PLATINUM BASED VERSUS ANTHRACYCLIN BASED NEOADJUVANT CHEMOTHERAPY IN NONMETASTATIC TRIPLE NEGATIVE BREAST CANCER (TNBC) PATIENTS

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ABSTRACT

Background: *Triple Negative Breast Cancer (TNBC) is a poor prognostic subtype of breast cancer. Response to neoadjuvant chemotherapy was proved to be associated with better survival. Platinum-based chemotherapy was suggested to be associated with better response in the neoadjuvant setting*

Aim of the work: *The current study is a phase III prospective study aimed at comparing platinum-based chemotherapy to anthracycline/taxanes conventional therapy in the neoadjuvant setting.*

Patients and Methods: *The study was carried out in Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Ain Shams University. Inclusion criteria: nonmetastatic breast cancer cases, age more than 18 years, ECOG performance status of 0-2, and tumor proved to be triple negative subtype. Exclusion criteria: chemotherapy treatment contraindications, pregnancy, history of prior malignancy, presence of distant metastasis, and bilateral cases.*

Results: *The study included 45 patients who fulfilled the eligibility criteria. Patients were randomly allocated into 2 groups, Group A: included 22 patients received anthracycline containing regimen (FEC or FAC) followed by Docetaxel and Group B: included 23 patients received platinum-based chemotherapy (Cisplatin or Carboplatin) combined with Docetaxel. Three patients in each arm had pCR in tumor, while one patient in each arm had PD. In axillary lymph nodes, complete regression occurred in 8 patients of group A and 11 patients of group B. Treatment was well tolerated in both groups.*

Conclusion: *Platinum based chemotherapy in treatment of TNBC was well tolerated and had non inferior outcome compared to the classic anthracycline/taxanes based treatment, yet better biological understanding of the TNBC subtypes is mandatory for better treatment outcome.*

Keywords: *TNBC, neoadjuvant, platinum, breast cancer.*

INTRODUCTION:

Breast cancer is the most frequent type of cancer in women[(1)]. Over the years, the prognosis of the disease improved significantly, and this could be partly attributed to the better understanding of the molecular patterns of the disease[(2)]. The better understanding of breast cancer is that it is a heterogeneous group of diseases, including different entities that vary in morphology, biological behavior, clinical outcome, and response to therapy[(3)]**.** Being divided into different molecular subtypes, each subtype of breast cancer has its own prognosis. Triple-negative breast cancer (TNBC) which is defined by the lack of Estrogen receptors

(ER), Progesterone receptors (PR), and Human Epidermal Growth Factor Receptor2 (Her-2neu) expression, makes up to 15-20 % of breast cancers[4&5]**.** At least six different triple-negative subtypes are identified with different biology and sensitivity to therapies**.** The risk of distant recurrence appears to peak at 3 years from diagnosis[6]**.** TNBC being nonresponsive to endocrine therapy or Her2 targeted therapy, is thus treated by chemotherapy. Conventional chemotherapy containing anthracycline and taxanes is the accepted treatment on TNBC[7]**.**

In TNBC patients, achieving a pathological response with neoadjuvant treatment is an important surrogate of better outcome [7&8]. Though being restricted to the conventional chemotherapy for decades[9], new therapies have been incorporated into the treatment of subgroups of TNBC[2,10&11]. Higher rates of response to neoadjuvant treatment have been described with platinum-based chemotherapy[10&12-14]. Platinum compounds cause cessation of DNA replication and apoptosis of the tumor cell[15]. Thus, TNBC appears to have high response rate with platinum-based compounds being associated with limited DNA repair capacity[10,16&17].

AIM OF THE WORK:

The current study is a phase III prospective study that aimed at comparing Platinum based chemotherapy coupled with taxanes to the classic anthracycline-based chemotherapy followed by taxanes regarding pathologic response, toxicity, Progression free survival (PFS) and overall survival (OS) in TNBC patients treated with neoadjuvant chemotherapy.

PATIENTS AND METHODS:

The study was carried out on patients with TNBC treated at Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Ain Shams University in the period between September/2013 till August/2017. Eligibility Criteria: Female patients, age more than 18 years, ECOG performance status of 0-2, pathologically proven as invasive breast carcinoma, nonmetastatic, proved to be Estrogen receptors (ER) -ve, Progesterone receptors (PR) -ve and Her2 status score 0-1 by immunohisto-chemistry (IHC) analysis and confirmed by SISH (only for HER2 score+2 by IHC). Exclusion criteria: any comorbidities that contraindicate the use of chemotherapy treatment, pregnancy, lactation, history of prior malignancy, presence of distant metastasis, and bilateral cases.

Metastatic work up done before treatment included radiological studies (CT-chest, pelviabdominal CT and isotopic Bone scan). Pretreatment assessment included laboratory investigations (Complete blood picture, kidney function tests, and liver function tests) and Echocardiography for those to receive anthracycline as per the guidelines of the breast clinic.

Patients who fulfilled the eligibility criteria were randomly allocated into 2 groups, **Group A**, received anthracycline containing regimen (FEC or FAC) followed by Docetaxel as follows: 5 Fluorouracil 500 mg/m^2 IV, Epirubicin 100 mg/m^2 or Adriamycin 50mg/m^2 IV, and Cyclophosphamide 500 mg/m2 IV on D1 of each cycle. Cycle repeated every 3 weeks for 3 repetitive cycles, followed by Docetaxel 75mg/m^2 IV D1, 3-weekly cycle, for 3 cycles (starting 3 weeks after last cycle of FEC or FAC).

Group B: received Cisplatin or Carboplatin combined with Docetaxel as follows: Platinum compound (Cisplatin 80 mg/m^2 IV D1 every 3 weeks for 6 cycles or Carboplatin AUC 5 IV Day 1 weekly for 3 weeks) for 6 cycles combined with Docetaxel 75mg/m^2 IV D1, 3-weekly cycle, for 6 cycles.

Radiopaque clips were inserted to detect the anatomical site of the primary lesion

before starting treatment. Patients were evaluated clinically after each cycle. Radiological studies were performed after every 3 cycles. Pathological response was assessed in the surgical specimen. After surgery patients completed their radiotherapy adjuvant treatment. Post treatment follow up was done once after surgery and every 3 months thereafter.

Response Criteria:

Pathological response was defined as follows: Pathological Complete Response (pCR); absence of all detectable disease after the treatment. Pathological Partial response (pPR); more than 50% tumor regression, according to WHO grading of the clinical response (18)**.** Tolerability was evaluated according to National Cancer Institute (NCI) CTC v.4 toxicity scale. Progression free survival (PFS) is defined as, time from day of diagnosis to any breast cancer related event**.**

Statistical Analysis:

Data were collected, revised, coded, and entered to the Statistical Package for Social Science (SPSS) version 23 and the Qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered ± significant as the following:

P > 0.05: Nonsignificant, P < 0.05: Significant, and P < 0.01: Highly significant.

RESULTS:

Initial recruitment included 51 patients. During the neoadjuvant treatment 6 patients were excluded (Developed metastases or referral to surgery due to tumor progression) These patients were excluded from the study. Thus, the study included 45 patients (22 patient in arm A and 23 patients in arm B). Group A patients had mean age of 46.36 ± 14.19 and group B patients had mean age of 47.87±12.55, family history of breast cancer was positive in 3 patients of group B. Most patients had pathology of IDC (81% and 91% of both groups respectively). The histopathological analysis revealed that 91% of group A and 82.6% of group B had G-II infiltrating ductal carcinoma. Fifty percent and 48.6% of both groups respectively presented with clinical tumor size of T3. Data of the patients are shown in table (1).

All patients received 6 cycles of chemotherapy as designed, none had been excluded due to side effects, 2 patients of each arm had minor treatment delays due to grade 2 or 3 side effects.

The neoadjuvant treatment showed benefit in most patients. There was complete disappearance of the primary tumor pCR in 3 patients of each group. Tumor improved to less than 5 cm in 15 patients in group A and 14 patients in group B versus 4 patients in each group before treatment. Regarding the N stage 8 patients in group A compared to 11 patients in group B became N0 versus 3 and 2 in both groups before treatment respectively. Patients improved to N1 in 10 and 9 patients of both groups respectively. The improved T and the N stage between both groups was statistically nonsignificant.

Toxicity to chemotherapy was recorded for both arms. Regarding hematologic toxicity only 1 patient of group A had grade 3 anemia, 3 and 5 patients of both groups respectively had grade 2 neutropenia. Thrombocytopenia of grade 2 occurred in 2 patients of group 2. The non-hematological side effects were more vomiting in group B; grade 2 in 9 patients. Peripheral neuropathy in arm B was more pronounced with grade 1and 2 neuropathies recorded in 11 patients but it was not recorded in group A.

Follow up after Surgery showed that, 15/22 patients (68.2%) at group A and 13/23 patients (56.5%) at group B, had no relapse. (Table:3).

Table (1): Patients and tumor characteristics in both arms before treatment.

		ARM A		ARM B		P-value	Sig.
		No=22	%	No=23	%		
Age	Mean ± SD Range	46.36 ± 14.19 23 – 71		47.87±12.55 25 – 73		0.708	NS
Family History	No	22	100.0%	20	87.0%	0.079	NS
	Yes	0	0.0%	3	13.0%	0.079	NS
Pathology	Infiltrating duct carcinoma	18	81.8%	21	91.3%	0.349	NS
	Infiltrating Lobular carcinoma	2	9.1%	1	4.3%	0.523	NS
	Inflammatory carcinoma	1	4.5%	1	4.3%	0.974	NS
	Medullary carcinoma	1	4.5%	0	0.0%	0.301	NS
Pathology grade	I	0	0.0%	1	4.3%	0.322	NS
	II	20	90.9%	19	82.6%	0.413	NS
	III	2	9.1%	3	13.0%	0.078	NS
Clinical T	T2	4	18.2%	4	17.4%	0.943	NS
	T3	11	50.0%	11	47.8%	0.884	NS
	T4	7	31.8%	8	34.8%	0.833	NS
Clinical N	N0	3	13.6%	2	8.7%	0.598	NS
	N1	0	0.0%	2	8.7%	0.157	NS
	N2	15	68.2%	15	65.2%	0.833	NS
	N3	4	18.2%	4	17.4%	0.943	NS

SD: Standard Deviation, T: tumor stage, N: nodal stage, Sig.: Significant value, NS: not significant

Table (2): response in primary tumor and lymph nodes with treatment

		Group B, N=22 (%)		Group B, N=23 (%)		P value	Significance
		Before (%)	After (%)	Before (%)	After (%)		
T stage	T0	0(0)	3(13.6)	0(0)	3(13)	0.956	NS
	T1	0(0)	5 (22.7)	0 (0)	9(39.1)	0.234	NS
	T2	4 (18.2)	10 (45.5)	4 (17.4)	5 (22)	0.091	NS
	T3	11(50)	2(9.1)	11(48)	3 (13)	0.673	NS
	T4	7 (32)	1 (4.5)	8 (35)	1 (4.3)	0.974	NS
	NA	0 (0)	1 (4.5)	0(0)	2 (8.7)	0.577	NS
	Total	22(100)	22 (100)	23 (100)	23 (100)		
N stage	N0	3 (13.6)	8 (36.6)	2 (8.7)	11(48)	0.436	NS
	N1	0 (0)	10 (45.5)	2 (8.7)	9 (39)	0.943	NS
	N2	15 (68.2)	3 (13.6)	15 (65)	1 (4.3)	0.273	NS
	N3	4 (18.2)	0 (0)	4 (17.4)	0 (0)	0.577	NS
	NA	0 (0)	1 (4.5)	0 (0)	1 (4.5)	0.721	NS
	Total	22 (100)	22 (100)	23 (100)	23 (100)		

T: Tumor, N: Lymph nodes, NA: Not available

Table (3): Recurrence at arm A vs arm B.

		ARM A		ARM B		Test value*	P-value	Sig.
		No.22	%	No.23	%			
Recurrence	Yes	6	27.3%	8	34.8%	0.296	0.586	NS
	No	15	68.2%	13	56.5%	0.650	0.420	NS
	NA	1	4.5%	2	8.7%	0.311	0.577	NS
Site of Recurrence	No	18	81.8%	17	73.9%	0.554	0.456	NS
	SCLN	0	0.0%	2	8.7%	2.002	0.157	NS
	Breast	1	4.5%	0	0.0%	1.069	0.301	NS
	Chest Wall	1	4.5%	1	4.3%	0.001	0.974	NS
	Axillary LN	1	4.5%	0	0.0%	1.069	0.301	NS
	NA	1	4.5%	3	13.0%	1.003	0.316	NS
Site of distant metastasis	No	16	72.7%	13	56.5%	1.289	0.256	NS
	Contralateral	0	0.0%	1	4.3%	0.978	0.322	NS
	Bone	2	9.1%	2	8.7%	0.002	0.964	NS
	Lung	0	0.0%	4	17.4%	4.199	0.040	S
	Liver	2	9.1%	0	0.0%	2.188	0.139	NS
	NA	2	9.1%	3	13.0%	0.178	0.673	NS

NA: not available, Sig.: significance, No.:number, SCLN: Supraclavicular LNs

Progression Free survival (PFS) and overall survival (OS) were measured for both groups and there was non-statistically significant difference between both groups in this regard (Table:4)

Table (4): Overall Survival & Progression Free Survival Group A vs. Group B.

		ARM A	ARM B	Test value	P-value	Sig.
		No.= 22	No.= 23			
O.S (Months)	Median	674 days 22.5 months	600 days 20 months	-0.569	0.572	NS
	Range	365 – 1451	286 – 1448			
PFS (Months)	Median	610 days 20.3 months	569 days 19 months	-0.687	0.496	NS
	Range	191 – 1218	145 – 1103			

PFS: Progression Free Survival, OS: Overall Survival, Sig: Significance, NS: not significant

DISCUSSION:

The prognosis of TNBC is still unsatisfactory despite the great progress in genotype profiles[12]. Many trials reported that there is association between response to neoadjuvant chemotherapy and outcome in TNBC[17]. Platinum based neoadjuvant chemotherapy was reported to have significantly elevated pCR rate of TNBC patients in several trials compared to non-platinum- based therapies[15]. Pathological complete response was recommended as a marker of better DFS in early cases[17].

In this prospective phase III study of TNBC patients managed by neoadjuvant treatment, we compared platinum-based regimen (platinum/ taxanes) to the standard regimen of the anthracycline/ taxanes. In the current study there was no difference regarding the pathological response to neoadjuvant therapy when treated by either modality. Pathological CR was achieved in 13% of patients treated with neoadjuvant platinum-based chemotherapy. A retrospective study of 144 patients reported on the use of neoadjuvant platinum-based chemotherapy in TNBC (either cisplatin or

carboplatin) combined with docetaxel reported a pCR of 31 %[19]. The small number of patients achieving pCR could be attributed to the small sample size in the current study.

Survival whether OS or PFS was not affected by the use of platinum-based neoadjuvant chemotherapy in the current study, and it was not different when treating patients with the conventional anthracycline based chemotherapy. Though reported by many, the better survival with the use of platinum-based neoadjuvant chemotherapy has been widely questionable [17,20-22]. Bian et al 2021,[17] in a meta-analysis of TNBC patients treated with platinum-based regimen found that Platinum-based regimens could be of DFS benefit in early TNBC patients, compared with standard regimens that lack the platinum compounds. The benefit of platinum-based therapy was demonstrated whether it was added to the anthracycline/taxane regimen or used in combination with taxanes alone. Addition-ally, it was proved regardless platinum compounds were used as adjuvant or neoadjuvant treatment. The benefit was in terms of better DFS but was marginal or no benefit for the OS. Survival benefit was also suggested in metastatic TNBC patients in a metanalysis by Egger et al 2020 for platinum- based compounds[23].

TNBC is a heterogenous disease with multiple subtypes[4,6]. TNT study comparing carboplatin to Docetaxel in TNBC patients showed no difference in response, PFS or OS but patients with a BRCA1/2 germline mutation had significantly better response and PFS in the carboplatin arm[24]. It was reported that EGFR abnormalities were associated with worse response to anthracycline[25]. Tumor-infiltrated lymphocytes (TILs) are also reported to be associated with TNBC in 20% of cases. Clinical data suggested a predictive role of TILs in terms of pCR in patients treated with neoadjuvant treatment, mainly with platinum regimens[26].

Clearly, there is a major need to better understanding the characteristics and the clinical behavior of TNBCs with an aim to develop effective treatments for this subtype. The identification of molecular targets is essential for designing of clinical trials that investigate new treatment strategies for better survival outcomes.

Limitations of the study:

The current study lacks any molecular target identification to further subclassify TNBC cases hence no response advantage was detected for the platinum-based regimen, the small sample size and the fact that considerable proportion of patients present to the oncology department after surgical management further reduced the number of patients recruited

Conclusion:

platinum based neoadjuvant chemo-therapy was non inferior to classical anthracycline/taxane neoadjuvant treatment. Better understanding of the intrinsic molecular genetic subtypes is crucial for better outcome.

Ethical considerations:

Study was approved by the local ethical committee at the faculty of medicine Ain shams university and all patients signed informed consent for before their inclusion in the trial.

Conflicts of Interest: The authors state that the publishing of this paper is free of any conflicts of interest.

REFERENCES:

1. Yin, L., Duan, J. J., Bian, X. W., & Yu, S. C. (2020). Triple-negative breast cancer molecular subtyping and treatment progress. *Breast cancer research: BCR*, *22*(1), 61. https://doi. org/10. 186/s 13058-020-01296-5

2. Untch M, Huober J, Jackisch C, et al. (2017). Initial treatment of patients with primary breast cancer: evidence, controversies, consensus: spectrum of opinion of German specialists at the 15th international St. Gallen breast cancer conference (Vienna 2017). Geburtshilfe Frauenheilkd. 2017; 77(6): 633–44.
3. Gass, P., Lux, M. P., Rauh, C. et al. (2018). Prediction of pathological complete response and prognosis in patients with neoadjuvant treatment for triple-negative breast cancer. *BMC cancer*, *18*(1), 1051. https://doi.org/10. 1186/s12885-018-4925-1
4. Carey, L., Winer, E., Viale, G., Cameron, D., & Gianni, L. (2010). Triple-negative breast cancer: disease entity or title of convenience?. *Nature reviews. Clinical oncology*, *7*(12), 683–692. https://doi.org/10.1038/nrclinonc.2010.154
5. Adel, A.M. and Abdelghani, D. (2020) Correlation between Cancer Breast Subtypes and Age at Presentation in Egyptian Patients; Single Institution Experience. Journal of Cancer Therapy, 11, 26-34. https://doi.org/10.4236/jct.2020.111003
6. Burstein, M. D., Tsimelzon, A., Poage, G. M., et.al. (2015). Comprehensive genomic analysis identifies novel subtypes and targets of triple-negative breast cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research*, *21*(7), 1688–1698. https://doi.org/10.1158/1078-0432.CCR-14-0432
7. Hahnen, E., Lederer, B., Hauke, J., et.al. (2017). Germline Mutation Status, Pathological Complete Response, and Disease-Free Survival in Triple-Negative Breast Cancer: Secondary Analysis of the GeparSixto Randomized Clinical Trial. *JAMA oncology*, *3*(10), 1378–1385. https://doi.org/10. 1001/ jamaoncol. 2017. 1007
8. Schneeweiss, A., Lux, M. P., Janni, W., et.al. (2018). Update Breast Cancer 2018 (Part 2) - Advanced Breast Cancer, Quality of Life and Prevention. *Geburtshilfe und Frauen-heilkunde*, *78*(3), 246–259. https: //doi. org/10.1055/s-0044-101614
9. Curigliano, G., Burstein, H. J., Winer, E. P., et.al., (2017). De-escalating and escalating treatments for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017. *Annals of oncology : official journal of the European Society for Medical Oncology*, *28*(8), 1700–1712. https://doi.org/10.1093/annonc/mdx308
10. Denkert, C., Liedtke, C., Tutt, A., & von Minckwitz, G. (2017). Molecular alterations in triple-negative breast cancer-the road to new treatment strategies. *Lancet (London, England)*, *389*(10087), 2430–2442. https://doi.org/10.1016/S0140-6736(16)32454-0
11. Lux MP, Janni W, Hartkopf AD, et al. Update breast cancer 2017 - implementation of novel therapies. Geburtshilfe Frauenheilkd. 2017;77(12):1281–90.
12. Hahnen, E., Lederer, B., Hauke, J., et al. (2017). Germline Mutation Status, Pathological Complete Response, and Disease-Free Survival in Triple-Negative Breast Cancer: Secondary Analysis of the GeparSixto Randomized Clinical Trial. *JAMA oncology*, *3*(10), 1378–1385. https://doi.org/10.1001/jamaoncol.2017.1007
13. Loibl, S., Weber, K. E., Timms, et al. (2018). Survival analysis of carboplatin added to an anthracycline/taxane-based neoadjuvant chemotherapy and HRD score as predictor of response-final results from GeparSixto. *Annals of oncology : official journal of the European Society for Medical Oncology*, *29*(12), 2341–2347. https://doi.org/10.1093/annonc/mdy460
14. Von Minckwitz G, Loibl S, Schneeweiss A, et al. Abstract S2-04: Early survival analysis of the randomized phase II trial investigating the addition of carboplatin to Gass et al. BMC Cancer (2018) 18:1051 Page 7 of 8 neoadjuvant therapy for triple-negative and HER2-positive early breast cancer (GeparSixto). Cancer Res.

2016;76:S2-04. https://doi.org/10.1158/1538-7445. SABCS15-S2-04.

15. Von Minckwitz G, Hahnen E, Fasching P, et al. (2014). Pathological complete response (pCR) rates after carboplatin-containing neoadjuvant chemotherapy in patients with germline BRCA (g BRCA) mutation and triple-negative breast cancer (TNBC): results from GeparSixto. J Clin Oncol. 32(15 Suppl):1005.
16. Von Minckwitz G, Timms K, Untch M, et al. (2016)Homologous repair deficiency (HRD) as measure to predict the effect of carboplatin on survival in the neoadjuvant phase II trial GeparSixto in triple-negative early breast cancer [abstract]. In: Proceedings of the 2016 San Antonio Breast Cancer Symposium. Cancer Res. 2017;77(4 Suppl):Abstract nr P1-09-02.
17. Lei Bian1,4, Ping Yu2,4, Jiahuai Wen3,4, et al. (2021) Survival benefit of platinum-based regimen in early stage triple negative breast cancer: A meta-analysis of randomized controlled trials. *NPJ Breast Cancer*. 2021;7(1):157. Published 2021 Dec 21. doi:10.1038/s41523-021-00367-w
18. Subbiah, V., Chuang, H. H., Gambhire, D., & Kairemo, K. (2017). Defining Clinical Response Criteria and Early Response Criteria for Precision Oncology: Current State-of-the-Art and Future erspectives. *Diagnostics (Basel, Switzerland)*, *7*(1), 10. https://doi.org/10. 3390/diagnostics70100101
19. Hurley, J., Reis, I. M., Rodgers, S. E., et al. (2013). The use of neoadjuvant platinum-based chemotherapy in locally advanced breast cancer that is triple negative: retrospective analysis of 144 patients. *Breast cancer research and treatment*, *138*(3), 783–794. https://doi.org/10.1007/s10549-013-2497-y
20. Iwase, M., Ando, M., Aogi, K., et al. (2020). Long-term survival analysis of addition of carboplatin to neoadjuvant chemotherapy in HER2-negative breast cancer. *Breast cancer research and treatment*, *180*(3), 687–694. https://doi.org/10.1007/s10549-020-05580-y
21. Du, F., Wang, W., Wang, Y., et al. (2020). Carboplatin plus taxanes are non-inferior to epirubicin plus cyclophosphamide followed by taxanes as adjuvant chemotherapy for early triple-negative breast cancer. *Breast cancer research and treatment*, *182*(1), 67–77. https://doi.org/10.1007/s10549-020-05648-9
22. Geyer, C. E., Sikov, W. M., Huober, J., et al. (2022). Long-term efficacy and safety of addition of carboplatin with or without veliparib to standard neoadjuvant chemotherapy in triple-negative breast cancer: 4-year follow-up data from BrighTNess, a randomized phase III trial. *Annals of oncology: official journal of the European Society for Medical Oncology*, *33*(4), 384–394. https://doi.org/10.1016/j.annonc.2022.01.009
23. Egger, S. J., Chan, M., Luo, Q., & Wilcken, N. (2020). Platinum-containing regimens for triple-negative metastatic breast cancer. *The Cochrane database of systematic reviews*, *10*(10), CD013750. https://doi.org/10. 1002/ 14651858. CD013750
24. 24- Tutt, A., Tovey, H., Cheang, M., et al. (2018). Carboplatin in BRCA1/2-mutated and triple-negative breast cancer BRCAness subgroups: the TNT Trial. *Nature medicine*, *24*(5), 628–637. https://doi.org/10.1038/s41591-018-0009-7
25. Liu, D., He, J., Yuan, Z., et al. (2012). EGFR expression correlates with decreased disease-free survival in triple-negative breast cancer: a retrospective analysis based on a tissue microarray. *Medical oncology (Northwood, London, England)*, *29*(2), 401–405. https://doi.org/10.1007/s12032-011-9827-x

26. Salgado, R., Denkert, C., Demaria, S., et al. International TILs Working Group 2014 (2015). The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILs Working Group 2014. *Annals of oncology : official journal of the European Society for Medical Oncology*, *26*(2), 259–271. https://doi.org/10.1093/annonc/mdu450

دراسه مقارنه بين العلاج الكيمائي المحتوي على عقار البلاتينول والمحتوي على الانثراسيكلين كعلاج مقدم للجراحه في علاج اورام الثدي السالبه المستقبلات

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نبذه عن البحث: اورام الثدي السالبه المستقبلات تعتبر من الاورام الصعبه في الغلاج لعدم استجابتها للعلاج الهرموني او المضاد لمستقبلات her2 واثبتت عده دراسات ان عقار البلاتينول فعال لعلاجها

الهدف من البحث: مقارنه بين العلاج الكيمائي المحتوي على عقار البلاتينول والمحتوي على الانثراسيكلين كعلاج مقدم للجراحه في علاج اورام الثدي السالبه المستقبلات من حيث الاستجابه ومعدل الاعاشه

طريقه البحث: اشتملت الدراسه على ٤٥ مريض مقسمين الى مجموعتين المجموعه الاولى ٢٢ مريضه وتلقو علاج يحتوي على الانثراسيكلين والمجموعه الثانيه ٢٣ مريضه وتلقو علاج يحتوي على البلاتينول

النتائج : لم يكن هناك فرق بين المجموعتين من حيث الاستجابه للعلاج ولا معدل الاعاشه

الخلاصه: علاج اورام الثدي ثلاثيه المستقبلات بواسطه عقار البلاتينول ادى الى نتائج مشابهه للعلاج التقليدي بواسطه الانثراسيكلين لذا لابد من استخدام التحاليل الجينيه لمعرفه الانواع سالبه المستقبلات من سرطان الثدي التي قد تستجيب لهذا العلاج