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Original article

Difference in Outcome between Luminal A, Luminal B in Early Stage Breast Cancer Retrospective Study

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Abstract

Background: Breast carcinoma is the most prevalent carcinoma in female worldwide, about 2.3 million new breast carcinoma cases and 685,000 breast carcinoma deaths worldwide in 2020. These tumors are heterogeneous in terms of histology (mainly ductal, lobular, mixed ductal and lobular, cribriform, mucinous, medullary, and tubular carcinomas), natural history, and response to treatment. **Objective:** To find retrospectively prognostic parameter difference between breast carcinoma subtypes Luminal A, Luminal B. and 5-year rates of (OS), (DFS) in female diagnosed with luminal early-stage breast carcinoma at clinical oncology department, faculty of Medicine, Beni-Suef University Hospital from Jan 2015 till December 2019. **Patients and Methods:** the current study is retrospective cross-sectional, conducted in Clinical Oncology Department in Beni-Suef University from Jan 2015 till Dec 2019**. Results:** There was significantly difference between luminal A, luminal B regarding age, as most patients more than 60 yrs old had luminal A breast cancer. There no significantly differences between luminal A, luminal B regarding DFS,OS but time of DFS, OS in luminal A was longer،as luminal A is

the best prognosis of molecular subtypes. There was significantly differences between luminal A, luminal B regarding chemotherapy, which most of luminal A not received chemotherapy, because luminal A breast cancer less benefit of chemotherapy. There was significant association between T3 and younger age less than 40 years but from 40 to 60 and above 60 there was no significant association with T1, 2&3.There was a significant association between ages more than 60 years and lower Ki67.There was significant higher overall survival in patients without comorbitities than patients with DM or HTN or both. **Conclusion:** The current study, Luminal B almost depend on high ki67 which is not riable test, so no significantly difference between Luminal A, Luminal B regarding OS, DFS. But time of DFS, OS is longer in Luminal A than Luminal B, this confirm Luminal A is the best prognosis of molecular subtypes of breast carcinoma.

1. Introduction:

Breast carcinoma is the most prevalent carcinoma in female worldwide, about 2.3 million new breast carcinoma cases and 685,000 breast carcinoma deaths worldwide in 2020 [1].

These tumors are heterogeneous in terms of histology (mainly ductal, lobular, mixed ductal and lobular, cribriform, mucinous, medullary, and tubular carcinomas), natural history, and response to treatment [2].

Breast cancer included 4 molecular subtypes with Luminal A (58.5%) subtype is the most common, followed by triple negative (16%), luminal B (14%), and Her_{2neu} positive (11.5%) [3].

Luminal A breast cancer is characterized by the high expression of ERs and PRs, low Ki67< 20% and negative Her_{2neu}. These cancers tend to be of a lower grade and have a better prognosis than the other subtypes. When compared to the luminal A subtype, luminal B Tumors often have lower expression levels of Estrogen-regulated genes(ER), lower or no progesterone Receptor (PR) expression, Her_{2neu} may be positive or negative, higher tumor grade, high nodal positivity, higher expression of Ki67 > 20%, and activation of growth factor receptor

signaling pathways, such as IGF-1R and PI3K/AKT/mTOR [4]**,** Luminal B tumors are considered to have low sensitivity to endocrine treatment and high sensitivity to chemotherapy than Luminal A tumors [5].

The optimal Ki67 cut-off that could differentiate luminal A and B tumors is unknown, although a cut-off of 14% is accepted in some studies. There is no fixed value at which the different luminal tumors are distinguished. The clinical guidelines for early-stage breast carcinoma published by the European Society for Medical Oncology (ESMO) in 2019 proposes a cut-off of 20%. In a study by Escala Cornejo et al., to identify the best Ki67 cut-off for determining luminal breast cancer subtypes using immunohistochemical (IHC) analysis and pam50 genomic classification they concluded that increasing the Ki67 cut-off to >20% leads to a better surrogate classification based on immunohistochemistry and to a higher sensitivity ,low specificity in classifying the luminal subtypes [6].

A variety of clinical, pathological, molecular and genetic (as Oncotype DX or MammaPrint)are used for treatment decisions in the adjuvant setting in early stage luminal breast carcinoma (e.g., whether chemotherapy (CT) administration is appropriate or not, based on the risk of recurrence) but genetic tests are expensive so not routinely used in developing countries inspite it is cost effective so most of oncologist are still depending on clinical and pathological data in decision making in early stage luminal breast carcinoma [7].

2. Aim Of The Work:

The aim of current study is to find retrospectively prognostic parameter difference between breast cancer subtypes Luminal A, Luminal B. and 5-year rates of overall survival (OS), Disease free survival (DFS) in women diagnosed with luminal early stage breast cancer at clinical oncology department, faculty of Medicine, Beni-Suef University Hospital from Jan 2015 till December 2019.

3. Patients And Methods:

- **Type of study:** This is a retrospective cross sectional study.
- **Site of study:** Oncology department, Beni-suef University hospital.
- **Date and period of the study:** years of study from January 2015 to December 2019.

Target Population: During the period of data collection all female patients with early stage Luminal A, Luminal B breast cancer attended the oncology Clinic and department was included in this study.

Data collection: Data was obtained from Beni-Suef University hospital, data was populated using manual review of each patient file. Data was collected on demographic characteristics, biomarkers

profile (ER, PR, Her_2, ki67) of the tumer, therapy modalities (surgery, chemotherapy type, regemin, radiotherapy) and patients of Luminal A, Luminal B breast cancer, disease recurrence, and survival outcome.

Inclusion criteria:

Included*:* All patients with histopathological diagnosis of early invasive ductal or lobular breast cancer stage I,II. Stage I: T0N1 /T1N1 /T2N0. Stage II: T2N1 /T3N0 regardless age, sex, or menopausal status. Luminal A breast cancer: ER, RR positive, Her_2 negative, ki67 Low . Luminal B breast cancer divide into: a) Luminal B 1: ER positive, and Her_2 negative, either PR low or Ki67 high b) Luminal B2: ER positive, Her_2 positive, any PR,any Ki67 . In Luminal B PR may be not expressed. Pt diagnosed with luminal A, Luminal B breast carcinoma in the last 5 years from (January 2015 _December 2019).

Exclusion criteria:

Included: Advanced breast cancer stage lll, lV. Patients with DCIS , TN breast carcinoma. Her_2 enriched breast carcinoma.. Patients diagnosed before January 2015, After December 2019.

Study end point:

Primary end point: OS, which is defined as the time of the date of diagnosis for a disease, such as cancer, that patients diagnosed with the disease are still alive.

Secondary end point: DFS ,which is defined as the time of curative surgery till the date of a first relapse, secondary cancer after the initial diagnosis, or death from any cause,

Ethical consideration: Ethical approval was sought from faculty of medicine Beni-Suef University ethical committee. Patients' data was confidential and anonymous. Patients' data had been for identifying the characteristics not identity. Approval No/ FMBSUREC/10102021/Saleh

Statistical analysis

Data analysis: The date was coded to fit the program of statistical analysis (SPSS) Statistical package for special sciences version 22 under window 7. Random sample of 10% of potential participants will be selected and reviewed to ensure an adequate quality of data.

Statistical analysis: Description of qualitative variables was by frequency and percentage. Description of qualitative variables was in the form of mean and standard deviation (mean ± SD). Chi-square (X2) test was used for comparison of qualitative variables with each other. Comparison between quantitative variables had been carried by using: Student t-test of two independent samples. One way ANOVA test (analysis of variance) was used instead of t-test in case of more than two independent samples. Correlation and mulivariable logistic regression analysis. For more statistical analysis; suitable statistical tests of significance were used. P-Values < 0.05 was considered as statistically significant.

4. Results:

The current study included 129 patients with breast carcinoma, data collected with manual review of each patient file from Beni-suef University hospital from Dec 2015 till Jan 2019.

Table 1: Patient's and Disease characteristics:

Items	Luminal A (no=55)	Luminal B (no=74)	P-value
Age Median (range)	50 (33-65)	55(35-80)	0.348
Age less than 40 40-60 more than 60	 5(9.1%) 26(47.3%) 24(43.6%)	 14(18.9%) 44(59.5% **16(21.6%)**	 **0.020***
Family history Negative Positive	 52(94.5%) 3(5.5%)	 66(89.2%) 8(10.8%)	 0.352
TNM stage 1A 1B 2A 2B	 12(21.8%) 0(0.0%) 25(45.5%) 18(32.7%)	 12(16.2%) 1(1.4%) 29(39.2%) 32(43.2%)	 0.480
ER positive	55(100.0%)	69(93.2%)	------
PR positive	55(100.0%)	65(87.8%)	
Her_2 positive	0(0.0%)	18(24.3%)	
Ki67≥20%	0(0.0%)	67(90.5%)	
Surgery MRM CBS	 36(65.5%) 19(34.5%)	 50(67.6%) 24(32.4%)	 0.801
Regimen of chemo (no=101) Neoadjuvant Adjuvant Both	(no=33) 3(9.1%) 28(84.8%) 2(6.1%)	(no=68) 7(10.3%) 53(77.9%) 8(11.8%)	 0.639
Chemotherapy -No -4 cycles AC -4 cycles AC+12 taxol -Taxol only	 **22(40.0%)** 17(30.9%) 11(20.0%) 2(3.6%)	 6(8.1%) 29(39.2%) **35(47.3%)** 1(1.4%)	 ***<0.001***

Items	Luminal A (no=55)	Luminal B (no=74)	P-value
-6 cycles AC	3(5.5%)	3(4.1%)	
Time to start chemo (no=101)(month)	2.2±1	1.6±1.1	0.246
Radiotherapy	38(69.1%)	57(77.0%)	0.312
Hormonal No Tamoxifen Femara Aromasin Tamoxifen and Femara Tamoxifen and Aromasin	 0(0.0%) 33(60.0%) 12(21.8%) 1(1.8%) 8(14.5%) 1(1.8%)	 2(2.7%) 50(67.6%) 8(10.8%) 0(0.0%) 13(17.6%) 1(1.4%)	0.326
anti Her$_2$	0(0.0%)	12(16.2%)	
LHRH	8(14.5%)	18(24.3%)	0.171

There was insignificant difference between patients with luminal A and B regarding presence of comorbidities and family history, and median age, but luminal A is more prevalent in patients> sixty years while luminal B incidence is higher in patients< 40 years with significant **P-value 0.020.**

There was insignificant difference between patients with luminal A and B regarding the TNM staging and hormonal receptors, in luminal B, estrogen receptors were positive in 93.2%, progesterone receptors were positive in 87.8%, Her$_2$ positive in 24.3% and Ki67 high in 90.5%, in luminal A, estrogen receptors were positive in 100%, progesterone receptors were positive in 100%.

In this study 77% of patients were categorized luminal B depending on high Ki67 as a single factor,There was insignificant difference between patients with luminal A and B regarding the type of surgery, regimen of chemotherapy, time to start chemotherapy, radiotherapy, hormonal therapy and LHRH but,Forty percent of luminal A patients did not receive chemotherapy, and nearly 47.3% of patient with luminal B breast cancer received four cycles of Adriamycin, endoxan followed by twelve weeks of taxol with significant P- value <0.001, table 1.

Table 2: frequency and proportion of incidence of death and relapse of luminal A, luminal B:

Items	**Luminal A (no=55)**	**Luminal B (no=74)**	**P-value**
Death	2(3.6%)	5(6.8%)	0.698
Relapse	4(7.3%)	13(17.6%)	0.087

This table showed that there was no significant difference between Luminal A and B regarding the proportion of occurrence of death and relapse.

Table 3: (DFS) and (OS) of the study of Luminal A and B patients:

Mean(95%CI)	**Luminal A (no=55)**	**Luminal B (no=74)**	**P-value Log Rank (Cox mantel)**
DFS	81.5(77.3,85.8)months	74.7(70.2,79.3) months	0.113
OS	83.5(80.2,86.9) months	81.2(77.9,84.4) months	0.465

There was no statistically significandly difference between patients with luminal A and luminal B regarding the Disease free survival, However, DFS was longer in patients with luminal A [mean95%CI was 81.5(77.3, 85.8) months] than luminal B [mean95%CI was 74.7(70.2, 79.3) months], table 9, There was no statistically significantly difference between patients with luminal A and luminal B regarding the OS, However, Overall survival was longer in patients with luminal A [mean95%CI was 83.5(80.2, 86.9) months] than luminal B [mean95%CI was 81.2(77.9, 84.4) months], table 3.

Table 4: Patient's and Disease characteristics of luminal A, luminal B Her_2 _ve and luminal B Her_2 +ve patients:

Items	Luminal A (no=55)	Luminal B H, Her_2 -ve (no=56)	Luminal B, Her_2 +ve (no=18)	P-value
Age Median (range)	50 (33-65)	52(30-70)	54(35-80)	0.543
Comorbidities				
No	39(70.9%)	45(80.4%)	17(94.4%)	
DM	4(7.3%)	2(3.6%)	0(0.0%)	0.446
HTN	8(14.5%)	7(12.5%)	0(0.0%)	
Both	4(7.3%)	2(3.6%)	1(5.6%)	
Family history				
Negative	52(94.5%)	49(86.0%)	20(95.2%)	0.199
Positive	3(5.5%)	8(14.0%)	1(4.8%)	
TNM				
1A	12(21.8%)	9(16.1%)	3(16.7%)	
1B	0(0.0%)	0(0.0%)	1(5.6%)	0.237
2A	25(45.5%)	22(39.3%)	7(38.9%)	
2B	18(32.7%)	25(44.6%)	7(38.9%)	
ER	55(100.0%)	53(94.6%)	16(88.9%)	----
PR	55(100.0%)	50(89.3%)	15(83.3%)	
Her_2	0(0.0%)	0(0.0%)	18(100.0%)	
Ki67	0(0.0%)	52(92.9%)	15(83.3%)	
Surgery				
MRM	36(65.5%)	37(66.1%)	13(72.2%)	0.863
CBS	19(34.5%)	19(33.9%)	5(27.8%)	
Regimen of chemo (no=101)	(no=33)	(no=50)	(no=18)	0.236

Items	Luminal A (no=55)	Luminal B H, Her2 -ve (no=56)	Luminal B, Her2 +ve (no=18)	P-value
neo adjuvant	3(9.1%)	4(8.0%)	3(16.7%)	
adjuvant	28(84.8%)	42(84.0%)	11(61.1%)	
both	2(6.1%)	4(8.0%)	4(22.2%)	
Chemotherapy				
-No	**22(40.0%)**	6(10.7%)	0(0.0%)	
-4 cycles Adriamycin and Endoxan (AC)	17(30.9%)	28(50.0%)	1(5.6%)	
-4 AC+12 taxol	11(20.0%)	19(33.9%)	16(88.9%)	**<0.001***
-Taxol only	2(3.6%)	0(0.0%)	1(5.6%)	
-6 AC	3(5.5%)	3(5.4%)	0(0.0%)	
Time to start chemo (no=101)	2.2±1	1.6±1.1	1.6±1.1	0.511
Radiotherapy	38(69.1%)	44(78.6%)	13(72.2%)	0.520
Hormonal				
No	0(0.0%)	0(0.0%)	2(11.1%)	
Tamoxifen	33(60.0%)	42(75.0%)	8(44.4%)	
Femara	12(21.8%)	6(10.7%)	2(11.1%	**0.030***
Aromasin	1(1.8%)	0(0.0%)	0(0.0%)	
Tamoxifen and femara	8(14.5%)	7(12.5%)	6(33.3%)	
Tamoxifen and aromasin	1(1.8%)	1(1.8%)	0(0.0%)	
anti Her2	0(0.0%)	0(0.0%)	12(66.7%)	
LHRH	8(14.5%)	11(19.6%)	7(38.9%)	0.082

There was insignificantly difference between the three groups regarding the presence of comorbidities and family history ,age , the TNM staging **.**

There was insignificantly difference between the three groups regarding the type of surgery, regimen of chemotherapy, time to start chemotherapy, radiotherapy, hormonal therapy and LHRH but, receiving chemotherapy was significantly lower in luminal A. Anti Her_2 was given in 66.7% of luminal B Her_2 +ve. All patients with Her_2 +ve received chemotherapy and 4 cycles AC plus 12 weeks paclitaxel was the most commonly used regimen but in luminal A 40% of patients didn't receive chemotherapy with 4 cycles AC the most commonly used regimen, table 4.

Table 5: frequency and proportion of incidence of death and relapse of luminal A, luminal B Her_2 -ve and luminal B Her_2 +ve patients:

Items	**Luminal A (no=55)**	**Luminal B Her_2-ve (no=56)**	**Luminal B Her_2 +ve (no=18)**	**P-value**
Death	2(3.6%)	4(7.1%)	1(5.6%)	0.869
Relapse	4(7.3%)	10(17.9%)	3(16.7%)	0.087

This table showed that there was no significantly difference between Luminal A, B Her2 positive and negative regarding the proportion of occurrence of death and relapse.

Table 6: DFS and OS of the study of luminal A, luminal B Her_2 -ve and luminal B Her_2 +ve patients:

Mean(95%CI)	**Luminal A (no=55)**	**Luminal B Her_2 -ve (no=56)**	**Luminal B Her_2 +ve (no=18)**	**P-value Log Rank (Cox mantel)**
DFS	81.5(77.3,85.8) (Median=81) months	74.8(69.8,79.9 (Median=72)) months	70.6(61.2, 80) months (Median=71)	0.284
OS	83.5(80.2,86.9) (Median=82) months	81.1(77.4, 84.8) months (Median=80)	77.1(71.6, 82.6) months (Median=76)	0.751

There was no statistically significant difference between patients with luminal A and luminal B regarding Disease free survival,Overall survival However, the time to (DFS) was longer in patients with luminal A [mean95%CI was 83.5(80.2, 86.9) months] than luminal B Her_2 -ve [mean95%CI was 74.8(69.8, 79.9) months} and luminal B Her_2+ve [mean95%CI was 70.6(61.2, 80) months], table 14, The time to death (OS) was longer in patients with luminal A [mean95%CI was 83.5(80.2, 86.9) months] than luminal B Her_2-ve [mean95%CI was 81.2(77.9, 84.4) months} and luminal B Her_2 +ve [mean95%CI was 77.1(71.6, 82.6) months] but this difference was statistically not significant (P value 0.751), table 12,

Table 7: Association between the TNM staging ,age:

		stage				Total
		1A	1B	2A	2B	
age	less than 40	4	0	6	9	19
		16.7%	0.0%	11.1%	18.0%	14.7%
	40-60	12	0	31	27	70
		50.0%	0.0%	57.4%	54.0%	54.3%
	more than 60	8	1	17	14	40
		33.3%	100.0%	31.5%	28.0%	31.0%
Total		24	1	54	50	129
		100.0%	100.0%	100.0%	100.0%	100.0%
P-value		0.744				

There was no significantly association between age categories ,TNM staging, table 7.

Table 8: Association between the ER and age.

		ER		**Total**
		Negative	**Positive**	
Age	less than 40	0_a	19_a	19
		0.0%	15.3%	14.7%
	40-60	4_a	66_a	70
		80.0%	53.2%	54.3%
	more than 60	1_a	39_a	40
		20.0%	31.5%	31.0%
Total		5	124	129
		100.0%	100.0%	100.0%
P-value		0.448		

There was no significantly association between age categories , Estrogen receptors, table 8.

Table 9: Association between the PR and age:

		PR		Total
		Negative	**Positive**	
Age	less than 40	2	17	19
		22.2%	14.2%	14.7%
	40-60	4_a	66_a	70
		44.4%	55.0%	54.3%
	more than 60	3	37	40
		33.3%	30.8%	31.0%
Total		9	120	129
		100.0%	100.0%	100.0%
P-value		0.775		

There was no significantly association between age categories ,progesterone receptors, table 9.

Table 10: Association between the Her_2 and age:

		Her_2		Total
		Negative	**Positive**	
Age	less than 40	16	3	19
		14.4%	16.7%	14.7%
	40-60	60_a	10_a	70
		54.1%	55.6%	54.3%
	more than 60	35	5	40
		31.5%	27.8%	31.0%
Total		111	18	129
		100.0%	100.0%	100.0%
P-value		0.973		

There was no significantly association between age categories , Her_2 receptors, table 10.

Table11: Association between the Ki67 and age:

		Ki67		Total
		Low<20%	**High≥20%**	
Age	less than 40	6_a	13_a	19
		9.7%	19.4%	14.7%
	40-60	30_a	40_a	70
		48.4%	59.7%	54.3%
	more than 60	26_a	14_b	40
		41.9%	20.9%	31.0%
Total		62	67	129
		100.0%	100.0%	100.0%
P-value		**0.024***		

There was a significantly association between age more than 60 years and low Ki67 with significant P- value, 0.024, table 11.

Table12: Comparison between patients with different comorbidities regarding the overall survival in luminal A and B:

Luminal	**Comorbidities**	**Mean**				**P-value of Log rank test**
		Mean	**Std. Error**	**95% Confidence Interval**		
				Lower Bound	**Upper Bound**	
B	No	83.217	1.239	80.789	85.645	**0.004***
	DM	45.000	.000	45.000	45.000	
	HTN	61.429	7.010	47.689	75.168	
	Both	56.667	8.437	40.130	73.203	

NB: There was no statistics computed for Luminal A as only one patient with no comorbidities and one with HTN were died SE: standard error

Patients without comorbidities had a significantly higher overall survival than patients with diabetes mellitus (DM) or hypertension (HTN) or both with significant P-value, 0.004, table 12.

Table 13: Comparison between patients with age lower and higher than 40 years regarding the DFS in luminal A and B:

Luminal	Age	Mean				P-value of Log rank test
		Mean(month)	Std. Error	95% Confidence Interval		
				Lower Bound	Upper Bound	
A	≤40 years	70.600	10.196	50.615	90.585	0.225
	>40 years	82.343	2.054	78.317	86.370	
B	≤40 years	72.804	5.557	61.912	83.695	0.747
	>40 years	75.186	2.525	70.238	80.134	

SE: standard error

There was no significantly difference between patients in different age categories regarding the DFS in luminal A and B table 13.

5. Discussion:

In the current study, it was retrospectively investigated the difference in outcome between luminal A luminal B in early stage breast cancer patients treated at the Clinical Oncology department, Beni Seuf University Hospital.

This study included 129 patients.

In this study, the percent of each of the molecular subtypes was 42.6 % for the luminal A type, 57.4% for the luminal B type, in contrast other studies published in Egypt which found that incidence of luminal A was more common than luminal B (44.3% versus 24.6% respectively) [4], in united states, USA (55% luminal A and 17% luminal B) [8], Tunis (51.5% luminal A and 16% luminal B) [9], Japan (71% luminal A and 8% luminal B) [10], China (65.3% luminal A and 19% luminal B) [11], and Algeria (50.6% luminal A and 19.% luminal B) [12], but other studies confirm the current results luminal B cancer was more prevalent (69%) than luminal A (31%) [4]**.** The results are in concordance with other studies conducted in Italy (34% luminal A and 36% luminal B) [13] and Saudi Arabia (3.9% luminal A and 16% luminal B) Al Tamimi et al. [14] which found luminal B subtypes more prevalent than luminal A. The variation in the commonest profile of breast carcinoma explains the heterogeneity of breast carcinoma around the world. In the current study many patients were categorized luminal B depending on high Ki67 as a single factor (strong positive ER, PR and negative Her_2) and central lab is not available, being Ki67 value can vary from lab to lab and many studies showed that Ki67 by immunohistochemistry isn't reliable test [15, 16].

Molecular subtypes of breast carcinoma have a significantly difference in distribution of

elderly breast carcinoma compared to their younger patient where elderly patient more prevalent Luminal A Pandit et al. [17] and less prevalent Her_2 +ve and TN subtypes. Elderly patient have better prognosis in comparison to younger patient [18]. In the current study luminal A is more common in patients> 60 years (43,6 %),which is significant P value(0,020).

Family history was positive only in 5,5% in luminal A,10,8% in luminal B with no significant difference, although family history of breast carcinoma is one of the major risk factors, about (five –ten%) cases of breast carcinoma are associated with a family history [19].

In this study, there was insignificant difference between patients with luminal A ,B regarding the TNM staging which most of patients were T2 63,6% in luminal A,66,2% in luminal B,N0 which was 54,5% in luminal A,68,9% in luminal B. But in other studies there was significantly differences in (T) size (p= 0.009), LN mets (p= 0.019), between luminal A, luminal B [20].

There was insignificant difference between patients with luminal A , B regarding the type of surgery, regimen of chemotherapy, time to start chemotherapy, radiotherapy, hormonal therapy and LHRH.

In the current study Tamoxifen was most used in two groups 60% in lumial A,67,6 % in luminal B due to the benefits of ***In Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*** a meta-analysis of individual patient data from twenty trials (n=21 457) in early breast carcinoma of about five years of TAM versus no adjuvant TAM, with about eighty% compliance**.** In (ER)+ve disease (n=10 645), allocation to about five years of TAM substantially decreased recurrence rates throughout the first ten years (RR 0·53 [SE 0·03] during years 0–4 and RR 0·68 [0·06] during years 5–9 [both 2p<0·00001]; but RR 0·97 [0·10] during years 10–14, suggesting no further gain or loss after ten years. In ER +ve disease, the RR was nearly independent of PR status (or level), age, nodal status, or use of chemotherapy**.** breast carcinoma mortality was decreased by about a third throughout the first fifteen years (RR 0·71 [0·05] during years 0–4, 0·66 [0·05] during years 5–9, and 0·68 [0·08] during years 10–14; p<0·0001 for extra mortality reduction during each separate time period. overall non breast carcinoma mortality was little affected, although small absolute increases in thromboembolic and uterine carcinoma mortality (both only in females older than 55 years), so all cause mortality was substantially decreased. In ER -ve disease, TAM had little or no effect on breast carcinoma recurrence or mortality (21).

That there was insignificant difference between patients with luminal A and B regarding the OS ,DFS.

DFS was longer in patients with luminal A [mean95%CI was 81.5(77.3, 85.8) months]

than luminal B [mean95%CI was 74.7(70.2, 79.3) months] with no significant P- value. OS was longer in patients with luminal A [mean95%CI was 83.5(80.2, 86.9) months] than luminal B [mean95%CI was 81.2(77.9, 84.4)] with no significant. because Luminal A has been associated with a highly good prognosis, with a more indolent clinical course, and generally shows less LN involvement [4]. Due to the positive status of HR , patients benefit from (ET) [23], but Luminal B has been associated with an intermediate prognosis, with more likely of locoregional recurrence when compared to Luminal A [4, 24].

Subgroup luminal B Her$_2$ -ve , luminal B Her$_2$ +ve :

There was insignificant difference between luminal A, luminal B Her$_2$ -ve , luminal B Her$_2$ +ve regarding the presence of comorbidities , family history but, age was different significantly between them, which was more than 60 yrs old in about 43,6 % of luminal A patients with significant P- value, 0,050.

There insignificant difference between luminal A, luminal B regarding TNM staging.

There was insignificant difference between luminal A, luminal B Her$_2$ -ve ,luminal B Her$_2$ +ve regarding the type of surgery, regimen of chemotherapy, time to start chemotherapy, radiotherapy, hormonal therapy and LHRH but receiving chemotherapy was significantly lower in luminal A which was 40%. Many studies showed that adjuvant chemotherapy can decrease the (RR) [25]. However, due to tumor heterogeneity, chemotherapy of different breast carcinoma molecular subtypes has multiple effects [25, 26]. In this study chemotherapy not improve the Overall survival of patients with luminal A subtype breast carcinoma (HR 1.73, 95% CI 1.23, and 2.43). Interestingly, patients who received (ET) only had better prognosis compared to patients who received both chemotherapy and (ET), regardless of whether the LN mets. The RFS/DFS of luminal A breast carcinoma patients did not appear significant associations, which indicated that chemotherapy did not decrease the risk of disease recurrence,10,7 % in luminal B Her$_2$ -ve, zero % in luminal B Her$_2$ +ve as Her$_2$ overexpression show benefit of chemotherapy Newton et al. [27] and anti Her$_2$ was Significantly higher in luminal B Her$_2$ +ve, due to the benefit of anti Her$_2$ (trastuzumab) benefits for patients who are treated with adjuvant chemotherapy, in this study the patients treated concurrently with trastuzumab and continue treatment to complete a year of therapy. Adjuvant trastuzumab was also used for those who were treated neoadjuvantly with chemotherapy and Her$_2$ directed therapy and experience a pathologic complete response.

There are substantial clinical benefits for including anti Her$_2$ therapy in management of early-stage, Her$_2$ +ve breast carcinoma. The benefits of adding trastuzumab to adjuvant chemotherapy in patients with Her$_2$ +ve tumors were emphasized in a 2021 meta-analysis of seven trials of chemotherapy + trastuzumab

versus chemotherapy alone included approximately 14,000 patients [28]:

Improvement in breast carcinoma recurrence ([HR] 0.66, 95% CI 0.62-0.71). Absolute ten - year recurrence risk was reduced by nine percent. The reduction in recurrence was highest in years zero to one after randomization (HR 0.53), with benefits persisting through years two to 4 (HR 0.73) and 5 to 9 (HR 0.80), with little F/U beyond ten years. Reductions in recurrence risks occurred independent of patient characteristics and tumor estrogen receptor (ER) status. The higher-risk the tumor, the greater the absolute reductions in five-year recurrence (eg, 5.7 percent in N0 disease, and 6.8 percent in N1 to N3 disease) Improvement in breast carcinoma mortality (HR 0.67, 95% CI 0.61-0.73). 10-year breast carcinoma mortality was reduced by 6.4 percent.

These results are consistent with those from a previous meta-analysis as well [28]. Subsequent data show adding trastuzumab to adjuvant chemotherapy results in durable survival benefits for patients with Her_2 +ve breast carcinoma.This was apparent in the combined analysis of the North Central Cancer Treatment Group N9831 trial and the National Adjuvant Breast and Bowel Project B-31 clinical trials. With a median on-study time of 8.4 years, adding trastuzumab resulted in a thirty-seven percent improvement in Overall survival (HR 0.63, 95% CI 0.54-0.73) and a forty percent improvement in DFS (HR 0.60, 95% CI 0.53-0.68) [29].

There was significant association between T3 and lower age less than 40 years a but from 40 to 60 and above 60 there was no significant association with T1,2,3,according to breast carcinoma in young females may be more aggressive and less likehood to respond to treatment [30].

There was a significant association between age more than 60 years and lower Ki67, which most of older age is luminal A that ki67 low

There was significant higher overall survival in patients without comorbidities than patients with DM or HTN or both (P-value 0,004).

6. Conclusion:

The current study, Luminal B almost depend on high ki67 which is not riable test, so no significantly difference between Luminal A, Luminal B regarding OS, DFS. But time of DFS, OS is longer in Luminal A than Luminal B, this confirm Luminal A is the best prognosis of molecular subtypes of breast carcinoma.

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