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Cost-Effectiveness of Biomarker Testing Among Early-Stage Breast Cancer Patients in Switzerland

Clinical solid tumor oncology

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Background and Objective:

- Multigene assays (MGAs) are used in clinical practice to complement clinicopathologic information to optimize adjuvant treatment decisions.
- To date, the Oncotype DX Breast Recurrence Score® test is the only MGA with the ability to predict adjuvant chemotherapy benefit (helping to minimise over- and undertreatment) validated by evidence from randomized clinical trials, and supported by major relevant guidelines e. g. NCCN (1).
- Other prognostic commercially available assays include MammaPrint®, EndoPredict® and Prosigna®.
- In Switzerland, early-stage HR+/HER2- breast cancer (BC) patients may receive adjuvant chemotherapy (CT) followed by endocrine treatment to reduce the risk of recurrence. However, CT does not improve survival for all patients and can result in treatment-related toxicities. CT is associated with significant direct (healthcare) and indirect (work productivity) costs.
- This analysis aims to provide a cost-effectiveness evaluation of the Oncotype DX test in Switzerland.

Methods:

- An economic model was developed based on best practice guidelines for state-transition modeling for economic evaluation (2). It is assumed that a patient receives the Oncotype DX test (Exact Sciences; 3,850 Swiss Francs) or another MGA in one arm and no test in the comparator arm (utilizing clinical pathological factors: age, menopausal status, tumor size, grading, nodal status, hormon receptor level, Ki67).
- The cost-effectiveness model uses a mixed structure with a decision-tree component to stratify patients according to test Recurrence Score (RS) and use of CT, followed by a Markov component to estimate the long-term costs and outcomes of the chosen treatment. The model included a Swiss payer and societal perspective.
- The costs and consequences of CT decisions were estimated over a lifetime horizon and all future costs and outcomes were discounted at a rate of 3 % per year (see table 1 for input data).

Table 1: Outcome distribution of the model for early-stage HR+/HER2- breast cancer patients, comparing clinical risk only and Oncotype DX

	BC patients	Allocated chemotherapy (%)		
		RS	Clinical risk only	Oncotype DX: Reduction vs. clinical risk only
N0	60 %	13 %	24 %	45 %
N1	34 %	27 %	68 %	61 %
Total	94 %*	18 %	40 %	55 %

- The long-term impact of distant recurrence of BC, acute myeloid leukemia (AML), chronic heart failure (CHF) as long-term adverse events of chemotherapy was extrapolated beyond the horizon of the clinical study using a Markov model with five mutually exclusive health states: “recurrence-free”, “distant recurrence”, “AML”, “CHF” and “death”.

*Model included N0 and N1 patients, representing 94 % of early-stage HR+/HER2- BC patients.

Overview of model inputs (details on request)

- Patient’s Recurrence Score distribution and distant recurrence probabilities for the Oncotype DX test were derived from the TAILORx (N0) and RxPONDER (N1) trials.
- The probability to develop AML was based on a meta-analysis (3).
- Standardised incidence of CHF are based on Clinical Practice Research Datalink (CPRD) longitudinal data from 2002-2014 (4).
- CT allocation reflected Swiss clinical practice, informed by expert opinion, and incorporated Swiss drug costs (details on request).
- The impact of breast cancer recurrence and chemotherapy AEs on health-related quality of life (HRQoL) in the model was estimated using health state utility values and utility decrements.
- The analysis included as well cost for testing, management of adverse events, and terminal care (references upon request).

Results:

- Use of MGA testing, such as the Oncotype DX test, is estimated to improve outcomes (increase in Quality Adjusted Life Years (QALY) and overall Life Years (LY)) at a lower overall cost to the Swiss healthcare payer and society.
- These outcomes demonstrate clinically meaningful trends that support the utility of genomic testing, such as Oncotype DX test by reducing chemotherapy-indication by approx. 50 % of patients compared to no testing.
- These benefits are observed as early as ten years for both N0 and N1 patients and continue to improve over a lifetime.
- When taking indirect cost such as loss of productivity into account as well, the cost saving is even higher (see table 2).

Table 2: Cost-effectiveness of Oncotype DX versus No testing (clinical risk only) in N0 and N1 patients.

		Direct cost				Including societal cost			
		10 years		Lifetime		10 years		Lifetime	
		No testing	Oncotype	No testing	Oncotype	No testing	Oncotype	No testing	Oncotype
N0 pts	**Total cost (Swiss Francs)**	24,834	23,850	49,979	46,160	35,348	31,597	71,524	63,222
	QALYs	6.51	6.56	13.19	13.44	6.51	6.56	13.19	13.44
	Life years	8.32	8.36	17.36	17.68	8.32	8.36	17.36	17.68
N1 pts	**Total cost (Swiss Francs)**	31,661	29,327	57,776	55,442	44,781	39,528	82,109	77,244
	QALYs	6.50	6.52	13.06	13.21	6.5	6.52	13.06	13.21
	Life years	8.31	8.33	17.11	17.37	8.31	8.33	17.11	17.37

- Besides the therapy de-escalating aspect, an escalating effect is also observed when utilizing the Oncotype DX test, resulting in better patient outcomes and therefore lower costs (figure 1). These costs are different for N0 vs. N1, primarily driven by fewer distant recurrence events (N0) and less utilization of CT (N1).
- From a societal perspective, one cost driver is loss of productivity, which accounts in the N0 case for 27 % of cost with Oncotype DX® versus 30 % in the clinical risk alone group.
- Within the model, cost-effectiveness of the Oncotype DX test was also dominant versus all other commercially available assays including MammaPrint, EndoPredict and Prosigna. Mean total direct cost differences for HR+/HER2- patients of Oncotype DX vs. Mammaprint: -6,170 CHF; Oncotype DX vs. Endopredict: -14,848 CHF; Oncotype DX vs. Prosigna: -14,683 CHF.

Figure 1a: Mean lifetime cost by category for Oncotype DX versus clinical pathological factors (no testing) in N0 patients

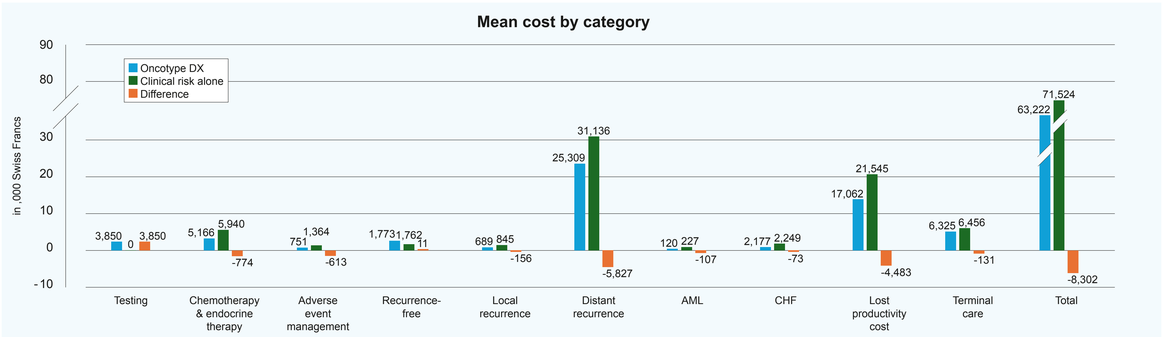
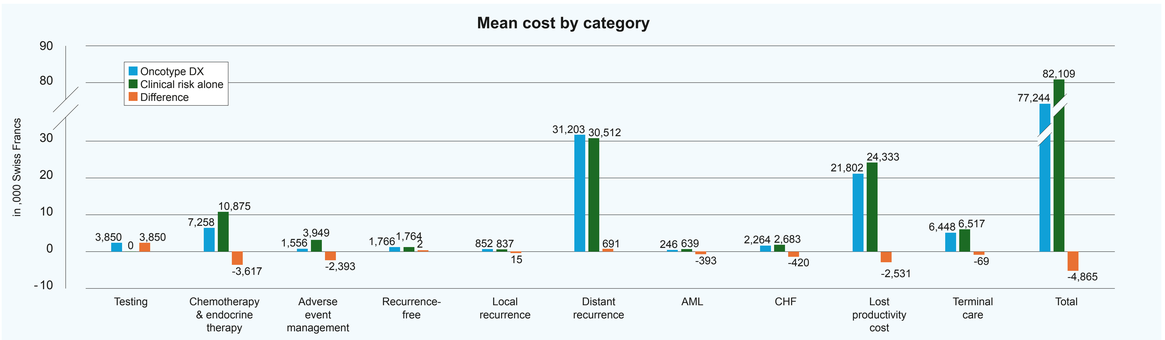


Figure 1b: Mean lifetime cost by category for Oncotype DX versus clinical pathological factors (no testing) in N1 patients



- One-way deterministic analyses confirmed results. Within these analyses, varying the N0 high-risk patient hazard ratio had the biggest impact and showed highest variation. Additionally, the discount rate had the second highest impact given the model’s long-term perspective.
- Results were also confirmed by probabilistic sensitivity analysis including a cost-effectiveness acceptability curve illustrating that cost-effectiveness is already reached in more than 90 % of simulations with a willingness-to-pay threshold of 0 Swiss Francs. With an acceptability threshold of 12,000 Swiss Francs all simulations were cost-effective which is a valid assumption in the Swiss health care context.

Conclusion:

- The numerical differences observed in total cost, QALYs and LY are clinically meaningful and support the utility of the Oncotype DX test in early-stage HR+/HER2- breast cancer patients.
- In summary, usage of the Oncotype DX test results in significant cost savings for the Swiss health system and leads to better clinical outcomes for breast cancer patients.
- The results of this study are in line with health economic assessments in other countries (e. g. Belgium, Germany, Italy and England).

References:

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Disclosures:

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