JBUON 2019; 24(5): 2180-2197
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
Email: editorial_office@jbuon.com

ORIGINAL ARTICLE

AROME-ESO Oncology Consensus Conference: access to cancer care innovations in countries with limited resources. Association of Radiotherapy and Oncology of the Mediterranean Area (AROME–Paris) and European School of Oncology (ESO – Milan)

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Summary

Purpose: *Cancer is a leading cause of mortality worldwide. Its incidence is still increasing, particularly in developing countries. Recent progresses further strengthen the differences between low/middle and high-income countries. This*

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Received: 22/04/2019; Accepted: 26/05/2019

situation calls for joint action to reduce inequities in cancer outcomes among the patients. The Association of Radiotherapy and Oncology of the Mediterranean Area (AROME) and the European School of Oncology (ESO), have initiated joint conferences devoted to access to innovations in oncology in the Mediterranean area. The heterogeneity of the economic, political and cultural situations of the different participating countries, offers the opportunity to develop consensus conference.

Methods: *Cancer prevention and treatment strategies were discussed according to existing international guidelines. The Scientific committee prepared 111 questions with an objective to prioritize the access to treatments and innovations in low/middle-income Mediterranean countries. The results from the votes of 65 oncology experts, coming from 16 countries and 33 institutions have been analysed and access priorities classified accordingly.*

Results: *Ninety six percent of the proposed general recommendations concerning national health care strategies, oncology education, and treatment organization were considered to be high priorities. Regarding access to systemic treatments, 41% of the drugs without validated predictive markers and 53% of those with validated predictive markers were considered to be 1st level priority. Only 4 biological tests were considered to be 1st level priority to access to innovation.*

Conclusions: *AROME-ESO consensus offers to cancer specialists from developing countries a basis for discussion with health authorities and payers on the prioritization of access to innovations in cancer care.*

Key words: *cancer, guidelines, emerging countries, innovations, access, inequities*

Introduction

According to recent epidemiological data, cancer is not only the second leading cause of death in the world with nearly 9 million deaths in 2015 [1], but it is estimated that the number of new cases will increase by about 70% over the next two decades reaching 25 million new cases per year worldwide [2].

Approximately 70% of deaths from cancer occur in low- and middle-income countries [3]. Late-stage presentation and inaccessible diagnosis and treatment are common in these regions. In 2015, only 35% of low-income countries reported having pathology services generally available to the public sector. More than 90% of high-income countries reported that treatment services are available, compared to less than 30% of low-income countries [4]. Only 1 in 5 low- and middle-income countries have the necessary data to drive cancer policy [5].

Over the past 10 years, due to enhanced knowledge in cancer biology and new technologies, dozens of new oncology treatments have been launched, some of which involved cancers without any active treatment, particularly in advanced and metastatic stages. However, most of these drugs are not yet available in low- and middle-income countries and, even when they are registered, are frequently not reimbursed.

The counterpart of access to these new treatments is a steady and exponential increase in healthcare spending on cancer treatments and diagnosis. For example, the total annual economic cost of cancer in 2010 was estimated at approximately 1.16 trillion US dollars [6]. The GDP of all the high-income countries for the same year was 45.2 trillion US dollars compared to 20.4 trillion US dollars for the GDP of all the middle-income countries and 0.3 trillion US dollars for the low-income countries [7]. Overall, high-income regions spend 5-10 times more on cancer control on a per capita basis than low- and middle-income countries. Most countries are struggling to embrace this evolution, in particular the regulatory systems, diagnostic and treatment infrastructure, and financing mechanisms that are required to meet the population needs.

Concerning access to these new treatments, the gap between high-income countries and middle- and low-income countries is increasing, especially since low-income countries have to treat more frequently patients in advanced and metastatic situations, in which the great majority of the new drugs are registered.

The Mediterranean area has always been an important place of exchange, having moved the region from an intercultural to a multicultural status. The overall improvement in the level of education and the development of new communication technologies have made it possible to modify access to knowledge. However, for many political, economic or cultural reasons, access to some of the innovations resulting from these advances has been very different between the North and the South, and also between the West and the East.

Since the end of the last century, the Mediterranean space has changed profoundly. On the one hand, there is a reapproachment of knowledge but, paradoxically, remoteness from the innovations resulting from it, notably in the field of care and, in a growing way, concerning the prevention and treat-

ment of cancers. Among the different reasons for the migration of peoples within the Mediterranean area, migrations nourished with "therapeutic hope" are more and more frequent and among the most dramatic because they are often doomed to failure.

The Association of Radiotherapy and Oncology of the Mediterranean Area (AROME) is a nongovernmental organization, founded in 2006 and based on a collaborative network of colleagues involved in the management of cancers. AROME aims to improve the prevention and management of cancers by reducing inequalities within the Mediterranean area [8]. The integration of any innovation into everyday practice must take into account the epidemiological and organizational realities of different countries. This is why AROME meetings are built on a perpetual exchange between the various actors of the Mediterranean cancer care network, concerning the issues, the limits, and the challenges of the access to these new practices [9]. Thus, AROME has put in place clinical guidelines, taking into account a different level of access to cancer care in the Mediterranean area, and allowing the definition of care evolving from minimal but acceptable requirements to the optimal requirements to which we all aspire [10].

The European School of Oncology (ESO) is a nongovernmental organization, founded in 1982, with a mission reflected in its motto "Learning to Care". ESO helps shorten the time needed to transfer knowledge from research centers to daily practice. Due to its financial independence, ESO has the rare privilege of being able to set its own priorities. Therefore, it pays particular attention to developing the transfer of knowledge in areas that are least supported by industry, such as loco-regional treatments, non-doctors' cancer care professional education, rare pathologies, particularly in countries and regions with limited economic resourceS [11]. Various members of AROME have been involved in several ESO courses and are part of the ESO Core Faculty.

Because of their implications for the diffusion of knowledge, and the common objectives of improving practices to enable patients to better manage cancers in their countries of origin, AROME and ESO have joined forces to organize in 2015 and 2017 Regional Oncology Consensus Conferences: "Access to Cancer Care Innovations in Countries with Limited Resources", where 62 experts participants were mainly cancer specialists from low- and middle-income countries. The objective was to give the practitioners in these regions the opportunity to define their own priorities regarding cancer care innovations. Here we report and discuss the conclusions of these two first conferences.

Methods

A set of 111 recommendation statements were prepared before the AROME-ESO Consensus Conferences by the Scientific Committee on the basis of existent knowledge. The set of statements was presented, discussed and voted upon during the two consensus sessions of the meetings by 62 panellists. Additional changes in the wording of statements were made during the session. Main available literature supporting each statement is provided as references.

There were two categories of questions. The first category concerned comprehensive treatment strategies that did not involve a particular molecule or technique of treatment or diagnosis, and this category of questions focused on general public health and cancer care organization. The second category concerned the role of diagnostic and therapeutic strategies specific to pathologies with a potential impact on survival and/or quality of life. For each question, the experts had three possible answers. For the first category of questions, the experts expressed their agreement or not with the proposed recommendation *(yes (Y), no (N), or abstain (A))*. For the second category of questions, the experts had to express the priority level of integration of a management strategy *(high (HP), modest (MP) or low (LP))*. All panellists were instructed to vote on all questions using voting keypads. Each panellist response was captured, recorded, and immediately displayed with the percentage of votes cast for each type of response.

During the analysis of the results and the preparation of the manuscript, all the results of the votes were presented in tables, on the one hand, with an overall score ranging from 0 to 100 (called "consensus score") and, on the other hand, with the detail of the votes. The higher the consensus score, the stronger the consensus. The consensus score (CS) took into account the different types of questions. For the first category of questions, the percentage of positive responses (yes) corresponds to the CS since the other possible answers (no and abstention) were considered null. For the second category of questions, the percentage of responses considering a high, modest and low priority were assigned a coefficient 1, 0.5, and 0, respectively, to calculate the CS. According to the CS, three categories of priority regarding accessibility to innovations were defined: 1st level priorities ($100 \leq CS \geq 75$), 2nd level priorities ($75 < CS \geq 50$), 3rd level priorities ($CS < 50$). Since drugs are available according to the defined priorities, treatment strategies might follow the ESMO guidelines.

The level of evidence (LoE) regarding the statements are according the ESMO guidelines when available or other international guidelines updated with recent publications. The scoring was adapted from the Infectious Diseases Society of America-United States Public Health Coding Systema [12] (Table 1).

All the results in the manuscript are presented with the CS and LoE. The percentages of the votes are detailed in the tables.

Results

General recommendations (Table 1)

1. Patients' rights for innovation and accessibility

Experts have stated that innovation in cancer care is defined as the application of better solutions that positively impact epidemiology, treatment strategies and at least improve cancer survival and/or quality of life of cancer patients (expert opinion, 94 CS). Access to innovations need to be considered as a fundamental right for cancer patients (expert opinion, 100 CS). The panellists think that the applicability of an innovation in cancer care must be evaluated by the national oncology board, including healthcare professionals, patients and healthcare authorities, and including public and private payers (expert opinion, 97 CS).

2. Health democracy, population education and prevention

Because cancer innovations are not only access to new techniques and drugs, the panellists strongly agree that, in countries with limited resources, the first innovative cancer care measure must achieve reduction of the incidence of locally advanced and metastatic cancers at diagnosis (expert opinion, 95 CS), implying education of the population concerning cancer risk factors and screening for some early stage curable cancers (expert opinion, 97 CS). This will allow "long term" human and economic investment.

Table 1. General recommendations concerning national health care strategies regarding access to innovations in oncology

1	Innovation in cancer care is defined as the application of better solutions that positively impact epidemiology, treatment strategies and at least improve cancer survival and/or QoL of cancer patients.	94 CS Y(94%), N(3%), A(3%)
2	Access to innovations in cancer care is a fundamental right for patients.	100 CS Y(100%), N(0%), A(0%)
3	In countries with limited resources, the first innovative cancer care measure must achieve reduction of the incidence of locally advanced and metastatic cancers at diagnosis (prevention and early diagnosis).	95 CS Y(95%), N(0%), A(5%)
4	Education of the population concerning cancer risk factors (primary prevention) and screening (secondary prevention) for some early stage curable cancers is part of the previous strategy.	97 CS Y(97%), N(3%), A(0%)
5	Increasing significantly the price of tobacco is an important public health measure that impacts "long term" lung cancer epidemiology and mortality.	86 CS Y(86%), N(6%), A(8%)
6	Mammography screening is important public health project that might impact with sufficient participation and follow-up breast cancer mortality and QoL treatments.	94 CS Y(94%), N(6%), A(0%)
7	Colorectal screening is an important public health project that might impact with sufficient participation and follow-up colorectal cancer mortality and QoL treatments.	100 CS H(100%), M(0%), L(0%)
8	Cervical cancer screening is important public health project that might impact with sufficient participation and follow-up cervical cancer mortality and QoL treatments.	100 CS Y(100%), N(0%), A(0%)
9	HPV vaccination is an important public health project that might impact with sufficient participation and follow-up cervical cancer mortality and QoL.	83 CS Y(83%), N(7%), A(10%)
10	Prostate cancer screening (PSA) is important public health project that might impact with sufficient participation and follow-up prostate cancer mortality and QoL treatments.	48 CS Y(22%), N(52%), A(26%)
11	Population education and primary prevention are important public health projects that might impact melanoma mortality and/or QoL treatments.	100 CS Y(100%), N(0%), A(0%)
12	The applicability of an innovation in cancer care must be evaluated by national oncology boards, including healthcare professional, patients and healthcare authorities (payers).	97 CS Y(97%), N(3%), A(0%)

Green colot stands for Yes, and Red for No.

The experts wished to clarify the value of certain preventive measures. Thus, within the framework of primary prevention, experts retain the importance of increasing the price of tobacco (LoE 4A[13], 86 CS), HPV vaccination (LoE 1A[14], 83 CS), and educating the population about environmental risk factors such as exposure to UV radiations (LoE 4A[15], 100 CS).

Concerning secondary prevention (screening), the experts wanted to emphasize the importance of breast cancer screening with mammography (LoE 1A[16], 94 CS), colorectal cancer screening (LoE 2B[17],100 CS), and cervical cancer screening (LoE 1A[18], 100 CS), but consider that prostate cancer screening using systematic measurement of PSA level is not a priority (LoE 1A[19], 48 CS).

Patient advocacy groups are important supports for prevention activities, patient support and access to innovations (expert opinion, 97 CS). In order to educate patients, experts recommend to advice patients about the optimal treatment strategies according to international guidelines (even if they are not accessible or reimbursed) and the proposed strategy (even if it is not the optimal one) (expert opinion 97 CS).

3. Healthcare professionals' education

The education of healthcare professionals on cancer contributes to better integration of the innovations (expert opinion, 100 CS). The experts not only recommend that ESMO examination should be part of the evaluation of medical oncology degree (expert opinion, 91 CS), but also that it should be offered to all young cancer specialists an experience in specialized cancer units in a high-income country (expert opinion, 100 CS). However, because the main objective of the training investment of young specialists in cancer care in emerging countries is to improve care in their countries of origin, experts also wanted to emphasize the risk of brain drain, that is a double prejudice to the low- and middle-income countries in terms of educational investment and impact on public health (expert opinion, 88 CS).

Because a clear majority of solid tumours are initially addressed by surgeons, surgical oncologists must receive education on general oncology (expert opinion, 91 CS). The experts also wanted to emphasize that the quality of surgeons' education and practice might be a crucial point impacting patient curability and survival, particularly in some cancers such as gynaecological cancers (LoE 1A[20], 100 CS).

Since childhood cancers are more often curable, and this curability reflects the health organization of the country and the level of medical education, the panellists strongly recommend as high priorities investments in oncopediatry (education, treatment access, specific units) with participation in international clinical research programs (expert opinion, 83 CS).

Due to the aging of the population, education in oncogeriatry must be a part of oncology education (expert opinion, 89 CS).

4. Cancer diagnosis

Concerning diagnostic procedures, regarding the importance and the complexity of the pathological and biological diagnosis of cancers, the education of oncopathologists is mandatory (expert opinion, 100 CS), and the panellists recommend a reference expert centre for molecular diagnostics with quality control insurance for a population of 3 million inhabitants or, at least, one in countries with less than 3 million inhabitants (expert opinion, 94 CS). In case of diagnosed rare cancer, we recommend a second pathology and treatment opinion in a referent centre (LoE 1A, 97 CS).

New imaging techniques allow better cancer staging, and the panellists consider that access to PET-CT is crucial in some situations to define the optimal and efficient therapeutic strategy. The needs are estimated at one PET-CT facility per population of 0,6 to 1 million inhabitants (expert opinion, 82 CS).

5. Multidisciplinary boards

The experts also wanted to make recommendations concerning the general principles of multidisciplinary care for cancer patients. Multidisciplinary decisions are mandatory for treatment strategy decisions (without delaying the initiation of treatment) and are ideally organized in tumour boards, allowing better and earlier access to innovations (expert opinions, 100 CS). Out of life-threatening situation, a cancer treatment must not be initiated without a multidisciplinary tumour board decision (expert opinion, 86 CS).

6. General requirements concerning specific treatments tools and organization (radiotherapy, systemic treatments and palliative care)

In order to improve the quality of the surgical treatments, the experts recommend the process of accreditation for training and certified centres for specific cancer pathologies (LoE 1A, 97 CS).

Minimal requirements concerning radiotherapy are: to have access to a CT simulator (in RT or radiology departments), 3D treatment planning system (imaging fusion), linear accelerator with multileaf collimation and on-line electronic port vision

(ideally two machines at least to insure treatment continuum), QA/QC program and dosimetry equipment, and to create or have access to one centre of reference for particular techniques (paediatrics, stereotactic radiotherapy,...) (expert opinion, 91 CS). The estimated number of radiotherapy machines is one machine per every 500 new cases of cancer according to IAEA guidelines [21].

Regarding chemotherapy, the panellists strongly recommend that each country must make the WHO list of anticancer drugs available for treating patients [4]. Access to chemotherapy resources must be coordinated by physicians and pharmacists specializing in oncology (expert opinion, 85% consensus). National agencies and commissions concerning approval and reimbursement of cancer treatments should integrate medical oncology and patients' representatives (expert opinion, 94 CS). Generics and biosimilars are an economical opportunity by reducing the price of the actual reimbursed originals and enlarge accessibility to new innovations by redistribution of the resources without negative impact on the global cancer care budget (LoE 1A, 83 CS). However, to be approved and reimbursed, AROME-ESO strongly recommend not to consider generics and biosimilars out of

Table 2. Recommendations concerning access to innovations in gastrointestinal cancers

Recommendations concerning access to innovation in colorectal cancers		
1	For adjuvant colorectal cancers, access to oxaliplatinum and capecitabine is a priority with survival and/or QoL impact.	89 CS H(86%), M(6%), L(8%)
2	For adjuvant colorectal cancers, MSI screening is a priority with treatment strategy impact.	67.5 CS H(48%), M(39%), L(13%)
3	For metastatic colorectal cancers, access to RAS mutation status is a priority with treatment strategy impact.	78 CS H(64%), M(28%), L(8%)
4	For metastatic colorectal cancers, access to RAF mutation status is a priority with treatment strategy impact.	42 CS H(14%), M(56%), L(30%)
5	For RAS wild type metastatic colorectal cancers, access to anti-EGFR treatment is a priority with survival and/or QoL impact.	73.5 CS H(47%), M(53%), L(0%)
6	For metastatic colorectal cancers, access to anti-angiogenic drugs is a priority with survival and/or QoL impact.	66 CS H(47%), M(38%), L(15%)
Recommendations concerning access to innovation in gastric cancers		
7	For high risk non-metastatic gastric cancers, access to adjuvant chemotherapy is a priority with survival and/or QoL impact.	94.5 CS H(89%), M(11%), L(0%)
8	For high risk non-metastatic gastric cancers, access to adjuvant radiotherapy, usually in combination with chemotherapy, is a priority with survival and/or QoL impact.	60 CS H(41%), M(38%), L(21%)
9	For metastatic gastric cancers, access to HER2 testing is a priority with treatment strategy impact.	75.5 CS H(61%), M(29%), L(11%)
10	For HER2-positive metastatic gastric cancers, access to trastuzumab is a priority with survival and/or QoL impact.	80.5 CS H(67%), M(27%), L(6%)
11	For metastatic gastric cancers, access to taxanes is a priority with survival and/or QoL impact.	81 CS H(62%), M(38%), L(0%)
Recommendations concerning access to innovation in pancreatic cancers		
12	For metastatic pancreatic cancers, access to gemcitabine is a priority with survival and/or QoL impact.	93 CS H(86%), M(14%), L(0%)
13	For metastatic pancreatic cancers, access to erlotiib is a low priority without clinically relevant survival and quality of life impact.	14.5 CS H(3%), M(23%), L(74%)

Green stands for high priority, Orange for modest priority and Red for low priority for Panelists in terms of access to innovations.

those registered by EMEA and/or FDA (expert opinion, 88 CS). Experts also wanted to remember that academic and industry sponsored cancer clinical trials had to be facilitated in emerging countries, in order to improve access to innovations (expert opinion, 94 CS).

Unfortunately, a large proportion of cancers remain incurable in countries with limited resources and, even for cured patients, treatment toxicities are a major issue. Therefore, access to palliative medicine and supportive care (opioids, analgesic specific treatments) is considered a high priority (expert opinion, 89.5 CS), including access to bone antiresorptive agents (expert opinion, 81.5 CS).

AROME-ESO recommend a process of accreditation for cancer treatment activities taking into account the number of patients treated in the centres (expert opinion, 91 CS).

Finally, all the panellists support WHO Cancer Control Prevention guidelines, the statements of the Global Action Plan for the Prevention and Control of NCDs 2013-2020 [4] and the ESO - World Oncology Forum initiative [11].

Tumour types-oriented recommendations

Gastrointestinal cancer (Table 2)

Gastro-intestinal tumours are among the most frequent cancers in emerging countries with limited resources, affecting females and males equally [5]. Much progress has been made in recent years, regarding screening and treatment of some of these cancers. Experts wanted to emphasize the importance of some that might be considered as a priority.

Table 3. Recommendations concerning access to innovations in lung cancers

Recommendations concerning access to innovation in non-metastatic lung cancers		
1	For lung cancers that might benefit from local treatment, access to TEP-FDG is a priority with treatment strategy impact	77.5 CS H(58%), M(39%), L(2%)
Recommendations concerning access to treatment without predictive factors in metastatic lung cancers		
2	For metastatic lung cancers, access to taxanes is a priority with survival and/or QoL impact.	93 CS H(86%), M(14%), L(0%)
3	For metastatic lung cancers, access to gemcitabine is a priority with survival and/or QoL impact.	86.5 CS H(76%), M(21%), L(3%)
4	For metastatic lung cancers, access to pemetrexed is a priority with survival and/or QoL impact.	59.5 CS H(31%), M(57%), L(11%)
5	For metastatic non-squamous lung cancers, access to anti-angiogenic drugs is a priority with survival and/or QoL impact.	45.5 CS H(16%), M(53%), L(29%)
6	For metastatic lung cancers, access to immune check-point drugs is a priority with survival and/or QoL impact.	46 CS H(23%), M(46%), L(31%)
Recommendations concerning access to targeted treatments with biologic predictors of efficacy in metastatic lung cancers		
7	For metastatic lung cancers, access to EGFR mutation status is a priority with treatment strategy impact.	84 CS H(71%), M(26%), L(3%)
8	For EGFR mutated metastatic lung cancers, access to EGFR-TKI is a priority with survival and/or QoL impact.	87 CS H(74%), M(26%), L(0%)
9	For metastatic lung cancers, access to ALK rearrangement status is a priority with treatment strategy impact.	68 CS H(47%), M(42%), L(11%)
10	For ALK rearranged metastatic lung cancers, access to ALK-TKI is a priority with survival and/or QoL impact.	74.5 CS H(58%), M(33%), L(9%)
11	For metastatic lung cancers, access to MEK mutation status is a priority with treatment strategy impact.	28 CS H(5%), M(46%), L(49%)

Green stands for high priority, Orange for modest priority and Red for low priority for Panelists in terms of access to innovations.

1. Colorectal cancers

For colorectal cancers, the importance of screening was discussed previously. Once the cancer is diagnosed, in adjuvant situations access to oxaliplatin and capecitabine is a high priority, with survival and potential quality of life impact (LoE 1A [17], 89 CS), while MSI screening was not considered to be a high priority by all, particularly if chemotherapy with oxaliplatin is planned (LoE 4D[17], 67.5 CS). In metastatic situations, access to *RAS* mutation status is a first level priority (LoE 1A [22], 96 CS), but not RAF (LoE 1B [22], 73 CS). Access to anti-angiogenic drugs (LoE 1A [22], 81 CS), and anti-EGFR treatments in RAS wild type cancers (LoE 1A [22], 86 CS) are considered to be also first-level priorities by the experts.

2. Gastric cancers

Gastric cancers are still a very frequent disease in emerging countries and experts wanted to emphasize several important treatment needs. In cases of non-metastatic high-risk gastric cancer, priorities concerning adjuvant treatment are, firstly, access to chemotherapy (LoE 1A [23], 94.5 CS), while adjuvant radiotherapy is clearly a second level priority (LoE 1B [23], 60 CS). In cases of metastatic gastric cancers, determination of HER2 status is crucial (LoE 1A [23], 75.5 CS), leading to the use of trastuzumab (LoE 1A [23], 80.5 CS). Among chemotherapy drugs, access to taxanes is also considered to be a high priority with survival impact, in complement to other usually accessible drugs such as 5FU (or capecitabine) and platinum salts (LoE 1A [23], 81 CS).

3. Pancreatic cancers

Metastatic pancreatic cancers are more and more frequently diagnosed, and access to gemcitabine in this situation is considered by the experts to be a first level priority in the low- and middle-income countries (LoE 1A [24], 93 CS), while access to nab-paclitaxel is considered a second level priority (LoE 1A, 54 CS) and erlotinib a third level (LoE 1D [24], 14.5 CS).

Lung cancers (Table 3)

Lung cancers are still one of the major causes of cancer mortality all around the world and are increasing, particularly in emerging countries [5]. Because just a small proportion of these cancers are curable when diagnosed at an early stage, the experts considered that primary preventing strategies are crucial to reducing the incidence of lung cancers. In addition to education on risk factors, experts consider that significantly increasing the price of tobacco is an important public health measure, as mentioned previously. Because TNM staging is crucial for treatment strategy decision, panellists consider that access to PET-FDG is a first level priority for lung cancers that might benefit from local treatment (LoE 1A [25], 77.5 CS).

1. Lung cancers' chemotherapy drugs

In cases of metastatic disease, chemotherapy is still the most frequent treatment administered. The experts wanted to emphasize the importance of access to several chemotherapy drugs in metastatic lung cancers and, particularly among the more recent ones, according to priorities: first taxanes (LoE 1A [26], 93 CS), then gemcitabine (LoE 1A [26], 86.5 CS), and finally pemetrexed (LoE 2A [26], 70 CS).

2. Lung cancers' targeted treatments

Recent progress has also been made with new targeted treatments. Several of these are particularly important in some adenocarcinomas of the lung, and possible biological tests might predict the effectiveness of the drugs [26]. This is why experts consider that it is important to have access to EGFR mutation status (LoE 1A [26], 84 CS), ALK rearrangement status (LoE 1A [26], 82 CS) and, less importantly, ROS mutation status (LoE 3A, 65 CS) and MEK mutation status (LoE 3A [26], 28 CS). All these biological tests are crucial to offer better access to drugs targeting tyrosine kinase inhibitors (TKIs) targeting EGFR (LoE 1A [26], 87 CS) and TKIs targeting ALK (LoE 1A [26], 85 CS).

Other approaches are treatments targeting the tumour micro-environment. Access to immunotherapy is considered a first level priority (LoE 1A [26], 76 CS) and anti-angiogenic drugs a second level priority (LoE 1A [26], 52 CS) are considered a second level priority.

Breast cancers (Table 4)

The incidence of breast cancers is increasing worldwide, and half of breast cancer cases are diagnosed in emerging countries [5]. Therefore, experts consider that mammography screening is an important public health project, as stated before. Access to BRCA or other factors of genetic predisposition status for patients with personal and/or family history suggesting a genetic risk of breast cancers is a second level priority (LoE 2A [27], 74 CS), since it can modify potentially loco-regional treatment strategies, essentially in young non-menopausal patients.

1. Non-metastatic breast cancers

Because a high proportion of non-metastatic breast cancers are curable, the quality of the

adjuvant treatments for the high risk of the relapsing non-metastatic patient is also crucial. In adjuvant situations in general, access to taxanes and anthracyclines (LoE 1A [16], 97 CS), aromatase inhibitors (LoE 1A [16], 92 CS), and 1-year trastuzumab for HER2-positive tumours (LoE 1A [16], 97 CS) are high priorities with survival impact.

In case of high risk of relapse adjuvant situation, experts also consider that access to LHRH agonists for premenopausal HR positive cancers (LoE 1B [16], 86 CS) and pertuzumab for HER2 posi-

Table 4. Recommendations concerning access to innovations in breast cancers

Recommendations concerning access to innovation in non-metastatic breast cancers		
1	For patients with personal and/or familial history suggesting a genetic risk of breast cancer, access to BRCA mutation status is a priority with treatment strategy impact.	74 CS H(52%), M(44%), L(4%)
2	For adjuvant breast cancers, access to taxanes and anthracyclines is a priority with survival and/or QoL impact.	97 CS H(97%), M(0%), L(3%)
3	For HER2-positive adjuvant breast cancers, access to trastuzumab is a priority with survival and/or QoL impact.	97 CS H(97%), M(0%), L(3%)
4	For hormone receptor positive adjuvant breast cancers, access to aromatase inhibitors is a priority with survival and/or QoL impact.	92 CS H(84%), M(16%), L(0%)
5	For non-menopausal hormone receptor positive adjuvant breast cancers, access to LHRH agonists is a priority but not consensually considered as a high priority.	72 CS H(55%), M(34%), L(11%)
Recommendations concerning access to innovation in metastatic breast cancers		
6	For HER2-positive metastatic breast cancers, access to pertuzumab is a priority with survival and/or QoL impact.	78.5 CS H(63%), M(31%), L(6%)
7	For HER2-positive metastatic breast cancers, access to T-DM1 is a priority with survival and/or QoL impact.	49 CS H(14%), M(70%), L(16%)
8	For HER2-positive metastatic breast cancers, access to lapatinib is a priority with survival and/or QoL impact.	56 CS H(28%), M(56%), L(17%)
9	For HR-positive metastatic breast cancers, access to both aromatase inhibitors (steroidal and non-steroidal) is a priority with survival and/or QoL impact.	88 CS H(76%), M(24%), L(0%)
10	For HR-positive metastatic breast cancers, access to fulvestrant is a priority with survival and/or QoL impact.	66 CS H(42%), M(48%), L(10%)
11	For HR-positive metastatic breast cancers, access to everolimus is a priority with survival and/or QoL impact.	35.5 CS H(17%), M(37%), L(46%)
12	For HR-positive metastatic breast cancers, access to palbociclib is a priority with survival and/or QoL impact.	30 CS H(15%), M(30%), L(55%)
13	For metastatic breast cancers, access to capecitabine is a priority with survival and/or QoL impact.	83.5 CS H(73%), M(21%), L(6%)
14	For metastatic breast cancers, access to vinorelbine is a priority with survival and/or QoL impact.	62.5 CS H(39%), M(47%), L(14%)
15	For metastatic breast cancers, access to eribulin is a priority with survival and/or QoL impact.	28.5 CS H(13%), M(31%), L(56%)
16	For metastatic breast cancers, access to bevacizumab is a priority with survival and/or QoL impact.	23.5 CS H(4%), M(39%), L(57%)

Green stands for high priority, Orange for modest priority and Red for low priority for Panelists in terms of access to innovations.

tive cancers (LoE1B, 83 CS) but not for treatment with neratinib (LoE 1B, 48 CS).

2. Metastatic breast cancers

In metastatic situation, priorities depend on subtypes of breast cancers. In HER2-positive metastatic breast cancers, access to pertuzumab (LoE 1A [28], 78.5 CS) and T-DM1 (LoE 1A [28], 87 CS) are considered as the highest priority, followed by access to lapatinib (LoE 1B [28], 65 CS).

For endocrine responsive metastatic breast cancers, access to aromatase inhibitors (both steroidal and non-steroidal) (LoE 1A [28], 88 CS) and fulvestrant are the highest priorities (LoE 1A [28], 95 CS). Access to endocrine treatment modulating agents is considered a second level priority for CDK 4/6 inhibitors (LoE1A, 70 CS) and everolimus (LoE 1B [28], 54 CS).

Concerning chemotherapy for metastatic breast cancer, experts considered that access to capecitabine is a high priority (LoE 1B [28], 83.5 CS), but access to vinorelbine (LoE 1B [28], 59 CS) is a second level priority. They consider eribulin (LoE 1B [28], 40 CS) or bevacizumab (LoE 1A [28], 23.5 CS) as a third level priority.

Gynaecologic cancers

All gynaecologic cancers are potentially curable by loco-regional treatments when diagnosed early. Furthermore, some of them might benefit from primary or secondary prevention. This is why, as a general statement, the panellists wanted to remember that, for operable gynaecological cancers, education and specialization of surgeons influence the survival of operated patients, as stated previously. Nearly 90% of cervical cancer deaths occurred in developing countries, where it is the third leading cause of death [5]. This is why primary prevention (HPV vaccination) and secondary prevention (screening) were considered as a general public health priority.

1. Particular considerations regarding radiotherapy for gynaecologic cancers

In case of radiotherapy indication in localized cervical cancers access to IMRT (LoE 1A, 82CS) and/or brachytherapy (LoE 1A, 98 CS) is considered a high priority.

2. Chemotherapy drugs for gynaecologic cancers

Regarding systemic treatments, access to platinum salts at any stage of the gynaecologic cancer is mandatory, particularly for ovarian cancers that might be treated several times during the disease course with this chemotherapy class (LoE 1A [29,30,31] 100 CS). Access to taxanes is considered a high priority for stage III and recurrent ovarian cancers (LoE 1A [29], 100 CS), metastatic cervical cancers (LoE 1A [30], 92 CS), and metastatic endometrial cancers (LoE 1A [31], 90.5 CS). For metastatic ovarian cancer, access to gemcitabine (LoE 2A [29], 79.5 CS) and liposomal anthracyclines (LoE 1A [29], 70 CS) are also considered to be important.

Other drugs are clearly considered as second level priorities in metastatic ovarian cancers, such as vinorelbine (LoE 3B, 59 CS) and trabectedin (LoE 1B [29], 17 CS). Topotecan is also considered a second level priority in metastatic cervical cancers (LoE 2B [30], 63 CS).

3. Targeted drugs for gynaecologic cancers

Access to bevacizumab is a first level priority for sage III (LoE 1B [29], 87 CS) and metastatic ovarian cancers (LoE 1A [29], 82 CS), while it is a second level priority for metastatic cervical cancers (LoE 1A [30], 70 CS).

Determination of BRCA status (LoE 1A [32], 74.5 CS) for PARP inhibitor treatments (LoE 1A [32], 90 CS) is also considered as important for ovarian cancers.

Urologic cancers

The experts wish to emphasize that in the case of certain urological cancers such as prostate or bladder cancers, the functional sequelae of locoregional treatments can be important and have a negative impact on patients' quality of life. As a result, the quality of the assessment of the initial stage of the disease is important before any discussion in a multidisciplinary meeting.

1. Prostate cancers

Prostate cancers will be more and more frequent cancers in males throughout the world while life expectancy becomes longer and longer. However, the experts do not consider that screening is an important public health project as was previously stated in this manuscript.

In case of radiotherapy indication in localized prostate cancers access to IMRT (LoE 1A, 84CS) is considered a first level priority and brachytherapy a second level priority (LoE 1A, 63 CS).

Experts considered that the main needs lie in metastatic situations. In cases of total androgen deprivation resistance, the panellists' votes made it possible to identify the following priorities: access to docetaxel first (LoE 1A [19], 100 CS), followed equally by abiraterone (LoE 1A [19], 89 CS) and enzalutamide (LoE 1A [19], 89 CS), followed by cabazitaxel (LoE 1A [19], 54 CS).

2. Renal cancers

Concerning renal cell cancers, progress has been made since targeted therapies were developed. Access to these drugs is still difficult in countries with limited resources and this is why panellists have prioritized the importance of access according to the clinicopathological situation and type of drug. For good prognosis metastatic renal cell cancers, access to anti-angiogenic drugs in first line (sunitib, bevacizumab or pazopanib) treatment is a first level priority with survival impact (LoE 1A [33], 92 CS), but a second level priority in second line is for sorafenib, everolimus or axitinib (LoE 2B [33], 70 CS). For poor prognosis metastatic renal cell cancers, access to temsirolimus is considered a second level priority (LoE 3B [33], 66 CS).

Concerning immunotherapy for metastatic renal cell cancers, experts consider that it is also a high priority (LoE 1A, 77CS).

3. Urothelial cancers

Experts also wanted to remember key strategies for the treatment of urothelial cancers. In cases of non-metastatic high-risk urothelial cancers, access to adjuvant MVAC chemotherapy protocol is considered a priority with survival impact (LoE 1A [34], 81.5 CS). For local pelvic recurrence, access to radiotherapy is also high priority with survival and quality of life impact (LoE 1A [34], 96.5 CS). In metastatic situations, access to gemcitabine is a high priority with survival and quality of life impact (LoE 1A [34], 89 CS) and also immunotherapy (LoE1A, 81CS).

Cutaneous cancers

Cutaneous cancers are the most frequent cancers worldwide. Among them, metastatic malignant cutaneous melanoma is considered as one of the most aggressive cancers. Panellists wanted to emphasize that UV irradiation has been identified as a major carcinogen involved in melanoma genesis. Thus, prevention of UV exposure is a critical population education point previously mentioned.

1. Melanoma

For diagnosed high risk non-metastatic melanoma, experts consider that access to a sentinel node biopsy procedure for clinical node negative cutaneous melanoma is a standard of care (LoE 1A [35], 96 CS) and that access to interferon alpha is a modest priority with modest survival impact (LoE 2B [35], 46 CS). Regarding determination of new biological predictors, the panellists consider that access to RAF mutation is a modest priority in non-metastatic situations (LoE 4C, 43 CS), while it is a high priority in metastatic situations (LoE 1A [35], 92.5 CS) due to a high priority for access to BRAF inhibitors (LoE 1A [35], 93.5 CS). Access to MEK inhibitors (LoE 2B [35], 86 CS) and BRAF/MEK inhibitors combo are high priorities (LoE 1A, 92 CS). Immune-checkpoint treatments such as PDL1 and CTLA4 directed antibodies (LoE 1A [35], 94 CS) are also high priority. Regarding chemotherapy agents for metastatic melanoma, access to dacarbazine (LoE 2C [35], 73.5 CS) and temozolomide (LoE 2C [35], 45.5 CS) are also considered to be a priority.

2. Basal cell carcinoma

Basal cell carcinomas are a subtype of skin cancer usually treated by surgery and/or radiation therapy. These treatments are the first treatment choice (LoE 1A [36], 100 CS). However, if locoregional treatments have been applied without success, then access to hedgehog pathway inhibitors is considered as a priority (LoE 2A [36], 61 CS). Yet, the experts stress that this approach is not a priority in cases of mixed basal cell carcinoma and squamous cell carcinoma (LoE 1A [36], 22 CS).

Sarcomas

Sarcomas are a group of frequent heterogeneous cancers, and panellists recommended that sarcomas should be treated in expert centers to optimally define treatment indications and techniques, and especially for locoregional treatments (LoE 3A [37], 100 CS). Access to expert surgeons and, if indicated, adjuvant radiotherapy (LoE 3A [37], 86.5 CS) and anthracyclines (LoE 1A [37], 77.5 CS) is a high priority. Also, regarding systemic treatments in metastatic situations, access to ifosfamide combined with mesna (LoE 3B [37], 90 CS) is a high priority with potential survival impact. Experts considered that access to pazopanib (LoE 1B37, 60 CS), trabectedin (LoE 2B [37], 39 CS) and eribulin in leiomyosarcomas and adipocytic sarcomas (LoE 2B [37], 39 CS) are not first level priorities.

Head and neck cancers

Head and neck cancers are relatively frequent in emerging countries, because of tobacco exposure and also because of some virus exposures [38]. For many years, the gold standard of treatment has been based on locoregional approaches for curable diseases (surgery and radiotherapy) and platinum, 5FU, methotrexate and taxanes-based chemotherapy [38]. In recent years, several trials have demonstrated the potential importance of EGFR targeting drugs in head and neck cancers. For this reason, ac-

cess to cetuximab in combination with radiotherapy in locoregional treatments (LoE 2B [38], 85 CS), and with chemotherapy in metastatic disease (LoE 2A [38], 75 CS) is considered a high priority by the experts.

Special considerations on brain tumours

Because brain tumours (primary or secondary) are relatively frequent but potentially not treated according to international guidelines, panellists wanted to emphasize the importance of access to stereotaxic radiotherapy as a priority at least for the quality of life (LoE 2B [39], 90 CS), and the need to access to temozolomide for primary brain tumours (LoE 2B [39], 83 CS). Access to bevacizumab for glioblastoma is considered a second level priority (LoE 2A, 63 CS).

Discussion

Cancer became more and more frequent worldwide and many innovations are actually dramatically changing the face of these diseases. We consider that access to innovation is a fundamental right of patients in general and particularly in cancer patients, since these diseases are usually life-threatening. On the basis of this statement, we agree with the recent European Cancer Patient's Bill of Rights [40]. However, we have seen that any declaration or law concerning access to care as old, legitimate and ethical cannot now escape the epidemiological and economic realities of the countries concerned. The applicability of these intentions is even more difficult because they are often decided for the low- and middle-income countries on the basis of high-income countries' experiences. This is why we wanted, after three days of updates concerning different topics in oncology, to ask experts from various Mediterranean regions with different fields of expertise to prioritize access to innovations according to their everyday needs.

About one-third of deaths from cancer are due to five leading behavioural and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, and alcohol use. It is estimated that 30% to 50% of cancers could be primarily prevented just by avoiding these risk factors and also cancer-causing infections [41]. The latter are responsible for up to 25% of cancer cases in low- and middle-income countries [42]. This is why the experts of the AROME-ESO consensus conference clearly emphasized the importance of primary and secondary prevention, particularly in cases of frequent and fatal diseases, that will ensure the lower social costs of these diseases. The experts wished to highlight the importance of a prevention policy with a very high level of consensus. These recommendations are based on levels of evidence in the literature, also demonstrating the limitations of certain preventive measures related either to a particular type of cancer such as prostate cancer, or to the importance of accompanying these measures in terms of public health. For example, tobacco use is the most important risk factor for cancer and is responsible for approximately 22% of cancer deaths [41]. Indeed, prevention has a limited impact without a political and healthcare organization that systematically includes education of populations, training of caregivers and promotion of these measures. It is for this reason that we think that, within the Mediterranean area, countries that have already begun to reflect on this issue could be of great help in implementing these measures in other low- and middle-income countries.

Even if these measures were implemented quickly, there would be a delay of several years before the economic benefits could be seen and, in the meantime, the care needs of patients diagnosed with cancer will only increase. Moreover, due to a more difficult health situation, the low- and middle-income countries will have to take care of patients with more advanced disease [43] initially, not only with increasing needs for new systemic treatments but also good quality supportive care [44]. Consequently, the second immediate challenge is to meet the needs of patients with regard to access to treatment innovations, particularly in advanced and high risk non-metastatic cancers.

We could have simply resumed the international guidelines and stuck to the level of proof in order to prioritize the different treatment strategies. For example, experts support the WHO essential cancer drug list and also ESMO guidelines. These guidelines that we have cited to define the level of evidence use well-established methodology to assess the clinical impact of the treatment, but do not take into account this impact in a particular health system. There are not only significant differences in socioeconomic status, health education, and preventive activities, but also sometimes cultural differences, as well as different geographic distributions of specific types of cancers. A second approach could have been an assessment of the treatment interest according to the QALY approach. We have to remember that the QALY approach was originally developed by economists, aimed at applying the "utility theory" to public health [45]. It is essential to recall the limits of this approach in the context of current treatment prices because the QALY is itself indexed to GDP, whereas the cost of these treatments is not. If we are not vigilant, this

Table 5. Level of consensus concerning systemic treatments access without validated predictive markers (companion test)

Treatments		*First level priorities*	*Second level priorities*	*Third level priorities*
Oxaliplatin	adjuvant	Colorectal cancers 89 CS		
Taxanes	adjuvant	Ovarian cancers 100 CS Breast cancers 97 CS		
	metastatic	Ovarian cancers 100 CS Prostate cancers 100 CS (docetaxel) Lung cancers 93 CS Cervical cancers 92 CS Endometrial cancers 90.5 CS Gastric cancers 81 CS	Prostate cancers 56.5 CS (cabazitaxel)	
Anthracyclines	adjuvant	Adult sarcomas 77.5 CS		
Gemcitabine	metastatic	Pancreatic cancer 93 CS Urothelial cancers 89 CS Lung cancers 86.5 CS Ovarian cancers 79.5 CS		
Pemetrexed	metastatic		Lung cancers 59.5 CS	
Capecitabine	adjuvant	Colorectal cancers 93 CS		
	metastatic	Breast cancers 83.5 CS		
Vinorelbine	metastatic		Breast cancers 62.5 CS Ovarian cancers 59 CS	
Eribulin	metastatic			Leiomyosarcomas and adipocyte sarcomas 39 CS Breast cancers 28.5 CS
Topotecan	metastatic		Cervical cancers 55 CS	
Ifosfamide + mesna	metastatic	Soft tissue sarcomas 90 CS		
Platinum salts	metastatic	Ovarian cancers 100 CS		
Liposomal anthracyclines	metastatic		Ovarian cancers 74.5 CS	
Trabectedin	metastatic			Ovarian cancers 33 CS Soft tissue sarcomas 35 CS
Abiraterone	metastatic		Prostate cancers 67.5 CS	
Enzalutamide	metastatic		Prostate cancers 58 CS	
Temsirolimus	metastatic			Renal cell cancers 39.5 CS
Interferon alpha	adjuvant			Melanoma 47 CS
DTIC	metastatic		Melanoma 73.5 CS	
Temozolomide	metastatic	Primary brain tumors 82 CS		Melanoma 43.5 CS
Hedgehog inhibitors	Non-metastatic		Pure basal cell carcinomas ineligible for loco regional treatment 71.5 CS	
Pazopanib	metastatic			Soft tissue sarcomas 36.5 CS
Antiangiogenic drugs	adjuvant		Ovarian cancers 66.5 CS	
	metastatic	Ovarian cancers 82 CS Renal cell cancers 82 CS (first line)	Colorectal cancers 66 CS Renal cell cancers 59 CS (second line)	Lung cancers 45.5 CS Breast cancers 23.5 CS Cervical cancers 39 CS

leads to hasty conclusions, such as that of WHO, which indexes the value of the cost of a life-saving treatment to the GDP per capita, thereby endorsing inequalities in access to innovations, even if it wishes to fight against them. Therefore, we believe that the level of evidence, or the QALY, does not define priorities alone for access to innovations in emerging countries. Thus, we wanted to set up a score to highlight all the public health actors, the priorities and the economic and organizational stakes. It is essential to note that the measures with the highest consensus score are those relating to the organization of care, the technical quality of care, including new methods of diagnosis, the importance of the multidisciplinary approach, and access to the oldest treatments with the highest level of evidence. Regarding new drugs, we believe that the conclusions of this consensus conference will help the payers of the low- and middle-income countries not only to prioritize access to the drugs (Tables 5 and 6), but also help in the investment in diagnostic tools (Table 7) that will help optimize treatment strategy.

Once the priorities have been defined, there remain two important obstacles to the availability of these innovations. The first is to shorten accessibility to innovations, and the second their financing. The two are related, although there are complementary solutions.

Regarding the rapidity of access to innovation, it is crucial to remember that the first possible access to innovations for a patient is usually in the context of a clinical trial. AROME-ESO experts wanted to emphasize the importance of the organization of the cancer care system in low- and middle-income countries, in order to increase the rate of patients participating in trials. However, political and organizational efforts are not the only ones to be made. Education of the patients regarding clinical trials is also an important challenge in these countries. The second aspect regarding the rapidity of access to innovation is to shorten the

Table 6. Level of consensus concerning systemic treatments access with validated predictive markers (companion tests)

Treatments		*First level priorities*	*Second level priorities*	*Third level priorities*
Anti-EGFR treatments	adjuvant		Head and neck cancers In combination with radiotherapy 72.5 CS	
	metastatic	Lung cancers 87 CS	Colorectal 73.5 CS Head and neck cancers 63 CS	
ALK inhibitors	metastatic	Lung cancers 74.5 CS		
Trastuzumab	adjuvant	Breast cancers 97 CS		
	metastatic	Gastric cancers 80.5 CS		
Pertuzumab	metastatic	Breast cancer 78.5 CS		
T-DM1	metastatic			Breast cancer 49 CS
Lapatinib	metastatic		Breast cancer 56 CS	
Aromatase inhibitors	adjuvant	Breast cancers 92 CS		
	metastatic	Breast cancers 88 CS		
Fulvestrant	metastatic		Breast cancers 66 CS	
Everolimus	metastatic			Breast cancers 35.5 CS
Palbociclib	metastatic			Breast cancers 30 CS
LHRH agonists	adjuvant		Breast cancers 72 CS	
PARP inhibitors	metastatic		Ovarian cancers 67.5 CS	
BRAF inhibitors	metastatic	Melanoma 93.5 CS		
MEK inhibitors	metastatic		Melanoma 55 CS	
Immune check-point drugs	metastatic		Melanoma 61 CS	Metastatic lung cancers 46 CS

Table 7. Level of consensus concerning diagnostic tools that might impact treatment strategies

Biological tests	*First level priorities*	*Second level priorities*	*Third level priorities*
MSI screening		Adjuvant colorectal cancers 67.5 CS	
RAS mutation	Metastatic colorectal cancers 78 CS		
RAF mutation	Metastatic melanoma 92.5 CS		Metastatic colorectal cancers 42 CS Adjuvant melanoma 17 CS
HER2 testing	Metastatic gastric cancers 75.5 CS		
EGFR testing	Metastatic lung cancers 84 CS		
ALK rearrangement		Metastatic lung cancers 68 CS	
MEK testing			Metastatic lung cancers 28 CS
BRCA testing		Metastatic ovarian cancers 74.5 CS Non-metastatic breast cancers 74 CS	
Imaging Test	*First level priorities*	*Second level priorities*	*Third level priorities*
TEP-FDG	Non-metastatic lung cancers 77.5 CS		

time to new drug approval. For example, in the United States, initiatives including "breakthrough therapy designation" may have contributed to the shortened time to approval. This is why we think that prioritizing access to innovations according to local epidemiology and needs will help authorities to take faster decisions regarding approvals. However, the complexity and duration of the drug regulatory process vary widely from country to country, and international cancer societies and organizations might help to convince some country to simplify the process in the context of first level priority access.

Last but not least is the financial support of access to all these drugs. The total cost of cancer treatments measured at the ex-manufacturer price reached more than 1 billion $ in 2015 in the USA, representing an increase in constant dollars of 11.5% over the prior year [46]. Payers are seeking assurance of the value that results from their expenditure, and this is why evaluation of the importance of any new innovative approach is mandatory. This tension will amplify over the next years, as an important pipeline of new anticancer therapies reaches a growing number of patients worldwide. Moreover, the importance to optimally define the target population and how to manage efficacy and safety assessment of these drugs will grow. This is why healthcare professional education is critical, and patients followed in specialized cancer departments crucial. But the challenge that remains the most important to date, and if the future does not change, is the constant and exponential increase in the cost of new cancer treatments [47]. The first regulatory initiative would be to put in place tools to better evaluate the cost of developing a treatment (including failures of treatment that did not result in registration), as well as the benefits for the companies, the patient and the society. The key element is the calculation of the impact on society in the countries with different incomes. Globalization, which does not take into account these differences, now results in "standardized" prices that do not facilitate access to innovations in these countries. Different economic solutions have already been cited in other journals giving an update on this major issue for low- and middle-income countries. Among them, generics and biosimilars (with quality control process of approval), and compulsory licensing are the most promising, but clearly need international mobilization and collaboration between high and low- and middle-income countries [48].

Conclusion

Advances in survival outcome and quality of care for cancer patients are related in general to the quality of healthcare providers' education and access to innovative treatment strategies. In the last few years, much progress has been made to improve patients' outcome. However, these improvements are of limited access in many developing countries. The first AROME-ESO consensus conference on access to cancer care innovations in countries with limited resources, provides national oncology boards, including healthcare professionals, patients and healthcare authorities, concrete arguments to prioritize the investments that are considered to be crucial to improve patients' outcomes and reduce cancer mortality. The heterogeneity of the

economic, political and cultural situations of the different countries, living in the same historical Mediterranean area, offers a unique opportunity to develop collaboration based on the shared experiences of each other to build a space of care where inequalities tend to be reduced. Even more, for countries with limited resources, the clear definition of objectives, public health constraints and the possibility of sharing resources will allow the implementation of specific solutions. We hope that the AROME-ESO consensus conferences will help to improve this practice and facilitate access to innovations in these countries. Reducing differences in the diagnosis and treatment and their optimization between the countries of the Mediterranean region is one of the goals of our future actions.

Disclosures

- Matti Aapro reports personal fees from Amgen, BMS, Celgene, Clingen, Eisai, Genomic Health, GSK, Helsinn, Hospira, JnJ, Novartis, Merck, Merck Serono, Mundipharma, Pfizer, Pierre Fabre, Roche, Sandoz, Tesaro, Teva, Vifor Pharma, Bayer Schering, Cephalon, lpsen, OrthoBiotech, Kyowa Hakko Kirin, Sanofi, Talho, outside the submitted work;
- François Clément Bidard reports personal fees and non-financial support from Amgen, AstraZeneca, personal fees from Lilly, grants, personal fees and non-financial support from Novartis and Pfizer, non-financial support from Roche, outside the submitted work;
- Michele De Laurentis reports personal fees from Astra Zeneca, Novartis, Pfizer, outside the submitted work;
- Ivana Durutovic reports grants and personal fees from Roche, Novartis, MSD, Astellas, outside the submitted work;
- Joseph Gligorov reports grants and personal fees from Eisai, Genomic Health, Novartis, MSD, Pfizer, Pierre Fabre, Roche; personal fees from Daichi, Ipsen, Lilly, Macrogenics, Mylan, Onxeo, outside the submitted work;
- Jadranka Lakicevic reports grants and personal fees from Roche, Novartis, Bayer Schering Pharma, Janssen Cilag, grants from Astellas, personal fees from AstraZeneca, outside the submitted work;
- Nikola Milasevic reports grants and personal fees from Roche, Novartis, Inpharm; personal fees from Merck; grants from MSD, outside the submitted work; .
- Liljana Stamatovic reports personal fees and non-financial support from Roche, Pfizer, AstraZeneca, Novartis outside the submitted work;
- Davorin Radosavljevic reports personal fees and non-financial support from Roche, MSD; Pfizer, Astra Zeneca, Merck, Boehringer Ingelheim, Amicus, outside the submitted work;
- Vladimir Todorovic reports personal fees and non-financial support from Roche, Novartis, Sanofi, Astra Zeneca, MSD, Merck, outside the submitted work.
- Suzana Vasovic reports personal fees and non-financial support from Roche, Novartis, Astra Zeneca, Pfizer
- Edouard Vrdoljak reports personal fees from Abbott, Astellas, Astra Zeneca, MSD, Merck, Amgen, Novartis, Servier; grants and personal fees from BMS, Roche, Pfizer outside the submitted work;
- Oliver Arsovski, Nada Babovic,Yazid Belkacemi, Semir Beslija, Mouna Bourhafour, Hamouda Boussen, Franco Cavalli, Timur Ceric, Bojana Cetnikovic, Nada Cicmil, Nebojsa Crnogorac, Enkelejda Cuedari, Tomislav Dragovic, Zoran Dzamic, Radan Dzodic, Zivka Eri, Ahmed Khalil, Khaldoun Kherrou, Dhurata Koroveshi, Vladimir Kovcin, Nevenka Lukovac, Snezana Knzevic-Usaj, Abraham Kuten, Ivan Markovic, Milan Markovic, Nenad Mijalkovic, Daniela Miladinova, Giorgio Mustacchi, Dragana Ognjenovic, Aleksandra Pantelic, Nicholas Pavlidis, Anila Kristo Pema, Lazar Popovic, Nina Radosevic, Sinisa Radulovic, Ivana Rosic, Nevena Secen, Milan Sorat, Petar Stefanovski, Dusanka Tesanovic, Zoran Tomasevic, Zorica Tomasevic, Pauletta Tsoutsou, Igor Stojkovski, Sedat Turkan, Nino Vasev, Ferenc Vicko, Damir Vrbanec, Filip Vukmirovic, Jean-Jacques Zambrovski, Bojan Zaric, had nothing to disclose.

Conflict of interests

Matti Aapro reports personal fees from Amgen, BMS, Celgene, Clingen, Eisai, Genomic Health, GSK, Helsinn, Hospira, JnJ, Novartis, Merck, Merck Serono, Mundipharma, Pfizer, Pierre Fabre, Roche, Sandoz, Tesaro, Teva, Vifor Pharma, Bayer Schering, Cephalon, lpsen, OrthoBiotech, Kyowa Hakko Kirin, Sanofi, Talho, outside the submitted work;François Clément Bidard reports personal fees and non-financial support from Amgen, AstraZeneca, personal fees from Lilly, grants, personal fees and non-financial support from Novartis and Pfizer, non-financial support from Roche, outside the submitted work;Michele De Laurentis reports personal fees from Astra Zeneca, Novartis, Pfizer, outside the submitted work;Ivana Durutovic reports grants and personal fees from Roche, Novartis, MSD, Astellas, outside the submitted work;Joseph

Gligorov reports grants and personal fees from Eisai, Genomic Health, Novartis, MSD, Pfizer, Pierre Fabre, Roche; personal fees from Daichi, Ipsen, Lilly, Macrogenics, Mylan, Onxeo, outside the submitted work;Jadranka Lakicevic reports grants and personal fees from Roche, Novartis, Bayer Schering Pharma, Janssen Cilag, grants from Astellas, personal fees from AstraZeneca, outside the submitted work;Nikola Milasevic reports grants and personal fees from Roche, Novartis, Inpharm; personal fees from Merck; grants from MSD, outside the submitted work; .Liljana Stamatovic reports personal fees and non-financial support from Roche, Pfizer, AstraZeneca, Novartis outside the submitted work;Davorin Radosavljevic reports personal fees and non-financial support from Roche, MSD; Pfizer, Astra Zeneca, Merck, Boehringer Ingelheim, Amicus, outside the submitted work;Vladimir Todorovic reports personal fees and non-financial support from Roche, Novartis, Sanofi, Astra Zeneca, MSD, Merck, outside the submitted work.Suzana Vasovic reports personal fees and non-financial support from Roche, Novartis, Astra Zeneca, Pfizer, Edouard Vrdoljak reports personal fees from Abbott, Astellas, Astra Zeneca, MSD, Merck, Amgen, Novartis, Servier; grants and personal fees from BMS, Roche, Pfizer outside the submitted work; Oliver Arsovski, Nada Babovic,Yazid Belkacemi, Semir Beslija, Mouna Bourhafour, Hamouda Boussen, Franco Cavalli, Timur Ceric, Bojana Cetnikovic, Nada Cicmil, Nebojsa Crnogorac, Enkelejda Cuedari, Tomislav Dragovic, Zoran Dzamic, Radan Dzodic, Zivka Eri, Ahmed Khalil, Khaldoun Kherrou, Dhurata Koroveshi, Vladimir Kovcin, Nevenka Lukovac, Snezana Knzevic-Usaj, Abraham Kuten, Ivan Markovic, Milan Markovic, Nenad Mijalkovic, Daniela Miladinova, Giorgio Mustacchi, Dragana Ognjenovic, Aleksandra Pantelic, Nicholas Pavlidis, Anila Kristo Pema, Lazar Popovic, Nina Radosevic, Sinisa Radulovic, Ivana Rosic, Nevena Secen, Milan Sorat, Petar Stefanovski, Dusanka Tesanovic, Zoran Tomasevic, Zorica Tomasevic, Pauletta Tsoutsou, Igor Stojkovski, Sedat Turkan, Nino Vasev, Ferenc Vicko, Damir Vrbanec, Filip Vukmirovic, Jean-Jacques Zambrovski, Bojan Zaric, had nothing to disclose.

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