The Gulf Journal of Oncology

Indexed By PubMed and Medline Database

Issue 40, September 2022
ISSN No. 2078-2101

The Official Journal of the Gulf Federation For Cancer Control

Table of Contents

Original Articles

Review Article

Case Reports

Conference Highlights/Scientific Contributions

Original Article

The Prognostic Significance of CD10 Expression in Invasive Breast Carcinoma in Tunisian Patients

Saadia Makni[1,2], Manel Mellouli[1,2], Ines Saguem[1,2], Ons Boudawara[1,2], Naourez Gouiaa[1,2], Tahya Sallemi Boudawara[1,2], Jihene Feki[2,3], Rim Kallel[1,2]

[1]Department of Pathology and Research Laboratory, Habib Bourguiba University Hospital, 3029, Sfax, Tunisia.
[2]Medical School of Sfax, University of Sfax, 3029, Sfax, Tunisia.
[3]Department of Medical Oncology, Habib Bourguiba University Hospital, 3029, Sfax, Tunisia.

Abstract

Background: Breast cancer is the first female cancer worldwide. Its prognosis depends mainly on pathological stage and histological grade. These classical prognostic factors are essential but may be insufficient to predict the outcome of the disease. Research focuses on identifying new prognostic factors such as CD10, which is a cell surface metalloproteinase.

Objective: This study aims to evaluate CD10 expression on stromal and tumor cells in invasive breast carcinomas and its correlations with other clinicopathological factors and survival.

Methods: A series of 100 cases of breast carcinoma of no special type diagnosed from 2009 to 2011, was investigated in this study. CD10 expression was detected by immunohistochemistry. Stromal CD10 expression (≥10% stromal positivity was considered positive) and tumor cells expression (≥1% stained carcinomatous cells) were noted. Statistical correlations were analyzed with different known prognostic parameters; survival analysis were performed using SPSS 22.0.

Results: Stromal CD10 expression was seen in 60% of the cases. It showed positive correlation with high tumor grade (p=0,012) and distant metastasis (p=0,02). CD10 expression on tumor cells was observed in 10% of the cases. It was associated with high tumor grade (p=0,009), hormone receptor negativity (estrogen receptor: p<0,0001), progesterone receptor: p=0,005), triple–negative phenotype (p=0,001), and Ki67 overexpression (p=0,046). Stromal CD10 expression was significantly associated to a shorter overall survival (p=0,029) and disease–free survival (p=0,05) in univariate analysis.

Conclusion: Given these results, it can be concluded that CD10 expression predict an aggressive behavior of breast cancer. This marker can be introduced as a determinant prognostic factor.

Keywords: Invasive breast carcinoma; CD10; Stromal cell; prognosis

I–Introduction

Breast cancer is the first cancer among women in the world in terms of incidence and mortality with an estimated 2 million new cancer cases diagnosed in 2018 (24,2% of all female cancers), and 626000 deaths (15% of all female mortality by cancer)[1]. In Tunisia, according to the register of the southern Tunisian cancers, the estimated incidence of breast cancer is 30 cases per 100000 women (33,4% of all female cancers)[2].

This malignancy has an unpredictable behavior regarding its metastatic potential and its response to treatment. Clincopathological prognostic factors including tumor and nodal stage, tumor grade, molecular markers (hormone receptor status, Her–2 score) and proliferation index Ki67 are essential to predict the outcome of the disease, but the recognition of new markers is crucial to better understand the molecular mechanisms of carcinogenesis, which opens up new therapeutic perspectives.

Recently, several studies have investigated the role of stromal markers such as CD10 antigen in the development of breast tumors and in assessing its prognosis.

Corresponding Author: Saadia Makni, Departement of pathology, Habib Bourguiba University Hospital., El Ain Road Km 0.5, 3029. Sfax–Tunisia,
Phone : +216 20 330 432 / +216 74 240 341,
Fax : +216 74 243 427, E Mail : olfa_saadia@yahoo.Fr

CD10 or CALLA antigen «Common Acute Lymphoblastic Leukemia Antigen» is a cell surface of 90 to 110 KDa, which belongs to the zinc–dependent metalloprotease family. It is frequently expressed in bone marrow lymphoid stem cells, pro–B lymphoblast, various lymphoma subtypes, renal cell carcinoma and endometrial stromal sarcoma. Several recent studies have shown that stromal CD10 expression is associated with aggressive behavior in various epithelial tumors[3–7].

The aims of our study were: To estimate the expression of CD10 on stromal and tumor cells in invasive breast carcinoma, to assess the prognostic significance of CD10 expression on stromal and tumor cells and to examine the association of this expression with other clinicopathological prognostic factors.

II–Materials and Methods

This is a retrospective study included 100 surgical specimens diagnosed as invasive breast carcinoma of no special type, in the department of pathology, Habib Bourguiba University Hospital of Sfax (Tunisia), between 2009 and 2011.

Clinical features:

Clinical data were collected from patient's medical files. They included age, menopausal status, family history of breast cancer, distant metastasis at diagnosis and outcomes.

Pathological evaluation:

For each specimen, the following pathological data were retrieved: tumor multifocality, tumor size, histological grade (according to Nottingham modification of Scarff Bloom Richardson system (SBR)[8,9], presence of lymphovascular invasion (LVI), presence of perineural invasion (PNI), tumor necrosis, concomitant carcinoma in situ (CIS), Paget disease, surgical margin status, tumor and nodal stage, estrogen (ER) and progesterone receptor (PR) status[10], Her–2 status[11] and proliferation index Ki67 (considered overexpressed if ≥20%)[12,13]. Tumors were classified into 5 molecular sub–types[10,13,14] : Luminal A, Luminal B Her2 positive, Luminal B Her2 negative, Her2 overexpression and Triple negative.

Immunohistochemical staining for CD10:

The expression of CD10 (clone 56C6; dilution 1:30; Leica) was evaluated by immunohistochemistry (IHC), on neoplastic and stromal cells, by two pathologists.

We used 3 µm slices, dried overnight at 40°C, deparaffinized in xylene and then rehydrated in alcohol at 100°C then at 95°C and washed with distilled water.

For antigen retrieval, the sections were placed in a water bath with basic buffer (pH 9) for 40 min until the temperature reached 98°C. Then, slices were cooled at room temperature for 20 min, and incubated in hydrogen peroxide (H2O2, 3%) for 10 min to block endogenous peroxidase activity.

The sections were thoroughly washed with distilled water and washed for 5 min with phosphate buffered saline (PBS). The primary antibody for CD10 was applied at 1:30 dilution for 1h at room temperature. following this, sections were incubated with biotin–conjugated secondary antibody for 20 min and then incubated using streptavidin biotin system for 20 min at room temperature. Each step was followed by PBS wash for 5 min. Sections were immersed in 3, 3 diaminobenzidine a substrate–chromogen solution for 20 min. Finally, the slides were counterstained with Mayer hematoxylin, permanently mounted, and viewed with a standard light microscope.

The immunostaining of CD10 on stromal cells was considered positive if ≥10% of fusiform cells exhibited positive signal. CD10 expression on tumor cells was considered positive if staining was found in at least one neoplastic cell (≥1%).

Statistical Analyses:

Data were analyzed using SPSS software (version 22.0). Correlation studies between CD10 expression and clinicopathological parameters was performed using Chi–square and Fisher's exact tests. Overall survival (OS) was defined as time from initial surgery to date of death or last follow up. Disease–free–survival (DFS) was defined as time after treatment during which no sign of cancer is found.

The survival analysis was evaluated according to the Kaplan–Meier method and compared by the log–rank test. The threshold of statistical significance was set at 5% (p–value ≤0.05).

III–Results

Population characteristics:

The age of patients ranged from 21 to 80 years (mean: 50,5 years). Thirty–five patients have family history of breast cancer.

Macroscopic examination found a single nodule in 83 cases. The mean tumor size was 3,5cm. Histologically, most cases (61%) were assigned as grade II according to modified SBR, followed by grade III (23%). LVI and PNI were observed respectively in 56 and 27 cases. Tumor necrosis was recorded in 18 cases and concomitant CIS in 81 cases. Paget disease was noted in 6,7% of cases (5 patients among 75 patients who underwent radical mastectomy). Surgical margin were positive in 12 cases.

Most of our cases were staged as pT2 (54%) according to the TNM staging, followed by pT1 (24%), and pT3 category (14%).

Lymph node involvement was found in 58 cases. It was staged as pN1 (1–3 involved nodes) in 32 cases and pN2 (4–9 involved nodes) in 15 cases.

At diagnosis, eight patients had distant metastasis.

Tumors were hormonal receptor positive in 74 cases (ER+:74% ; PR+:63%), Her2 was positive in 28 cases, Ki67 was overexpressed in 50 cases.

Concerning molecular classification, 36 cases were classified as Luminal B Her2 negative, 20 cases as Luminal A, 18 cases as Luminal B Her2 positive, 15 cases as triple negative and 11 cases as Her2 overexpression.

The median follow up was 53,3 months. The 5–year OS rate was 82,1%, The 5–year DFS rate was 80,1%.

Stromal CD10 expression and correlations with other clinicopathological factors:

Stromal CD10 positivity was seen in 60 cases, out of which 18 cases showed strong immunoreactivity (Fig.1) and 17 cases showed weak immunoreactivity.

Correlations between stromal CD10 expression and clinicopathological factors were listed in Table 1. Stromal CD10 staining was more significantly associated with grade III tumors (p=0,012) and with distant metastasis at diagnosis (p=0,02). Meanwhile, all clinical data and other pathological features had no association with CD10 stromal expression (Table 1).

Univariate survival analysis showed that stromal expression of CD10 was associated with OS and DFS. The 5–year OS rate was 74,5% in tumors with stromal CD10 staining and 89,8% in tumors without stromal CD10 expression (p=0,029) (Fig.2). The 5–year DFS rate was 75% in tumors with stromal CD10 expression and 88,3% in tumors without stromal CD10 staining (p=0,05) (Fig.3).

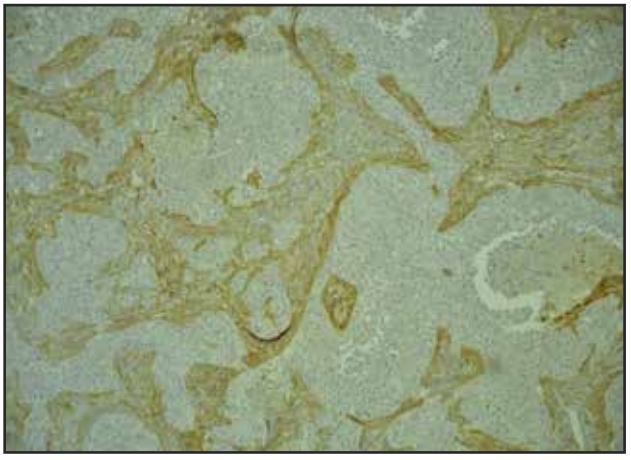

Figure 1: Strong stromal CD10 staining (IHC×200)

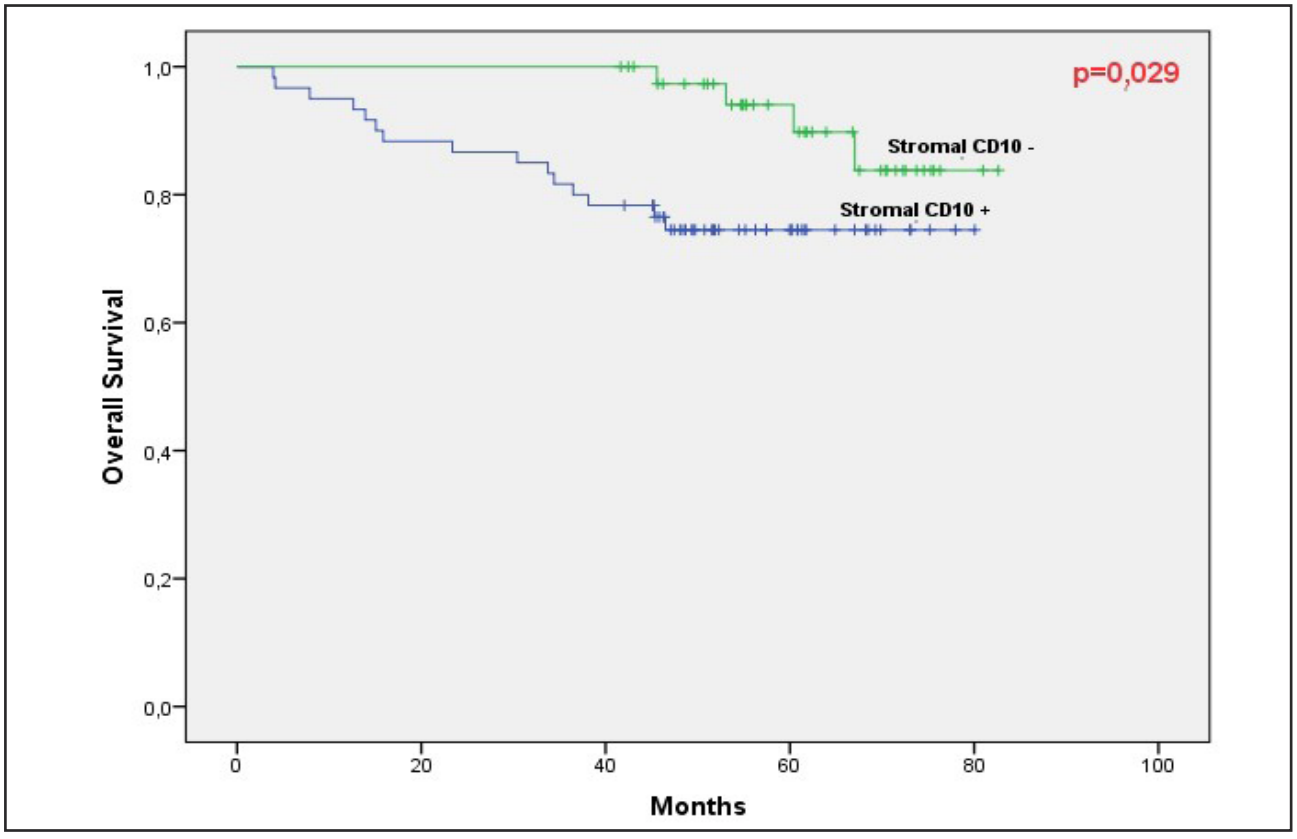

Figure 2: Kaplan–Meier curves of overall survival according to stromal CD10 expression

		Stromal CD10 expression		P
		<10% (n=40)	≥10% (n=60)	
Age	≤45 year (n=35)	10 (25%)	25 (41,7%)	0,087
	>45 year (n=65)	30 (75%)	35 (58,3%)	
Hormonal status	Menopaused (n=45)	16 (40%)	29 (48,3%)	0,412
	Not menopaused (n=55)	24 (60%)	31 (51,7%)	
Family history of breast cancer	Yes (n=30)	13 (32,5%)	17 (28,3%)	0,656
	No (n=70)	27 (67,5%)	43 (71,7%)	
Multifocality	Yes (n=17)	8 (20%)	9 (15%)	0,514
	No (n=83)	32 (80%)	51 (85%)	
Tumor size	≤3 cm (n=56)	23 (57,5%)	33 (55%)	0,805
	>3 cm (n=44)	17 (42,5%)	27 (45%)	
SBR grading	III (n=23)	4 (10%)	19 (31,6%)	**0,012**
	I+II (n=77)	36 (90%)	41 (68,4%)	
LVI	Yes (n=56)	21 (52,5%)	35 (58,3%)	0,565
	No (n=44)	19 (47,5%)	25 (41,7%)	
PNI	Yes (n=27)	14 (35%)	13 (21,6%)	0,141
	No (n=73)	26 (65%)	47 (78,4%)	
Tumor necrosis	Yes (n=18)	5 (12,5%)	13 (21,6%)	0,242
	No (n=82)	35 (87,5%)	47 (78,4%)	
CIS	Yes (n=81)	31 (77,5%)	50 (83,3%)	0,466
	No (n=19)	9 (22,5%)	10 (16,7%)	
Paget disease (/75 cases)	Yes (n=5)	2/32 (6,2%)	3/43 (6,9%)	1,00
	No (n=70)	30/32 (93,8%)	40/43 (93,1%)	
Surgical margin status	Positive (n=12)	6 (15%)	6 (10%)	0,535
	Negative (n=88)	34 (85%)	54 (90%)	
Lymph node metastasis	N+ (n=58)	23 (57,5%)	35 (58,3%)	0,934
	N– (n=42)	17 (42,5%)	25 (41,7%)	
Tumor stage	≤pT2 (n=77)	34 (85%)	43 (71,7%)	0,121
	>pT2 (n=23)	6 (15%)	17 (28,3%)	
Distant metastasis	M0 (n=92)	40 (100%)	52 (86,7%)	**0,02**
	M1 (n=8)	0 (0%)	8 (13,3%)	
ER	Positive (n=74)	30 (75%)	44 (73,3%)	0,852
	Negative (n=26)	10 (25%)	16 (26,7%)	
PR	Positive (n=63)	29 (72,5%)	34 (56,6%)	0,108
	Negative (n=37)	11 (27,5%)	26 (43,4%)	
Her2 Status	Amplified (n=28)	8 (20%)	20 (33,3%)	0,146
	Not amplified (n=72)	32 (80%)	40 (66,7%)	
Triple negative phenotype	Yes (n=15)	7 (17,5%)	8 (13,3%)	0,568
	No (n=85)	33 (82,5%)	52 (86,7%)	
KI67 expression	<20% (n=50)	23 (57,5%)	27 (45%)	0,221
	≥20% (n=50)	17 (42,5%)	33 (55%)	
Tumor cell CD10 expression	Positive (n=10)	4 (10%)	6 (10%)	1,00
	Negative (n=90)	36 (90%)	54 (90%)	

Table 1: Correlation between Stromal CD10 expression and clinicopathological factors in breast cancer
Abbreviations: SBR: Scarff–Bloom–Richardson; LVI: Lymphovascular Invasion; PNI: Perineural Invasion; CIS: Carcinoma In Situ; Her–2: Human Epidermal Growth 2; ER: estrogen receptor; PR: progesterone receptor
Bold highlighted values indicate significance ($p \leq 0.05$).

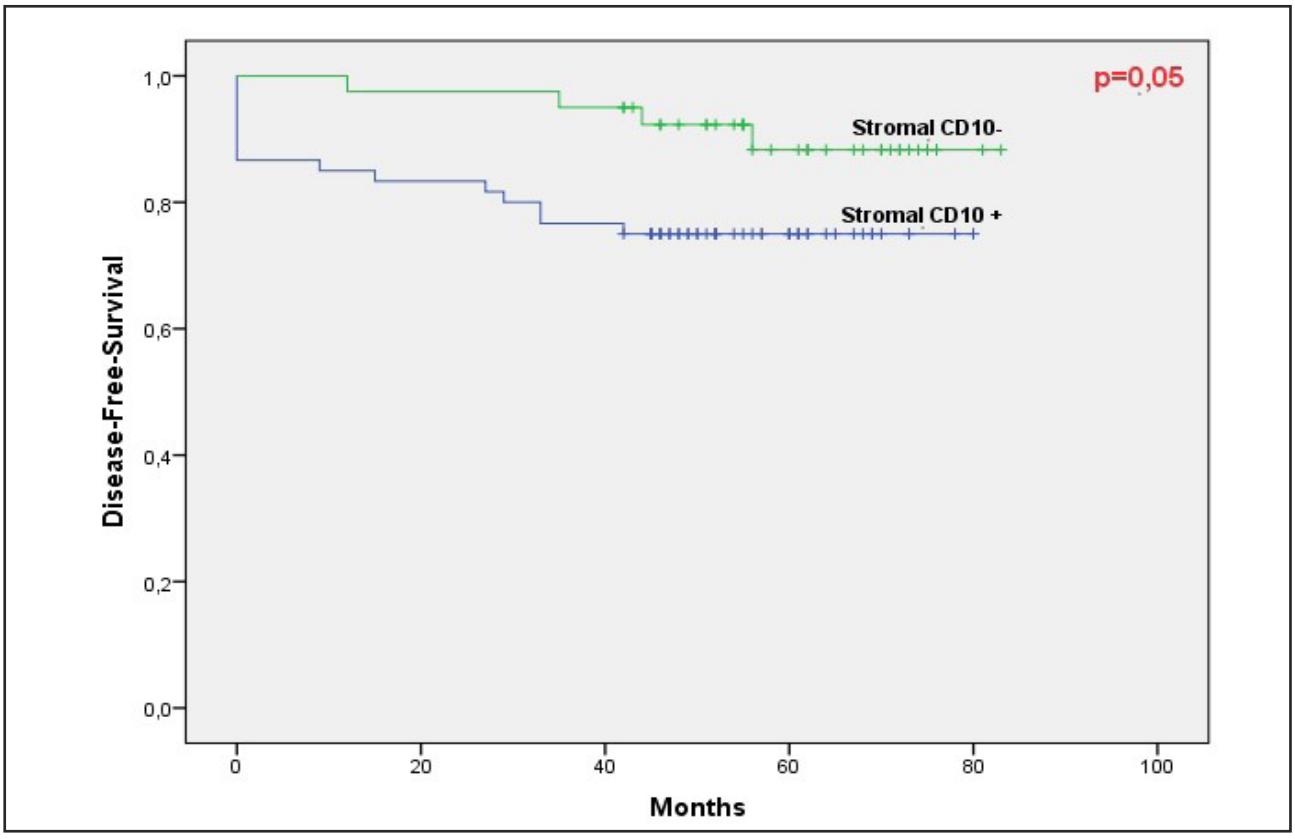

Figure 3: Kaplan–Meier curves of disease–free–survival according to stromal CD10 expression

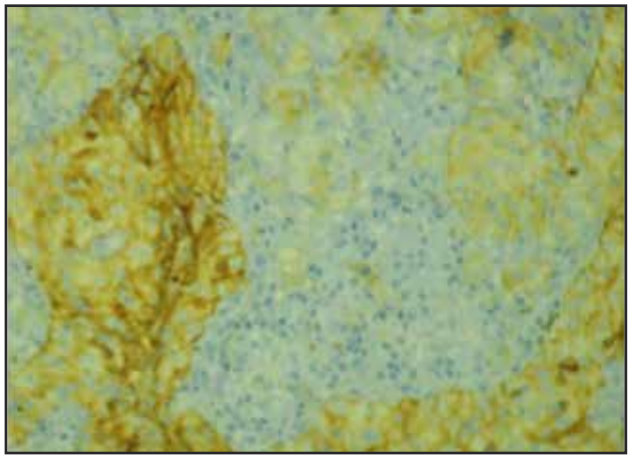

Figure 4: Strong CD10 positivity on neoplastic cells (IHC×400)

CD10 tumor cells expression and correlations with other clinicopathological factors:

Tumor cells CD10 positivity was observed in 10 cases (Fig.4), out of which 6 concomitant staining for CD10 in the stromal cells.

CD10 expression on neoplastic cells correlated with a high tumor grade (p=0,009), ER negativity (p<0,0001), PR negativity (p=0,005), triple negative phenotype (p=0,001) and high proliferative index Ki67 (p=0,046). No correlation has been proven with tumor size (p=0,328), lymph node metastasis (p=0,934) or Her2 positivity (p=1,00) (Table 2).

In univariate analysis, CD10 expression on tumor cells was not a significant prognostic factor for both OS and DFS.

Multivariate analysis, including family history of breast cancer, tumor size, tumor grade, LVI, tumor and nodal stage, stromal CD10 expression and distant metastasis, was performed in order to identify the independent prognostic factors. Results showed that only tumor grade (p=0,007) and distant metastasis (p<0,000) were the significant independent prognostic factors for OS (Table 3).

IV–Discussion

CD10 is produced by myofibroblastic cells in tumor stroma of breast carcinoma, and it has been demonstrated that it breaks down collagen and other protein components of the extracellular matrix, which promotes proliferation, invasion and metastasis of tumor cells[4,5,15–26].

CD10 Stromal expression in invasive breast carcinoma varies between 18 and 82,76%[4,5,16–26]. Our result is similar to those of the literature with a rate of 60%. The difference observed in the frequency of the marker expression could be explained by the different criteria used for scoring stromal CD10 expression, the heterogeneity of various clinicopathologic parameters and the variation in immunohistochemical protocols.

		CD10 tumor cells expression		P
		Negative (n=90)	Positive (n=10)	
Age	≤45 year (n=35)	33 (36,7%)	2 (20%)	0,487
	>45 year (n=65)	57 (63,3%)	8 (80%)	
Hormonal status	Menopaused (n=45)	40 (44,4%)	5 (50%)	0,750
	Not menopaused (n=55)	50 (55,6%)	5 (50%)	
Family history of breast cancer	Yes (n=30)	28 (31,1%)	2 (20%)	0719
	No (n=70)	62 (68,9%)	8 (80%)	
Multifocality	Yes (n=17)	15 (16,6%)	2 (20%)	0,677
	No (n=83)	85 (83,4%)	8 (80%)	
Tumor size	≤3 cm (n=56)	52 (57,8%)	4 (40%)	0,328
	>3 cm (n=44)	38 (42,2%)	6 (60%)	
SBR grading	III (n=23)	17 (18,8%)	6 (60%)	**0,009**
	I+II (n=77)	73 (81,2%)	4 (40%)	
LVI	Yes (n=56)	51 (56,6%)	5 (50%)	0,745
	No (n=44)	49 (43,4%)	5 (50%)	
PNI	Yes (n=27)	26 (28,8%)	1 (10%)	0,280
	No (n=73)	64 (71,2%)	9 (90%)	
Tumor necrosis	Yes (n=18)	14 (15,5%)	4 (40%)	0,077
	No (n=82)	76 (84,5%)	6 (60%)	
CIS	Yes (n=81)	74 (82,2%)	7 (70%)	0,396
	No (n=19)	16 (17,8%)	3 (30%)	
Paget disease (/75 cases)	Yes (n=5)	5/67 (7,4%)	0/8 (0%)	1,00
	No (n=70)	61/65 (92,6%)	8/8 (100%)	
Surgical margin status	Positive (n=12)	11 (12,2%)	1 (10%)	1,00
	Negative (n=88)	79 (87,8%)	9 (90%)	
Lymph node metastasis	N+ (n=58)	54 (60%)	4 (40%)	0,314
	N– (n=42)	36 (40%)	6 (60%)	
Tumor stage	≤pT2 (n=77)	68 (75,6%)	9 (90%)	0,446
	>pT2 (n=23)	22 (24,4%)	1 (10%)	
Distant metastasis	M0 (n=92)	82 (91,2%)	10 (100%)	1,00
	M1 (n=8)	8 (8,8%)	0 (0%)	
ER	Positive (n=74)	72 (80%)	2 (20%)	**<0,0001**
	Negative (n=26)	18 (20%)	8 (80%)	
PR	Positive (n=63)	61 (67,7%)	2 (20%)	**0,005**
	Negative (n=37)	29 (32,3%)	8 (80%)	
Her2 Status	Amplified (n=28)	25 (27,7%)	3 (30%)	1,00
	Not amplified (n=72)	65 (72,3%)	7 (70%)	
Triple negative phenotype	Yes (n=15)	9 (10%)	6 (60%)	**0,001**
	No (n=85)	81 (90%)	4 (40%)	
Ki67 expression	<20% (n=50)	48 (53,4%)	2 (20%)	**0,046**
	≥20% (n=50)	42 (46,6%)	8 (80%)	
Stromal CD10 expression	<10% (n=40)	36 (40%)	4 (40%)	1,00
	≥10% (n=60)	54 (60%)	6 (60%)	

Table 2: Correlation between CD10 tumor cells expression and clinicopathological factors in breast cancer
Abbreviations: SBR: Scarff–Bloom–Richardson; LVI: Lymphovascular Invasion; PNI: Perineural Invasion; CIS: Carcinoma In Situ; Her–2: Human Epidermal Growth 2; ER: estrogen receptor; PR: progesterone receptor
Bold highlighted values indicate significance (p≤0.05).

	OS		DFS	
	p	HR	p	HR
Family history of breast cancer	0,553	0,466	0,593	0,545
Tumor size	0,056	6,526	0,264	2,423
SBR grading	**0,007**	**10,35**	0,060	4,153
LVI	0,972	0,877	0,965	0,862
Tumor stage	0,551	0,732	0,320	1,470
Lymph node metastasis	0,161	1,860	0,121	1,772
CD10 Stromal expression	0,081	9,154	0,643	1,509
Distant metastasis	**<0,0001**	**219,299**	–	–

Table 3: Multivariate analysis of prognostic factors for overall survival and disease–free–survival
Abbreviations: SBR: Scarff–Bloom–Richardson; LVI: Lymphovascular Invasion; HR: Hazard Ratio
Bold highlighted values indicate significance (p≤0.05).

Prognostic significance of stromal CD10 expression in breast carcinoma was investigated for the first time by Iwaya et al. in 2002: It was associated to lymph node metastasis (p=0,038)[4].

The following studies evidenced a significant association between stromal CD10 expression and other prognostic factors namely high tumor grade, big tumor size, lymph node metastasis, distant metastasis, ER/PR negativity and Her2 overexpression[16,17,19,21,23–26]. In our study, stromal CD10 expression was associated to high tumor grade (p=0,012) and distant metastasis at diagnosis (p=0,02).

Regarding the prognostic relevance of stromal CD10 expression, survival analysis concluded to a decreased OS (p=0,029) and DFS (p=0,05), similarly to the literature[4, 16].

Few studies have investigated the relationship between stromal CD10 expression and Ki67. In 2011, Puri et al. demonstrated a significant association with a high proliferative index Ki67 (p=0,027)[18]. This association was also proven by Vo et al. in 2015[22], and Dhande et al in 2019[26]. In our study 55% of tumors with a high proliferative index, overexpressed CD10 in stromal component without reaching statistical significance (p=0,221).

CD10 expression on tumor cells was 10% in our study. This frequency varies from 6,5% to 20%, and CD10 expression was, in the literature, significantly associated to ER negativity, PR negativity and high tumor grade[22,25,27–29].

Livasy et al. investigated the relationship between tumor expression of CD10 and the different molecular subtypes in 46 cases: 11% of basal–like phenotype tumors expressed CD10 (2/18), 8% of overexpressing Her2 tumors was positive for CD10 (1/12) and all tumors of Luminal phenotype were CD10 negative (0/16)[28].

In the present study, CD10 expression on tumor cells was correlated to ER negativity (p<0,0001), PR negativity (p=0,005), triple negative phenotype (p=0,001) and high tumor grade (p=0,009), which is concordant to previous studies[22,25,27–29]. This work is the first study concluded to a significant association between CD10 expression on tumor cells and high proliferative index Ki67 (p=0,046).

To conclude, our results demonstrate that CD10 expression is a marker of less differentiated carcinoma, it predict an aggressive behavior of breast cancer, so it could represent a new therapeutic target[30].

Conflict of Interest: The authors have no conflict of interest in this article.

Acknowledgement: We wish to thank all people who directly and indirectly contributed for this study. We express our gratitude to the technical staff of the department of pathology.

Ethics statement:

The Ethics Committee of the Medical Faculty of the University of Sfax has given approval for the study (LR18SP10)

Funding (Financial Disclosure)

This research did not receive any specific grant from funding agencies in the public, commercial, or not–for–profit sectors.

Statement of human rights

We have conducted a retrospective study, for this type of study formal consent is not required.

References

1. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin D M, Pineros M, Znaor A, Bray F. Estimating the global cancer incidence and mortality in 2018 : GLOBOCAN sources and methods. Int J Cancer 2019;144(8):1941–1953.

2. Ghribi Ben Ghazi W, Sellami A, Sellami Boudawara T. Incidence des cancers dans le gouvernorat de Sfax 2003–2005. Regist Cancer Sud Tunis MSP–CHU H Bourguiba Sfax–INSP. 2017;28–9.

3. Turner AJ, Tanzawa K. Mammalian membrane metallopeptidases: NEP, ECE, KELL, and PEX. FASEB J. 1997;11(5):355–364.

4. Iwaya K, Ogawa H, Izumi M, Kuroda M, Mukai K. Stromal expression of CD10 in invasive breast carcinoma: a new predictor of clinical outcome. Virchows Arch. 2002;440(6):589–593.

5. Jana SH, Jha BM, Patel C, Jana D, Agarwal A, others. CD10–a new prognostic stromal marker in breast carcinoma, its utility, limitations and role in breast cancer pathogenesis. Indian J Pathol Microbiol. 2014;57(4):530.

6. Chu P, Arber DA. Paraffin–section detection of CD10 in 505 nonhematopoietic neoplasms. Am J Clin Pathol. 2000;113(3):374–382.

7. Atique M, Abbasi MS, Jamal S, Khadim MT, Akhtar F, Jamal N. CD10 expression intensity in various grades and stages of urothelial carcinoma of urinary bladder. J Coll Physicians Surg Pak. 2014;24(5):351–355.

8. Lakhani S, Ellis I, Schnitt S, Tan P, van de Vijver M. WHO classification of tumours of the breast. 4th ed IARC; 2012.

9. Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long–term follow–up. Histopathology. 1991;19(5):403–410.

10. Hammond MEH, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer (unabridged version). Arch Pathol Lab Med. 2010;134(7):e48–e72.

11. Wolff AC, Hammond MEH, Hicks DG, Dowsett M, McShane LM, Allison KH, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol. 2013;31(31):3997–4013.

12. Franchet C, Duprez–Paumier R, Lacroix–Triki M. Cancer du sein luminal et apport des classifications intrinsèques moléculaires: comment identifier les tumeurs luminales A et B en 2015? Bull Cancer (Paris). 2015;102(6):S34–S46.

13. Dowsett M, Nielsen TO, A'Hern R, Bartlett J, Coombes RC, Cuzick J, et al. Assessment of Ki67 in breast cancer: recommendations from the International Ki67 in Breast Cancer working group. J Natl Cancer Inst. 2011;103(22):1656–1564.

14. Zemmouri Y, De Croze D, Salomon AV, Rouzier R, Bonneau C. Caractérisation moléculaire des cancers du sein en pratique clinique. Gynécologie Obstétrique Fertil. 2016;44(5):285–292.

15. De Wever O, Mareel M. Role of tissue stroma in cancer invasion. J Pathol 2003;200:29–47.

16. Makretsov NA, Hayes M, Carter BA, Dabiri S, Gilks CB, Huntsman DG. Stromal CD10 expression in invasive breast carcinoma correlates with poor prognosis, estrogen receptor negativity, and high grade. Mod Pathol. 2007;20(1):84–89.

17. Kim H–S, Kim GY, Kim YW, Park Y–K, Song J–Y, Lim S–J. Stromal CD10 expression and relationship to the E–cadherin/–catenin complex in breast carcinoma. Histopathology. 2010;56(6):708–719.

18. Puri V, Jain M, Thomas S. Stromal expression of CD10 in invasive breast carcinoma and its correlation with ER, PR, HER2–neu, and Ki67. Int J Breast Cancer. 2011;2011:437957.

19. Mohammadizadeh F, Salavati M, Afshar Moghaddam, N. CD10 expression in stromal component of invasive breast carcinoma: A potential prognostic determinant. J Res Med Sci. 2012;17(Spec 2):S194–9.

20. Thomas S, Babu RJ, Agarwal K, Puri V, Jain M, Andley M, et al. Effect of neoadjuvant chemotherapy on stromal CD10 antigens in breast cancer–A preliminary study. Indian J Cancer. 2013;50(1):46.

21. Taghizadeh–Kermani A, Jafarian AH, Ashabyamin R, Seilanian–Toosi M, Pourali L, Asadi M, et al. The stromal overexpression of CD10 in invasive breast cancer and its association with clincophathologic factors. Iran J Cancer Prev. 2014;7(1):17–21.

22. Vo T–ND, Mekata E, Umeda T, Abe H, Kawai Y, Mori T, et al. Prognostic impact of CD10 expression in clinical outcome of invasive breast carcinoma. Breast Cancer. 2015;22(2):117–128.

23. Devi BA, Sekhar SC, Saritha C, Anil SS, Rani HS. A study on stromal CD10 expression in invasive breast carcinoma. IAIM. 2016;3(6):142–7.

24. Nema S, Narang S. CD–10: An Emerging biomarker in Prognostication of Infiltrating Duct Carcinoma Breast. Ann Pathol Lab Med. 2016;3(3):A171–175.

25. Louhichi T, Saad H, Dhiab MB, Ziadi S, Trimeche M. Stromal CD10 expression in breast cancer correlates with tumor invasion and cancer stem cell phenotype. BMC Cancer. 2018;18(1):49.

26. Dhande AN, Sinai Khandeparkar SG, Joshi AR, Kulkarni MM, Pandya N, et al. Stromal expression of CD10 in breast carcinoma and its correlation with clinicopathological parameters. South Asian J Cancer. 2019;8(1):18–21.

27. Kesse–Adu R, Shousha S. Myoepithelial markers are expressed in at least 29% of oestrogen receptor negative invasive breast carcinoma. Mod Pathol. 2004;17(6):646–652.

28. Livasy CA, Karaca G, Nanda R, Tretiakova MS, Olopade OI, Moore DT, et al. Phenotypic evaluation of the basal–like subtype of invasive breast carcinoma. Mod Pathol. 2006;19(2):264–271.

29. Arora G, Girdhar M, Baghla A, Lajpal K, Manjari M, Jagga K, et al. Comparing the expression of myoepithelial cell markers CD10 and smooth muscle actin with the estrogen receptor status in the invasive carcinoma breast: An immunohistochemical study. Clin Cancer Investig J. 2013;2(1):20.

30. Pan C, Cardarelli PM, Nieder MH, Pickford LB, Gangwar S, King DJ, et al. CD10 is a key enzyme involved in the activation of tumor–activated peptide prodrug CPI–0004Na and novel analogues: implications for the design of novel peptide prodrugs for the therapy of CD10+ tumors. Cancer Res. 2003;63(17):5526–5531.