

Clinical Risk Assessment of the Healthcare Improvement Scotland Report

**“Clinical Management of Breast
Cancer in NHS Tayside”**

Clinical Risk Assessment of the Healthcare Improvement Scotland Report “Clinical Management of Breast Cancer in NHS Tayside” April 2019.

Provide by the **Immediate Review Group** (TOR and Membership Annex A).

Situation.

An individual in NHS Tayside contacted the Chief Medical Officer for Scotland (CMO), the Chief Pharmaceutical Officer for Scotland (CPO) and the previous Cabinet Secretary for Health & Sport to raise concerns relating to the breast cancer clinical management guidelines in use locally and alleged ‘under-dosing’ of oncology medicines, lack of informed consent and a separate, but related, bullying and harassment complaint. The concerns that were raised led to the CMO and the CPO commissioning Healthcare Improvement Scotland (HIS) to undertake an investigation into the clinical management of breast cancer in NHS Tayside. This investigation has now concluded and a draft final report has been produced, due to be published on April 1st 2019. This report highlights some key areas for concern;

- A. It appears that patients in NHS Tayside are being treated differently from the patients in the rest of NHS Scotland with chemotherapy in the adjuvant and neo-adjuvant setting. The decision to treat differently lacks robust evidence or multidisciplinary consultation. This practice was exposed by the failure of the North of Scotland Cancer Network, (NOSCAN), to agree on a Clinical Management Guideline, (CMG), for the management of breast cancer. The recommendations relevant to this in the HIS report are A and B.**
- B. Patients in NHS Tayside are not being offered Oncotype DX (Predictive Molecular Testing) to aid further decision making in patients at intermediate risk of recurrence after surgery. NICE Guidance is extant on this issue as of December 2018 (recommendation C).**
- C. Breast Cancer patients in NHS Tayside were not informed during the consent process of these variations in clinical practice (recommendation D).**

The Immediate Review Group was commissioned by the CMO and CPO to deliver informed consensus risk assessment relating to this variation in clinical practice in NHS Tayside.

Specifically the group will advise the CMO and CPO on the following main questions:

- Is the variation in practice confirmed in NHS Tayside seen elsewhere in NHS Scotland (the HIS report would say not) or in NHS England? Is this variation considered to be within acceptable best current clinical practice? This question specifically related to a reduction in the doses of docetaxel and epirubicin within the FEC-T chemotherapy regimen given to adjuvant (after surgery), and neo-adjuvant (before surgery) patients. In addition, the routine use of myelopoietic growth factors, (e.g. filgrastim), to facilitate safe delivery of chemotherapy was not employed whilst giving this less intensive regimen.
- The IRG will specifically assess the risk of a reduction in dose across the duration of adjuvant/neo-adjuvant treatment. Can an estimate of harm/increased risk of recurrence be made? Can this be mitigated in any way? The estimation of risk will facilitate any NHS Scotland decision to inform or recall the cohort of relevant patients and influence the communication given and action taken.
- Is there a risk to NHS Tayside patients of not using molecular profiling to further aid decision making in intermediate risk patients to receive adjuvant chemotherapy?
- Would established best practice mandate that such a variation against universally adopted practice be communicated to patients during the consent process?

Risk Assessment.

Adjuvant and neo-adjuvant chemotherapy.

Doses of epirubicin and docetaxel in the FEC-T regimen were reduced by 25% in the adjuvant and neo-adjuvant treatment of breast cancer patients in NHS Tayside in 2016 (initially to 75mg/m² for docetaxel but later to 80mg/m²). The evidence base for this decision was not clear to the visiting HIS team in October 2018. It was also clear that this decision was at variance with other NOSCAN breast cancer colleagues, illustrated by failure to agree a CMG across the network. In addition to the dose reductions, filgrastim supportive therapy was not routinely given as primary prophylaxis against neutropenic sepsis. The decision to reduce doses was taken by the Tayside oncologists based on observed significant toxicity. The view of the IRG was as follows;

- The regimen used, FEC75:T75/80 (meaning FEC with 75mg/m² of epirubicin for 3 or 4 cycles followed by docetaxel 75mg/m² (later increased to 80mg/m²), is not a regimen that has been directly compared to any other standard regimen in clinical trials.
- In studies comparing different doses of epirubicin within a FEC regimen, there is evidence that higher doses are more effective.
- Thus it is likely that the FEC75 used for 3 cycles in Tayside offers less benefit than the more standard FEC100, particularly when used for only 3 cycles.

- The use of taxanes after anthracycline-based chemotherapy in the adjuvant setting reduces the relative risk of recurrence by 16%. (references available). Thus reducing the dose by 20-25% could reduce the benefit to perhaps 12% rather than 16%, with the absolute loss of benefit for an individual patient depending on the risk of recurrence after surgery.
- There is acknowledgement that planned doses of chemotherapy are likely to differ from actual delivered doses, but such differences are very difficult to quantify.
- There is a broad range of doses and regimens within adjuvant breast cancer treatment that have been tested in many clinical trials. Whilst the NHS Tayside approach may be within the range of doses tested within these trials, because all patients considered to warrant adjuvant chemotherapy are given lower doses, including the fittest and those with the highest risk, there may be a proportion of patients who are being undertreated, and are disadvantaged by not being offered the higher doses.
- There were significant concerns raised about the failure of regional medicines governance arrangements in the decisions made by the NHS Tayside consultants to routinely use lower than standard chemotherapy doses. The implication in the HIS report is that these were made without multi-professional scrutiny and agreement.
- The overall assessment of the increased risk of recurrence within the treated cohort is extremely difficult to quantify but probably of the order of 1-2%.
- Compliance with regional network governance processes was deficient. Failure of these structures to provide oversight of the changes made by individual oncologists may have led to the small but significant relative increased risk of recurrence in a cohort of women in NHS Tayside.

Access to Oncotype DX (or molecular profile testing) of patients in NHS Tayside.

NICE guidance 34 confirmed that **EndoPredict, (EPclin score), Oncotype DX Breast Recurrence Score** and **Prosigna** are recommended as options for guiding adjuvant chemotherapy decisions for patients with oestrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, lymph node (LN)-negative (including micrometastatic disease) early breast cancer if they have an intermediate risk of distant recurrence using a validated tool such as PREDICT or the Nottingham Prognostic Index. The tests add information to guide the decision-making for adjuvant chemotherapy. It is estimated these tests could be applied to 10-15% of all adjuvant patients. Oncotype DX was endorsed for use in this context by the NHS Scotland Molecular Pathology Evaluation Panel, (MPEP) in January 2016 and is universally deployed in the other 4 cancer centres in Scotland. It is worth noting that within “Beating Cancer; Ambition and Action” (2016), Scottish Government policy is to allow access to Oncotype DX testing for appropriate patients. The view of the panel was as follows;

- Molecular profiling to facilitate decision-making in adjuvant chemotherapy for ER+ve, Her2-ve and lymph node negative patients is routine clinical practice

in the UK. Whilst Oncotype DX testing is endorsed by the MPEP in NHS Scotland, that committee may adapt its guidance to be congruous with NICE DG34 and endorse the other two tests.

- If no testing is offered in NHS Tayside, that would be at variance with clinical practice in the rest of NHS Scotland and almost certainly in England.
- There is acknowledgement that the consequences of only using NHS PREDICT as a decision tool, without the added value of molecular profiling is uncertain and currently controversial.

Consent

The HIS report recommendation D recommends that where clinical practice is different from that supported by the wider oncological community, patients should be informed of this. NHS Scotland has a national SACT Governance Group which is hosting a national review of consent for cancer systemic therapy, and this group should consider this recommendation as part of its remit. The view of the panel was as follows;

- It is not clear whether the consent communication to patients changed when the dose adjustments were made in 2016.
- There was a consensus view that SACT consent is regimen based and patients are not consented to specific doses of drugs within that regimen.
- Variations in care of this level are common to most or all medical interventions and are in most circumstances considered to be below the threshold of requiring explicit pro-active consent. The difference in this case is that a decision was made to reduce the prescribed doses of 2 of the most important drugs in the adjuvant therapy of breast cancer, at variation with other centres, to all patients. There was also a decision to withdraw a medicine which is universally applied to reduce the risk of neutropenic sepsis in adjuvant chemotherapy for breast cancer (filgrastim).
- There is acknowledgement that the Tayside oncology team may not have known that they were universally out of step with the other Scottish centres and thus did not consider adjusting the consent process. However, after the publication of the HIS report they will be aware and may be obliged to inform patients going forward.
- A risk of harm of 1-2%, allows an estimate that around 1 patient per year in NHS Tayside may have suffered an adverse outcome. Although in terms of population outcomes this is a small risk, it is accepted that the principles of duty of candour mean that there needs to be a communication to the relevant cohort of treated patients (adjuvant and neo-adjuvant breast cancer patients receiving SACT with the FEC-T regimen between 2016 and 2019) of the variation in care delivered in NHS Tayside. Failure to disclose delivers an increased risk, although significant concerns were raised about the potential serious downsides of such a disclosure in terms of patient anxiety, staff morale and departmental reputation. The clinical group were of the view that the utmost care and preparation needs to be in place to manage this process.

Summary.

The IRG was convened rapidly and had no access to specific patient data or demographic information. The conclusions and recommendations are based on the information provided in the HIS report, and access to some very basic information provided by NHS Tayside colleagues on the patient toxicity which led to the dose adjustments. This information was unable to convince members of the IRG that these decisions were valid, evidence based, nor managed through an appropriate clinical governance process for review and challenge.

It is strongly recommended that there is a review of the medicines governance, decision making and sign off processes in NHS Tayside. There need to be clear roles and responsibilities of the appropriate committees that will approve the use of protocols. If these protocols are not in line with regional or national clinical management guidelines, but are approved, then there needs to be agreement on the expected documentation and communication to patients. If the committee does not approve a protocol, then there should be a clear process for appeal and final decision.

The current reduced dose adjuvant and neo-adjuvant regimen being used by NHS Tayside is at variance with that used in the other NHS Scotland centres. Whilst the decision to reduce doses in 2016 was taken in the best interests of patients, and based on an audit of toxicity, this decision lacked robust challenge or consultation. It reflected a unilateral internal decision to adopt practice which was judged by the IRG as being out with best current practice, and close to being unacceptable. The decision to withdraw the concurrent prescribing of supportive growth factors to better allow safe delivery of treatment was similarly criticised by the IRG. The estimate of harm is judged to be in the order of an increased risk of recurrence for 1 patient per year in NHS Tayside.

The access to molecular testing for a proportion of adjuvant patients to facilitate better decision making in the intermediate group of patients (10-15% of all adjuvant patients), should be the same for NHS Tayside patients as those in the rest of NHS Scotland. Failure to comply with this will create a unique risk in NHS Tayside. Compliance with the use of Oncotype DX testing in appropriate patients will eliminate the variance, and allow NHS Tayside to be compliant with NHS Scotland MPEP guidance, NICE Guidance, and the recommendations in current cancer policy.

The issue of consent is complex. In general oncologists consent patients to the risks and side effects of SACT regimens specific for their cancer. However, in general the consent process is not specific to regimen doses. Patients will generally experience the same generic toxicities when given lower doses of chemotherapy within a regimen. The consent process for SACT is under scrutiny in NHS Scotland in a process hosted by the National SACT Governance Group. This group will consider the NHS Scotland consent process for SACT in light of the Montgomery Report, and should host any agreed change in consent processes going forward. However, colleagues now know, (post publication of the HIS Report on April 1st 2019), that they are prescribing treatment which is different from that being prescribed in the rest of

NHS Scotland, (lower doses and no supporting growth factors), and should be directed to inform patients prospectively.

Annex A

Clinical Management of Breast Cancer in NHS Tayside – Immediate Review Group (IRG)

Terms of Reference (ToR)

1. Background

An oncology lead pharmacist in NHS Tayside contacted the CMO, CPO and the previous Cabinet Secretary for Health & Sport to raise concerns relating to the breast cancer clinical management guidelines and alleged ‘under-dosing’ of oncology medicines, lack of informed consent and a separate, but related, bullying and harassment complaint. The latter will be considered separately from this work being the responsibility of NHS Tayside.

The CMO and CPO commissioned Healthcare Improvement Scotland (HIS) to undertake an investigation into the clinical management of breast cancer in NHS Tayside. This investigation has now concluded and a draft final report has been produced. This report highlights some key areas for concern;

- A. Patients in NHS Tayside were being treated differently from the patients in the rest of NHS Scotland with chemotherapy in the adjuvant and neo-adjuvant setting. The decision to treat differently lacked evidence or multidisciplinary consultation.
- B. Breast Cancer patients in NHS Tayside were not informed during the consent process of that difference and the potential consequences.
- C. Patients in NHS Tayside were not offered Oncotype DX Testing in the planning of therapy.

2. Purpose

This group will advise the CMO and CPO on the content and implications for patients of the HIS report. It will assess the potential risk of the variation in practice. Thereafter, will work with NHS Tayside on the practical response to allay concerns and/or recall patients.

Specifically the group will advise the CMO and CPO on the following main questions:

- Is the variation in practice seen elsewhere in NHS Scotland (the HIS report says not) or in NHS England? Is this variation considered to be within acceptable clinical practice?
- The IRG will specifically assess the risk of a reduction in dose across the duration of adjuvant/neo-adjuvant treatment. Can an estimate of harm/increased risk of recurrence be made? Can this be mitigated in any way?

- Is the practice of using NHS Predict rather than offering Oncotype DX testing seen elsewhere? Is any harm caused mitigated by the NHS Predict tool use?
- Would established best practice mandate that such a variation against universally adopted practice be communicated to patients during the consent process?

3. Governance

The group will report to the CMO and CPO who will then report to the Cabinet Secretary for Health & Sport.

4. Membership

The membership will consist of:

Name	Profession/Position	Affiliation
Professor David Cameron	Professor of Medical Oncology and Director of Cancer Services	NHS Lothian
Dr Hilary Dobson	Consultant Breast Radiologist, Clinical Lead National Cancer QPI Group	University of Edinburgh
Dr David Dunlop (Chair)	Senior Medical Office-Oncology	Scottish Government
Professor David Dodwell	Senior Research Fellow and Clinical Oncologist	Oxford University Hospitals
Pauline McIlroy	Advanced Breast Clinical Nurse Specialist	NHS Greater Glasgow & Clyde
Jatinder Harchowal	Chief Pharmacist	Royal Marsden NHS Foundation Trust, London.

Members will be expected to attend each meeting of the group.

5. Meetings

Due to the time pressure on this process meetings will be virtual.



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