Evaluación de un panel de 21 genes y su impacto en la terapia adyuvante según el score de recurrencia (RS), en la Fundación Hospital San Pedro en el Departamento de Nariño

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RESUMEN

Introducción: El cáncer de mama femenino se ha convertido en el cáncer más comúnmente diagnosticado en todo el mundo, con 2.26 millones de nuevos casos estimados en para el año 2020 y representa más de 1 de cada 10 nuevos diagnósticos de cáncer cada año. El cáncer de mama invasivo en etapa temprana presenta, biomarcadores que son de gran utilidad en el momento de dirigir la estrategia sistémica adyuvante, como el estado de los receptores hormonales (RH), receptor del factor de crecimiento epidérmico humano 2 (HER2), la estratificación ganglionar, entre otros. Estos han servido para guiar los ensayos de firmas genéticas, los cuales han modificado el panorama del tratamiento del cáncer de mama temprano.
El Oncotype DX® es un ensayo que evalúa el riesgo de recurrencia del cáncer de mama con el fin de ayudar a individualizar el tratamiento.

Objetivo: Evaluar el impacto de los resultados del score de recurrencia de la prueba Oncotype DX®, frente a la definición del tratamiento aplicado en una cohorte de mujeres con cáncer de mama en la Fundación Hospital San Pedro (Pasto-Colombia) en el periodo comprendido desde año 2015 al año 2022.

Metodología: Mediante análisis retrospectivo en 90 registros de pacientes que contaban con la información de la firma genética de 21 genes (Oncotype DX®) en la institución de salud, se realizó análisis descriptivo o exploratorio para las variables categóricas y se utilizaron frecuencias, porcentajes y promedios, para la distribución de la características clínico-patológicas con relación a los puntos de corte de los Score de recurrencia se empleó un análisis bivariado a través de tablas de contingencia, con la prueba Chi cuadrado de Person, para determinar el nivel de significancia entre las variables ($p= 0,05$). El tiempo de corte del seguimiento de la población en estudio fue hasta el 29 de septiembre del año 2022. Para la determinación de la supervivencia global (SG), se utilizó la herramienta estadista de Kaplan-Meier con la fecha del momento del diagnóstico y/o fecha del procedimiento quirúrgico, cuando no se contaba con la información registrada del diagnóstico, hasta el momento de muerte o la última evolución a pacientes vivas con corte hasta última fecha de seguimiento.

Resultados: De los 90 registros, las características clínico-patológicas que mostraron asociación significativa respecto al RS fueron; el tamaño y la extensión del tumor primario, la presencia de ganglios linfáticos regionales, la metástasis a distancia y el tratamiento después del resultado de Oncotype DX®. Además, se observaron correlaciones significativas entre la decisión de modificar el tratamiento

previamente iniciado y los resultados de Oncotype DX®. Las tasas de SG de la población de estudio fueron superiores al 90 % y las puntuaciones de RS oscilaron entre el 80 % y el 96 %.

Conclusiones: La prueba Oncotype DX® es una herramienta capaz de predecir el beneficio de la terapia adyuvante (quimioterapia y/o tratamiento endocrino), basando las decisiones respecto a un cuadro clínico claro de la biología tumoral individual, en pacientes con cáncer de mama invasivo en etapa temprana, mejorando la supervivencia general de esta patología.

Palabras clave: Cáncer de mama, Oncotype DX®, quimioterapia, RS (Score de Recurrencia), supervivencia global (SG), terapia adyuvante.

ABSTRACT

Introduction: Female breast cancer has become the most commonly diagnosed cancer worldwide, with an estimated 2.26 million newly diagnosed cases for the year 2020 and represents more than 1 in 10 newly diagnosed cancer diagnoses every year. An early stage of invasive breast cancer exhibits biomarkers that have a great deal of value when it comes to directing adjunctive systemic strategies, such as hormone receptor status (RH), human epidermal growth factor receptor 2 (HER2), and ganglionic stratification, which have helped to guide the trials of genetic companies, which have been modified, and how early breast cancer can be treated. Oncotype DX® is an assay that assesses the risk of recurrence of breast cancer with the aim of helping to individualize treatment.

Aim: Evaluation of the impact of the recurrence score of the Oncotype DX® test compared to the definition of the treatment applied to a cohort of women with breast cancer at the Fundación Hospital San Pedro (Pasto-Colombia) between the years 2015 - 2022.

Method: Through a retrospective analysis in 90 records of patients who had the information of the genetic signature of 21 genes (Oncotype DX®) in the health institution, a descriptive or exploratory analysis was performed for the categorical variables, frequencies, percentages and averages were used, for the distribution of the clinicopathological characteristics in relation to the cut-off points of the recurrence score, a bivariate analysis was used through contingency tables, with the Chi-square test of Person, to determine the level of significance between variables ($p= 0,05$). The follow-up study population cutoff time was until September 29, 2022. For the determination of overall survival (OS), the Kaplan-Meier statistical tool was used with the date of diagnosis and/or date of the surgical procedure, when the

recorded information of the diagnosis was not available, until the time of death or the last evolution to live patients with cut-off until the last follow-up date.

Results: Of the 90 records, the clinicopathological characteristics associated with significant RS were; size and extent of primary tumor, presence of regional lymph nodes, distant metastasis, and treatment after Oncotype DX® result. Furthermore, significant correlations were observed between the decision to modify the treatment previously initiated and the Oncotype DX® results. The OS rates of the study population were greater than 90% and the RS ranged from 80% to 96%.

Conclusions: The Oncotype DX® test is a tool capable of predicting the benefit of adjuvant therapy (chemotherapy and/or endocrine treatment), basing decisions on a clear clinical picture of individual tumor biology, in patients with invasive breast cancer at an early stage, improving the general survival of this pathology.

Key Words: Breast cancer, Oncotype DX®, chemotherapy, RS (Recurrence Score), overall survival (OS), adjuvant therapy

REFERENCIAS BIBLIOGRÁFICAS

1. Yin W, Wang J, Jiang L, Kang YJ. Cancer and stem cells. Exp Biol Med. 2021;246:1791–801. Available from: https://doi.org/10.1177/15353702211005390
2. Seelige R, Searles S, Bui JD. Innate sensing of cancer ' s non-immunologic hallmarks. Curr Opin Immunol [Internet]. 50:1–8. Available from: https://doi.org/10.1016/j.coi.2017.09.005
3. Senga SS, Grose RP. Hallmarks of cancer—the new testament. Open Biol [Internet]. 2021;11(1):0–2. Available from: https://doi.org/10.1098/rsob.200358
4. World Health Organization. Cáncer [Internet]. 2022 [cited 2022 Aug 3]. Available from: https://www.who.int/es/news-room/fact-sheets/detail/cancer
5. Mehraj U, Ganai RA, Macha MA, Hamid A, Zargar MA, Bhat AA, et al. The tumor microenvironment as driver of stemness and therapeutic resistance in breast cancer: New challenges and therapeutic opportunities. Cell Oncol [Internet]. 2021;44(6):1209–29. Available from: https://doi.org/10.1007/s13402-021-00634-9
6. Yamauchi H, Takei J. BRCA1/BRCA2 Pathogenic Variant Breast Cancer: Treatment and Prevention Strategies. Int J Clin Oncol. 2018;23(1):45–51. Available from: https://doi.org/10.3343/alm.2020.40.2.114
7. Coughlin SS. Epidemiology of Breast Cancer in Women. Breast Can. Ahmad

A, editor. Vol. 1152, Advances in Experimental Medicine and Biology. Springer; 2019. 9–29 p. Available from: https://doi.org/10.1007/978-3-030-20301-6_2

8. Harnan S, Tappenden P, Cooper K, Stevens J, Bessey A, Rafia R, et al. Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer: a systematic review and economic analysis. Health Technol Assess (Rockv) [Internet]. 2019;23(30):1–327. Available from: https://doi.org/10.3310/hta23300
9. Saha T, Solomon J, Samson AO, Gil-Henn H. Invasion and metastasis as a central hallmark of breast cancer. J Clin Med [Internet]. 2021;10(16):1–12. Available from: https://doi.org/10.3390/jcm10163498
10. Soerjomataram I, Bray F. Planning for tomorrow: global cancer incidence and the role of prevention 2020–2070. Nat Rev Clin Oncol [Internet]. 2020;203–11. Available from: http://dx.doi.org/10.1038/s41571-021-00514-z
11. Rincon-silva NG. Inmunoterapia aplicada para el tratamiento de cáncer mediante vacunas desarrolladas con biomateriales. Rev Cuba Quim [Internet]. 2020;32(1):20–40. Available from: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S2224-54212020000100020&lng=es&tlng=es. Recuperado el 21 de agosto de 2022
12. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin [Internet]. 2021;71(3):209–49. Available from: https://doi.org/10.3322/caac.21660
13. International Agency for Research on Cancer (WHO). Estimated number of deaths in 2020, worldwide, both sexes, all ages [Internet]. Vol. 144, World Health Organization-Global cancer Observatory. 2022. Available from: https://gco.iarc.fr/today/online-analysis-pie?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=total&sex=0&cancer=39&type=1&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=7&group
14. International Agency for Research on Cancer (WHO). Estimated number of new cases in 2020, worldwide, both sexes, all ages [Internet]. Vol. 291, World Health Organization-Global cancer Observatory. 2020. Available from: http://gco.iarc.fr/today
15. International Agency for Research on Cancer (WHO). Cancer Tomorrow [Internet]. World Health Organization-Global cancer Observatory. [cited 2022 Aug 3]. Available from: https://gco.iarc.fr/
16. Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing

importance of cancer as a leading cause of premature death worldwide. Cancer [Internet]. 2021;127(16):3029–30. Available from: https://doi.org/10.1002/cncr.33587

17. World Health Organization. Cancer Today-Data visualization tools for exploring the global cancer burden in 2020 [Internet]. International Agency for Research on Cancer (IARC). 2022 [cited 2022 Aug 3]. Available from: https://gco.iarc.fr/today/data/factsheets/populations/170-colombia-fact-sheets.pdf
18. International Agency for Research on Cancer (WHO). Estimated number of new cases from 2020 to 2040, Both sexes, age [0-85+] Breast Colombia [Internet]. World Health Organization-Global cancer Observatory. Available from: https://gco.iarc.fr/tomorrow/
19. Marzo-Castillejo M, Guiriguet Capdevila C, Coma Redon E. The impact of COVID-19 on cancer diagnosis delay: possible consequences. Aten Primaria [Internet]. 2021;53(9):20–1. Available from: https://doi.org/10.1016/j.aprim.2021.102142
20. Jones D, Neal RD, Duffy SRG, Scott SE, Whitaker KL, Brain K. Impact of the COVID-19 pandemic on the symptomatic diagnosis of cancer: the view from primary care. Lancet Oncol [Internet]. 2020;21(6):748–50. Available from: http://dx.doi.org/10.1016/S1470-2045(20)30242-4
21. Vanni G, Tazzioli G, Pellicciaro M, Materazzo M, Paolo O, Cattadori F, et al. Delay in breast cancer treatments during the first COVID-19 lockdown. a multicentric analysis of 432 patients. Anticancer Res [Internet]. 2020;40(12):7119–25. Available from: https://doi.org/10.21873/anticanres.14741
22. Moraliyage H, De Silva D, Ranasinghe W, Adikari A, Alahakoon D, Prasad R, et al. Cancer in Lockdown: Impact of the COVID-19 Pandemic on Patients with Cancer. Oncologist [Internet]. 2021;26(2):e342–4. Available from: https://doi.org/10.1002/onco.13604.
23. Kaufman HW, Chen Z, Niles J, Fesko Y. Changes in the Number of US Patients with Newly Identified Cancer before and during the Coronavirus Disease 2019 (COVID-19) Pandemic. JAMA Netw Open [Internet]. 2020;2019(8):2020–2. Available from: https://doi.org/10.1001/jamanetworkopen.2020.17267
24. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England , UK : a national , population-based , modelling study. Lancet Oncol [Internet]. 2020;21(8):1023–34. Available from: http://dx.doi.org/10.1016/S1470-2045(20)30388-0
25. Bao T, Davidson NE. Gene Expression Profiling of Breast Cancer. Adv Surg

[Internet]. 2008;42(C):249–60. Available from: https://doi.org/10.1016/j.yasu.2008.03.002

26. Paik S, Shak S, Kim C, Baker J, Cronin M, Baehner FL, et al. A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer. n engl j med [Internet]. 2004;27(351):2817–43. Available from: https://doi.org/10.1056/NEJMoa041588
27. Boer RH De, Lindeman GJ, Mann GB. Spotlight on the utility of the Oncotype DX ® breast cancer assay. Int J Salud la mujer [Internet]. 2018;10:89–100. Available from: https//doi.org/10.2147/IJWH.S124520
28. Syed YY. Oncotype DX Breast Recurrence Score®: A Review of its Use in Early-Stage Breast Cancer. Mol Diagnosis Ther [Internet]. 2020;24(5):621–32. Available from: https://doi.org/10.1007/s40291-020-00482-7
29. Ramírez G. Predictores genéticos en cáncer mamario. Importancia de la prueba de 21 genes para predecir la tasa de recurrencia y la indicación de la quimioterapia. Rev Colomb Cirugía [Internet]. 2010;25(4):300–8. Available from: https://www.redalyc.org/articulo.oa?id=355534496008
30. Paik S, Tang G, Shak S, Kim C, Baker J, Kim W, et al. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. J Clin Oncol [Internet]. 2006;24(23):3726–34. Available from: https://doi.org/10.1200/JCO.2005.04.7985
31. 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 [Internet]. 2018;379(2):111–21. Available from: https://doi.org/10.1056/NEJMoa1804710
32. Gluz O, Nitz UA, Christgen M, Kates RE, Shak S, Clemens M, et al. West German Study Group Phase III PlanB Trial: First prospective outcome data for the 21-gene recurrence score assay and concordance of prognostic markers by central and local pathology assessment. J Clin Oncol. 2016;34(20):2341–9. Available from: https://doi.org/10.1200/JCO.2015.63.5383
33. Ferlay J, Parkin DM, Colombet M, Soerjomataram I, Piñeros M, Znaor A, et al. Cancer statistics for the year 2020 : An overview. Int J Cancer. 2021;149(February):778–89. Available from: https://doi.org/10.1002/ijc.33588
34. Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Piñeros M, Znaor A, et al. Global Cancer Observatory: Cancer Today [Internet]. International Agency for Research on Cancer. 2020 [cited 2022 Aug 3]. Available from: https://gco.iarc.fr/today/home
35. Bravo LE, Muñoz N. Epidemiology of cancer in Colombia. Colomb Med. 2018;49(1):09–12. Available from: https://doi.org/10.25100/cm.v49i1.3877

36. Ministerio de Salud y Protección Social - Instituto Nacional de Cancerología E. Plan Decenal Para el Control del Cáncer en Colombia Para el Período 2012 – 2021 [Internet]. Bogotá, D.C.; 2021. 1–124 p. Available from: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/IA/INCA/plan-nacional-control-cancer.pdf
37. Godone RLN, Leitão GM. Clinical and molecular aspects of breast cancer : Targets and therapies. Biomed Pharmacother [Internet]. 2018;106(January):14–34. Available from: https://doi.org/10.1016/j.biopha.2018.06.066
38. Kim MY. Breast Cancer Metastasis. In: Translational Research in Breast CancerAvances en Medicina Experimental y Biología,. Springer; 2021. p. 183–204. Available from: https://doi.org/10.1007/978-981-32-9620-6_9
39. Barzaman K, Karami J, Zarei Z, Hosseinzadeh A, Kazemi MH, Moradi-Kalbolandi S, et al. Breast cancer: Biology, biomarkers, and treatments. Int Immunopharmacol. 2020;84(February). Available from: https://doi.org/10.1016/j.intimp.2020.106535
40. Petkov VI, Miller DP, Howlader N, Gliner N, Howe W, Schussler N, et al. Breast-cancer-specific mortality in patients treated based on the 21-gene assay: a SEER population-based study. npj Breast Cancer. 2016;2(1). Available from: https://doi.org/10.1038/npjbcancer.2016.17
41. Sparano JA, Gray RJ, Ravdin PM, Hayes DF. Clinical and Genomic Risk to Guide the Use of Adjuvant Therapy for Breast Cancer. N Engl J Med. 2019;380(25):2395–405. Available from: https://doi.org/10.1056/NEJMoa1904819
42. 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):2005–14. Available from: https://doi.org/10.1056/NEJMoa1510764
43. Burstein HJ, Curigliano G, Loibl S, Dubsky P, Gnant M, Poortmans P, et al. Estimating the benefits of therapy for early-stage breast cancer: The St. Gallen International Consensus Guidelines for the primary therapy of early breast cancer 2019. Ann Oncol [Internet]. 2019;30(10):1541–57. Available from: https://doi.org/10.1093/annonc/mdz235
44. Burguin A, Diorio C. Breast Cancer Treatments : Updates and New Challenges. J Pers Med [Internet]. 2021;1–54. Available from: https://doi.org/10.3390/jpm11080808
45. Arnedos M, Gligorov J. St Gallen International Consensus Guidelines in early breast cancer: Experts to prevent patients' overtreatment and breaking the bank? Ann Oncol [Internet]. 2019;30(10):1533–5. Available from: https://doi.org/10.1093/annonc/mdz292

46. Dubsky P, Pinker K, Cardoso F, Montagna G, Ritter M, Denkert C, et al. Breast conservation and axillary management after primary systemic therapy in patients with early-stage breast cancer: the Lucerne toolbox. Lancet Oncol. 2021;22(1):e18–28. Available from: https://doi.org/10.1016/S1470-2045(20)30580-5
47. Varga Z, Sinn P, Seidman AD. Summary of head-to-head comparisons of patient risk classifications by the 21-gene Recurrence Score® (RS) assay and other genomic assays for early breast cancer. Int J Cancer. 2019;145(4):882–93. Available from: https://doi.org/10.1002/ijc.32139.
48. Hanahan D. Hallmarks of Cancer : New Dimensions. Cancer Discov [Internet]. 2022;12(January):31–46. Available from: https://doi.org/10.1158/2159-8290.CD-21-1059
49. Bougias H, Stogiannos N. Breast MRI: Where are we currently standing? J Med Imaging Radiat Sci [Internet]. 2022;53(2):203–11. Available from: https://doi.org/10.1016/j.jmir.2022.03.072
50. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. Br J Radiol. 2022;95(1130):7–9. Available from: https://doi.org/10.1259/bjr.20211033
51. Akram M, Iqbal M, Daniyal M, Khan AU. Awareness and current knowledge of breast cancer. Biol Res. 2017;50(1):1–23. Available from: https://doi.org/10.1186/s40659-017-0140-9
52. Alkabban, Fadi M. Ferguson T. Breast Cancer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2022 [cited 2022 Oct 16]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482286/
53. Yeo SK, Guan J. Breast Cancer: Multiple Subtypes within a Tumor? Trends Cancer. 2018;3(11):753–60. Available from: https://doi.org/10.1016/j.trecan.2017.09.001
54. Hortobagyi GN, Edge SB, Giuliano A. New and Important Changes in the TNM Staging System for Breast Cancer. Am Soc Clin Oncol Educ B. 2022;38:457–67. Available from: https://doi.org/10.1200/EDBK_201313
55. Zhang B, Zhang Z, Gao B, Zhang F, Tian L, Zeng H, et al. Raman microspectroscopy based TNM staging and grading of breast cancer. Spectrochim Acta Part A Mol Biomol Spectrosc [Internet]. 2023;285(October 2022):121937. Available from: https://doi.org/10.1016/j.saa.2022.121937
56. Nicolini A, Ferrari P, Duffy MJ. Prognostic and predictive biomarkers in breast cancer: Past, present and future. Semin Cancer Biol. 2018;52(August 2017):56–73. Available from: https://doi.org/10.1016/j.semcancer.2017.08.010
57. Badve SS, Baehner FL, Gray RP, Childs BH, Maddala T, Liu ML, et al. Estrogen- and progesterone-receptor status in ECOG 2197: Comparison of

immunohistochemistry by local and central laboratories and quantitative reverse transcription polymerase chain reaction by central laboratory. J Clin Oncol [Internet]. 2008;26(15):2473–81. Available from: https://ascopubs.org/doi/pdf/10.1200/JCO.2007.13.6424

58. Baehner FL, Achacoso N, Maddala T, Shak S, Quesenberry CP, Goldstein LC, et al. Human epidermal growth factor receptor 2 assessment in a case-control study: Comparison of fluorescence in situ hybridization and quantitative reverse transcription polymerase chain reaction performed by central laboratories. J Clin Oncol [Internet]. 2010;28(28):4300–6. Available from: https://doi.org/10.1200/JCO.2009.24.8211
59. Andre F, Ismaila N, Henry NL, Somerfield MR, Bast RC, Barlow W, et al. Use of biomarkers to guide decisions on adjuvant systemic therapy for women with early-stage invasive breast cancer: ASCO clinical practice guideline update-integration of results from TAILORx. J Clin Oncol. 2019;37(22):1956–64. Available from: https://doi.org/10.1200/JCO.19.00945
60. Burstein HJ, Curigliano G, Thürlimann B, Weber WP, Poortmans P, Regan MM, et al. Customizing local and systemic therapies for women with early breast cancer: the St. Gallen International Consensus Guidelines for treatment of early breast cancer 2021. Ann Oncol. 2021;32(10):1216–35. Available from: https://doi.org/10.1016/j.annonc.2021.06.023
61. World Health Organization. Decade of Healthy Ageing 2020-2030 [Internet]. 2020. Available from: https://cdn.who.int/media/docs/default-source/decade-of-healthy-ageing/final-decade-proposal/decade-proposal-final-apr2020-en.pdf?sfvrsn=b4b75ebc_25&download=true
62. Nitz U, Gluz O, Christgen M, Kates RE, Clemens M, Malter W, et al. Reducing chemotherapy use in clinically high-risk , genomically low-risk pN0 and pN1 early breast cancer patients : five-year data from the prospective , randomised phase 3 West German Study Group (WSG) PlanB trial. Breast Cancer Res Treat. 2019;165(3):573–83. Available from: https://doi.org/10.1007/s10549-017-4358-6
63. Stemmer SM, Steiner M, Rizel S, Ben-baruch N, Uziely B, Jakubowski DM, et al. Ten-year clinical outcomes in N0 ER + breast cancer patients with Recurrence Score-guided therapy. npj Breast Cancer [Internet]. 2019;8–13. Available from: http://doi.org/10.1038/s41523-019-0137-3
64. Joseph Gligorov, Xavier B. Pivot, William Jacot, Hervé L. Naman, Dominique Spaeth, Jean-Louis Misset, Rémy Largillier, Jean-Loup Sautiere, Anne de Roquancourt, Christophe Pomel, Philippe Rouanet, Roman Rouzier, Frederique M. Penault-Llorca for TF. Prospective Clinical Utility Study of the Use of the 21-Gene Assay in Adjuvant Clinical Decision Making in Women With Estrogen Receptor-Positive Early Invasive Breast Cancer : Results From

the SWITCH Study. Oncologist. 2015;20(8):873–9. Available from: https://doi.org/10.1634/theoncologist.2014-0467

65. Loncaster J, Armstrong A, Howell S, Wilson G, Welch R, Chittalia A, et al. Impact of Oncotype DX breast Recurrence Score testing on adjuvant chemotherapy use in early breast cancer : Real world experience in Greater Manchester , UK. Eur J Surg Oncol [Internet]. 2017;43(5):931–7. Available from: http://doi.org/10.1016/j.ejso.2016.12.010
66. Rath MG, Uhlmann L, Fiedler M, Heil J, Golatta M, Dinkic C, et al. Oncotype - DX ® in breast cancer patients : clinical experience , outcome and follow - up — a case – control study. Arch Gynecol Obstet [Internet]. 2018;297(2):443–7. Available from: https://doi.org/10.1007/s00404-017-4618-z
67. Lin NU, Perez EA, Goldstein LJ, Chia SKL, Thind SD, Rastogi P, et al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. N Engl J Med. 2021;385:2336–2347. Available from: https://doi.org/10.1056/NEJMoa2108873