of your reference population**
4. **Please indicate the number of Hospital Pharmacists in your centre's Oncology Area**
5. **Please select the scope of your centre's Pharmacy and Therapy Commission where binding decisions related to the access to drugs are taken (REQUIRED)** *(Please select an option)*

☐ Hospital

☐ Hospital Groups

☐ Healthcare District

☐ Province

☐ Region

☐ Does not exist

**Do you know the number of members of the aforementioned Commission? (REQUIRED)**

☐ Yes ☐ No

If yes, please indicate:

a. **Number of members of the aforementioned Commission:**

(Range 1-20) Please click here to select a number

b. **Number of Medical Oncologists participating in the Commission:**

(Range 1-20) ☐ I don't know

c. **Number of Hospital Pharmacists participating in the Commission:**

(Range 1-20) ☐ I don't know ☐ No

d. **Does The Medical Director participate in the aforementioned Commission?**

☐ Yes

☐ No

e. **Does any member of the Regional Health Service participate in the aforementioned Commission?**

☐ Yes

☐ No

## Appendix 2. Data on the access to analysed drugs and indications

1. **Do you know if the drug has been requested to the binding Pharmacy and Therapy Commission for its use in the centre?**

   □ Yes

   □ No

   **If yes, when has the application been submitted (month and year)?**

   Please include month and year

   **If no, what was the main reason for not application?** *(Multiple choice answer)*

   □ Unofficial negative answer

   □ Excessive delay

   □ Excessive burocracy

   □ It does not affect my prescription

   □ Other reason. Please specify

2. **Has the use of this drug been approved at the hospital?**

   Yes □ No □ Pending of assessment □

   **If no, is there any referral procedure available for referring the patient to another centre where he can have access to the drug?**

   Yes □ No □

   **If no, is there any prescription procedure available for accessing the drug?**

   Yes □ No □

3. **When has the drug been assessed (month and year)?**

   Please include month and year

   □ I do not know the date

   □ The drug has not been assessed

4. **If the drug has been approved, has it been approved with the same conditions than the ones included in the Data Sheet/ Therapeutic Positioning Report?**

□ It has been approved with the SAME conditions than the ones included in the Data Sheet/Therapeutic Positioning Report

□ It has been approved with MORE restrictive conditions than the ones included in the Data Sheet/Therapeutic Positioning Report

□It has been approved with LESS restrictive conditions than the ones included in the Data Sheet/Therapeutic Positioning Report

□ The drug has not been approved

5. **When was the drug prescribed to the first patient (month and year)?**

Please include month and year

□ The information is not available.

□ The drug has not been prescribed to any patient although it is available.

6. **The use of the drug in the hospital is regulated according to criteria established by… Please select one or multiple options** *(Multiple choice answer)*

□ Data Sheet/ Therapeutic Positioning Report

□ Regional

□ Hospital's Pharmacy and Therapy Commission

□ SEOM Assessment Report

□ Genesis Assessment Report

□ Unavailable information

□ Drug is not available at the centre

□ Other Please specify

7. **How many patients have been treated with this drug in 2014?**

Please include number of patients

8. **Do you identify barriers/ limitations for accessing this drug at your centre?**

No □ Yes □

If **yes,** please select one or multiple options related to the drug access barriers at your centre *(Multiple choice answer)*

□ Criteria established by the centre are more restrictive than the ones included in the Data Sheet.

□ A justification report is required for each patient.

□ Debt ceiling systems have been established.

□ No medical oncologists participate in the Pharmacy and Therapy Commission.

□ Lack of hospital budget

□ Burocracy, lack of transparency in information and bad management of delays

□ Regional Harmonization Commission

□ Another drug with the same indication and lower price has been approved

□ Treatment sequence is not allowed for the same indication

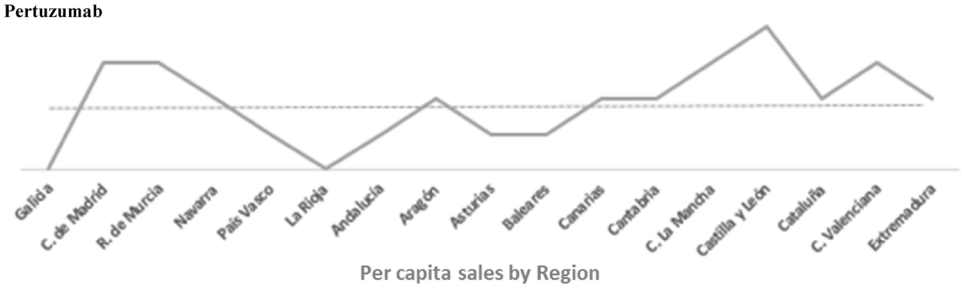
□ Other use barriers. Please specify

9. **Please include other relevant comments.**

## Appendix 3. Consumption results by drug and Region. Per capita sold units rate or per capita sales (according to the information provided by laboratories) and region of some of the analysed drugs standardized to 100,000 inhabitants

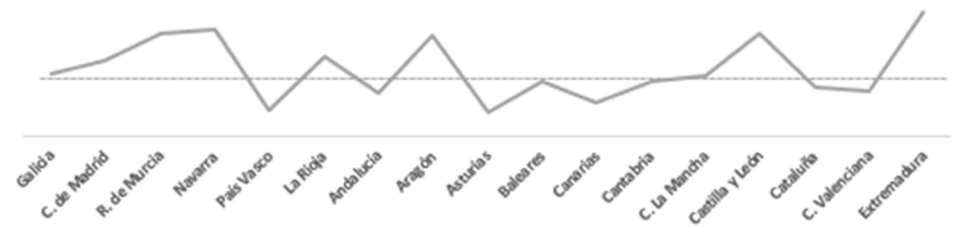
1. **Breast cancer**

**Pertuzumab**




Per capita sales by Region

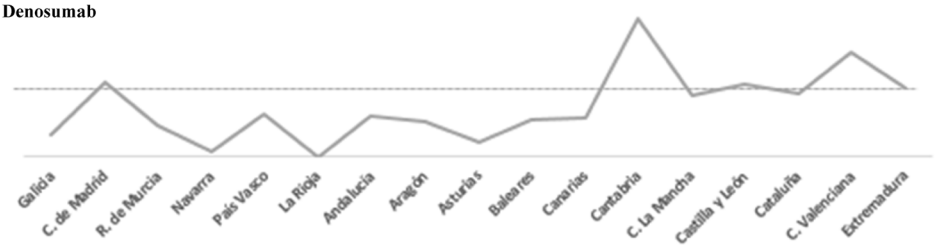
**Nab-Paclitaxel**




Per capita sold units rate by Region

**2. Support treatment**

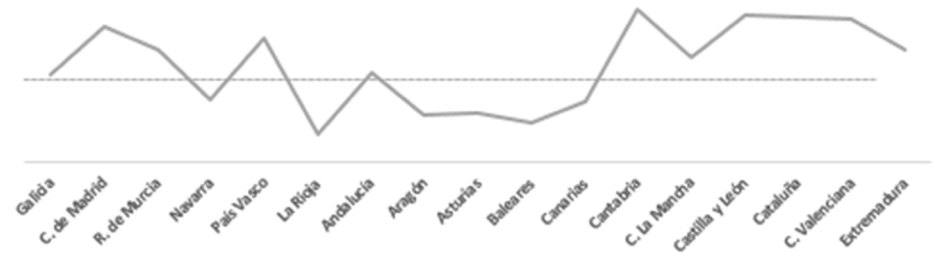
**Denosumab**




Per capita sold units rate by Region

**3. Melanoma**

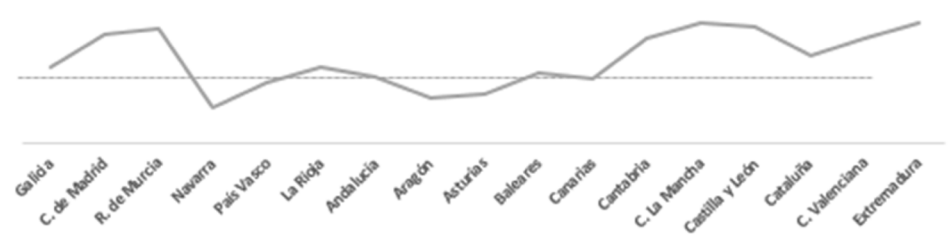
**Ipilimumab**




Per capita sold units rate by Region

**4. Prostate cancer**

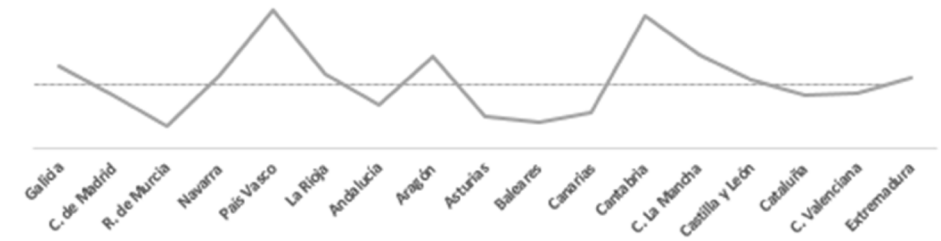
**Abiraterona**



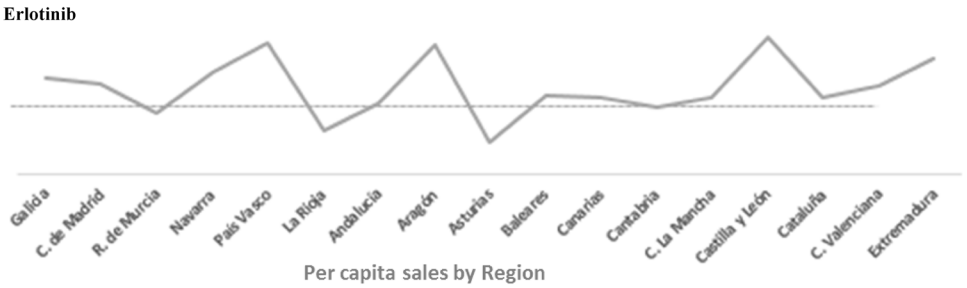

% Per capita sold units rate by Region

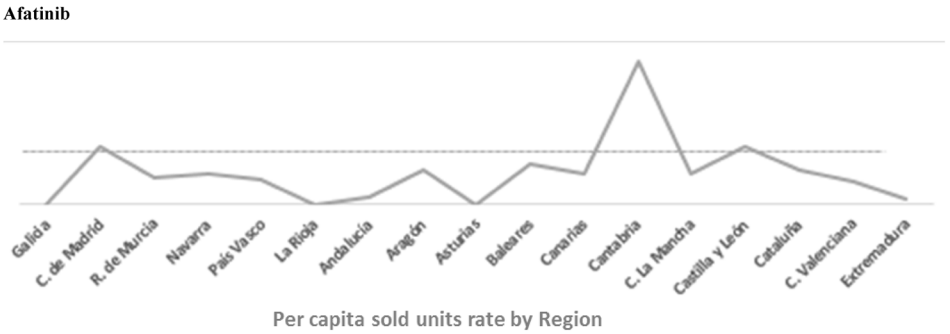
**5. Lung cancer EGFR +**

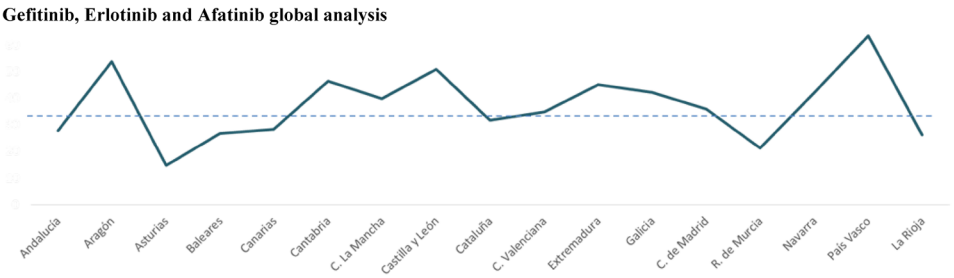
**Gefitinib**




Per capita sold units rate by Region




## Appendix 4. Participant hospitals per Region

| Region | Number of hospitals requested to participate in the study | Number of centers that finally participate in the study | Participation rate (%) |
|---|---|---|---|
| Andalucía | 18 | 10 | 56 |
| Aragón | 7 | 3 | 43 |
| Asturias | 2 | 1 | 50 |
| Baleares | 3 | 3 | 100 |
| Canarias | 4 | 2 | 50 |
| Cantabria | 2 | 1 | 50 |
| Castilla La Mancha | 7 | 4 | 57 |
| Castilla y León | 8 | 3 | 38 |
| Cataluña | 25 | 13 | 52 |
| Ceuta | 1 | 0 | 0 |
| C de Madrid | 23 | 13 | 57 |
| C. Valenciana | 20 | 12 | 60 |
| Extremadura | 4 | 1 | 25 |

continued

| Region | Number of hospitals requested to participate in the study | Number of centers that finally participate in the study | Participation rate (%) |
|---|---|---|---|
| Galicia | 9 | 5 | 56 |
| La Rioja | 1 | 1 | 100 |
| Navarra | 1 | 1 | 100 |
| País Vasco | 6 | 2 | 33 |
| Región de Murcia | 3 | 2 | 67 |
| Total | **144** | **77** | **53.5** |

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