RESEARCH ARTICLE

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mTOR Levels and Metastasis in Luminal Breast Cancer: Implications for Prognosis and Treatment

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Abstract

Background: Breast cancer (BC) is the most common cancer in women, with metastasis being the leading cause of mortality. The *PI3K/PTEN/Akt/mTORC1* signaling pathway plays a crucial role in cancer cell proliferation, angiogenesis, and invasion, with mammalian target of rapamycin (mTOR) serving as a key regulator. Activation of mTOR is associated with tumor growth and resistance to therapy in luminal and human epidermal growth factor receptor 2 positive (*HER2*-positive) BC subtypes. This study aims to explore the relationship between serum mTOR levels and metastasis in luminal, *HER2*-positive and *HER2*-negative BC subtypes to assess the potential of mTOR as a predictive biomarker and therapeutic target. **Methods:** This preliminary cross-sectional study included BC patients with luminal *HER2*-positive or *HER2*-negative subtypes. Serum mTOR levels were measured using a Human ELISA kit. The optimal cut-off point for mTOR was determined using a Receiver Operating Characteristic (ROC) curve analysis. Statistical associations between mTOR levels and metastasis were performed using the Chi-square or Fisher's exact test, and the prevalence ratio (PR) with a 95% confidence interval was calculated. **Results:** The ROC curve demonstrated an AUC of 0.996, with an optimal cut-off point for serum mTOR levels at 13.32 ng/mL, showing 100% sensitivity and 96.4% specificity for predicting metastasis. The mean mTOR level was 58.39±250.91 ng/mL, with 50% exhibiting elevated levels (≥13.32 ng/mL). Notably, mTOR levels were significantly higher in *HER2*-positive cases (113.59±381.87 ng/mL) compared to *HER2*-negative cases (17.45±14.83 ng/mL; p=0.040). Elevated mTOR levels were significantly associated with metastasis (p<0.001), with a PR of 0.037 (95% CI: 0.005-0.253). **Conclusions:** Increased serum mTOR levels (≥13.32 ng/mL) are significantly linked to the presence of metastasis, particularly in *HER2*-positive BC. These findings suggest serum mTOR as a promising biomarker for metastasis risk and a potential therapeutic target in luminal BC.

Keywords: Metastasis- mTOR- *HER2*- biomarker- breast cancer

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Introduction

Breast cancer (BC) is the most common type of cancer among women, with a global incidence of 2.3 million cases in 2020 and a mortality rate of 685,000 deaths [1]. While the incidence of BC is higher in developed countries, mortality rates are, paradoxically, greater in developing nations [2]. Risk factors for BC include reproductive, hormonal, and lifestyle factors. Increased early detection through mammography screening has contributed to higher diagnosis rates in developed countries [3].

Based on molecular characteristics, BC is classified into several subtypes: estrogen receptor (ER)-positive, progesterone receptor (PR)-positive, human epidermal growth factor receptor 2 (*HER2*)-positive, and triple-negative breast cancer (TNBC). The luminal subtype (ER-positive and/or PR-positive) is the most common, whereas the *HER2*-positive subtype is characterized by rapid proliferation and responsiveness to *HER2*-targeted therapy (3). Metastasis, which accounts for over 90% of cancer-related deaths, is a primary contributor to the high mortality rates associated with BC [4, 5]. The *PI3K/PTEN/Akt/mTORC1* signaling pathway plays a crucial role in BC metastasis [6–8], with mammalian target of rapamycin (mTOR) acting as a key regulator of cancer cell proliferation, angiogenesis, invasion, and adaptation to new environments [9–11].

In luminal and *HER2*-positive subtypes, mTOR activation is associated with tumor growth and resistance to hormonal and *HER2*-targeted therapies [12, 13]. Although inhibitors such as rapamycin and its derivatives have been developed as adjunct therapies, their effectiveness

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remains a challenge. While the role of the PI3K/Akt/mTOR pathway in BC metastasis is well-established, and its activation in luminal and *HER2*-positive subtypes is linked to tumor growth and therapy resistance, specific investigations into serum mTOR levels as a predictive biomarker for metastasis, particularly within *HER2*-stratified luminal BC subtypes, remain limited, especially in the Indonesian population. Therefore, this study aims to investigate the relationship between serum mTOR levels and the presence of metastasis in luminal *HER2*-positive and *HER2*-negative breast cancer subtypes to further assess the potential of mTOR as a biomarker for metastasis risk and a therapeutic target.

Materials and Methods

This preliminary cross-sectional study was conducted at Dr. Wahidin Sudirohusodo Hospital and Hasanuddin University Hospital, Makassar, over one year period (August 2023 to July 2024). The study included BC patients diagnosed with luminal *HER2*-positive or *HER2*-negative subtypes.

Inclusion Criteria were patients diagnosed with luminal BC subtypes (*HER2*-positive or *HER2*-negative), patients with known metastatic status confirmed through radiological examination, and patients who provided informed consent. Exclusion criteria include patients with incomplete medical records and patients who declined participation. A total sampling method was used for participant selection.

Metastasis Assessment

Metastasis was defined as the spread of BC to other organs, confirmed through diagnostic imaging such as head CT scan (for the brain), chest X-ray/CT scan (for the lungs), abdominal ultrasound/CT scan (for the liver), and bone scan, X-ray, or CT scan/MRI of the spine (for bones and other organs) [14, 15].

BC staging

BC staging was determined according to the TNM system from the American Joint Committee on Cancer (AJCC), encompassing stages IA, IB, IIA, IIB, IIIA, IIIB, IIIC, and IV [16, 17].

mTOR Levels Measurement

Serum mTOR levels were measured via venous blood serum analysis using a Human ELISA kit (BT Lab, catalog no. E3693Hu. Results were expressed in ng/mL. The optimal cut-off point for serum mTOR levels to predict metastasis was determined using a Receiver Operating Characteristic (ROC) curve analysis. This analysis aimed to identify the value that maximized both sensitivity and specificity for distinguishing between patients with and without metastasis. Serum mTOR levels were subsequently classified as elevated (≥ the optimal cut-off point) or not elevated (< the optimal cut-off point).

Data Analysis

Data analysis was performed using IBM SPSS version 21 (Armonk, NY: IBM Corp.). The relationship between mTOR levels and metastasis was analyzed using the Chi-square test or Fisher's exact test in cases with small expected values. ROC analysis was conducted to determine the optimal serum mTOR cut-off point for predicting metastasis, assessing its diagnostic performance through sensitivity and specificity. The association between mTOR levels and metastasis was further quantified using the prevalence ratio (PR) with a 95% confidence interval (CI). Results were considered statistically significant at $p < 0.05$.

Results

The ROC curve analysis demonstrated excellent diagnostic performance with an Area Under the Curve (AUC) value of 0.996 (99.6%), as illustrated in Figure 1. This value indicates the superior discriminatory ability of serum mTOR levels in distinguishing between patients with and without metastasis.

The optimal cut-off point for serum mTOR levels was determined to be 13.32 ng/mL. At this threshold, the test achieved a sensitivity of 100%, indicating that all metastatic cases could be accurately identified. Concurrently, a specificity of 96.4% confirmed the test's capability to precisely identify most patients without metastasis.

Patient age and cancer duration showed no statistically significant relationship with serum mTOR levels, and were therefore excluded from further analysis. The mean mTOR level was 58.39±250.91, with 50% of participants experiencing elevated mTOR levels (Table 1).

Further analysis revealed a significant association between elevated serum mTOR levels (≥13.32 ng/mL) and the presence of metastasis ($p<0.001$) with a prevalence ratio (PR) of 0.037 (95% CI: 0.005–0.253). This indicates that elevated mTOR levels increase the risk of metastasis in luminal BC by 0.037 times, as presented in Table 2. Clinically, this finding is highly relevant, given that 100% of patients with elevated mTOR levels were confirmed

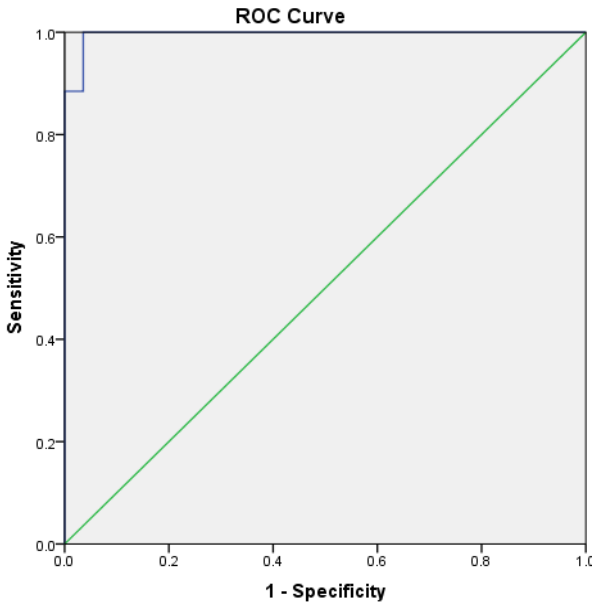

Figure 1. ROC Curve Analysis of Serum mTOR Levels in Breast Cancer Metastasis.

Table 1. Characteristics of Participants

Variable	Frequency (%)	BC Subtype		p-value
		Luminal *HER2*-positive (n=23) (%)	Luminal *HER2*-negative (n=31) (%)	
Age (Mean±SD) (years)	48.31±43	50.83±8.87	46.45±9.54	0.092[a]
≥ 60	6 (11.10)	2 (8.70)	4 (12.90)	0.488[d]
< 60	48 (88.90)	21 (91.30)	27 (81.70)	
Duration of BC (mean±SD) (months)	10.48±4.96	10.87±5.75	10.19±4.37	0.964[b]
BC stage				
IIB	5 (9.30)	0 (0.00)	5 (16.10)	0.018*[c]
IIIA	13 (24.10)	7 (30.40)	6 (19.40)	
IIIB	12 (22.20)	2 (8.70)	10 (32.30)	
IV	24 (44.40)	14 (60.90)	10 (32.30)	
Metastasis				
Present	26 (48.10)	14 (60.90)	12 (38.70)	0.107[c]
Absent	28 (51.90)	9 (39.10)	19 (61.30)	
mTOR levels (Mean±SD) (ng/mL)	58.39±250.91	113.59±381.87	17.45±14.83	0.040*[b]
Elevated (≥13.32)	27 (50.00)	14 (60.90)	13 (41.90)	0.169[c]
Not elevated (<13.32)	27 (50.00)	9 (39.10)	18 (58.10)	

Note: BC, breast cancer; mTOR, mammalian target of rapamycin

Table 2. Association between Serum mTOR Levels and Clinicopathological Features of Luminal BC Patients

Clinical Feature	mTOR Elevated (≥13.32 ng/mL)	mTOR Not Elevated (<13.32 ng/mL)	p-value	Prevalence Ratio (95% CI)
Metastasis	26 (100%)	1 (3.6%)	<0.001*	0.037 (0.005–0.253
HER2 status	14 (60.9%)	13 (41.9%)	0.040*	–
Stage IV	24 (88.9%)	0 (0.0%)	0.011*	–

Note: mTOR, mammalian target of rapamycin; Chi-square or Fisher exact test; *significant at p<0.05

Table 3. Serum mTOR Levels in Luminal *HER2*+ vs *HER2*− Patients

BC Subtype	Mean m TOR ± SD (ng/mL)	% Elevated	p-value
HER2-positive	113.59 ± 381.87	60.9	0.040*
HER2-negative	17.45 ± 14.83	41.9	

to have metastasis, compared to only 3.6% in the group with non-elevated mTOR levels. The proportion of *HER2*-positive patients with elevated mTOR levels was also higher (60.9% vs. 41.9%). Furthermore, elevated serum mTOR levels were significantly associated with Stage IV breast cancer (p=0.011), where all patients (100%) with Stage IV disease presented with elevated mTOR levels (Table 2).

Additionally, this study identified a significant relationship between serum mTOR levels and *HER2* status and cancer stage. Patients with *HER2*-positive status exhibited significantly higher mean serum mTOR levels (113.59±381.87 ng/mL) compared to *HER2*-negative patients (17.45±14.83 ng/mL) (p=0.040) (Table 3).

Discussion

This study significantly demonstrates that elevated serum mTOR levels (≥13.32 ng/mL) exhibit a strong and significant association with the incidence of metastasis in luminal BC patients, particularly within the *HER2*-positive subtype. This finding is substantiated by the ROC curve analysis, which revealed exceptional predictive capability with an AUC of 0.996 (99.6%). This affirms that serum mTOR levels serve as a highly reliable indicator for determining metastasis in luminal BC. Furthermore, with an optimal cut-off point of 13.32 ng/mL, serum mTOR levels achieved 100% sensitivity and 96.4% specificity in predicting metastasis, suggesting that this biomarker holds substantial potential for accurate metastasis risk identification in this patient population.

The characteristics of the study cohort indicate that the majority of participants were under 60 years of age (88.9%), with a mean age of 48.31 ± 43 years. Although the mean age and duration of breast cancer did not exhibit statistically significant relationships with serum mTOR levels, the clinical distribution of participants provides important context. The majority of metastatic patients in this study were at Stage IV (92.4%), while non-metastatic patients tended to be in Stage IIIA and IIIB. This stage distribution was statistically significant (p<0.001). Moreover, a significant difference was observed in the mean mTOR levels between *HER2*-positive (113.59 ± 381.87 ng/mL) and *HER2*-negative patients (17.45 ± 14.83 ng/

mL) (p=0.040), with a higher prevalence of elevated mTOR levels in the *HER2*-positive group. The correlation between elevated mTOR and advanced disease stage, as well as the significant differences in mTOR levels across *HER2* subtypes, further reinforces the potential role of mTOR as a metastasis biomarker in the clinical context of luminal breast cancer.

Biological Role of mTOR in Cancer Pathophysiology and Metastasis

The central role of mTOR in cancer pathophysiology, particularly in breast cancer, is widely recognized [18, 19]. As a member of the phosphoinositide kinase-related kinase (PIKK) family, mTOR functions as a primary regulator of cellular responses to various stimuli, including amino acid availability, energy status, oxygen levels, and growth factor receptor signaling [6, 20]. mTOR activation is a hallmark of various cancer types, including breast cancer, and plays a crucial role in tumorigenesis [9, 10, 18, 19]. mTOR forms two distinct complexes, mTORC1 and mTORC2, through interactions with Raptor or Rictor [21, 22]. The activation of mTORC1, in particular, phosphorylates key substrates such as p70S6K1 and 4EBP1, directly driving cancer cell proliferation and growth by regulating protein synthesis essential for cell growth [9, 10, 18, 19].

Beyond proliferation, the mTOR pathway significantly contributes to the metastatic process through several mechanisms. mTOR influences angiogenesis, the formation of new blood vessels crucial for tumor oxygen and nutrient supply, by promoting the release of angiogenic factors such as vascular endothelial growth factor [7, 23]. This enhanced angiogenesis supports tumor growth and facilitates the dissemination of cancer cells to other organs via the bloodstream. In the metastatic process itself, mTOR regulates cancer cell migration and invasion by modulating proteins that influence cell motility [24]. The activation of the mTOR pathway increases the ability of cancer cells to move and penetrate surrounding tissues, which is a pivotal step in metastasis. Furthermore, the mTOR pathway interacts synergistically with other signaling pathways involved in metastasis, such as the PI3K/AKT pathway, strengthening proliferation, migration, and invasion signals, thereby increasing overall metastatic potential [24]. mTOR activation also enhances the resistance of cancer cells to apoptosis (programmed cell death), enabling these cells to survive longer and increasing their likelihood of spreading to other organs [24]. Research in human and animal models has also demonstrated that inhibition of the mTOR pathway can suppress breast cancer metastasis, with mTOR inhibitors like rapalogs showing potential in reducing the invasion, migration, and metastatic potential of cancer cells [7, 8].

Comparison with Literature and Clinical Implications

This study, demonstrating a strong association between elevated serum mTOR levels and metastasis, is consistent with previous research that underscores the pivotal role of the mTOR pathway in breast cancer progression and aggressiveness. For instance, a study by An et al. [18] reported that high expression of phosphorylated mTOR (p-mTOR) in invasive breast carcinomas correlated with more aggressive tumor characteristics. However, their study utilized tissue expression rather than serum levels and did not specifically focus on metastasis prediction. Similarly, Giotta Lucifero et al. [25] and Gargalionis et al. [20] highlight the importance of the mTOR pathway in various oncological contexts and tumor mechanobiology, supporting the notion that mTOR dysregulation contributes to malignant behaviors, including metastasis.

The novelty of our study lies in several crucial aspects. First, our utilization of serum mTOR levels as a biomarker offers a non-invasive and more accessible approach compared to protein expression analysis in biopsy tissues. This ease of sample collection has significant practical implications for routine screening, monitoring, and metastasis prediction in clinical practice. Second, the stratification of patients into luminal *HER2*-positive and *HER2*-negative subtypesallowed us to explore the role of mTOR more specifically within the biological heterogeneity of breast cancer, highlighting significant differences in mTOR levels between these subtypes. This supports the idea that mTOR pathway activation may play a varied or more prominent role in specific subtypes, particularly *HER2*-positive, consistent with the crosstalk between the *HER2* and *PI3K/Akt/mTOR* pathways. Third, this study was conducted within the Indonesian population, providing valuable data on this biomarker in a demographic that may possess distinct genetic or environmental characteristics.

The clinical implications of these findings are substantial. With high sensitivity and specificity, serum mTOR levels hold the potential to serve as a reliable predictive biomarker for metastasis risk, enabling the early identification of high-risk patients. This could facilitate more informed clinical decisions, such as intensified surveillance or modification of therapeutic plans for high-risk patients. Furthermore, these findings reinforce the potential of the mTOR pathway as a therapeutic target in luminal breast cancer. mTOR-targeting drugs, such as everolimus and sirolimus (rapalogs), have demonstrated efficacy in delaying disease progression in breast cancer, especially in luminal subtypes resistant to endocrine therapy. Identifying patients with high serum mTOR levels can assist in the selection of patients most likely to respond to mTOR inhibitor therapy, guiding more personalized and effective treatments. This approach could improve patient outcomes by suppressing tumor growth and cancer cell dissemination, as well as potentially overcoming resistance to standard therapies.

Study Limitations

Despite these promising findings, this study has several limitations. As a cross-sectional study, it can only establish an association between serum mTOR levels and metastasis, not a direct causal relationship. We cannot determine whether elevated mTOR levels precede or are a consequence of metastasis development. The relatively small sample size may also limit the generalizability of these findings to a broader population and hinder the detection of more subtle associations. Therefore, future research employing a prospective cohort study design with

a larger sample size is highly recommended. Prospective cohort studies would allow for longitudinal monitoring of serum mTOR levels and their correlation with metastasis development, thereby providing stronger evidence of causality and confirming the predictive role of mTOR over time.

In conclusion, this study demonstrates that a serum mTOR level cut-off of ≥13.32 ng/mL exhibits high predictive accuracy (100% sensitivity, 96.4% specificity, AUC 0.996) for metastasis in luminal *HER2*-positive and *HER2*-negative breast cancer. Elevated serum mTOR levels are significantly associated with an increased risk of metastasis. These findings underscore the potential utility of serum mTOR assessment as a valuable biomarker for metastasis risk stratification, which can aid in treatment planning and patient monitoring to ultimately improve clinical outcomes in breast cancer patients.

Author Contribution Statement

MMHN (Concept, Design, Resources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Writing Manuscript), PRI (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), MIK (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), ID (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), SAS (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), NS (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), JP (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), and MF (Concept, Design, Analysis and Interpretation, Critical Review). All authors read and approved the final version of the manuscript.

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Ethics approval

All research designs were reviewed and approved by the Health Research Ethics Committee of Dr Wahidin Sudirohusodo Hospital Faculty of Medicine, Hasanuddin University (protocol no. UH24050321).

Data availability statement

The data presented in this study are available on request from the corresponding author.

Competing interests

No competing interests were reported.

References

1. Chou CY, Shen TT, Wang WC, Wu MP. Favorable breast cancer mortality-to-incidence ratios of countries with good human development index rankings and high health expenditures. Taiwan J Obstet Gynecol. 2024;63(4):527-31. https://doi.org/https://doi.org/10.1016/j.tjog.2023.11.012.
2. Huang J, Chan PS, Lok V, Chen X, Ding H, Jin Y, et al. Global incidence and mortality of breast cancer: A trend analysis. Aging (Albany NY). 2021;13(4):5748-803. https://doi.org/10.18632/aging.202502.
3. Salvo EM, Ramirez AO, Cueto J, Law EH, Situ A, Cameron C, et al. Risk of recurrence among patients with hr-positive, her2-negative, early breast cancer receiving adjuvant endocrine therapy: A systematic review and meta-analysis. Breast. 2021;57:5-17. https://doi.org/10.1016/j.breast.2021.02.009.
4. Fong MY, Zhou W, Liu L, Alontaga AY, Chandra M, Ashby J, et al. Breast-cancer-secreted mir-122 reprograms glucose metabolism in premetastatic niche to promote metastasis. Nat Cell Biol. 2015;17(2):183-94. https://doi.org/10.1038/ncb3094.
5. 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. 2021;71(3):209-49. https://doi.org/10.3322/caac.21660.
6. Hynes NE, Boulay A. The mtor pathway in breast cancer. J Mammary Gland Biol Neoplasia. 2006;11(1):53-61. https://doi.org/10.1007/s10911-006-9012-6.
7. Jacobs BL, Goodman CA, Hornberger TA. The mechanical activation of mtor signaling: An emerging role for late endosome/lysosomal targeting. J Muscle Res Cell Motil. 2014;35(1):11-21. https://doi.org/10.1007/s10974-013-9367-4.
8. Foster KG, Fingar DC. Mammalian target of rapamycin (mtor): Conducting the cellular signaling symphony. J Biol Chem. 2010;285(19):14071-7. https://doi.org/10.1074/jbc.R109.094003.
9. Steelman LS, Martelli AM, Cocco L, Libra M, Nicoletti F, Abrams SL, et al. The therapeutic potential of mtor inhibitors in breast cancer. Br J Clin Pharmacol. 2016;82(5):1189-212. https://doi.org/10.1111/bcp.12958.
10. Zou Z, Tao T, Li H, Zhu X. Mtor signaling pathway and mtor inhibitors in cancer: Progress and challenges. Cell Biosci. 2020;10:31. https://doi.org/10.1186/s13578-020-00396-1.
11. Zhu K, Wu Y, He P, Fan Y, Zhong X, Zheng H, et al. Pi3k/akt/mtor-targeted therapy for breast cancer. Cells. 2022;11(16). https://doi.org/10.3390/cells11162508.
12. Creighton CJ. The molecular profile of luminal b breast cancer. Biologics. 2012;6:289-97. https://doi.org/10.2147/btt.S29923.
13. Garcia-Martinez L, Zhang Y, Nakata Y, Chan HL, Morey L. Epigenetic mechanisms in breast cancer therapy and resistance. Nat Commun. 2021;12(1):1786. https://doi.org/10.1038/s41467-021-22024-3.
14. Ikhlas M, Ferianto D, Syamsu SA, Ganda IJ, Smaradania N, Sampepajung E, et al. Pleiotrophin serum level and metastasis occurrence in breast cancer patients. Breast Dis. 2024;43(1):93-8. https://doi.org/10.3233/bd-249003.
15. Cangara H. Expression of estrogen receptor (ER), progesterone receptor (PR), and human epi- dermal growth factor receptor-2 (HER-2) in growth and metastases of breast cancer. Nusantara Medical Science Journal. 2017;1(3):98-103. https://doi.org/10.20956/nmsj.v1i3.2227.
16. Zhu H, Doğan BE.American joint committee on cancer's staging system for breast cancer, eighth edition: Summary for clinicians. EJBH.. 2021;17(3):234–8. https://doi.org/10.4274/ejbh.galenos.2021.2021-4-3.
17. Saleh D, Hamdani W, Syamsu SA, Smaradania N. Correlation between CD44 and human Epidermal Growth Factor Receptor 2 Expression with distant metastasis

on women non-luminalBreast Cancer. Indonesia Surg J. 2024;1(1):4-9.
18. An J, Jeong H, Lee Y, Woo SU, Seo JH, Kim A. Phosphorylated akt and phosphorylated mtor expression in breast invasive carcinomas: Analysis of 530 cases. J Breast Cancer. 2010;13(4):337-48.
19. Sihto H, Lundin J, Lundin M, Lehtimäki T, Ristimäki A, Holli K, et al. Breast cancer biological subtypes and protein expression predict for the preferential distant metastasis sites: A nationwide cohort study. Breast Cancer Res. 2011;13(5):R87. https://doi.org/10.1186/bcr2944.
20. Gargalionis AN, Papavassiliou KA, Basdra EK, Papavassiliou AG. Mtor signaling components in tumor mechanobiology. Int J Mol Sci. 2022;23(3). https://doi.org/10.3390/ijms23031825.
21. Panwar V, Singh A, Bhatt M, Tonk RK, Azizov S, Raza AS, et al. Multifaceted role of mtor (mammalian target of rapamycin) signaling pathway in human health and disease. Signal Transduct Target Ther. 2023;8(1):375. https://doi.org/10.1038/s41392-023-01608-z.
22. Jhanwar-Uniyal M, Wainwright JV, Mohan AL, Tobias ME, Murali R, Gandhi CD, et al. Diverse signaling mechanisms of mtor complexes: Mtorc1 and mtorc2 in forming a formidable relationship. Adv Biol Regul. 2019;72:51-62. https://doi.org/10.1016/j.jbior.2019.03.003.
23. Beca F, Andre R, Martins DS, Bilhim T, Martins D, Schmitt F. P-mtor expression is associated with better prognosis in luminal breast carcinoma. J Clin Pathol. 2014;67(11):961-7. https://doi.org/10.1136/jclinpath-2014-202320.
24. Ito K, Ogata H, Honma N, Shibuya K, Mikami T. Expression of mtor signaling pathway molecules in triple-negative breast cancer. Pathobiology. 2019;86(5-6):315-21. https://doi.org/10.1159/000503311.
25. Giotta Lucifero A, Luzzi S, Brambilla I, Trabatti C, Mosconi M, Savasta S, et al. Innovative therapies for malignant brain tumors: The road to a tailored cure. Acta Biomed. 2020;91(7-s):5-17. https://doi.org/10.23750/abm.v91i7-S.9951.