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Trastuzumab Persistence Between Two Adjuvant Breast Cancer Treatment Regimens Among US Health Plan Enrollees: a Comparative Effectiveness Analysis

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Background: Approved US indications for trastuzumab include adjuvant treatment of HER2-overexpressing breast cancer (BC) in anthracycline-based (ACTH) or non-anthracycline-based (TCH) regimens. This study compared trastuzumab persistence across regimens for US health plan enrollees.
Materials and Methods: This retrospective cohort study used the IMS LifeLink™ Health Plan Claims Database. The cohort included adult adjuvant BC patients, defined as patients aged 18+ years with a mastectomy or lumpectomy and with a primary BC diagnosis (index diagnosis) between 1/1/2006 and 12/31/2008. Patients were required to have a second primary BC diagnosis within 90 days of the first and have no evidence of any other primary or secondary malignant neoplasm within 180 days before or 90 days after the index diagnosis. Patients also were required to have a trastuzumab claim (index claim) and $\geqslant$1 carboplatin, cyclophosphamide, taxane, or anthracycline claim within 210 days of the index diagnosis, with no evidence of trastuzumab use before the index diagnosis. Patient regimens were classified as ACTH (doxorubicin, cyclophosphamide, a taxane, trastuzumab) or TCH (docetaxel, carboplatin, trastuzumab), based on therapies observed on or after the index claim. Patients with $\geqslant$2 trastuzumab claims were followed to evaluate duration of trastuzumab use, or persistence, defined as the time from the index claim to earliest of trastuzumab discontinuation, new malignant neoplasm, end of health plan enrollment, or 360 days after the index claim. Data were compared across regimens using the Kaplan–Meier estimator and Cox proportional hazards models.
Results: 550 BC patients met all study criteria (291 ACTH, 259 TCH, 46 unassigned); TCH-treated patients were older (median 52 years vs. 50 years; P = 0.018). For years 2006–2008, the annual share of the cohort initiating ACTH decreased from 69.3% to 35.2%; patients initiating TCH increased from 26.7% to 56.5%. ACTH-treated patients persisted on trastuzumab for fewer days (mean = 256, median = 334) than did TCH patients (mean = 282, median 344, P = 0.018). Fewer ACTH than TCH patients remained persistent on trastuzumab at day 90 (83% vs. 91%), day 180 (71% vs. 79%), day 270 (61% vs. 72%), and day 360 (20% vs. 26%). ACTH patients still persisted less after adjusting for age, region, plan type, prescriber specialty, and comorbidities (HR = 0.77, 95% CI [0.63, 0.95]).
Conclusions: The share of adjuvant BC patients initiating TCH versus ACTH increased from 2006 to 2008. TCH patients persisted on trastuzumab longer than those receiving ACTH. Further analyses will evaluate whether regimens also differ in weight-adjusted cumulative trastuzumab doses received during therapy.

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Decision Impact and Economic Evaluation of the 21-gene Recurrence Score (RS) Assay for Physicians and Patients in Japan

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Background: The 21-gene Recurrence Score (RS) was validated in Japanese women (Toi et al, Cancer, 2010). St. Luke's International Hospital (Tokyo, Japan) directed a prospective study on the treatment impact of the RS for women with early-stage breast cancer (ESBC) with estrogen receptor positive (ER+) disease. We assessed the utility and economic value of the RS for management of ESBC from a Japanese societal perspective.
Materials and Method: A multi-center study enrolled 90 patients with ER+ ESBC, including pre- and post-menopausal women with LN− disease and post-menopausal women with LN+ disease. All participating physicians and patients completed pre- and post-RS questionnaires on treatment recommendations and confidence in decision making. We adapted a published Markov model to evaluate the value of RS testing. The probability of individual's risk of recurrence and the chemotherapy benefit predicted by the RS were derived from published trials. The decision impact of the RS and direct costs representative of the 90 patients were obtained from St. Luke's and published literature. The model accounted for both direct costs to health system and to the patients for adjuvant treatment. Cost included chemotherapy drugs, management of adverse events and recurrence, and patients' expenses.
Results: 90 cases, (73 LN− and 17 LN+) are included in this cohort. Prior to RS testing, 53% (39/73) of LN− and 82% (14/17) LN+ patients were recommended to adjuvant chemotherapy plus hormone therapy (CHT). After RS testing, 29% (21/73) of LN− patients and 12% (2/17) LN+ patients were treated with CHT. RS led to 25% CHT reduction in LN− cohort and 71% CHT reduction in LN+ cohort. Direct savings in USD, per patient tested in this cohort, in the costs of chemotherapy, adverse events plus monitoring, patient expenses, and recurrence were: $2133, $750, $102, and $45, respectively. Including cost of the RS, the adoption of the RS increased management cost by $1,769 per patient tested. By reducing the chemotherapy disutility, and preventing recurrence, the RS increased the patient's quality adjusted life (QALYS) by 0.215 years. Use of RS in Japan costs $8,242 per QALY gained.
Conclusions: In Japan, RS reduced the use of chemotherapy and represents a cost effective approach to favorably affect the lives of women with ER+ ESBC.

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High Rates of Nonadherence to Aromatase Inhibitors in the Extended Adjuvant Setting

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Background: Aromatase inhibitors (AI) have shown impressive improvements in reducing mortality and recurrence in postmenopausal, hormone-receptor-positive (HR+) breast cancer patients and are often prescribed for 5 years or more. Despite prominent developments in adjuvant ET, adherence in the first 5 years of therapy is persistently low, with rates similar in patients treated with AI, Tamoxifen (TAM), or a sequence of both [1–6]. In the extended adjuvant setting little is known about nonadherence. Though increasingly evident that more than 5 years of adjuvant ET is beneficial in terms of survival, many are plagued by adverse effects, with the risk of nonadherence interfering with the additional benefit of extended treatment [1,7]. The aim of this study was to investigate early treatment discontinuation (ETD) in the extended adjuvant setting.
Methods: 1262 patients were randomised in the IDEAL trial is a prospective, open-label phase III trial comparing efficacy and safety of 2.5 years with 5 years of extended adjuvant treatment with LET (2.5 mg once daily) in HR+ postmenopausal early breast cancer patients after 5 years of adjuvant ET. Nonadherence was defined as early discontinuation of LET for all reasons, excluding death, recurrence or protocol completion.
Results: 1262 patients were included in the present analysis. 197 patients (15.6%) were classified as nonadherent. 162 patients (12.8%) discontinued due to toxicities. Further analyses showed significant differences in prior ET as well as the interval between prior ET and first dose of LET. Patients treated 3−2 years AI after 2−3 years TAM had less early discontinuation than patients treated with 5 years AI or 5 years TAM (logrank p = 0.005). As expected, there were differences in the type of AI used prior, with patients on LET most compliant (logrank p = 0.034).
Conclusions: Low nonadherence was found in extended adjuvant setting than in the first 5 years of ET [8]. Toxicities were the major reasons for ETD, and it has yet to be determined who will derive most benefit from extended adjuvant treatment.

Table 1. Nonadherence and prior endocrine therapy (ET)

	N	Nonadherence (%)	HR (95% CI)	Logrank p value
Prior ET				
5 years TAM	165	37 (22.4)	1 (ref)	0,005
5 years AI	325	58 (17.8)	0.938 (0.620–1.421)	
TAM → AI	772	102 (13.2)	0.605 (0.414–0.884)	
Interval between prior ET and first dose of letrozole				
0 to <6 months	1107	155 (14)	1 (ref)	0.001
6 to <12 months	68	16 (23.5)	1.784 (1.066–2.987)	
12 to 27 months	87	24 (27.6)	1.949 (1.266–2.999)	