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The use of EndoPredictTM and ProsignaTM for early invasive breast cancer

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Direction des services de santé et de l'évaluation des technologies

Québec

This is the English summary of the guidance entitled Utilisation d'EndoPredict[MC] et de Prosigna[MC] dans les cas de cancer du sein invasif précoce published in October 2018.

The complete version of this guidance (in French) is available on the website of INESSS in the Publications section.

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SUMMARY

Historically, the decision to add adjuvant chemotherapy for treatment of early breast cancer has rested solely on prognostic clinical-pathological factors, including age, height, grade of the tumor, nodal status as well as biomarker expression such as estrogen and progesterone receptors (ER, PR) and epidermal growth factor receptor 2 (HER2). Multigene profiling essays were developed to clarify the risk of distant breast cancer recurrence in women, to limit adjuvant chemotherapy administration only to patients who can reap potential benefits of it.

Since 2012, Quebec patients have had access to Oncotype DX™ tests in the public health system. Recently, certain professional bodies have incorporated EndoPredict™ and Prosigna™ testing in their recommendations on treatment of patients with breast cancer. Unlike Oncotype DX™ EndoPredict™ and Prosigna™ can be done in Québec's laboratories. Within this context, the *Direction générale de cancérologie* (DGC) and the *Direction de la biovigilance et de la biologie médicale* (DBBM) of the MSSS mandated the *Institut national d'excellence en santé et en services sociaux* (INESSS) to evaluate the clinical utility as well as clinical and analytical validity of EndoPredict™ and Prosigna™ compared to Oncotype DX™.

The findings from a review of collected scientific data were discussed between experts in this field, the CEPO and members of the *Comité scientifique des analyses de biologie médicale*.

According to available data, EndoPredict™ or Prosigna™ help determine the risk of breast cancer recurrence within 10 years. No prospective studies, however, have demonstrated the impact of these tests on a patient's clinical course, both in terms of overall survival and progress-free survival.

The prognostic value of EndoPredict™ and Prosigna™ has been assessed in prospective-retrospective randomized studies or observational studies on RO+, HER-, N0 and N+ patients. The limited data available suggest that EndoPredict™ and Prosigna™ provide additional clinical information for N0 patients. The results of these tests should identify which women with breast cancer (RO+, HER2- and N0) do have a low risk of 10-year distant cancer recurrence. Also, the recurrence rate for women in this category should be similar to that of women assessed through Oncotype DX™ testing. In patients with lymph nodes (N+), the prognostic value has not been established to characterize the group of patients for which these tests are effective.

A few publications have assessed the analytical validity of the two tests. The tests were performed by their manufacturers on a limited number of samples. In order to confirm the clinical validity of EndoPredict™ and Prosigna™, independent studies must be conducted on a larger sampling of patients.

The comparative studies of various tests conducted on the same population show inconsistency between the results obtained with EndoPredict™, Prosigna™ and Oncotype DX™. The limited number of patients and distant recurrences as well as the

absence, in certain cases, of follow-up have failed to determine which of these three tests delivers the most reliable results to evaluate the risk of distant cancer recurrence. Furthermore, there are insufficient economic data to rule on the efficiency of these tests as regards stratification of distant recurrence risk in patients with breast cancer.
Our discussions with experts have highlighted the limits of the data supporting the utility and validity of EndoPredict™ and Prosigna™. While Oncotype DX™ is widely used in clinical practice, the experts have expressed some concerns about the comparison of these two new tests with Oncotype DX™ and the impossibility to conclude to the superiority of any of these tests.

Considering that:

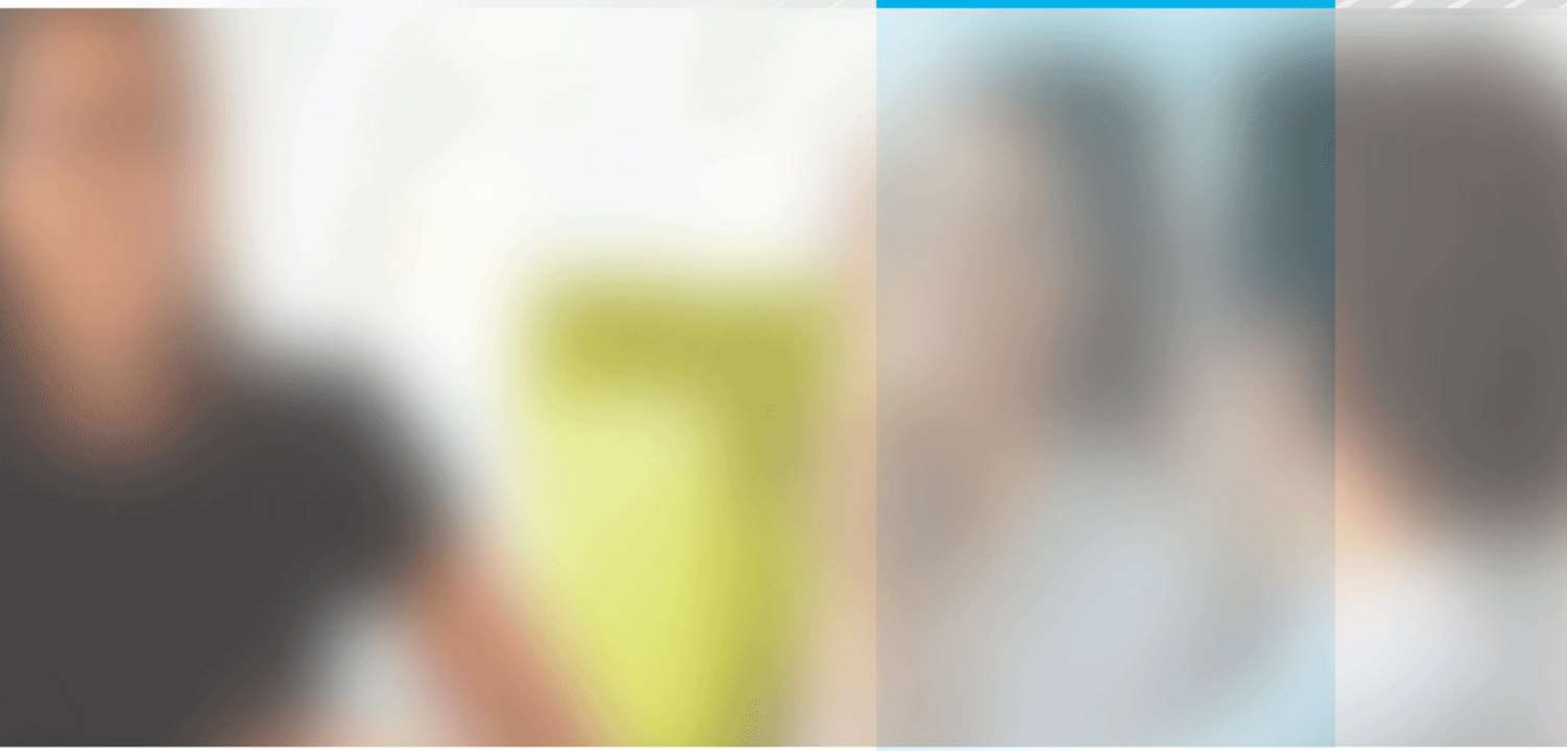
- there are no data available to rule on the clinical utility and predictive value of EndoPredictMC and Prosigna™;
- the inconsistency between the results obtained with EndoPredict™, Prosigna™ and Oncotype DX™ for the same patient and the impossibility to determine which of these three tests delivers the most reliable result to evaluate distant recurrence risk;
- ongoing studies will make it possible to achieve a more accurate appreciation of the added value of these tests in clinical decision-making;
- the synthesis of available clinical value studies of the new EndoPredict™ and Prosigna™ tests has highlighted the remaining uncertainties of the comparator, Oncotype DX™;

The INESSS recommends to not include EndoPredict™ and Prosigna™ testing in the *Répertoire québécois et système de mesure des procédures de biologie médicale*. A re-evaluation can be performed once new data are published.

Caution:

Although Oncotype DX™ is widely used, it has never been thoroughly evaluated for its clinical utility nor has it ever been evaluated by a regulatory agency.

The best strategies allowing to stratify prognosis of patient with breast cancer (RH +, HER2-, N0 or N +), to assess the risk of distant recurrence and to whether or not to administer chemotherapy remain tainted with uncertainty.



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