Pharmacoeconomics: Can we afford new drugs for breast cancer?

Bringing value to cancer therapy
A new tool to score anticancer treatments and assess drug value.

WE NEED YOU
Find out how you can join us to change the lives of breast cancer patients together.
Can we afford progress in cancer care?

This newsletter highlights some challenges of the ever-increasing cost of new breast cancer drugs. Questions are being asked about the affordability of this progress: new drugs brought to market as a result of real progress in basic and translational science, and co-ordinated multi-national clinical trial programmes involving companies, academicians and thousands of patients. But, the median monthly cost of new drugs at the time of their FDA approval has risen 100-fold over 40 years – from US$100 in the 1970s to US$10 000 in 2015.1

But, can we afford NOT to make progress in cancer care? Worldwide, just over half a million people die each year from breast cancer. That is too many women (and men), so further progress is needed to reduce, or even eliminate, this unwelcome premature mortality. BIG was created to facilitate and expedite research to lead to more breast cancer cures through improvements in treatment, including systemic therapy.

In the Jenny Bryan’s interviews, although different views are discussed, there seems to be a consistency in calling for a change to the whole system: what options exist for that? It is expensive to develop new drugs: many fail at an early stage, and those costs need to be recouped. A pharmaceutical company presumably does this from the subsequent sales of the successful drugs. Precision medicine may reduce overall drug use, but won’t obviate the need to recoup the cost of failed compounds. Could healthcare purchasers support the costs of trials and then legitimately buy approved drugs at a much lower price? Could we use academic research structures, if they were better funded by healthcare systems, to reduce the cost of doing large phase III trials?

Pharmaceutical companies charge prices that the market can absorb. But it is not a true competitive market, in that each drug developed has a monopoly for many years, and competitors have to go through the same expensive clinical trial programme to get to the point where the efficacy and safety data on a “me-too” agent are at least as good as the front runner. What options exist to force price restraint as part of the deal for regulatory approval of a monopoly drug?

But is it the role of the regulator to limit the profit to be made from innovation? Whilst commercial companies need to take risks to develop drugs, we must recall that it is patients who take part in clinical trials, and most do so, especially in the early phases, more out of altruism than an expectation of benefit. How is their “investment” acknowledged in a system that allows drug prices to rise faster than inflation, so that the future patients they wanted to help are being priced out of access to the new drug?

In calling for a change to the whole system: what options exist for that? Perhaps the regulators should ensure that the “value” as well as the activity of a drug is better understood at the point of coming to market?

Clinicians traditionally see themselves as an advocate for each individual patient, balancing efficacy and toxicity when choosing a treatment. But each Euro spent on one patient is a Euro not available for another... should we advocate a better system that values the use of health-care money based on its purchasing power – the extra healthcare it buys – rather than how loudly its advocates shout?

Dr David Cameron
Professor of Oncology, University of Edinburgh & Director of Cancer Services, NHS Lothian, UK
BIG Executive Board Member

2 http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx accessed 19th January 2016
In the last three years, around 40 new anticancer drugs have been approved by US and European regulators, and pharmaceutical company pipelines are packed with promising new targeted therapies. But rising prices – averaging $10,000 per month for new agents in the US – are putting such pressure on healthcare budgets that medicines regulators, health economists and clinicians are focusing on how costs can be contained to create affordable and sustainable models for the future. Jenny Bryan discusses recent US and European initiatives and reports industry and patient advocate viewpoints on the way forward.

How can healthcare providers ensure they are getting value for money from the headline-grabbing, new generation of anticancer drugs streaming on to markets around the world? That is the multi-billion-dollar question challenging budget holders with the unenviable task of deciding who should have access to the latest advances in treatment.

As long ago as 2009, cancer drugs were costing the EU over €13 billion¹ – over a quarter of the total healthcare costs for the disease – and US data published in 2010 estimated drug costs at $125 billion, predicted to increase to $158 billion by 2020.² On both continents, healthcare costs for breast cancer were higher than for any other form of cancer and, in the EU, drug costs topped €3 billion – nearly half of overall costs for breast cancer.¹

¹The financial problem is real, the question is how it’s being dealt with and where this leads.
Certainly, some insurers are noting a rapid increase in the proportion of pay-outs that are going for cancer drugs and starting to question how long this can be sustained,” says Professor Clifford Hudis, Chief, Breast Medicine Service, Memorial Sloan Kettering Cancer Center, New York, USA.

Individual cancer drug prices vary between and within countries, depending on centrally agreed market access schemes and locally negotiated discounts. A recent analysis of European pricing showed that prices were generally higher in Sweden, Switzerland and Germany, and lower in Portugal, Spain, Greece and the UK. For example, the price of trastuzumab was reported 27% higher in Switzerland than in the UK.

“It’s clear that prices are being set according to what the market can bear and pricing for reimbursement is a dark art, with as many different schemes and prices as stars in the sky,” points out Professor Richard Sullivan, Director, Institute of Cancer Policy, King’s College London. “Official list prices bear no resemblance to what countries, healthcare institutions, clinicians and patients really pay and the actual prices are an unknown quantity. The best data come from the US where there is greater transparency, and you can see that it has a superheated market for cancer drugs.”

Professor Hudis believes that only a radical change in thinking about drug pricing can address affordability issues and points to the electronics industry as an example of how to combine innovation with competitive pricing:

“At present, the best predictor of the price of a drug is the year it was approved, with each drug a little more expensive than the last. The pharmaceutical industry is not the enemy, they price their drugs the way the market encourages them. So if we want to change that, we need to see how we can change the market forces. Pharmaceutical companies need to be incentivised to behave as they would in a normal market that competes on price.”

Dr David Montgomery, Medical Director for Oncology at Pfizer UK and Ireland, predicts that the cost of anticancer drugs will soon start to fall, as cheaper generics and biosimilars come on to the market when novel agents lose patent protection. He compares the current situation to the affordability bubble in cardiology following the introduction of new blood pressure and cholesterol medicines in the 1980s and 1990s:

“That led to significantly improved outcomes with patients living longer with fewer complications of heart attacks, less surgery and reduced costs, and was followed by a big fall in prices once generics were introduced. I think we will reach a similar equilibrium in oncology where, for every new medicine that is launched, several will come off patent.”

He adds that governments need to work with pharmaceutical companies to find ways to ensure patients get access to the medicines they need.

“Most companies would like to avoid two or three years struggling to get new medicines reimbursed so they can be prescribed to patients, which incurs additional costs on all sides,” he says.

In an effort to turn the debate towards using value as a measure of health benefit for money spent, both the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) last year published new scales, rating benefit of anticancer drugs/treatment regimens on the basis of whether they enable patients to live longer and better.

The ASCO framework also includes drug costs.

“Value tools make it clear what keeps a patient alive and what doesn’t and what the alternatives are, so maybe we can have more transparent discussions. They won’t necessarily drive prices down, but they will help people have more informed conversations,” says Professor Hudis.

More widespread use of personalised medicine, with treatment tailored to tumour biomarkers, may also impact on drug costs, though the direction of spend and the timeframe remain unclear.

Dr Peter Hall, Senior Lecturer in Cancer Informatics, at Edinburgh Cancer Research Centre, Edinburgh, UK, suggests that personalised medicine will lead to increased benefit and value if it demonstrates the advantage of spending money in a highly selected population:

“The same challenges will apply in assessing value, and I don’t think it will reduce drug costs per se, but it may very well lead to healthcare
cost savings. If targeted drugs can increase cure and reduce recurrence, we can make savings.”

Dr Montgomery agrees, and also points to the potential of personalised medicine for reducing treatment-related costs such as hospitalisation to manage side effects. “But there are currently too many uncertainties, he says, to be sure of the impact”.

What of patients themselves? Should they play a greater role in determining how healthcare providers spend taxpayers’ money on anticancer drugs?

Susan Knox, Executive Director of Europa Donna - The European Breast Cancer Coalition, an organisation with patient advocacy groups in 47 European countries, urges greater involvement for such groups in national health technology assessment processes:

“People say they want patients to be involved but there is little transparency around negotiations between reimbursement agencies and pharmaceutical companies about pricing. We’ve sat on various committees aimed at helping patients understand more about health technology assessment procedures, but it hasn’t resulted in better access to such discussions for advocacy groups in many countries.”

She thinks it is unreasonable to expect patients to get involved in discussions about the cost effectiveness of their medicines when they are ill, but she does support broader educational initiatives aimed at helping the general public and patient advocates improve their understanding of the issues:

“It’s important that people understand their health system, the rising costs of medical care and the decisions that need to be made about access to treatment. As advocates we believe patients should have access to all treatments that have been proven effective. That said, in Europe at least, people understand and don’t expect that governments can afford to pay for absolutely every treatment, especially those where there is little advantage. But there is certainly a place for more education about how and why these decisions are made.”

Professor Sullivan, whose research has included studies of attitudes to drug availability amongst sick patients, healthy volunteers and clinicians, agrees that, when the issues are explained, people do not believe that healthcare providers should offer all treatments, whatever the cost.

“People understand the trade-offs if you explain them, but what is clear across all groups, including clinicians, is that people don’t want to make those decisions at an individual level, they want to live within a managed system,” he concludes. “What we now need is a rational discussion, with public involvement, around the thresholds for willingness to pay. People are good rationalisers in these situations but they need the opportunity to hear the evidence and understand the debate away from the confrontational arena in which these things are so often presented.”

Pharmacoeconomic assessment to improve decision-making

In pharmacoeconomic analyses, the health benefits of anticancer treatments and other therapies are typically measured in terms of quality adjusted life year (QALY) gained, and clinicians and health economists believe that this remains the most useful measure.
“QALYs get a lot of criticism but we do need a universal measure of health benefit that is relevant across all diseases and that’s what QALYs give us. Cancer-specific measures help us to prioritise treatments and support accelerated regulatory approvals, but we still need to calculate cost per QALY to make a proper statement about value within a national healthcare system where cancer is just one of the many diseases that need to be treated,” says Dr Hall.

In the UK, the National Institute for Health and Care Excellence (NICE) generally uses a threshold of £30 000 per QALY (up to £50 000 for end of life drugs) above which it is unlikely to approve a drug, and other national health technology authorities have used similar cut-offs.

“The threshold depends on the healthcare provider’s budget and the bigger the budget, the higher the threshold. If you look at the decisions that NICE has been making on cancer drugs in recent years, the threshold is probably closer to £50 000,” says Dr Hall.

He points to the growing trend towards conditional approval of new drugs, with the requirement for Phase 3 trials and collection of additional “real world” data before authorisation is confirmed. These data typically include response rate, survival, uptake, toxicity and the characteristics of the population in which the drug is used.

“One of the concerns is that when you move from a relatively fit clinical trial population to a less fit, real world population, patients may be more susceptible to toxicities, so a period of intense observation can identify the true level of toxicity and its impact on quality of life and hence the value of treatment,” adds Dr Hall.

As he explains, early access schemes can be expensive to administer unless an efficient data capture system is in place. In England, the National Cancer Intelligence Network (NCIN) plays an important role in collecting data throughout the cancer journey, and other National Health Service (NHS) data capture systems facilitate analysis of healthcare costs in routine clinical practice.

“The UK has the advantage of having a single healthcare provider, so one system is able to capture all the necessary data. This is much harder in countries such as the US where there are many different providers and data have to be gathered from multiple insurers whose systems haven’t been designed to give standardised information,” Dr Hall explains.

“Some data, such as toxicity-related hospitalisation, are more generalisable across healthcare systems”, he adds. Thus, if a treatment is typically associated with a week’s hospitalisation in one country, this information can be used to calculate costs in another country, based on local prices.

“From a global perspective, the most important thing is for the oncology community to engage with health economists in collecting data for value assessments so that we can reduce the delay in getting new treatments to patients. Alongside this, there is a need for pharmaceutical companies to engage not only with the FDA and EMA in setting up appropriate clinical trials, but with reimbursement decision makers and health economists.”

**Bringing value to cancer therapy: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MBCS)**

The European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS), published in 2015, stratifies the magnitude of clinical benefit for new cancer treatments for solid tumours on the basis of trial outcomes indicating that patients live longer and/or better. It grades adjuvant and neoadjuvant therapies used with curative intent on a scale of A to C, with A and B indicating a high level of clinical benefit, and new treatments used without curative intent on a scale of 1 to 5, with grades 4 and 5 representing a high level of proven clinical benefit.

Professor Sullivan, who was involved in the development of the scale, explains that the hierarchy of trial outcomes on which these grading systems are based starts with overall survival (OS) as the gold standard, followed by progression-free survival (PFS), disease-free.
survival (DFS), and finally response rate (RR), with each adjusted according to toxicity and quality of life (QoL). The curative intent scale allows favourable assessment of studies with early data showing a high DFS, but requires that these are re-evaluated when mature survival data are available.

“There was general consensus that you couldn’t get the top score if you only had PFS as an outcome for a drug and, as a result, very few trials of drugs used for curative intent scored A or B, and 40% of trials of non-curative agents had benefits in the 1 to 3 category,” says Professor Sullivan. “Using the scale, many trials that were published in leading journals were found not to be the game changers they were originally thought to be.”

Amongst breast cancer trials, the HERA study of chemotherapy +/- trastuzumab as neoadjuvant treatment for HER-2 positive tumours achieved an A grade, and the EMDILIA study of T-DM1 as second-line treatment of metastatic disease after trastuzumab achieved a grade 5. The CLEOPATRA trial of trastuzumab+chemotherapy +/- pertuzumab as first line treatment for metastatic disease was graded 4, as was the EGF104900 trial of lapatinib +/- trastuzumab.

Further analyses of other trials are being carried out and some institutions are already starting to use the scale to make reimbursement decisions.

**ASCO scale for grading drug costs**

The American Society of Clinical Oncology (ASCO) has developed a conceptual value framework to enable new treatment regimens to be compared with standard of care (SoC) in terms of clinical benefit and toxicity, in order to generate a net health benefit (NHB) score. Once fully developed, ASCO plans that physicians and patients can use the framework to view these parameters alongside direct treatment costs to facilitate shared decision making about the value of different approaches.

Professor Hudis, who was involved in developing the ASCO framework, points out that the clinician’s role has traditionally been to identify the most appropriate treatment for each patient, balancing efficacy against toxicity, but value has not been a primary part of this responsibility.

“The ASCO tool helps them to start to incorporate value into their thinking and make choices where efficacy and toxicity are similar but costs may differ widely. We need to be able to deal with these issues in a transparent way, and the value framework allows people to compare across regimens rather than dealing with absolute cost,” he explains.

As with ESMO-MCBS, two versions of the value framework have been developed: for advanced cancer and for potentially curative adjuvant or neoadjuvant treatment.

For advanced disease, clinical benefit is rated 1 to 5, based on improvement in median OS for a new treatment compared to SoC or, if median OS data are not available, median PFS or, if that is not available or treatment was only evaluated in a single-arm study, response rate (RR). Scores are then weighted according to the clinical meaningfulness of OS, PFS or RR as endpoints to gain a maximum of 80 points that can be attributed to survival. Bonus points are assigned for certain statistically significant improvements in cancer symptoms and treatment interval.

For the curative framework, clinical benefit is also rated 1 to 5 and then weighted according to whether OS or DFS data are available so that the maximum survival benefit is 80 points.

In both scenarios, toxicity is calculated as the relative toxicity of the new agent against the comparator regimen, with a maximum score of 20, based on the frequency of common terminology criteria for adverse events (CTCAE) grade 3 to 5.

The Net Health Benefit (NHB) is then calculated by combining clinical benefit and toxicity scores, and bonus points, so the maximum score is 130 for the advanced disease framework and 100 for the curative framework.

For advanced disease, cost is based on monthly cost of treatment (drug acquisition cost and patient cost) while, for curative treatment, cost reflects the total cost (drug acquisition cost and outpatient requests.

---

**The UK Cancer Drugs Fund**

Since 2011, some cancer drugs that would not be available on the NHS in England because they failed to meet NICE cost effectiveness thresholds or were awaiting appraisal, have been reimbursed through the Cancer Drugs Fund (CDF) (worth £340 million in 2015/16). The Fund scores cancer drugs on clinical effectiveness (OS, PFS, quality of life (QoL), toxicity and unmet medical need), and takes account of clinical support for drug applications to the fund. Once a drug is on the CDF list, clinicians can apply for funding for individual patients through an online service that provides almost immediate approval.

As the CDF has come under increasing cost pressure, it was decided to incorporate it within NICE. Under the proposed new scheme, starting in April 2016, NICE will appraise all new cancer drugs that are expected to receive marketing authorisation and publish guidance within 90 days of this being received. It will then recommend whether a drug should go into routine use, be used within the CDF, or not go into routine use. Drugs used via the CDF will be available for a predetermined period while further evidence is collected. At the end of this time, it will go through a further short assessment by NICE and, on the basis of the updated evidence, receive a positive recommendation and go into routine use, or a negative recommendation, allowing it to be used only on the basis of individual funding requests.

As part of this, as the CDF has come under increasing cost pressure, it was decided to incorporate it within NICE. Under the proposed new scheme, starting in April 2016, NICE will appraise all new cancer drugs that are expected to receive marketing authorisation and publish guidance within 90 days of this being received. It will then recommend whether a drug should go into routine use, be used within the CDF, or not go into routine use. Drugs used via the CDF will be available for a predetermined period while further evidence is collected. At the end of this time, it will go through a further short assessment by NICE and, on the basis of the updated evidence, receive a positive recommendation and go into routine use, or a negative recommendation, allowing it to be used only on the basis of individual funding requests.
patient cost) of a standard duration treatment regimen. Costs include those of supportive care drugs required to administer anticancer treatment (e.g., antiemetics).

Professor Hudis stresses that the ASCO value framework is not a finished product and will require continuing input and refinement:

“It’s already helping to put value front and centre of our dialogue, and the fact that we’re talking about it is a major step forward. It’s likely to be used by policy makers, insurers, doctors and pharmaceutical companies, and we’re already seeing regulators in some countries asking for it to be included in new drug submissions.”

### The industry viewpoint

With a US list price of $9850 per month, Pfizer’s new breast cancer drug, palbociclib, is not the most expensive drug for the disease and, says a Wall Street Journal report, the company turned down the option of setting a higher price that would risk antagonising clinicians and payers and suck the air out of the launch campaign early in 2015.

Dr David Montgomery explains that pricing decisions balance the level of unmet need, the likely impact on patients and the disease, the cost of other treatments, and the potential to reduce other health-related costs:

“In the UK, our aim is to make our oncology medicines available at prices that are affordable to taxpayers and a good deal for patients. If we don’t set prices that the NHS considers sensible, our medicines won’t get used.”

Pfizer, like other companies making new cancer medicines, has had medicines turned down for use in the NHS because they failed to meet the tough cost effectiveness criteria set by NICE, and Dr Montgomery questions not only the £30 000 threshold for most drugs but also the emphasis on OS in cost per QALY calculations.

“NICE uses cost per QALY criteria, which requires an understanding of the extra life a medicine gives. But most cancer drug trials are set up with PFS rather than OS because we are of course not comfortable with the idea that patients have to die to get a positive result,” he says. “Regulators will approve medicines on the basis of PFS, but health technology assessors like NICE want OS for reimbursement.”

Given that clinicians in other specialties, such as cardiology, routinely carry out large trials to demonstrate survival advantages of drug treatments, why can’t oncologists?

Dr Montgomery explains that, in contrast to the relatively healthy patients who take part in large trials of statins and other heart drugs with survival endpoints, patients in cancer drug trials generally have metastatic disease and may be dying. The new drugs available to them are likely to have received conditional approval under fast-track procedures based on results of Phase 1/2 trials, prior to confirmation in large Phase 3 studies.

“We are asking patients with terminal disease to take part in studies of a new medicine versus standard of care chemotherapy, where the new medicine has already been conditionally approved because of its promising early results, so patients can get it without agreeing to take part in a trial,” says Dr Montgomery. “We approach this by doing PFS trials where patients are closely monitored and, when those in the chemotherapy arm show pre-agreed levels of progression, they can switch to the new drug.”

Although this type of study design can produce strong PFS data to support a licence application or confirm a conditional approval, it cannot provide the head-to-head comparison of OS needed for health technology assessments (HTAs). Dr Montgomery explains that companies can model for survival in order to meet the need for cost effectiveness analyses. However, doubts about the true survival benefit add uncertainty to cost effectiveness calculations. He adds that uncertainty over the survival gain is the most common reason for cancer medicines to be declined by NICE.

“In the recent case of crizotinib for non-small cell lung cancer, NICE used methods that showed a cost per QALY of £115 000, which meant it was rejected, while the Scottish Medicines Consortium used different methods that gave a figure nearer to £40 000, which meant it was accepted under the end-of-life threshold of £50 000,” he says.

Dr Montgomery does not believe that the transfer of the Cancer Drugs Fund within NICE’s remit will help the situation. While it will enable more
“real world” data to be collected, including OS data on newly licensed agents, it will not be able to compare these results with those for standard care because of the switch to the new agent once progression has occurred.

As the Cancer Drugs Fund, ESMO-MCBS and ASCO value frameworks all use scoring systems that put a premium on OS evidence, with fewer points awarded for PFS-based studies, he questions how useful they will be in facilitating prescribing decisions.

“They partly assess the effectiveness of the medicines and partly assess the methodology of the trials, so you could have less effective medicines with survival benefits getting higher scores than better medicines that only have PFS measurements,” says Dr Montgomery.

He feels that another drawback is the use of data from registration studies, which may lead to companies having to choose a sub optimal comparator drug.

“The new scoring systems are too blunt and too crude and again enshrine OS benefit. They may be helpful for prioritising medicines in countries without the infrastructure for making funding decisions, but it would be a significant regressive step for countries such as France, Germany or the UK to introduce these tools that are cruder than what they already have,” he said.

Would differential pricing for cancer medicines across indications – allowing companies to charge more for medicines to treat cancers where they work best – be a better option for containing costs?

Dr Montgomery suggests that the industry is open to flexible approaches to pricing medicines and will work with governments to try and ensure that medicines can be made available to patients. He points out that, in the UK, the pharmaceutical industry underwrites the overall medicines bill so that it cannot exceed a set level, and this will cut the cost of medicines to the NHS by £4 billion over the five years of the scheme.

“Until we sort the fundamental issues related to HTAs effectively and get proper agreements with governments that are realistic and function to improve access, we will always face challenges with access to medicines,” concludes Dr Montgomery. “One of the issues driving that challenge is fear of ever expanding budgets, and I don’t think that’s correct. In the UK the medicines bill remains firmly under control and, in time, we’ll reach equilibrium as is the nature of the medicines life cycle.”

From the patient perspective

Greater involvement for patient advocacy groups in HTA procedures and clinical trial design could have a significant impact on containing cancer drug costs and helping to create more affordable models of care. Susan Knox points out that, while patients are often invited to discussions at the European Medicines Agency (EMA) about new drug approvals, this rarely happens on consultations about reimbursement.

“Just because a drug is approved by the EMA doesn’t mean it will be reimbursed in different EU countries and, if we aren’t informed when drugs are going through HTAs, we can’t advocate on behalf of patients,” she says. “While the European Network for Health Technology (EUnetHTA) has made progress in developing and harmonising HTAs across Europe, patient involvement is not automatically incorporated into the process in all countries.”
Meet the experts

Peter Hall, MD PhD
Clinical Senior Lecturer in Cancer Informatics, Edinburgh Cancer Research Centre, University of Edinburgh, UK

Clifford A. Hudis, MD
Chief, Breast Medicine Service, Department of Medicine
Vice President for Government Relations and Chief Advocacy Officer
Memorial Sloan Kettering Cancer Center
Professor of Medicine, Weill Cornell Medical College, New York, USA

Susan Knox,
CEO, Europa Donna—The European Breast Cancer Coalition

Dr David Montgomery MRCS FFPM
Medical Director - Pfizer Oncology UK and the Republic of Ireland

Richard Sullivan, MD, PhD
Director, Institute of Cancer Policy,
Co-Director, Conflict & Health Research Program,
King’s Health Partners Comprehensive Cancer Centre, King’s College London, UK

Europa Donna has run training courses on HTA methodology, but members have to rely on clinicians and other sources to tell them when HTAs concerning breast cancer drugs are underway in their countries; it is still quite rare for breast cancer advocates to be invited to participate in these discussions.7

“Pharmaceutical companies and reimbursing agencies in many countries still do not engage in public discussions about pricing decisions and their rationale. That needs to change, and we need much greater transparency about how these decisions are made,” says Ms Knox.

She feels that patient groups could make a greater contribution to discussions about changes to drug trial methodology to reduce the cost of trials required for marketing approval and also raise the possibility of shorter courses of treatment. She points to a study being carried out in Finland to investigate whether shorter drug regimens for some breast cancer patients could be as effective as longer, more expensive courses.

“All parties need to come together to look at different methods of doing research that could bring costs down for pharmaceutical companies and payers. If patient advocates are involved in these discussions, they can also play a role in communicating information to the wider public when such changes are made,” says Ms Knox.

She is optimistic that the newly launched European Commission Initiative on Breast Cancer (ECIBC) will also improve public awareness of and involvement in treatment access issues.8 The initiative is focused on developing a voluntary European quality assurance scheme for the full range of breast cancer services underpinned by evidence-based guidelines on screening and diagnosis. As Ms Knox concludes:

“From the patient perspective, the ECIBC is the most important project currently underway. Its working groups include key health professionals from the entire breast cancer field in Europe, and patient advocates as individuals and stakeholders are being consulted throughout the process to ensure a focus on patient/person-centred care. This initiative will ultimately have a huge impact on breast cancer services across all European countries, including access to new drugs.”

References

Bringing value to cancer therapy: Focus on the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS)

The European Society for Medical Oncology (ESMO) has developed a validated and reproducible scale, the ESMO - Magnitude of Clinical Benefit Scale (ESMO-MCBS) to assess the magnitude of clinical benefit for cancer medicines. A field testing of the scale was conducted on 77 cancer medicines across 10 cancer types. In this article, Dr Nawale Hajjaji from BIG Headquarters interviews Professor Martine Piccart, Chair of the Breast International Group (BIG), who has served as President of ESMO (2012-2013) and the European CanCer Organization (ECCO) (2014-2015).

What does this scale bring?

The great strength of this scale is to provide an objective starting point to assess drug value*, says Professor Martine Piccart. The ESMO-MCBS is an important first step to the critical public policy issue of value in cancer care, helping to frame the appropriate use of limited public and personal resources to deliver cost effective and affordable cancer care.

The contribution of the scale to value assessment is illustrated in Figure 1, alongside ASCO value framework and cost-effectiveness.

This scale uses a rational, standardised and validated approach to derive a relative ranking of the magnitude of clinically meaningful benefit that can be expected from a new anti-cancer treatment for solid tumours.

The goal of the ESMO-MCBS evaluation is to assign the highest grade to trials having adequate power for a relevant magnitude of benefit, and to make appropriate grade adjustment to reflect the observed magnitude of benefit.

The ESMO-MCBS implements a dual rule:
- taking into account the variability of the estimated hazard ratio (HR) of from a study, the lower limit of the 95% confidence interval (CI) for the HR is compared with specified threshold values,
- and the observed absolute difference in treatment outcomes is compared with the minimum absolute gain considered as beneficial.

At European Cancer Congress 2015, the ESMO-MCBS was received with great enthusiasm by patients and oncologists; pharmaceutical companies also expressed a favourable opinion.

---

* The great strength of this scale is to provide an objective starting point to assess drug value.

** Prof. Martine Piccart

---

Figure 1: ESMO-MCBS contribution to the landscape of value assessment
Figure 2: ESMO-MCBS scoring of new approaches to adjuvant therapy or new potentially curative therapies

Scoring therapies with curative intent
ESMO-MCBS Form 1

- **A**: HR > 0.65 AND Gain ≥ 3 months or Increase in 3 year survival alone ≥ 3%
- **B**: HR > 0.65–0.70 AND Gain 1.5–2.4 months or Increase in 2 year survival alone 3%–5%
- **C**: HR ≤ 0.65 AND Gain 2.5–2.9 months or Increase in 2 year survival alone 0–3%

Scores

Figure 3: ESMO-MCBS scoring of therapies that are not likely to be curative where primary outcome is OS (3A), PFS (3B), or quality of life (QoL), toxicity or response rate (RR) in non-inferiority studies (3C)

3A

Scoring therapies with non-curative intent
OS as endpoint
ESMO-MCBS Form 2a

- **A**: HR > 0.70 AND Gain ≥ 3 months, or Increase in 3 year survival alone ≥ 10%
- **B**: HR ≤ 0.70 AND Gain 3–4.9 months, or Increase in 3 year survival alone 5 to 10%
- **C**: HR ≤ 0.70 AND Gain 1.5–2.4 months, or Increase in 2 year survival alone 0–3%

Scores

3B

Scoring therapies with non-curative intent
PFS as endpoint
ESMO-MCBS Form 2b

- **A**: HR > 0.65 AND Gain ≥ 3 months
- **B**: HR ≤ 0.65 AND Gain ≥ 1.5 months
- **C**: HR = 0.65

Scores

3C

Scoring therapies with non-curative intent
QoL, toxicity or response rate (RR) as primary outcomes and for non-inferiority studies
ESMO-MCBS Form 2c

- **A**: Reduced toxicity or improved QoL using validated scale with evidence for non-inferiority or superiority in PFS/OS
- **B**: Improvement in some symptoms using a validated scale but without evidence of improved overall QoL
- **C**: RR is increased ≥ 20\% but without improvement in toxicity/ QoL/PFS/OS

Scores

How does the ESMO-MCBS score anti-cancer treatments?

Given the profound differences between the curative and palliative settings, the tool is presented in two parts.

- In form 1, the improvement of survival at 3 years or more or the improvement in disease-free survival (DFS) alone is used to score drugs from A (highest score) to C in the (neo)adjuvant setting (curative intent), as detailed in Figure 2.

- Form 2 (Figure 3) is used to evaluate non-curative interventions and scores drugs from 5 (highest score) to 1:
  - form 2a (Figure 3A) is used for studies with overall survival (OS) as the primary outcome, and is prognostically sub-stratified according to the OS in the control arm (OS > 1 year or ≤ 1 year), scores can be upgraded by 1 point when the experimental arm demonstrates improved quality of life (QoL) or delayed deterioration in QoL using a validated scale or substantial reduction in grade 3 or 4 toxicity;
  - form 2b (Figure 3B) is used for studies with progression-free survival (PFS) or time-to-progression (TTP) as primary outcomes and is similarly sub-stratified according to the PFS in the control arm (PFS > 6 months or ≤ 6 months), scores can be upgraded or downgraded depending on secondary outcomes such as toxicity data, improvement in OS or data derived from QoL;
  - form 2c (Figure 3C) is used for non-inferiority studies with QoL, toxicity or response rate as primary outcomes.

The ESMO-MCBS can only be applied to comparative research outcomes; it is not applicable when evidence of benefit derives from single-arm studies.

How can this scale be improved?

The ESMO-MCBS is a dynamic tool and its criteria will be revised on a regular basis pending peer reviewed feedback and developments in cancer research and therapies. “Moreover, future versions of the scale could integrate new variables, such as the results of outcome research and resumption of a professional activity”, explains Professor Piccart.

How will ESMO apply the ESMO-MCBS?

ESMO intends to apply this scale prospectively to each new anti-cancer drug/intervention that will be European Medicines Agency (EMA) approved. Drugs or treatment interventions that obtain the highest scores on the scale will be emphasized in the ESMO guidelines, with the hope that they will be rapidly endorsed by health authorities across the European Union.

More than anyone else, you know how much research is important and that you are part of the solution.

More than anyone else, you know that academic clinical trials are hard to fund but are critical to patients, who are at the hearth of our research.

We are striving to fundraise for research and clinical trials under the BIG umbrella through events such as The Designers’ Christmas Trees, the BIG Garden Party, and the BIG Time for Baby crowdfunding campaign (see BIG’s website).

But YOU can help us in a different way!

BIG against breast cancer is looking for connections that you believe can make a difference

☐ Are you directly or indirectly acquainted with an international celebrity? Maybe she or he could become the next BIG Ambassador of a specific breast cancer research campaign?

☐ Do you know a top designer who would be delighted to create something unique to support breast cancer research?

☐ Do you know a company whose CEO or board is impassioned by the breast cancer cause and would be keen to sensitise their company employees or their clients?

If you tick one or more of these boxes, please contact us today to share your precious advice.

Together, we can change the world for breast cancer patients.

Serge Schmitz – International Fundraising Director
serge.schmitz@BIGagainstbc.org
Tel +32 475 78 00 51

www.BIGagainstbreastcancer.org

Yesterday’s research results in
Today’s treatments and
Tomorrow’s cures
Our vision: Together we will find a cure for breast cancer through global research and collaboration.

The Breast International Group (BIG) is a not-for-profit organisation for academic breast cancer research groups from around the world.

Founded by leading European breast cancer experts in 1999, BIG now constitutes a network of 56 groups and data centres based in Europe, Canada, Latin America, the Middle East, Asia and Australasia. These entities are tied to several thousand specialised hospitals and research centres worldwide. About 30 clinical trials and several research programmes are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute and the North American Breast Cancer Group, so that together they act as a strong interacting force in the breast cancer research arena.

www.BIGagainstbreastcancer.org

The 56 breast cancer research groups of the BIG network

ABC
Austrian Breast & Coloelctal Cancer Study Group

AGO-B
Arbeitsgemeinschaft Gynäkologische Onkologie Breast Study Group

ANZ BCCT
Australia & New Zealand Breast Cancer Trials Group

ARCGOY-DINECO
Association de Recherche dans les Cancers dont Gynécologiques - Groupe d’Investigateurs Nationaux pour l’Etude des Cancers Ovariens et du sein

BOCS
Breast-Gynecological International Cancer Society

BIBE
Breast Intergroup of Eastern India

BOOG
Borstkanker Onderzoek Groep

BREAST
Breast European Adjuvant Study Team

CCTG
Canadian Cancer Trials Group

CEEOG
Central and East European Oncology Group

CTR
Cancer Therapeutics Research Group

DBCG
Danish Breast Cancer Cooperative Group

EORTC BC
European Organisation for Research and Treatment of Cancer, Breast Cancer Group

FBCG
Finnish Breast Cancer Group / Suomen Rintasyöpäryhmä

FBI
Francilien Breast Intergroup

GAICO
Grupo Argentino de Investigación Clinica en Oncologia

GBCT
Grupo Brasiliero de Estudos do Cancé de Mama

GER
German Breast Group

GECO PERU
Grupo de Estudios Clinicos Oncologicos Peruano

GEICAM
Grupo Español de Investigacion en Cancé de Mama

GOG
Gynecologic Oncology Group

GORIC
Italian Oncology Group for Clinical Research

GONO
Gruppo Oncologico Nord-Ovest

HBCS
Hellenic Breast Surgical Society

HeCoG
Hellenic Cooperative Oncology Group

HKBOG
Hong Kong Breast Oncology Group

HORG
Hellenic Oncology Research Group

IBCC
Icelandic Breast Cancer Group

IBCG
International Breast Cancer Group

IBG
Israel Breast Group

IBIS
International Breast Cancer Intervention Studies

ICCG
International Collaborative Cancer Group

ICON ARO
Indian Co-Operative Oncology Network

ICOR
All Ireland Cooperative Oncology Research Group

ICRC
Iranian Cancer Research Center

ICR-CTS
Institute of Cancer Research – Clinical Trials & Statistics Unit

IOSG
Indian Oncology Study Group

ITMO
Italian Trials in Medical Oncology

JBCRG
Japan Breast Cancer Research Group

LACOG
Latin American Cooperative Oncology Group

MICHELANGELO
Fondazione Michelangelo

NCCG
National Cancer Research Institute - Breast Cancer Clinical Studies Group

SABO
Swedish Association of Breast Oncologists

SAKK
Swiss Group for Clinical Cancer Research

SBCG
Sheba Breast Collaborative Group

SweBCG
Swedish Breast Cancer Group

SKMCH & RC
Shaukat Khanum Memorial Cancer Hospital & Research Centre

SLO
Société Luxembourgeoise d’Oncologie

SOLO
Society of Oncology

SUCCES
Study Group

TCOG
Taiwan Cooperative Oncology Group

TROG
Trans Tasman Radiation Oncology Group

UCBG
Unicancer Breast Group

WSG
Westdeutsche Studiengruppe
IMPROVING CARE AND KNOWLEDGE THROUGH TRANSLATIONAL RESEARCH IN BREAST CANCER

Late registration deadline: 13 April

BRUSSELS  BELGIUM

Conference Co-Chairs
Robert Coleman, Sheffield, UK
Philippe Bedard, Toronto, ON, Canada

PRE-IMPAKT TRAINING COURSE
11-12 MAY 2016

IMPAKT CONFERENCE
12-14 MAY 2016
Together

we will find a cure for breast cancer