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From: MSAC SECRETARIAT
Sent: Friday, 26 July 2019 12:15 PM
To: s 47F s 47F ; s 22
Cc: MSAC SECRETARIAT; s 47F
Subject: FW: For next week's MSAC - Application 1342.5 – Oncotype DX breast cancer assay [SEC=OFFICIAL]

Dear all

This late feedback was received today, we will add to the Consultation Feedback for 1342.5 on Sharepoint.

Kind Regards

s 22

MSAC Secretariat

Medical Services Technology Section | Office of Health Technology Assessment Branch
Technology Assessment and Access Division
Australian Government Department of Health

PO Box 9848, Canberra ACT 2601, Australia

From: hta
Sent: Friday, 26 July 2019 11:54 AM
To: MSAC SECRETARIAT ; hta ; MSAC ESC_Secretariat
Cc: s 22
Subject: For next week's MSAC - Application 1342.5 – Oncotype DX breast cancer assay [SEC=UNOFFICIAL]

Morning,

Graeme Suthers sent this to the HTA inbox.

Cheers, s 22

From: Graeme Suthers <Graeme.Suthers@sonichealthcare.com.au>
Sent: Friday, 26 July 2019 10:48 AM
To: hta <hta@health.gov.au>
Subject: Application 1342.5 – Oncotype DX breast cancer assay [SEC=No Protective Marking]

Dear MSAC,

Re Application 1342.5 – Oncotype DX breast cancer assay

I note that this application is to be considered by MSAC at its meeting next week.

The brief Agenda that was circulated by email notes that "Feedback and comments are welcome at any stage during the MSAC process". I recognise that the preparatory meetings and evaluations have been completed, but I will take you at your word and provide a brief comment. In doing so, I declare an interest (Sonic has been evaluating competing methods for estimating prognosis and predicting chemo-responsiveness for 5 years) and a conflict (we have chosen to provide a different gene expression assay).

The TAILORx trial has been the subject of three NEJM articles in recent years. This was a randomised trial of chemotherapy based on the result of the OncotypeDX test. It was not a randomised trial of the test itself as the participants were randomised on the basis of the OncotypeDX result alone.

- In 2015, the TAILORx triallists reported that both classic prognostic markers and OncotypeDX identified women at low risk of breast cancer recurrence[1]; they did not compare the performance of the two measures.
- Last year, they described using OncotypeDX alone to randomise women to chemotherapy, showing that women at low risk did not benefit from chemotherapy[2].
- They recently reported that clinical features can contribute to estimates of recurrence risk derived from OncotypeDX[3].

However, none of these publications provided a comparative assessment documenting the superiority of OncotypeDX over clinical features or classic prognostic markers.

Low recurrence risk has long been associated with the luminal A subtype[4], a subtype which is unresponsive to chemotherapy[5]. Hence the apparent predictive power of OncotypeDX could rest simply on the estimate of recurrence risk.

In 2013, a comparative study showed that OncotypeDX was less accurate than both clinical and histological features in estimating the risk of distant recurrence in the ATAC trial[6]. OncotypeDX does not report subtype, and there has been no study comparing the predictive power of OncotypeDX *versus* conventional markers.

1. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF*, et al*. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med* 2015; **373**(21)**:** 2005-2014.
2. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF*, et al*. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med* 2018; **379**(2)**:** 111-121.
3. Sparano JA, Gray RJ, Ravdin PM, Makower DF, Pritchard KI, Albain KS*, et al*. Clinical and Genomic Risk to Guide the Use of Adjuvant Therapy for Breast Cancer. *N Engl J Med* 2019; **380**(25)**:** 2395-2405.
4. Prat A, Fan C, Fernández A, Hoadley KA, Martinello R, Vidal M*, et al*. Response and survival of breast cancer intrinsic subtypes following multi-agent neoadjuvant chemotherapy. *BMC medicine* 2015; **13:** 303.
5. Nielsen TO, Jensen MB, Burugu S, Gao D, Jorgensen CL, Balslev E*, et al*. High-Risk Premenopausal Luminal A Breast Cancer Patients Derive no Benefit from Adjuvant Cyclophosphamide-based Chemotherapy: Results from the DBCG77B Clinical Trial. *Clin Cancer Res* 2017; **23**(4)**:** 946-953.
6. Dowsett M, Sestak I, Lopez-Knowles E, Sidhu K, Dunbier AK, Cowens JW*, et al*. Comparison of PAM50 risk of recurrence score with oncotype DX and IHC4 for predicting risk of distant recurrence after endocrine therapy. *J Clin Oncol* 2013; **31**(22)**:** 2783-2790.

Regards,

Graeme.

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