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BREAST CANCER DRUGS FUNDING AND TRIALS

A white paper, August 2017

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About Pink Ribbon

Pink Ribbon is a growing international network for breast cancer prevention and cure, seeking to help eliminate all breast cancer-related deaths.

In the UK, its current focus includes an annual conference called the Breast Cancer Forum, held in association with the Royal Society of Medicine, along with other specialist events, online news and information, networking, lobbying and social media.

Future planned events include the inaugural Pink Ribbon awards, to be launched in London and held in New York, and other promotional and campaigning work.

The team is led by publishing director, Gerard Dugdill.

The current steering panel for the forum is additionally:

Mike Dixon, consultant surgeon & professor, Edinburgh breast unit

Aleksandra Filopovic, clinical fellow in medical oncology, Imperial College, London

Mark Ho-Asjoe, consultant plastic surgeon, St Thomas' hospital

Donald Longmore, retired heart surgeon & author

Deborah Ruddy, consultant clinical geneticist, Guys & St Thomas

Susannah Stanway, consultant, medical oncology, breast unit, Royal Marsden NHS Foundation Trust

Ash Subramanian, breast care consultant, East Sussex Healthcare NHS Trust

Kathleen Thompson, pharmaceutical physician & author, *From Both Ends of the Stethoscope*

Chris Twelves, pharmacology & oncology professor, Leeds Cancer Research UK clinical center

Wendy Watson, founder, national hereditary breast cancer helpline.

- Dr Thompson, previously diagnosed with breast cancer, chaired the drugs funding and trials event.

A range of other patient campaigners also contribute to the projects.

For this conference and white paper these included: Metup UK lobbyist, Jo Taylor (@abcdiagnosis); Julia Bradford; breast and ovarian patient and campaigner, Alison Dagul, and Lesley Turner, patient advocate for the Catalyst Initiative (see page 8).

www.pinkribbon.co

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Introduction

This white paper arises out of the Pink Ribbon drugs funding & trials conference, held at the faculty of pharmaceutical medicine on 23 March 2017 (full programme provided on page 13-15).

The general theme to emerge from the conference is that the UK would benefit from enhanced communication between:

- Pharma, regulators and NICE to expedite drug and pricing approval;
- Regulators, NICE and hospitals to allow hospitals time to prepare for new drugs, for example through horizon scanning, with transparency on costs, efficacy and safety profile;
- Pharma and trials database creators, for example, Cancer Research UK (CRUK), to ensure information on clinical trials is effectively disseminated to those patients who may wish to take part – for the benefit of the patients themselves, as well as the national health service (NHS) and pharma.

We also need better communication:

...of raw data on patients, outcomes and trials to NHS England, and processed and analysed data from NHS England to all who can use it to benefit drug treatment, for example hospitals, researchers and pharma;

...between academia and pharma, and between pharma companies collaborating together more frequently to facilitate best use of different drugs (either using in combination or using for new indications);

...using artificial intelligence initiatives as an effective tool for interrogating available data to ensure no key efficacy signals are lost (while retaining data privacy).

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Headline points

1. Data

We need to make progress on data. Data is key to:

Understanding the scale of the problem and hence assigning adequate funding and resources

Thorough assessment of drugs: maximising speed and efficiency of new drug development and constantly monitoring response to marketed drugs in order to modify and improve treatment guidelines, leading to better treatment response, fewer side-effects, and on occasions removal of ineffective drugs with associated cost-savings.

Data must be recorded consistently and analysed in clinical use as an extension of clinical trials use. Can we improve on previous data collection initiatives with the Cancer Drugs Fund (CDF)?

Electronic connectivity could help share datasets and improve the precision medicine targets and trial accrual.

NB: There is a current mandate to collect data. The Office of Data Release (ODR) within Public Health England (PHE) has made strong progress in this area, but there are issues: not all hospitals have the resources or knowledge to provide high quality data. This is something the National Cancer Registration and Analysis Service (NCRAS) in PHE is working on currently and we expect to improve.

There are serious issues to address around how to use the data or extract it. Currently all requests for data analysis are assessed and, if approved, processed by the ODR. We need initiatives for freer access to this data whilst being aware of data protection requirements.

Future updates on collections systems may help provide better data, but we need more information on what these updates will lead to.

Summary:
We need to improve *communication* and quality of data both into NCRAS statistics and out again.

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2. Approvals.

We should also acknowledge the positives that have recently been put into place for all aspects of the approvals process. There have been lots of initiatives to expedite regulatory approval and the NICE process – earlier communication between pharma, regulators and NICE being the main one – allowing earlier drug approval. These are all good projects and are comparatively recent, for example horizon scanning (UK PharmaScan) and very innovative.

NB: Although there are numerous initiatives for getting new drugs approved quicker, there are knock-on effects such as little notice to prepare guidelines and processes within hospitals to accommodate new drugs. Drugs are being approved with very limited benefit – improvement in survival of just two months over current therapies, for example. Is there a need to reassess these rapid, limited approvals again to ensure that the most effective drugs can be funded? Perhaps we could set higher efficacy hurdles for approval.

There is also a tension between making promising drugs available earlier rather than waiting for full data, which carries the inherent risk that the medicines do not live up to their promise, or are better, therefore not appropriately priced. We must accelerate access but ensure continuous monitoring of efficacy and safety to widen use when more data become available but still allowing early use for promising medicines. Those that do not fulfill that promise can then be discontinued.

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3. Pricing.

We are facilitating new drugs, but the question remains, are we running out of money for drugs that do work? It may well be the NHS is underfunded and rationing all sorts of care and treatments, as well as limiting wage growth creating real terms pay cuts. Drugs may get a "tough rap" in that scenario, despite voluntary department of health - pharma schemes such as pharmaceutical price regulation scheme.

All that said, we need an eagle-eye view of all drugs and drug regimes and be ready to cut drugs and amend drug regimes as soon as we know a regime is sub-optimal – this links again with data analysis. Screening to allow better personalised medicine would also have the effect of reducing the amount of people being treated for drugs that don't work for them with associated patient benefit and cost savings. We could also de-escalate treatment in some patients based on the current evidence without compromising patient outcomes, and indeed reducing drug-related side-effects – this must be a priority.

Issues such as cost of new drugs, and early health economic discussions and pricing negotiation can also hopefully be further addressed through the accelerated access review (AAR); current initiatives could perhaps be reviewed to assess how we could expedite or improve the process.

NB: the creation of a new commercial group to create links between pharma and NICE has significance. But if prices are forced down too low, the UK market will become more unattractive for pharma. This could result in delayed availability of new drugs in the UK. The UK market could become so unattractive to pharma that it is given very low priority, given the benefits of producing drugs here compared with other countries, particularly after Brexit? At the time of writing, prices are better in Albania than the UK.

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4. National spend

There are new initiatives in place for pharma, NICE and NHS England to work together. The question remains – is the drugs bill going up? Factors such as confidential discounts may significantly cloud the picture. However, we are only spending around 8-9% of GDP on health, and a low amount on breast cancer medicines. Can we improve this? The optimal spend, in line with other European countries, would be 11%. USA spend of 17% may be unnecessarily high.

5. New paradigms

New paradigms for repurposing drugs are available, such as the Breast Cancer Now Catalyst programme. This new initiative by charity Breast Cancer Now bring together Europe's leading breast cancer researchers and the world's leading pharmaceutical companies to pool resources. The first partnership agreed has been with Pfizer which has provided substantial funding for research grants and has opened up its development pipeline of new drugs and existing oncology drugs to academic researchers. The projects to be funded will include preclinical research that could lead to repurposing existing drugs including new indications for already licensed drugs.

Other initiatives, such as that run by BenevolentBio, focus on artificial intelligence (AI) for drug discovery, looking at aspects such as efficiency, better target selection, optimisation of compound properties and areas of unmet need.

There is a huge cost of failed drugs. We need to get better at decommissioning. Such initiatives could investigate use of old drugs for new indications and drug combinations. The AAR project previously evaluated digital technology as an enabler of decisions on treatment and their use, but also to try to change care pathways to free up funds for other activities. Could it be extended to cover areas such as AI in respect of digital innovation? Can we merge initiatives such as AI with enhanced statistical data collection at NHS England?

These initiatives could help reduce fire fighting and silo approaches, for example between different pharma companies and between academia and pharma.

6. Screening

If we can screen in different ways, for example identifying genetic problems, e.g. a potential BRCA +ve; or working out if a tumor will respond to treatment, we can cut costs, perhaps use different budgets, and thus reserve funds for more expensive drugs. It is worth diverting precious funds from treatment to screening programmes for an overall win. BRCA screening, if not done before diagnosis, could occur before treatment or surgery.

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Further specific thoughts

1. Other, US data-based, initiatives, led by patient-driven data collection, have provided sharper information on the likely benefits of treatments. Can we achieve similar here, while acknowledging the good work already being done?

2. There are too many delays in hospital investigations for example with MRI scans so that sometimes by the time results are available they are no longer clinically useful. In addition, waiting several weeks for the results of tumour scans is extremely traumatic for patients.

3. There should be an entrepreneurial spirit among researchers, with additional awareness of considerations of intellectual property; this could take the form of industrial modules within PhDs. We should look at issues such as bringing industry more into academia, for example to look at questions such as content patents and method of use patents. We should look at other questions, such as how budgets are formed and development timelines raised, whether we can make people self-critical about their work with respect to the practical benefit of their research, whether government provide more funds, and whether we can bring in more private funding.

4. I-SPY is a good example of an academic study with industry participation.

5. We could prioritise drug discovery and development to drive the cost of treatment down with help of department of health / government funding, but we need to look at this would work in practice?

6. The time and cost of development could then be cut by conjoint working so that there was a downstream benefit to the NHS. This might raise the further issue of how acceptable would the cost of failures be, and how such costs would be covered.

7. We should improve pharmacovigilance in relation to direct patient reporting systems: increase patient education so they are aware they can and should report adverse events, and provide information on how it can be done.

8. We can look at using patient-based preferences to drive forward future benefit-risk assessment. Communication would be a key aspect of this, perhaps with patient panels consulted by the European Medicines Agency (EMA) and Medicines and Healthcare Products Regulatory Agency (MHRA). Can such organisations provide clarity on how such initiatives already take place?

9. We have a new revised Cancer Drug Fund (CDF). We need to introduce balance. We need to carefully control costs and negotiate with pharma at an early stage, but don't push down prices too much. We don't want pharma to desert the UK market, reducing research and development of riskier but more innovative drugs. Do we simply need to increase the percentage of GDP spent on drugs? If so, how?

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[cont.]

10. Clinical trials: if more people have access, drugs can get approved faster and more cost-effectively, which in turn creates a more vibrant market. Plus, more patients have access to new drugs at an early stage. However CRUK, for example, struggles to extract information for their trials database from a small number of pharma companies. Can pharma senior management educate staff to provide data or information on their trials? More communication and education of clinical trials personnel would enhance databases such as that held by CRUK. Pharma senior management would need to communicate positive benefits to staff. We can or should ensure trial results, if not data, are made available by the sponsor running the study after completion for analysis; this is a requirement but may be poorly complied with on occasions.

We need to look at whether improvements can be made to the way in which information on clinical trials databases, similar to the one held by Cancer Research UK, is gathered and communicated to interested parties in the UK.

Pooling and referring patients between centers may also help, as not all centers are able to take part in all studies.

NB: anyone running a trial in the UK has to register their trial with at least one of the following databases: - Clinicaltrials.gov - the ISRCTN Registry - EU Clinical Trials Register.

There is also the UK Clinical Trials Gateway, which is viewed as the national trials database. Is there an argument for reducing the number of databases, to provide a 'one stop shop' for patients and medical staff searching for trials?

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Specific recommended action points

Pink Ribbon would like to posit some specific actions points coming out of this white paper to build on its findings and push the agenda for an enhanced breast cancer drugs and trials regime, building on existing achievements.

1. Data
Investigate possibilities of better quality data flowing through NCRAS (see page 5, above).

We would also like potentially to work with the Cancer Drugs Fund to improve data collection regimes. This is an ongoing challenge affecting all parts of the data sourcing, preparation and usage cycle.

2. Trials databases
Pink Ribbon to investigate possibilities of further development of clinical trials databases.

Pink Ribbon is to set up meetings to investigate the possibilities of creating a single usable database for breast cancer trials in the UK and beyond, or look at how to better market existing databases. This will involve liaison with existing trials operators.

3. Artificial Intelligence
Investigate what data could be used for artificial intelligence interrogation

Pink Ribbon can investigate for example how study data or NHS pooled data is currently used.

We must be mindful of some key questions of relevance: who would own “analyses” and outcomes? Who would fund such activities and what would happen to them once created?

Pink Ribbon could take stock within the industry to see what next steps might be possible.

4. Funding
Analyse how extra funding could aid drug creation process

Pink Ribbon could potentially work with funders and government bodies to see what extra funding might be possible.

5. Lobbying
Determine specific lobbying goals.

Such goals could relate to the above tasks or be built around additional activities. Input from all sections of the breast cancer network would be welcomed: prevention and cure, hospitals, pharma, NHS, academia, support groups, government, media and so forth.

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BREAST CANCER CONFERENCE: DRUGS FUNDING & TRIALS

Achieving world-class patient outcomes

THURSDAY 23 MARCH 2017

Faculty of Pharmaceutical Medicine, 19 Angel Gate, 326a City Road,
London EC1V 2PT 9am-5pm

BRITAIN'S breast cancer patients are losing out: rising drug costs are making breast cancer drugs unaffordable for stretched NHS budgets while poor access to clinical trials and inadequate use of data is hindering research and drug development and patient access to drugs.

To understand what is needed to achieve world-class patient outcomes, Pink Ribbon hosted a new event, supported by Pfizer.

Building on the contents of the Accelerated Access Review and featuring a programme of world-renowned speakers, among the questions to be addressed at this exclusive event are:

- How effective is the current breast cancer drugs regime?
- What are the key challenges in drug approval and funding?
- How can drugs be developed and approved more quickly?
- How can we ensure new drugs reach patients more effectively?

Speakers included:
- Dr Kathleen Thompson (chair), Pharmaceutical Physician, Breast Cancer Patient & Author, *From Both Ends of the Stethoscope – Getting Through Breast Cancer by a Doctor Who Knows*
- Dr Bhawna Sirohi, Consultant Medical Oncologist, Program Training Director – Medical Oncology, Barts Cancer Institute, London
- Linda Landells, Associate Director – Technology Appraisals (Cancer Drugs Fund), National Institute for Clinical Excellence (NICE)
- Professor Peter Clark, Clinical Lead, CDF, NHS England

This exclusive event for oncology, pharmaceutical and health experts took place on Thursday 23 March between 9am and 5pm at the Faculty of Pharmaceutical Medicine, London EC1V 2PT. The full programme is over the page.

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The Breast Cancer Conference Programme

09.00 Registration & coffee + exhibition

09.30 Welcome and introduction Gerard Dugdill, publisher/coordinator Pink Ribbon

Chair: Dr Kathleen Thompson, pharmaceutical physician, breast cancer patient & author, *From Both Ends of the Stethoscope – Getting Through Breast Cancer by a Doctor Who Knows*

Section one: The problems

PATIENT PERSPECTIVES: How effective is the current breast cancer drugs regime?

09.40 Major issues: limits in availability of new effective treatments for metastatic breast cancer, poor access to clinical trials, inadequate use of data to facilitate research into cure, tissue banking.

Group discussion: Chair + patient advocates (Jo Taylor, MetupUK; Alison Dagul, breast and ovarian patient; Julia Bradford, Metup)

SYSTEM PERSPECTIVES: What are the key challenges in drug approval and funding?

Increasing breast cancer drug costs due to regulation, prevalence, survival rates, long drug approval time. NICE. UK lagging behind other countries. Funding restraints hindering prescription. Cancer Drugs Fund

10.15 *Medical perspective: cancer funding and research needs* Dr Aleksandra Filipovic, research fellow, department of surgery and cancer, Imperial College, London

10.30 *Pharma perspective: regulator approval and drug funding* Dr David Montgomery, medical director, Pfizer Oncology UK

10.45 *Buyer perspective: providing adequate cancer service and drugs* Ms. Raj Nijjar, Lead Cancer Pharmacist, Barts Health NHS Trust & Specialised Cancer Commissioning Pharmacist, NHS England – London Region

11.00 *Life science + patient perspective: accelerated access review opportunities*

Dr Stuart Dollow, Head, Global Clinical Development and Medical Affairs at UCB; Founder - Vermilion Life Sciences; also, external champion to the Accelerated Access Review

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[cont.]

11.15 *PANEL: are we clear now on the key challenges for the industry?*

11.30 Refreshments break

Section two: The solutions

1. **DRUG DEVELOPMENT: New ways to make and deliver drugs quickly and effectively**

Oncologist focus: new drug possibilities, personalized medicine, genomics

11.45 Dr Bhawna Sirohi, Consultant Medical Oncologist, Program Training Director – Medical Oncology, Barts Cancer Institute, London

12 *New ways of doing drug development*

Speaker one: New ways of funding research. Lesley Turner, patient advocate, Catalyst Initiative

Speaker two: Professor Jackie Hunter, CEO, BenevolentBio (drug discovery arm of BenevolentAI)

12.30 *Cancer patient data: linking the possibilities*

Dr Rachael Brock, national head of cancer registration, National Cancer Registration & Analysis Service, Public Health England (PHE)

12.45 *Clinical trial database creation: getting it perfect*

Sarah Kimber, patient information manager, Cancer Research UK

13.00 *PANEL: what one thing can we do to enhance innovative research?*

13.15 Lunch and exhibition

2. REGULATION: New approaches for approval, cost and reimbursement

14.15 *Regulatory approval of breast cancer drugs*

Dr Cecilia Chisholm, medical assessor in licensing division, medicines and healthcare products regulatory agency (MHRA)

14.35 R*egulation from an EU perspective*

Dr Francesco Pignatti, head of oncology, haematology and diagnostics, European Medicines Agency (EMA)

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[cont.]

14.50 *PANEL: how can we get the best possible regulation?* Panel: regulation section speakers + extra, NHS England, NHS

15.05 Tea break

3. FUNDING: Collaboration—getting new drugs to patients

15.20 Towards partnership approaches in funding

Open discussion

15.50 *The new Cancer Drugs Fund* Linda Landells, associate director – Technology Appraisals (Cancer Drugs Fund),

National Institute for Clinical Excellence (NICE)

16.05 *Making drugs available earlier: how can we achieve?* Professor Peter Clark, clinical lead, CDF, NHS England

16.25 *PANEL: what must we do to fund all patient needs?*

16.45 Chair's closing remarks + call to action via white paper

17.00 Close

Final comment on Scotland from Dr Philippa Whitford, breast surgeon, health spokesman for the parliamentary SNP (Scottish national party) group and Member for Central Ayrshire:

"The report is, of course, aimed at the English NHS with no comment regarding different Scottish structures. The key theme however, is common to all in how we pay for expensive new drugs. One difference you may find interesting is that the pharmaceutical price regulation scheme (PPRS) rebates in Scotland go to fund our drugs fund which is not limited to just cancer patients but is a 'New Drugs, Rare Diseases and End of Life' fund. This is proportionally three times the size of the CDF. In England PPRS rebates go into the core budget so save the treasury money rather than helping to fund new drugs."