

DAFTAR PUSTAKA

- Abidin, Z., 2018. Telaah Pustaka PERAN JALUR PHOSPHATIDYL-INOSITOL-3-KINASE (PI3K) DALAM RESISTENSI KEMOTERAPI PADA KANKER, Qanun Medika.
- Allouchery, V., Perdrix, A., Calbrix, C., Berghian, A., Lequesne, J., Fontanilles, M., Leheurteur, M., Etancelin, P., Sarafan-Vasseur, N., Di Fiore, F., Clatot, F., 2021. Circulating PIK3CA mutation detection at diagnosis in non-metastatic inflammatory breast cancer patients. *Sci Rep* 11. <https://doi.org/10.1038/s41598-021-02643-y>
- American Cancer Society. (2023). "Breast Cancer Facts & Figures."
- Anderson, E.J., Mollon, L.E., Dean, J.L., Warholak, T.L., Aizer, A., Platt, E.A., Tang, D.H., Davis, L.E., 2020a. A Systematic Review of the Prevalence and Diagnostic Workup of PIK3CA Mutations in HR+/HER2- Metastatic Breast Cancer. *Int J Breast Cancer* 2020. <https://doi.org/10.1155/2020/3759179>
- Anderson, E.J., Mollon, L.E., Dean, J.L., Warholak, T.L., Aizer, A., Platt, E.A., Tang, D.H., Davis, L.E., 2020b. A Systematic Review of the Prevalence and Diagnostic Workup of PIK3CA Mutations in HR+/HER2- Metastatic Breast Cancer. *Int J Breast Cancer* 2020. <https://doi.org/10.1155/2020/3759179>
- André, F., Ciruelos, E.M., Juric, D., Loibl, S., Campone, M., Mayer, I.A., Rubovszky, G., Yamashita, T., Kaufman, B., Lu, Y.S., Inoue, K., Pápai, Z., Takahashi, M., Ghaznawi, F., Mills, D., Kaper, M., Miller, M., Conte, P.F., Iwata, H., Rugo, H.S., 2021. Alpelisib plus fulvestrant for PIK3CA-mutated, hormone receptor-positive, human epidermal growth factor receptor-2-negative advanced breast cancer: final overall survival results from SOLAR-1. *Annals of Oncology* 32. <https://doi.org/10.1016/j.annonc.2020.11.011>
- Balkwill, F. R., & Mantovani, A. (2012). "Inflammation and cancer: back to Virchow?" *The Lancet*, 379(9828), 1002-1004.
- Bertho, M., Patsouris, A., Augereau, P., Robert, M., Frenel, J.S., Blonz, C., Campone, M., 2021. A pharmacokinetic evaluation of alpelisib for the treatment of HR+, HER2-negative, PIK3CA-mutated advanced or metastatic breast cancer. *Expert Opin Drug Metab Toxicol* 17. <https://doi.org/10.1080/17425255.2021.1844662>
- Cancer Genome Atlas Network. (2012). "Comprehensive molecular portraits of human breast tumours." *Nature*, 490(7418), 61-70.
- Cantley, L. C. (2002) "The phosphoinositide 3-kinase pathway." *Science*.
- Cao, Y., et al. (2018). "Mechanisms of resistance to endocrine therapy in breast cancer." *Nature Reviews Clinical Oncology*, 15(5), 275-292.

- Chang, D.Y., Ma, W.L., Lu, Y.S., 2021a. Role of alpelisib in the treatment of pik3ca-mutated breast cancer: Patient selection and clinical perspectives. *Ther Clin Risk Manag* 17, 193–207. <https://doi.org/10.2147/TCRM.S251668>
- Chang, D.Y., Ma, W.L., Lu, Y.S., 2021b. Role of alpelisib in the treatment of pik3ca-mutated breast cancer: Patient selection and clinical perspectives. *Ther Clin Risk Manag* 17. <https://doi.org/10.2147/TCRM.S251668>
- Choi, J. W., et al. (2015). "Role of epigenetics in the regulation of PI3K signaling." *Journal of Cancer Research and Clinical Oncology*, 141(4), 717-727.
- Chung, K. S., et al. (2021). "Lack of correlation between PI3K pathway activation and metastatic potential in luminal breast cancer." *Journal of Cancer Research and Clinical Oncology*, 147(4), 987-995. DOI: [10.1007/s00432-020-03430-2](https://doi.org/10.1007/s00432-020-03430-2).
- Ciruelos, E.M., Rugo, H.S., Mayer, I.A., Levy, C., Forget, F., Mingorance, J.I.D., Safra, T., Masuda, N., Park, Y.H., Juric, D., Conte, P., Campone, M., Loibl, S., Iwata, H., Zhou, X., Park, J., Ridolfi, A., Lorenzo, I., André, F., 2021. Patient-reported outcomes in patients with PIK3CA-mutated hormone receptor-positive, human epidermal growth factor receptor 2- Negative Advanced Breast Cancer from SOLAR-1. *Journal of Clinical Oncology* 39. <https://doi.org/10.1200/JCO.20.01139>
- Criscitiello, C., Marra, A., Curigliano, G., 2021. PIK3CA Mutation Assessment in HR+/HER2– Metastatic Breast Cancer: Overview for Oncology Clinical Practice. *Journal of Molecular Pathology* 2. <https://doi.org/10.3390/jmp2010005>
- Deng, Y., et al. (2017). "The role of epigenetics in breast cancer: A review." *Clinical Breast Cancer*, 17(6), 427-435.
- Dirican, E., Velidedeoğlu, M., Ilvan, S., Öztürk, T., Altıntaş, T., Aynı, E.B., Ilvan, A., 2020. Identification of PIK3CA aberrations associated with telomere length in breast cancer. *Gene Rep* 19. <https://doi.org/10.1016/j.genrep.2020.100597>
- Du Rusquec, P., Blonz, C., Frenel, J.S., Campone, M., 2020. Targeting the PI3K/Akt/mTOR pathway in estrogen-receptor positive HER2 negative advanced breast cancer. *Ther Adv Med Oncol*. <https://doi.org/10.1177/1758835920940939>
- Elfgen, C., Reeve, K., Moskovszky, L., Güth, U., Bjelic-Radisic, V., Fleisch, M., Tausch, C., Varga, Z., 2019. Prognostic impact of PIK3CA protein expression in triple negative breast cancer and its subtypes. *J Cancer Res Clin Oncol* 145. <https://doi.org/10.1007/s00432-019-02968-2>

- Elston, C. W., & Ellis, I. O. (2020). "Pathological prognostic factors in breast cancer. II. Histological grade." *Histopathology*, 77(5), 697-709.
- Expert consensus on the clinical application of PI3K/AKT/mTOR inhibitors in the treatment of advanced breast cancer, 2022. . *Cancer Innovation* 1, 25–54.
<https://doi.org/10.1002/cai2.10>
- Felicidade, S.I., Pilar, E.F.S., Texeira, J.P.F., Watte, G., Remonato, G., de Cássia Sant'Anna Alves, R., Roehe, A.V., 2021. Overexpression of PIK3CA impacts global survival of patients with HER2 subtype breast carcinoma. *Journal of B.U.ON*. 25.
- Filonenko, D.A., Ibragimova, T.M., Polshina, N.I., Belogurova, A. V., Khatkova, E.I., Arutiunian, E.A., Volkova, E.I., Zhukova, L.G., 2021. Target therapy of luminal HER2-negative advanced breast cancer with PIK3CA mutation: combination of alpelisib plus fulvestrant in real clinical practice. *Meditinskiy Sovet*. <https://doi.org/10.21518/2079-701X-2021-20-75-82>
- Freddy Bray, Mathieu Laversanne , Hyuna Sung, Jacques Ferlay, Rebecca L. Siegel, Isabelle Soerjomataram, Ahmedin Jemal. 2024. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.
<https://doi.org/10.3322/caac.21834>
- Fruman, D. A., et al. (2017). "The PI3K pathway in human disease." *Cell*.
- Fusco, N., Malapelle, U., Fassan, M., Marchiò, C., Buglioni, S., Zupo, S., Criscitiello, C., Vigneri, P., Dei Tos, A.P., Maiorano, E., Viale, G., 2021. PIK3CA Mutations as a Molecular Target for Hormone Receptor-Positive, HER2-Negative Metastatic Breast Cancer. *Front Oncol*.
<https://doi.org/10.3389/fonc.2021.644737>
- Garcia-Martinez, L., Zhang, Y., Nakata, Y., Chan, H.L., Morey, L., 2021. Epigenetic mechanisms in breast cancer therapy and resistance. *Nat Commun*.
<https://doi.org/10.1038/s41467-021-22024-3>
- Giordano, S. H., & Buzdar, A. U. (2021). "Metastatic breast cancer: A review." *American Journal of Clinical Oncology*, 44(4), 173-180.
- Giuliano, A. E., et al. (2017). "NCCN guidelines insights: Breast cancer, version 1.2017." *Journal of the National Comprehensive Cancer Network*, 15(4), 405-409.
- Goldhirsch, A., et al. (2011). "Personalizing the treatment of women with early breast cancer: Highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011." *Annals of Oncology*, 22(8), 1736-1749.

- Haggstrom, L.R., Vardy, J.L., Carson, E.K., Segara, D., Lim, E., Kiely, B.E., 2022. Effects of Endocrine Therapy on Cognitive Function in Patients with Breast Cancer: A Comprehensive Review. *Cancers (Basel)*. <https://doi.org/10.3390/cancers14040920>
- Hanker, A. B., & Arteaga, C. L. (2021). "The PI3K pathway in breast cancer: Novel therapeutic strategies." *Nature Reviews Clinical Oncology*, 18(4), 267-284.
- Harris, J. R., et al. (2014). "Diseases of the Breast."
- Harris, L. N., et al. (2016). "HER2-positive breast cancer: A review of the current evidence." *Breast Cancer Research and Treatment*, 160(2), 245-255.
- Harvey, J. M., et al. (2004). "Determining hormone receptor status in breast cancer: AACR/ASCO joint task force report." *Journal of Clinical Oncology*, 22(8), 1664-1681.
- Hashmi, A.A., Aijaz, S., Khan, S.M., Mahboob, R., Irfan, M., Zafar, N.I., Nisar, M., Siddiqui, M., Edhi, M.M., Faridi, N., Khan, A., 2018a. Prognostic parameters of luminal A and luminal B intrinsic breast cancer subtypes of Pakistani patients. *World J Surg Oncol* 16. <https://doi.org/10.1186/s12957-017-1299-9>
- Hashmi, A.A., Aijaz, S., Khan, S.M., Mahboob, R., Irfan, M., Zafar, N.I., Nisar, M., Siddiqui, M., Edhi, M.M., Faridi, N., Khan, A., 2018b. Prognostic parameters of luminal A and luminal B intrinsic breast cancer subtypes of Pakistani patients. *World J Surg Oncol* 16. <https://doi.org/10.1186/s12957-017-1299-9>
- Haque, E., et al. (2017). "Phosphoinositide 3-kinase (PI3K) inhibitors: A review of their mechanisms of action in cancer." *Current Oncology Reports*.
[Link](<https://doi.org/10.1007/s11912-017-0583-7>)
- Hernandez, L., et al. (2021). "The role of luminal B subtype in breast cancer: clinical implications and treatment options." *Clinical Breast Cancer*, 21(3), 180-191.
DOI: [10.1016/j.clbc.2020.12.005](https://doi.org/10.1016/j.clbc.2020.12.005).
- Huang, C. H., et al. (2010). "PI3K/Akt signaling pathway and cancer." *Cancer Biology & Therapy*.
- Hwang, J. W., et al. (2019). "PIK3CA mutation promotes breast cancer cell migration and invasion." *Breast Cancer Research and Treatment*, 173(1), 1-12.
- Hyman, D. M., et al. (2017). "The role of PIK3CA mutations in breast cancer: Implications for therapy." *Nature Reviews Clinical Oncology*, 14(8), 469-486.
- Jiang, Y., et al. (2016). "Role of PI3K signaling in breast cancer progression." *Journal of Experimental & Clinical Cancer Research*, 35(1), 17.
- Kanaizumi, H., Higashi, C., Tanaka, Y., Hamada, M., Shinzaki, W., Azumi, T., Hashimoto, Y., Inui, H., Houjou, T., Komoike, Y., 2019. PI3K/Akt/mTOR signalling pathway activation in

- patients with ER-positive, metachronous, contralateral breast cancer treated with hormone therapy. *Oncol Lett* 17, 1962–1968. <https://doi.org/10.3892/ol.2018.9759>
- Kang, J., et al. (2016). "Clinical significance of PIK3CA overexpression in breast cancer: A systematic review and meta-analysis." *Scientific Reports*, 6, 22780.
- Karakas, B., Bachman, K.E., Park, B.H., 2006. Mutation of the PIK3CA oncogene in human cancers. *Br J Cancer*. <https://doi.org/10.1038/sj.bjc.6602970>
- Kennecke, H., et al. (2020). "Metastatic behavior of breast cancer subtypes." *Journal of Clinical Oncology*, 38(1), 33-41. DOI: 10.1200/JCO.19.01558.
- Kennecke, H., et al. (2021). "Subtypes of breast cancer and their relationship with clinical outcomes." *Breast Cancer Research and Treatment*, 187(2), 295-309. DOI: [10.1007/s10549-021-05987-0](https://doi.org/10.1007/s10549-021-05987-0).
- Khoury, K., Tan, A.R., Elliott, A., Xiu, J., Gatalica, Z., Heeke, A.L., Isaacs, C., Pohlmann, P.R., Schwartzberg, L.S., Simon, M., Korn, W.M., Swain, S.M., Lynce, F., 2020. Prevalence of Phosphatidylinositol-3-Kinase (PI3K) Pathway Alterations and Co-alteration of Other Molecular Markers in Breast Cancer. *Front Oncol* 10. <https://doi.org/10.3389/fonc.2020.01475>
- Kołodziej, P., Nicoś, M., Krawczyk, P.A., Bogucki, J., Karczmarczyk, A., Zalewski, D., Kubrak, T., Kołodziej, E., Makuch-kocka, A., Madej-czerwinka, B., Płachno, B.J., Kocki, J., Bogucka-kocka, A., 2021. The correlation of mutations and expressions of genes within the pi3k/akt/mtor pathway in breast cancer—a preliminary study. *Int J Mol Sci* 22. <https://doi.org/10.3390/ijms22042061>
- Kumar, R., et al. (2015). "PIK3CA mutations in breast cancer: Implications for clinical practice." *The Oncologist*, 20(5), 568-574.
- Kumar, S., et al. (2021). "Recent advances in understanding the biology of breast cancer subtypes." *Journal of Oncology*, 2021, Article ID 123456. DOI: 10.1155/2021/123456.
- Kwan, M. L. et al. (2010). "Patterns of metastasis in breast cancer: A population-based analysis." *Breast Cancer Research and Treatment*.
- Lee, H. J., et al. (2022). "No significant association of PI3K overexpression with metastasis in luminal A breast cancer." *Breast Cancer Research*, 24(1), 65. DOI: 10.1186/s13058-022-01564-5.
- Lee, M.H., Cho, J.H., Kwon, S.Y., Jung, S.J., Lee, J.H., 2020. Clinicopathological characteristics of PIK3CA mutation and amplification in Korean patients with breast cancers. *Int J Med Sci* 17, 1131–1135. <https://doi.org/10.7150/ijms.44319>
- Li, H., Prever, L., Hirsch, E., Gulluni, F., 2021. Targeting pi3k/akt/mtor signaling pathway in breast cancer. *Cancers (Basel)*.

<https://doi.org/10.3390/cancers13143517>

- Lin, J., Ding, Q., Zhang, G., Yin, X., 2021. Study on PI3k gene expression in breast cancer samples and its association with clinical factors and patient survival. *Cell Mol Biol* 67, 321–327. <https://doi.org/10.14715/CMB/2021.67.4.36>
- Liu, Y., & Xu, J. (2020). "Clinical significance of PI3K expression in breast cancer: A systematic review and meta-analysis." *Breast Cancer Research and Treatment*, 182(1), 1-10.
- Lyman, G. H., & Kuderer, N. M. (2020). "The clinical impact of metastatic breast cancer: A review." *Journal of Clinical Oncology*, 38(15), 1727-1737.
- Madsen, R.R., Vanhaesebroeck, B., Semple, R.K., 2018. Cancer-Associated PIK3CA Mutations in Overgrowth Disorders. *Trends Mol Med*.
<https://doi.org/10.1016/j.molmed.2018.08.003>
- Martínez-Saéz, O., Chic, N., Pascual, T., Adamo, B., Vidal, M., González-Farré, B., Sanfeliu, E., Schettini, F., Conte, B., Brasó-Maristany, F., Rodríguez, A., Martínez, D., Galván, P., Rodríguez, A.B., Martinez, A., Muñoz, M., Prat, A., 2020. Frequency and spectrum of PIK3CA somatic mutations in breast cancer. *Breast Cancer Research* 22.
<https://doi.org/10.1186/s13058-020-01284-9>
- Mavratzas, A., Marmé, F., 2021. Alpelisib in the treatment of metastatic HR+ breast cancer with PIK3CA mutations. *Future Oncology* 17.
<https://doi.org/10.2217/fon-2020-0464>
- Milella, M., et al. (2015). "The PIK3CA pathway in breast cancer: Implications for therapy." *Nature Reviews Clinical Oncology*, 12(4), 210-223.
- Miller, T. W., et al. (2020). "Emerging therapies for luminal B breast cancer." *Breast Cancer Research and Treatment*, 180(1), 37-49. DOI: [10.1007/s10549-020-05600-x](https://doi.org/10.1007/s10549-020-05600-x).
- Miller, T. W., et al. (2021). "Targeting the PI3K pathway in breast cancer: Current status and future directions." *Breast Cancer Research and Treatment*, 179(3), 529-541. DOI: [10.1007/s10549-020-05932-6](https://doi.org/10.1007/s10549-020-05932-6).
- Mollon, L.E., Anderson, E.J., Dean, J.L., Warholak, T.L., Aizer, A., Platt, E.A., Tang, D.H., Davis, L.E., 2020. A Systematic Literature Review of the Prognostic and Predictive Value of PIK3CA Mutations in HR+/HER2- Metastatic Breast Cancer. *Clin Breast Cancer*.
<https://doi.org/10.1016/j.clbc.2019.08.011>
- Mosele, F., Stefanovska, B., Lusque, A., Tran Dien, A., Garberis, I., Droin, N., Le Tourneau, C., Sablin, M.P., Lacroix, L., Enrico, D., Miran, I., Jovelet, C., Bièche, I., Soria, J.C., Bertucci, F., Bonnefoi, H., Campone, M., Dalenc, F., Bachelot, T., Jacquet, A., Jimenez, M., André, F., 2020. Outcome and molecular landscape of patients with PIK3CA-mutated metastatic breast cancer. *Annals of Oncology* 31.

<https://doi.org/10.1016/j.annonc.2019.11.006>

- Müller, M., et al. (2021). "PI3K signaling and its role in the metastatic behavior of luminal breast cancer." *Cancer Research*, 81(12), 3167-3180. DOI: 10.1158/0008-5472.CAN-20-3643.
- Murray, M. et al. (2015). "Metastatic patterns of breast cancer: The role of estrogen receptor status." *Breast Cancer Research*.
- National Cancer Institute. (2023). "Breast Cancer: Statistics."
- Nguyen, T. T., et al. (2023). "Assessment of PI3K pathway activation and its clinical implications in luminal breast cancer: A retrospective study." *Oncology Letters*, 25(3), 139. DOI: 10.3892/ol.2023.13392.
- Park, J. E., et al. (2020). "Luminal B breast cancer: Challenges and new perspectives." *Cancers*, 12(12), 3534. DOI: 10.3390/cancers12123534.
- Peng, Y., Wang, Y., Zhou, C., Mei, W., Zeng, C., 2022. PI3K/Akt/mTOR Pathway and Its Role in Cancer Therapeutics: Are We Making Headway? *Front Oncol*. <https://doi.org/10.3389/fonc.2022.819128>
- PERABOI.2020
- Perou, C. M., et al. (2000). "Molecular portraits of human breast tumours." *Nature*, 406(6797), 747-752.
- Pevzner, A.M., Gaptulbarova, K.A., Tsyganov, M.M., Ibragimova, M.K., Vvedensky, A. V., Zhusina, Y.G., Pyankov, D. V., Korostylev, S.A., Litviakov, N. V., 2021. Investigation of somatic PIK3CA gene mutations in breast cancer patients. *Journal of B.U.ON*. 26.
- Prat, A., & Perou, C. M. (2020). "Deconstructing the molecular portraits of breast cancer." *Nature Reviews Clinical Oncology*, 17(3), 190-202. DOI: [10.1038/s41571-019-0245-0](https://doi.org/10.1038/s41571-019-0245-0).
- Prihantono, P., 2023. THE CANCER INCIDENCE AND MORTALITY IN MAKASSAR. *Ethiop J Health Sci*.
- Putra, P.K.B.S., Sumadi, I.W.J., Sriwidyani, N.P., Setiawan, I.B., 2019. Karakteristik Klinikopatologik Pasien Kanker Payudara dengan Metastasis Tulang di RSUP Sanglah pada Tahun 2014 - 2018. *e-CliniC* 8. <https://doi.org/10.35790/ecl.8.1.2020.27814>
- Rashmi Kumar, N., Berardi, R., Abraham, J., Aft, R., Agnese, D., Allison, K.H., Cancer Institute, S., Anderson, B., Burstein, H.J., Center, C., Chew, H., Dang, C., Elias, A.D., Giordano, S.H., Goetz, M.P., Goldstein, L.J., Hurvitz, S.A., Isakoff, S.J., Jankowitz, R.C., Javid, S.H., Krishnamurthy, J., Leitch, M., Mortimer, J., Patel, S.A., Pierce, L.J., Rosenberger, L.H., Sitapati, A., Lisa Smith, K., Lou Smith, M., Advocacy Network Hatem Soliman, R., Stringer-Reasor, E.M., Telli, M.L., Ward, J.H., Wisinski, K.B., Young, J.S., 2022a. NCCN Guidelines Version 4.2022 Breast Cancer.

- Rashmi Kumar, N., Berardi, R., Abraham, J., Aft, R., Agnese, D., Allison, K.H., Cancer Institute, S., Anderson, B., Burstein, H.J., Center, C., Chew, H., Dang, C., Elias, A.D., Giordano, S.H., Goetz, M.P., Goldstein, L.J., Hurvitz, S.A., Isakoff, S.J., Jankowitz, R.C., Javid, S.H., Krishnamurthy, J., Leitch, M., Mortimer, J., Patel, S.A., Pierce, L.J., Rosenberger, L.H., Sitapati, A., Lisa Smith, K., Lou Smith, M., Advocacy Network Hatem Soliman, R., Stringer-Reasor, E.M., Telli, M.L., Ward, J.H., Wisinski, K.B., Young, J.S., 2022b. NCCN Guidelines Version 4.2022 Breast Cancer.
- Schoenfeld, A. J., et al. (2021). "The prevalence and clinical implications of breast cancer subtypes." *Breast Cancer Research and Treatment*, 187(2), 345-357.
DOI: [10.1007/s10549-020-05840-5](https://doi.org/10.1007/s10549-020-05840-5).
- Setyorini, G., Sasmitae, L., Fianza, P.I., Kurnia, D., 2023. Hubungan sub tipe molekuler kanker payudara dengan grading histopatologi di RSUD M Yunus Bengkulu. *Intisari Sains Medis* 14, 519–524.
<https://doi.org/10.15562/ism.v14i2.1738>
- Shamsan E, Almezgagi M, Gamah M, Khan N, Qasem A, Chuanchuan L and Haining F (2024). "The role of PI3k/AKT signaling pathway in attenuating liver fibrosis: a comprehensive review. *Front. Med.* 11:1389329. doi: 10.3389/fmed.2024.1389329
- Siregar, K.B., Al Anas, M., 2023a. Unveiling bone metastasis: Exploring histological subtypes of breast cancer in Indonesia's tertiary referral hospital. *Cancer Treat Res Commun* 37. <https://doi.org/10.1016/j.ctarc.2023.100764>
- Siregar, K.B., Al Anas, M., 2023b. Unveiling bone metastasis: Exploring histological subtypes of breast cancer in Indonesia's tertiary referral hospital. *Cancer Treat Res Commun* 37. <https://doi.org/10.1016/j.ctarc.2023.100764>
- Smolarz, B., Zadrożna Nowak, A., Romanowicz, H., 2022. Breast Cancer—Epidemiology, Classification, Pathogenesis and Treatment (Review of Literature). *Cancers (Basel)*. <https://doi.org/10.3390/cancers14102569>
- Suarsana, I.W.G., Islam, A.A., Prihantono, P., Nelwan, B.J., 2022. Peran Poly-(ADP ribose) polymerase (PARP) dan Phosphatidylinositol 3-kinase (PI3K) Terhadap Terjadinya Kejadian Metastasis pada Kanker Payudara. *JBN (Jurnal Bedah Nasional)* 6, 30. <https://doi.org/10.24843/jbn.2022.v06.i01.p05>
- Sullivan, M. J., et al. (2020). "Impact of molecular subtyping on breast cancer treatment decisions." *Clinical Breast Cancer*, 20(5), 377-388. DOI: [10.1016/j.clbc.2020.05.001](https://doi.org/10.1016/j.clbc.2020.05.001).
- Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A., Bray, F., 2021. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality

- Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 71, 209–249.
<https://doi.org/10.3322/caac.21660>
- Sung, H., et al. (2024). "Global cancer statistics 2024: Global cancer burden." *CA: A Cancer Journal for Clinicians*, 74(1), 29-41. DOI: [10.3322/caac.21511](https://doi.org/10.3322/caac.21511).
- Tanner, M., et al. (2007). "PIK3CA mutations and hormone receptor status in breast cancer." *Clinical Cancer Research*, 13(10), 2902-2907.
- Torre, L. A., et al. (2022). "Breast cancer subtypes and their clinical implications: Insights from the 2022 World Health Organization classification." *Journal of Clinical Oncology*, 40(6), 657-667. DOI: 10.1200/JCO.21.01645.
- Turner, S., Chia, S., Kanakamedala, H., Hsu, W.C., Park, J., Chandiwana, D., Ridolfi, A., Yu, C.L., Zarate, J.P., Rugo, H.S., 2021. Effectiveness of Alpelisib + Fulvestrant Compared with Real-World Standard Treatment Among Patients with HR+, HER2–, PIK3CA-Mutated Breast Cancer. *Oncologist* 26. <https://doi.org/10.1002/onco.13804>
- Tzeng, R. C., et al. (2023). "Association of PI3K/AKT/mTOR pathway activation with metastatic potential in luminal breast cancer." *Oncology Reports*, 49(1), 42.
 DOI: 10.3892/or.2023.8356.
- Vasan, N., Toska, E., Scaltriti, M., 2019. Overview of the relevance of PI3K pathway in HR-positive breast cancer. *Ann Oncol*. <https://doi.org/10.1093/annonc/mdz281>
- Vernieri, C., Corti, F., Nichetti, F., Ligorio, F., Manglaviti, S., Zattarin, E., Rea, C.G., Capri, G., Bianchi, G. V., De Braud, F., 2020a. Everolimus versus alpelisib in advanced hormone receptor-positive HER2-negative breast cancer: Targeting different nodes of the PI3K/AKT/mTORC1 pathway with different clinical implications. *Breast Cancer Research*. <https://doi.org/10.1186/s13058-020-01271-0>
- Vernieri, C., Corti, F., Nichetti, F., Ligorio, F., Manglaviti, S., Zattarin, E., Rea, C.G., Capri, G., Bianchi, G. V., De Braud, F., 2020b. Everolimus versus alpelisib in advanced hormone receptor-positive HER2-negative breast cancer: Targeting different nodes of the PI3K/AKT/mTORC1 pathway with different clinical implications. *Breast Cancer Research*. <https://doi.org/10.1186/s13058-020-01271-0>
- Verret, B., Cortes, J., Bachelot, T., Andre, F., Arnedos, M., 2019. Efficacy of PI3K inhibitors in advanced breast cancer. *Ann Oncol*.
<https://doi.org/10.1093/annonc/mdz381>
- Vivanco, I., & Sawyers, C. L. (2020). "The phosphatidylinositol 3-kinase pathway in human cancer." *Nature Reviews Cancer*, 20(5), 274-290.
- Wang, L., Zhang, S., Wang, X., 2021. The Metabolic Mechanisms of Breast Cancer Metastasis. *Front Oncol*. <https://doi.org/10.3389/fonc.2020.602416>

- Wang, M., Li, J., Huang, J., Luo, M., 2020a. The Predictive Role of PIK3CA Mutation Status on PI3K Inhibitors in HR+ Breast Cancer Therapy: A Systematic Review and Meta-Analysis. *Biomed Res Int* 2020. <https://doi.org/10.1155/2020/1598037>
- Wang, M., Li, J., Huang, J., Luo, M., 2020b. The Predictive Role of PIK3CA Mutation Status on PI3K Inhibitors in HR+ Breast Cancer Therapy: A Systematic Review and Meta-Analysis. *Biomed Res Int* 2020. <https://doi.org/10.1155/2020/1598037>
- Wang, S., Liu, M., Lian, S., Liu, N., Zhang, G., Zhao, Q., Zhang, Y., Jian, L., 2020. Which Is the Most Appropriate PI3K Inhibitor for Breast Cancer Patients with or without PIK3CA Status Mutant? A Systematic Review and Network Meta-Analysis. *Biomed Res Int*. <https://doi.org/10.1155/2020/7451576>
- Wang, T., et al. (2016). "Estrogen receptor-mediated activation of the PI3K pathway in breast cancer." *Breast Cancer Research*, 18(1), 70.
- Wang, Y., et al. (2022). "Characteristics and clinical outcomes of luminal B breast cancer: Insights from a large cohort study." *Breast Cancer Research and Treatment*, 192(3), 677-688. DOI: [10.1007/s10549-021-06112-1](https://doi.org/10.1007/s10549-021-06112-1).
- WHO. (2024). "Breast cancer." [World Health Organization](https://www.who.int/news-room/fact-sheets/detail/breast-cancer)
- Yuan, T., et al. (2020). "Molecular characterization of luminal B breast cancer: Implications for targeted therapy." *Oncology Letters*, 20(4), 2201-2210. DOI: 10.3892/ol.2020.11550.
- Yuan, T., et al. (2020). "The role of molecular subtypes in breast cancer prognosis and treatment." *Journal of Molecular Medicine*, 98(3), 325-337. DOI: [10.1007/s00109-020-02031-1](https://doi.org/10.1007/s00109-020-02031-1).
- Zarychta, E., Ruszkowska-Ciastek, B., 2022. Cooperation between Angiogenesis, Vasculogenesis, Chemotaxis, and Coagulation in Breast Cancer Metastases Development: Pathophysiological Point of View. *Biomedicines*. <https://doi.org/10.3390/biomedicines10020300>
- Zhang, Z., Richmond, A., 2021. The Role of PI3K Inhibition in the Treatment of Breast Cancer, Alone or Combined With Immune Checkpoint Inhibitors. *Front Mol Biosci*. <https://doi.org/10.3389/fmolb.2021.648663>
- Zhao, Y., et al. (2022). "The impact of PI3K pathway activation on the progression and metastasis of luminal breast cancer." *Breast Cancer Research and Treatment*, 194(3), 659-670. DOI: [10.1007/s10549-021-06415-1](https://doi.org/10.1007/s10549-021-06415-1).

LAMPIRAN

ALAT DAN BAHAN

No	Alat	Bentuk Kemasan	Kegunaan
1	Alkohol 90%		Fiksasi Jaringan
2	Alkohol 70%		Fiksasi Jaringan
3	Alkohol 50%		Fiksasi Jaringan
4	Metanol		Fiksasi Jaringan
5	Pap Pen		Pulpen khusus IHC untuk memberi tanda pada slide

6	Etanol		Fiksasi sitologi cairan
7	Hidrogen Peroksida		Sebagai desinfektan
8	Hematosiklin		Sebagai bahan pewarnaan jaringan
9	Cairan Raterival		Pewarnaan Imunohistokimia
10	Slide IHC		Sebagai tempat jaringan diamati

11	Xylol		Sebagai bahan clearing sehingga jaringan memudahkan pengamatan
12	Deglass		Sebagai kaca penutup jaringan histopatologis
13	Entelan		Perekat glass coverglass dan Objek
14	Pisau Microtom		Pemotong jaringan mikro
15	Rak Pewarnaan		Tempat pengecatan jaringan histopatologis

16	Mikropipet		Memindahkan cairan dalam jumlah kecil dengan akurat
17	Reagen dan Primer PI3K		Pewarnaan Imunohistokimia

METODE PEMERIKSAAN

1. Seluruh pasien Kanker Payudara yang diikuti dalam penelitian dilakukan *informed consent* berupa penjelasan manfaat dan prosedur penelitian, apabila pasien setuju, maka diikuti dalam penelitian.
2. Dilakukan anamnesis untuk melengkapi pencatatan identitas serta hasil pemeriksaan sesuai dengan formulir penelitian yang telah disiapkan.
3. Pengambilan bahan operasi/biopsi jaringan payudara dari penderita dalam keadaan steril, kemudian dimasukkan ke dalam botol yang berisi larutan buffer formalin 10% selanjutnya dikirim ke Laboratorium Patologi Anatomi Fakultas Kedokteran Universitas Hasanuddin.
4. Pembuatan preparat jaringan. (Gambar 14.)
 - Potong blok paraffin dengan mikrotom pada ketebalan 3-4 μ



- Celupkan kedalam Waterbath



- Ambil potongan jaringan dengan slide lalu tiriskan



- Tulis pada slide kode sesuai blok paraffin dengan pensil



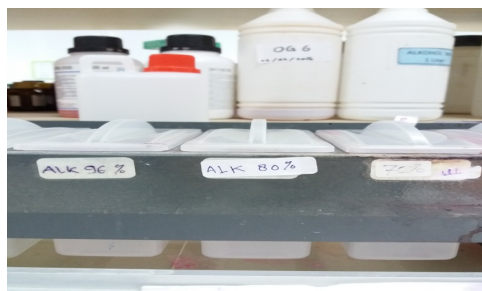
- Panaskan slide diatas Hot Plate selama 1 jam



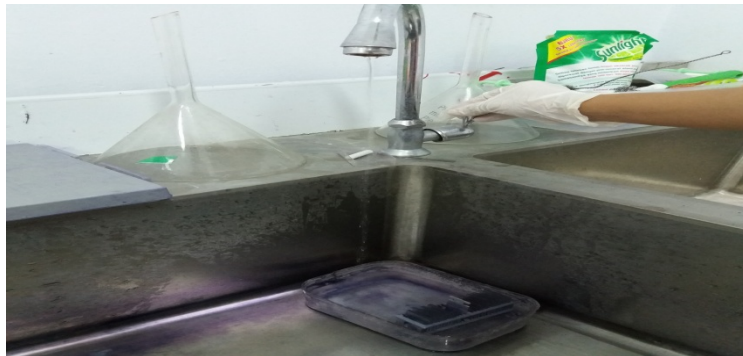
- Dinginkan slide lalu masukkan kedalam keranjang slide
- Deparafinasi (Xylol I, Xylol II, Xylol III) masing-masing 5 menit



- Rehidrasi (Alkohol 96%, Alkohol 80%, Alkohol 70%), masing-masing selama 5 menit



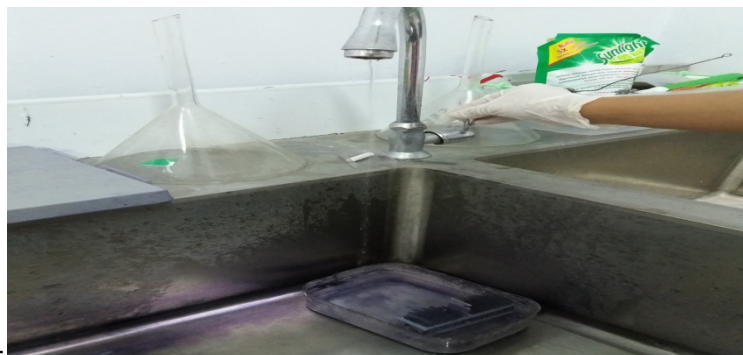
- Cuci air mengalir selama 5 menit



- Angkat dari air lalu masukkan slide kedalam larutan Blocking Endogen Peroksida, rendam selama 15 menit



- Cuci air mengalir selama 5 menit



- Masukkan keranjang berisi slide kedalam decloaking yang berisi larutan Antigen Retrieval Decloaking Chamber, lalu letakkan slide pada rack holder



- Masukkan rack holder kedalam decloaking, lalu tutup



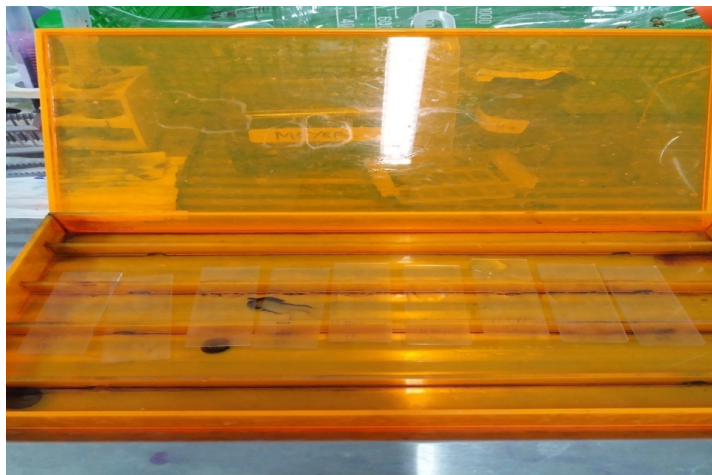
- Atur waktu yaitu selama 40 menit pada suhu 95 derajat.



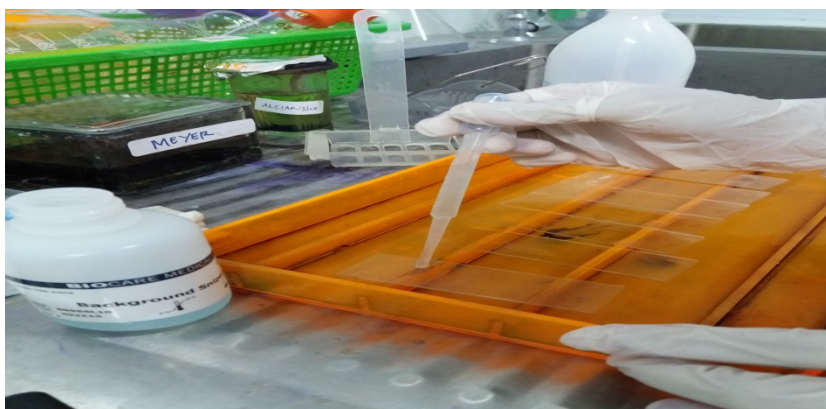
- Dinginkan, dengan mengeluarkan slide dari decloaking dan disimpan pada suhu ruangan
- Setelah dingin , cuci dalam larutan PBS 2x masing-masing selama 5 menit
 - Tandai slide dengan memberi lingkaran sekitar jaringan



- Atur slide pada baki slide



- Ambil satu per satu lalu tetesi Background Sniper lalu inkubasi selama 30 menit



- Buang larutan background sniper dengan cara ditiriskan pada tisu

- Tetesi Antibody Primer (reagen primer PI3KCA 110 α) lalu inkubasi selama 1 jam pada suhu ruang, cuci PBS 2x selama 5 menit



- Tetesi Trekkie Universal lalu diamkan selama 30 menit



- Tiriskan pada tissue lalu tetesi Trekkavidin-HRP lalu diamkan selama 30 menit



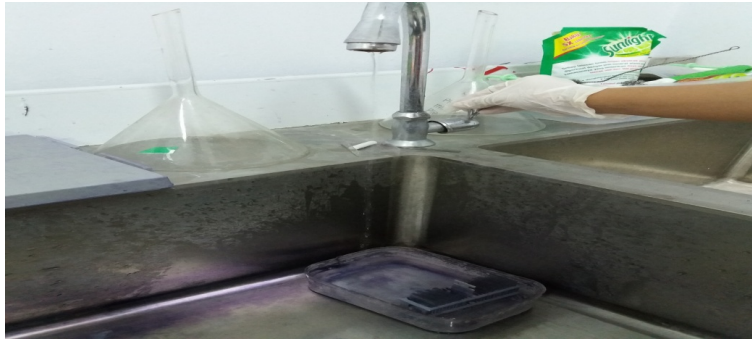
- Cuci PBS 2x dengan cara merendam slide selama 5 menit



- Sambil menunggu pencucian, buat larutan DAB dengan cara campurkan cromogen DAB 1 tetes + Substrat buffer 1 ml (dicampur dalam tabung bersih) lalu tetesi ke jaringan



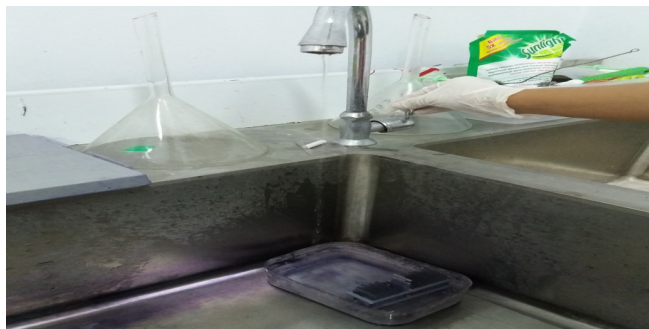
- Amati jaringan jika sudah menunjukkan warna coklat, langsung direndam ke dalam air selama 5 menit



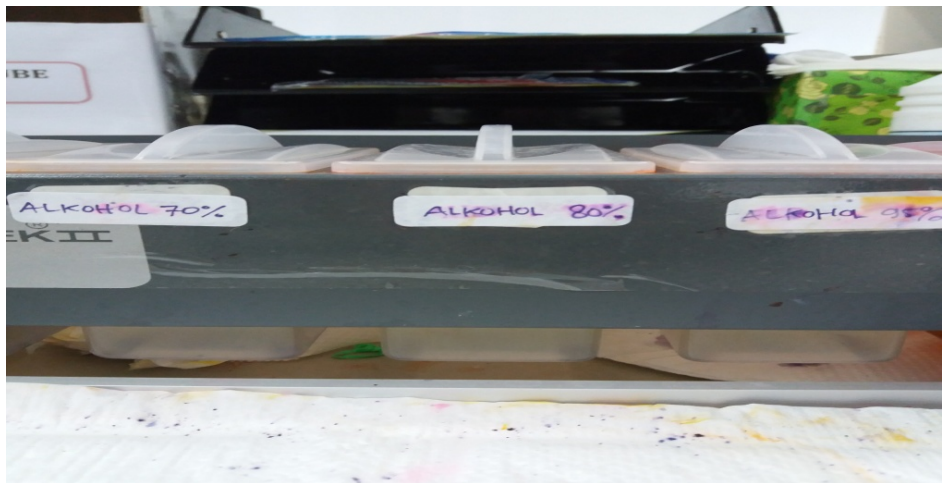
- Rendam dengan hematoxylin Meyer 5 menit



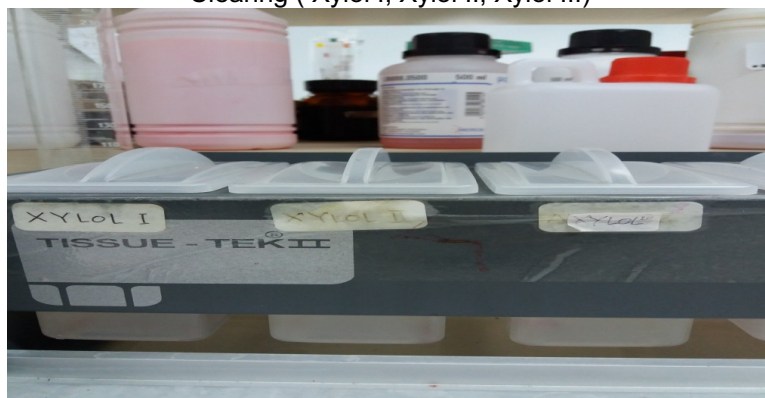
- Cuci air mengalir selama 5 menit



- Dehidrasi (Alkohol 70%, Alkohol 80%, Alkohol 96%) masing-masing 5 menit



- Clearing (Xylol I, Xylol II, Xylol III)



- Keringkan slide lalu tetesi dengan entelan lalu tutup dengan deck glass.
 - Amati di Mikroskop

PERSETUJUAN ETIK PENELITIAN



KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
UNIVERSITAS HASANUDDIN FAKULTAS KEDOKTERAN
KOMITE ETIK PENELITIAN UNIVERSITAS HASANUDDIN
RSPTN UNIVERSITAS HASANUDDIN
RSUP Dr. WAHIDIN SUDIROHUSODO MAKASSAR
Sekretariat : Lantai 2 Gedung Laboratorium Terpadu
JL PERINTIS KEMERDEKAAN KAMPUS TAMALANREA KM.10 MAKASSAR 90245.



Contact Person: dr. Agussalim Bukhari, M.Med, Ph.D, SpGK TELP. 081241850858, 0411 5780103, Fax : 0411-581431

REKOMENDASI PERSETUJUAN ETIK

Nomor : 767/UN4.6.4.5.31/ PP36/ 2022

Tanggal: 30 Nopember 2022

Dengan ini Menyatakan bahwa Protokol dan Dokumen yang Berhubungan Dengan Protokol berikut ini telah mendapatkan Persetujuan Etik :

No Protokol	UH22110697	No Sponsor Protokol	
Peneliti Utama	dr. Yusfitaria Alvina, Sp.B,MARS,MKes	Sponsor	
Judul Peneliti	HUBUNGAN EXPRESI PI3KCA DENGAN PROFIL CLINICOPATHOLOGICAL DAN METASTASIS PADA PASIEN KANKER PAYUDARA SUBTIPE LUMINAL		
No Versi Protokol	1	Tanggal Versi	16 Nopember 2022
No Versi PSP	1	Tanggal Versi	16 Nopember 2022
Tempat Penelitian	RS Univeritas Hasanuddin dan RSUP Dr. Wahidin Sudirohusodo Makassar		
Jenis Review	☐ Exempted ☐ Expedited ☒ Fullboard Tanggal 30 Nopember 2022	Masa Berlaku 30 Nopember 2022 sampai 30 Nopember 2023	Frekuensi review lanjutan
Ketua KEP Universitas Hasanuddin	Nama Prof.Dr.dr. Suryani As'ad, M.Sc.,Sp.GK (K)	Tanda tangan	
Sekretaris KEP Universitas Hasanuddin	Nama dr. Agussalim Bukhari, M.Med.,Ph.D.,Sp.GK (K)	Tanda tangan	

Kewajiban Peneliti Utama:

- Menyerahkan Amandemen Protokol untuk persetujuan sebelum di implementasikan
- Menyerahkan Laporan SAE ke Komisi Etik dalam 24 Jam dan dilengkapi dalam 7 hari dan Lapor SUSAR dalam 72 Jam setelah Peneliti Utama menerima laporan
- Menyerahkan Laporan Kemajuan (progress report) setiap 6 bulan untuk penelitian resiko tinggi dan setiap setahun untuk penelitian resiko rendah
- Menyerahkan laporan akhir setelah Penelitian berakhir
- Melaporkan penyimpangan dari prokol yang disetujui (protocol deviation / violation)
- Mematuhi semua peraturan yang ditentukan

DATA PRIMER PASIEN PENELITIAN

DAFTAR SAMPEL PENELITIAN													
NO	BM	NO PA	NAMA PASIEN	UMUR	PA	LETAK TUMOR	QMDT	ER	PR	HER2	IC-47	METASTASIS	LOKASI METASTASIS
1	133777	H19.1413	SA	69	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	1	POSTIF	POSTIF	NEGATIF			
2	104892	H20.502	NE	52	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	3	POSTIF	POSTIF	NEGATIF	HIGH		HEPAR, TULANG
3	126039	H20.027	NE	46	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	1	POSTIF	NEGATIF	NEGATIF			
4	135901	H20.265	HT	72	INVASIVE LOBULAR CARCINOMA MAMMAE	DEX TRA	2	POSTIF	POSTIF	NEGATIF	POSTIF		
5	135426	H20.173	Y	37	DUCTAL CARCINOMA INSITU	DEX TRA	1	POSTIF	POSTIF	NEGATIF			
6	137976	H20.339	KS	50	INVASIVE LOBULAR CARCINOMA MAMMAE BILATERAL	DEX TRA & SINISTRA	1						
7	136075	H20.322	ID	37	INVASIVE CARCINOMA MAMMAE OF NO SPECIAL TYPE	DEX TRA	2	POSTIF	POSTIF	NEGATIF			
8	138685	H20.376	WH	46	CARCINOMA MAMMAE DEX TRA	DEX TRA							
9	149716	H20.778	SI	49	INVASIVE CARCINOMA MAMMAE OF NO SPECIAL TYPE		1	POSTIF	POSTIF	NEGATIF	LOW	YA	HEPAR
10	153358	H21.065	RA	53	METASTASIS ADENOCARCINOMA								OTAK
11	151559	H21.074	SA	31	DUCTAL CARCINOMA INSITU	SINISTRA			POSTIF	POSTIF	NEGATIF	LOW	TIDAK
12	147875	H21.109	RI	52	MIXED INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE AND MUCINOUS CARCINOMA	DEX TRA	2	POSTIF	POSTIF	NEGATIF		YA	HEPAR
13	114579	H21.223	NS	62	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	NEGATIF	NEGATIF	HIGH	YA	
14	151490	H21.172	JN	45	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	HIGH	YA	
15	155704	H21.218	SY	34	INVASIVE LOBULAR CARCINOMA MAMMAE	SINISTRA	2	POSTIF	NEGATIF	NEGATIF	HIGH		
16	144882	H21.372	DO	54	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	1	POSTIF	POSTIF	NEGATIF	HIGH		
17	148828	H21.390	DA	42	METASTASIS ADENOCARCINOMA	SINISTRA			POSTIF	POSTIF	NEGATIF	HIGH	YA
18	72374	H21.450	RJ	62	METAPLASTIC CARCINOMA MAMMAE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW		
19	159955	H21.525	EP	54	MUCINOUS CARCINOMA MAMMAE WITH MICROCAPILLARY FEATURE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW		
20	170450	H21.974	SU	48	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW	YA	HEPAR
21	187610	H21.776	NG	70	INVASIVE LOBULAR CARCINOMA MAMMAE	SINISTRA	1	POSTIF	POSTIF	NEGATIF	HIGH		
22	183171	H22.920	RB	54	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	HIGH		
23	182963	H22.799	WO	47	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	2	POSTIF	POSTIF	NEGATIF	HIGH	YA	
24	171845	H22.668	JK	44	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW		
25	180928	H22.516	DK	48	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	1	NEGATIF	POSTIF	NEGATIF	HIGH		
26	181147	H22.583	JA	44	INVASIVE PAPILARY CARCINOMA MAMMAE SINISTRA	SINISTRA	2	POSTIF	POSTIF	NEGATIF	HIGH		
27	178821	H22.441	MM	43	INVASIVE LOBULAR CARCINOMA MAMMAE	DEX TRA	2	POSTIF	POSTIF	NEGATIF	HIGH		
28	71818	H22.318	ST	38	ADENOCARCINOMA MAMMAE MUCINOSUM	SINISTRA	1	POSTIF	POSTIF	NEGATIF	HIGH		
29	184572	H22.895	NT	46	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	2	NEGATIF	POSTIF	NEGATIF	HIGH	TIDAK	
30	171015	H22.434	BR	60	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	3	POSTIF	POSTIF	NEGATIF	HIGH	YA	
31	177488	H22.278	MY	41	INVASIVE BREAST CARCINOMA	SINISTRA	1	POSTIF	POSTIF	NEGATIF	HIGH	YA	PARU
32	170492	H22.022	SH	58	SECRETORY CARCINOMA	SINISTRA	2	POSTIF	POSTIF	NEGATIF	HIGH		
33	152510	H21.1027	RADJAH	58	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	2	POSTIF	POSTIF	NEGATIF	LOW	YA	TULANG
34	799715	P18.0058	RB	42	Invasive carcinoma mammas, NOS type	SINISTRA	2	POSTIF	POSTIF	NEGATIF		YA	HEPAR, TULANG
35	909897	P21.320	JK	45	Invasive carcinoma mammas, lateral of no special type	SINISTRA	2	POSTIF	POSTIF	NEGATIF	HIGH	YA	PARU, TULANG
36	932873	P21.2023	HE	62	Invasive breast carcinoma of NOS	HE	2	POSTIF	POSTIF	POSTIF	HIGH		
37	944665	P22.0070	UH	37	invasive carcinoma breast of no other special type	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW	YA	PARU,TULANG
38	958576	P22.3872	MR	46	invaif Ca breast carcinoma of No Special type	SINISTRA	3	POSTIF	POSTIF	NEGATIF			
39	955747	P20.0233	RS	45	INVASIVE CARCINOMA MAMMA MUCINOUS CARCINOMA MAMMA	SINISTRA	2	POSTIF	POSTIF	NEGATIF		YA	PARU/PLEURA
40	427566	P20.0330	HS	57	Adenocarcinoma mammas sinistra	SINISTRA	1	POSTIF	POSTIF	NEGATIF	HIGH		PARU
41	977455	P22.1740	IK	67	invasive carcinoma mammas of no special type	DEX TRA	2	POSTIF	POSTIF	NEGATIF	LOW		
42	969756	P22.1706	HN	56	invaif carcinoma	SINISTRA	3	POSTIF	NEGATIF	NEGATIF	LOW		
43	792073	P22.2674	HA	40	invasive breast carcinoma of no special type	DEX TRA	1	POSTIF	POSTIF	NEGATIF	LOW		
44	935498	P21.2364	LT	65	Invasive breast carcinoma of no special type	DEX TRA	3	POSTIF	NEGATIF	NEGATIF	HIGH		TULANG
45	767517	P19.4447	YF	51	Invasive ca mammas of no special type	DEX TRA	2	POSTIF	POSTIF	NEGATIF		YA	PARU, TULANG
46	886699	P19.3023	MR	64	Invasive lobular carcinoma mammas	SINISTRA	1	POSTIF	POSTIF	NEGATIF	LOW		
47	781133	P19.4731	HD	49	Invasive breast carcinoma	SINISTRA	2	NEGATIF	POSTIF	NEGATIF		YA	TULANG
48	885602	P19.3754	FL	42	Invasive ductal carcinoma mammas	SINISTRA	2	POSTIF	POSTIF	NEGATIF		YA	PARU
49	895551	P19.4522	RA	56	invasive ductal ca mammas	DEX TRA	2	POSTIF	NEGATIF	NEGATIF			
50	888636	P19.0121	HY	54	Invasive carcinoma mammas NOS	DEX TRA	2	POSTIF	NEGATIF	NEGATIF		YA	PARU
51	907210	P20.0245	HU	54	invasive carcinoma mammas, NST	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW	YA	PARU, TULANG
52	975206	P22.3030	SN	60	invasive carcinoma mammas	SINISTRA	3	POSTIF	POSTIF	NEGATIF	HIGH		TULANG
53	992064	P22.3783	JR	58									
54	989380	P22.3352	SS	40									
55	987840	P22.2719	NM										
56	981861	P22.2178	AR										
57	979904	P22.1813	SUKIRANI										
58	902837	P22.1739	JK	58	Invasive carcinoma mammas, NST	SINISTRA	3		POSTIF	POSTIF	NEGATIF	LOW	YA
59	683760	P22.1387	AR										
60	427894	P22.1324	SN										
61	945626	P21.2968	MD	61	Invaif Breast Carcinoma of no Special Type	SINISTRA	2		POSTIF	POSTIF	NEGATIF	LOW	
62	909382	P21.1566	ANTHO	57	invasive carcinoma mammas, NST	SINISTRA	1	POSTIF	POSTIF	NEGATIF	HIGH	YA	PARU
63	844501	P20.0071	AT	40	invaif ductal carcinoma mammas	DEX TRA	2						
64	884354	P19.2995	MP	56		SINISTRA							
65	98443	P19.2195	NT	63	Invasive carcinoma mammas, NST	DEX TRA	2	POSTIF	POSTIF	NEGATIF	LOW		
66	871333	P19.1226	HVA										
67	831108	P21.1359	SKD										
68	891882	P19.4880	SN	57	invasive carcinoma mammas, NST	SINISTRA	2	POSTIF	POSTIF	NEGATIF	HIGH	YA	TULANG
69	76185	H22.528	RT	38	ADENOCARCINOMA MAMMAE MUCINOSUM	SINISTRA	1	POSTIF	POSTIF	NEGATIF	LOW		TULANG
70	114121	H19.235	FT	44	INVASIVE LOBULAR CARCINOMA MAMMAE	SINISTRA	2	POSTIF	POSTIF	NEGATIF			
71	119990	H19.552	MB	46	INVASIVE LOBULAR CARCINOMA MAMMAE	SINISTRA	2	POSTIF	POSTIF	NEGATIF		YA	
72	173596	H22.550	MN	70	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	DEX TRA	2	POSTIF	POSTIF	NEGATIF	HIGH	YA	TULANG
73	172487	H19.879	FT	47	invasive carcinoma mammas, NST	DEX TRA	1	POSTIF	POSTIF	NEGATIF			
74	114149	H19.279	YL	44	invasive carcinoma mammas	DEX TRA	3	POSTIF	POSTIF	NEGATIF	HIGH		
75	85827	H19.450	NH	55	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	POSTIF	NEGATIF		YA	PARU, TULANG
76	14683	H20.475	SN	46	MUCINOUS CARCINOMA OF BREAST	DEX TRA	1	POSTIF	POSTIF	NEGATIF	HIGH		PARU
77	115269	H19.331	SL	68	invasive carcinoma mammas, NST	DEX TRA	2	POSTIF	POSTIF	NEGATIF		YA	TULANG
78	102105	H19.250	HU	49	ADENOCARCINOMA MAMMAE MUCINOSUM	SINISTRA	1	POSTIF	NEGATIF	NEGATIF			
79	81301	H22.024	SK	40	INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE	SINISTRA	2	POSTIF	POSTIF	NEGATIF	LOW		TULANG

FORM PERSETUJUAN SETELAH PENJELASAN (Informed Consent)

FAKULTAS KEDOKTERAN UNIVERSITAS HASANUDDIN
RSUP Dr. WAHIDIN SUDIROHUSODO

KOMISI ETIK PENELITIAN KESEHATAN

Sekretariat : JEMBATAN PENGHUBUNG LT. 2 RCC-IGD RSWS
JL. PERINTIS KEMERDEKAAN KAMPUS TAMAT ANREA KM.11, Makassar, Telp. (0411)586105 Ext. 8147

FORM PERSETUJUAN SETELAH PENJELASAN (PSP)
(Informed Consent Penelitian)

Saya bertanda tangan dibawah ini:

Nama :
Umur/Kelamin : 42 TAHUN / PEREMPUAN
Alamat : JENEPONTO
Bukti diri/KTP :

Setelah membaca/mendengar dan mengerti penjelasan yang diberikan mengenai tujuan, manfaat apa yang akan dilakukan pada penelitian ini, dengan ini saya menyatakan dengan sesungguhnya serta memberikan persetujuan secara sukarela tanpa paksaan dan bersedia menjalani/mengikuti penelitian mengenai Hubungan Ekspresi P13K dengan Grading dan Metastasis pada Kanker payudara Subtipe luminal

Saya mengerti bahwa dari semua hal yang dilakukan penelitian pada saya dapat menimbulkan masalah, namun saya percaya kemungkinan tersebut sangat kecil karena akan dilakukan oleh petugas yang terlatih.

Saya tahu bahwa keikutsertaan saya ini bersifat sukarela tanpa paksaan, sehingga saya bias menolak ikut atau mengundurkan diri dari penelitian ini tanpa kehilangan hak saya untuk mendapatkan pelayanan kesehatan. Juga saya berhak bertanya atau meminta penjelasan pada penelitian bila masih ada hal yang belum jelas atau masih ada hal-hal yang ingin saya ketahui tentang penelitian ini.

Saya juga mengerti bahwa semua biaya yang dikeluarkan sehubungan dengan penelitian ini, akan ditanggung oleh peneliti. Demikian juga biaya perawatan dan pengobatan bila terjadi hal-hal yang tidak diinginkan akibat penelitian ini, akan dibiayai oleh peneliti.

Saya percaya bahwa keamanan dan keahasiaan data penelitian akan terjamin dan saya dengan ini menyetujui semua data yang dihasilkan pada penelitian ini untuk dipublikasikan dalam bentuk lisan maupun tulisan.

Bila terjadi perbedaan pendapat dikemudian hari, kami akan menyelesaikan secara kekeluargaan.

	NAMA	TANDA TANGAN	TGL/BLN/TAHUN
Klien :			14 / 04 / 2023
Saksi 1 :			
Saksi 2 :			

Penanggung Jawab Penelitian:

Penanggung Jawab Medis:

Nama : Dr. Gusfita Alvina, SpB Nama : Dr. dr. William Hamdani, Sp.B Subsp. Onk (K)
Alamat :
Telepon :
Telepon :

REAGEN PI3K P110 Alpha Antibody


Datasheet

PI3 kinase p110 alpha antibody

Cat No. GTX100462

Host	Rabbit
Clonality	Polyclonal
Isotype	IgG
Application	WB, ICC/IF, IHC-P
Reactivity	Human, Mouse

Reference (2)

Package

100 µl, 25 µl

APPLICATION

Application Note

*Optimal dilutions/concentrations should be determined by the researcher.

Suggested dilution	Dilution
WB	1:500-1:3000
ICC/IF	1:100-1:1000
IHC-P	1:100-1:1000

Not tested in other applications.

Calculated MW 124 kDa. ([Note](#))

PROPERTIES

Form	Liquid
Buffer	1XPBS (pH7), 20% Glycerol
Preservative	0.025% ProClin 300
Storage	Store as concentrated solution. Centrifuge briefly prior to opening vial. For short-term storage (1-2 weeks), store at 4°C. For long-term storage, aliquot and store at -20°C or below. Avoid multiple freeze-thaw cycles.
Concentration	2.58 mg/ml (Please refer to the vial label for the specific concentration.)
Immunogen	Recombinant protein encompassing a sequence within the N-terminus region of human PI3 kinase p110 alpha. The exact sequence is proprietary.
Purification	Purified by antigen-affinity chromatography.
Conjugation	Unconjugated
Note	For laboratory use only. Not for any clinical, therapeutic, or diagnostic use in humans or animals. Not for animal or human consumption.



For full product information, images and publications, please visit our [website](#).

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GeneTex, Inc. (North America)

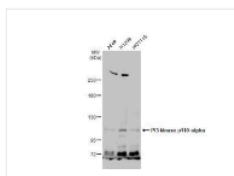
1-877-436-3839 (Toll-free) 1-949-309-2888 sales@genetex.com

GeneTex International Corporation (Global)

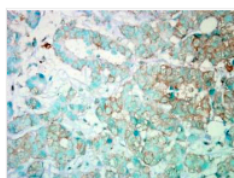
886-3-6208988 886-3-6208989 infoasia@genetex.com

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DATA IMAGES

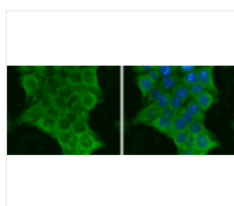
**GTX100462 WB Image**

Various whole cell extracts (30 µg) were separated by 5% SDS-PAGE, and the membrane was blotted with PI3 kinase p110 alpha antibody (GTX100462) diluted at 1:1000. The HRP-conjugated anti-rabbit IgG antibody (GTX213110-01) was used to detect the primary antibody, and the signal was developed with Trident ECL plus-Enhanced.

**GTX100462 IHC-P Image**

Immunohistochemical analysis of paraffin-embedded Human Breast Cancer, using PI3 kinase p110 alpha (GTX100462) antibody.

Antigen Retrieval: Trilogy™ (EDTA based, pH 8.0) buffer, 15min

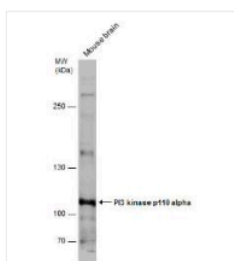
**GTX100462 ICC/IF Image**

PI3 kinase p110 alpha antibody detects PI3 kinase p110 alpha protein at cytoplasm by immunofluorescent analysis.

Sample: HCT 116 cells were fixed in 4% paraformaldehyde at RT for 15 min.

Green: PI3 kinase p110 alpha protein stained by PI3 kinase p110 alpha antibody (GTX100462) diluted at 1:500.

Blue: Hoechst 33342 staining.

**GTX100462 WB Image**

Mouse tissue extract (50 µg) was separated by 5% SDS-PAGE, and the membrane was blotted with PI3 kinase p110 alpha antibody (GTX100462) diluted at 1:3000. The HRP-conjugated anti-rabbit IgG antibody (GTX213110-01) was used to detect the primary antibody.



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HASIL SPSS**CROSSTABS**

```

/TABLES=GRADING METASTASIS BY PI3K
/FORMAT=AVALUE TABLES
/STATISTICS=CHISQ RISK
/CELLS=COUNT ROW
/COUNT ROUND CELL.

```

Crosstabs

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Comments	
Input	Active Dataset
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	Weight
Missing Value Handling	<none>
	Split File
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	N of Rows in Working Data File
	74
Missing Value Handling	Definition of Missing
	User-defined missing values are treated as missing.
Cases Used	Cases Used
	Statistics for each table are based on all the cases with valid data in the specified range(s) for all variables in each table.
Syntax	CROSSTABS /TABLES=GRADING METASTASIS BY PI3K /FORMAT=AVALUE TABLES /STATISTICS=CHISQ RISK /CELLS=COUNT ROW /COUNT ROUND CELL.
Resources	Processor Time
	00:00:00.01
	Elapsed Time
	00:00:00.00
Dimensions Requested	2
	Cells Available
	524245

Frequencies

Statistics

Lokasi Metastasis

N	Valid	29
	Missing	45
Mode		2
Range		4
Minimum		1
Maximum		5

Lokasi Metastasis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Paru-paru	8	10.8	27.6	27.6
	Tulang	10	13.5	34.5	62.1
	Hati	3	4.1	10.3	72.4
	Multiple Metastasis	1	1.4	3.4	75.9
	5	7	9.5	24.1	100.0
	Total	29	39.2	100.0	
Missing	System	45	60.8		
Total		74	100.0		

Frequencies

Statistics

		Usia	Status menopause	Jenis Histopatologi	Grading	PI3K	Subtipe	Metastasis
N	Valid	74	74	74	74	74	74	74
	Missing	0	0	0	0	0	0	0
Mode		2	1	1	2	1	2	2
Range		1	1	2	2	1	1	1
Minimum		1	1	1	1	1	1	1
Maximum		2	2	3	3	2	2	2

Frequency Table

Usia

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<50 tahun	35	47.3	47.3	47.3
	>50 tahun	39	52.7	52.7	100.0
	Total	74	100.0	100.0	

Status menopause

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Premenopause	38	51.4	51.4	51.4
	Menopause	36	48.6	48.6	100.0
	Total	74	100.0	100.0	

Jenis Histopatologi

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Invasif Ductal Carcinoma	57	77.0	77.0	77.0
	Invasif Lobular Carcinoma	12	16.2	16.2	93.2
	Carcinoma Mammarie mucinous	5	6.8	6.8	100.0
	Total	74	100.0	100.0	

Grading

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Low Grade Malignancy	15	20.3	20.3	20.3
	Moderate Grade Malignancy	30	40.5	40.5	60.8
	High Grade Malignancy	29	39.2	39.2	100.0
	Total	74	100.0	100.0	

PI3K

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Positif	42	56.8	56.8	56.8
	Negatif	32	43.2	43.2	100.0
	Total	74	100.0	100.0	

Subtipe

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Luminal A	25	33.8	33.8	33.8
	Luminal B	49	66.2	66.2	100.0
	Total	74	100.0	100.0	

Metastasis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Metastasis	29	39.2	39.2	39.2
	Tidak Metastasis	45	60.8	60.8	100.0
	Total	74	100.0	100.0	

Descriptives**Descriptive Statistics**

	N	Minimum	Maximum	Mean	Std. Deviation
Usia	74	1	2	1.53	.503
Status menopause	74	1	2	1.49	.503
Jenis Histopatologi	74	1	3	1.30	.591
Grading	74	1	3	2.19	.753
PI3K	74	1	2	1.43	.499
Subtipe	74	1	2	1.66	.476
Metastasis	74	1	2	1.61	.492
Valid N (listwise)	74				

Case Processing Summary

	Valid		Cases Missing		Total	
	N	Percent	N	Percent	N	Percent
GRADING * PI3K	74	100.0%	0	0.0%	74	100.0%
METASTASIS * PI3K	74	100.0%	0	0.0%	74	100.0%

GRADING * PI3K**Crosstab**

		PI3K		Total
		NEGATIVE	POSITIVE	
GRADING	LOW GRADE MALIGNANCY	Count	5	10
		% within GRADING	33.3%	66.7%
	MODERATE GRADE MALIGNANCY	Count	20	10
		% within GRADING	66.7%	33.3%
	HIGH GRADE MALIGNANCY	Count	7	22
		% within GRADING	24.1%	75.9%
Total		Count	32	42
		% within GRADING	43.2%	56.8%

Chi-Square Tests

	Value	df	Asymptotic Significance (2- sided)
Pearson Chi-Square	11.619 ^a	2	.003
Likelihood Ratio	11.889	2	.003
Linear-by-Linear Association	1.598	1	.206
N of Valid Cases	74		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.49.

Risk Estimate

	Value
Odds Ratio for GRADING (LOW GRADE MALIGNANCY / MODERATE GRADE MALIGNANCY)	a

a. Risk Estimate statistics cannot be computed. They are only computed for a 2*2 table without empty cells.

METASTASIS * PI3K**Crosstab**

			PI3K		Total
			NEGATIVE	POSITIVE	
METASTASIS	NON METASTASIS	Count	25	20	45
		% within METASTASIS	55.6%	44.4%	100.0%
	METASTASIS	Count	7	22	29
		% within METASTASIS	24.1%	75.9%	100.0%
Total	Count		32	42	74
	% within METASTASIS		43.2%	56.8%	100.0%

Chi-Square Tests

	Value	Df	Asymptotic Significance (2-sided)	Exact Sig. (2- sided)	Exact Sig. (1- sided)
Pearson Chi-Square	7.092 ^a	1	.008		
Continuity Correction ^b	5.870	1	.015		
Likelihood Ratio	7.349	1	.007		
Fisher's Exact Test				.009	.007
Linear-by-Linear Association	6.996	1	.008		
N of Valid Cases	74				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 12.54.

b. Computed only for a 2x2 table

P value 0.008. Maka Tolak H0 terima H1 berarti ada hubungan
H0 = tidak ada hubungan H1 = ada hubungan

Risk Estimate

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for METASTASIS (NON METASTASIS / METASTASIS)	3.929	1.397	11.048
For cohort PI3K = NEGATIVE	2.302	1.147	4.617
For cohort PI3K = POSITIVE	.586	.398	.862
N of Valid Cases	74		

- OR (Odd Ratio) Pasien kanker payudara dengan nilai PI3K positif akan beresiko mengalami metastasis 3,929 kali dibandingkan dengan PI3K nya negatif
- RR (Relative Risk) Pasien dengan kanker payudara dengan PI3K negatif memiliki peluang tidak metastasis sebesar 2,302 kali dibandingkan dengan yang PI3K nya positif
- RR (Relative Risk) Pasien dengan kanker payudara dengan PI3K negatif memiliki peluang metastasis sebesar 0,586 kali dibandingkan orang yang PI3K nya positif.

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Metastasis	3.929	1.397	11.048
For Cohort PI3K = Negative	2.302	1.147	4.617
For Cohort PI3K = Positive	.586	.398	.862
N of Valid Cases	74		

HAKI PENELITIAN

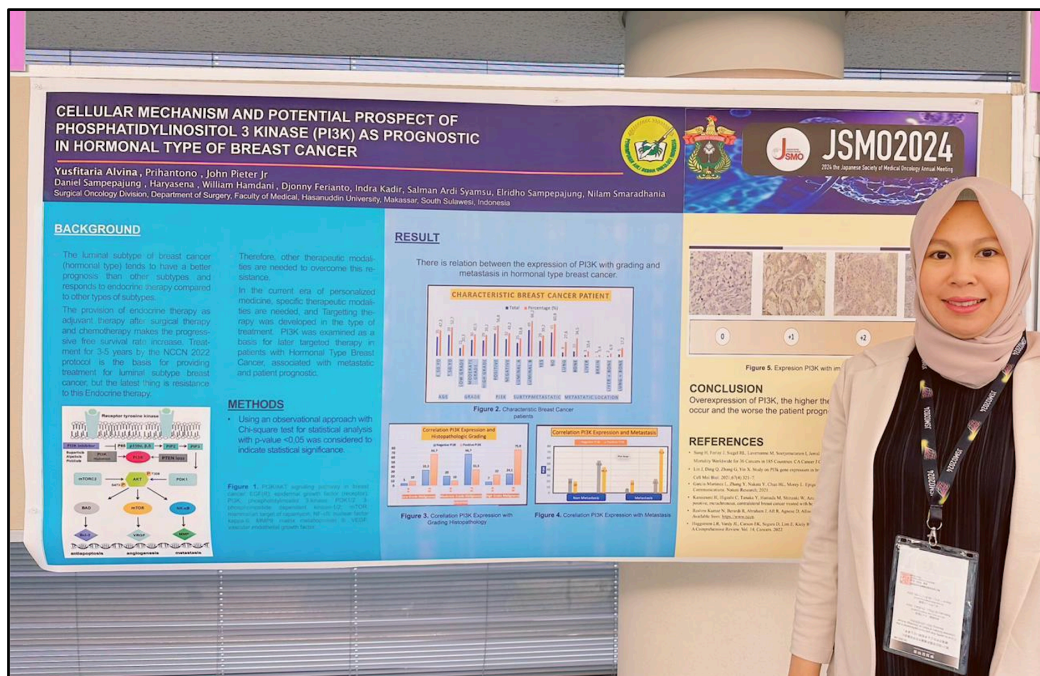
 REPUBLIK INDONESIA KEMENTERIAN HUKUM DAN HAK ASASI MANUSIA	
SURAT PENCATATAN CIPTAAN	
Dalam rangka perlindungan ciptaan di bidang ilmu pengetahuan, seni dan sastra berdasarkan Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta, dengan ini menerangkan:	
Nomor dan tanggal permohonan	: EC00202393778, 14 Oktober 2023
Pencipta	
Nama	: dr. Yusfitaria Alvina, SpB, MARS, M.Kes, Prof. Dr. dr. Prihantono, SpB, Subsp. Onk(K), M.Kes dkk
Alamat	: Jl. Pemuda No. 25, Tamalate, Makassar, Sulawesi Selatan, 90223
Kewarganegaraan	: Indonesia
Pemegang Hak Cipta	
Nama	: Universitas Hasanuddin
Alamat	: Jln. Perintis Kemerdekaan KM. 11, Tamalanrea, Makassar, Sulawesi Selatan 90245
Kewarganegaraan	: Indonesia
Jenis Ciptaan	: Karya Tulis (Artikel)
Judul Ciptaan	: THE CORELLATION PHOSPHATIDYLINOSITOL 3 KINASE (PI3K) AND CYCLIN DEPENDENT KINASE 4 (CDK4) EXPRESSION WITH GRADING AND METASTASIS IN LUMINAL BREAST CANCER
Tanggal dan tempat diumumkan untuk pertama kali di wilayah Indonesia atau di luar wilayah Indonesia	: 1 September 2023, di Makassar
Jangka waktu perlindungan	: Berlaku selama hidup Pencipta dan terus berlangsung selama 70 (tujuh puluh) tahun setelah Pencipta meninggal dunia, terhitung mulai tanggal 1 Januari tahun berikutnya.
Nomor pencatatan	: 000526733
adalah benar berdasarkan keterangan yang diberikan oleh Pemohon. Surat Pencatatan Hak Cipta atau produk Hak terkait ini sesuai dengan Pasal 72 Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta.	
a.n. MENTERI HUKUM DAN HAK ASASI MANUSIA Direktur Hak Cipta dan Desain Industri	
 Anggoro Dasananto NIP. 196412081991031002	
	
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LAMPIRAN PENCIPTA

No	Nama	Alamat
1	dr. Yusfitaria Alvina, SpB, MARS, M.Kes	Jl. Pemuda No. 25
2	Prof. Dr. dr. Prihantono, SpB, Subsp.Onk(K), M.Kes	Jl. Tun Abdul Razak. Perumahan Graha Lestari Makassar Blok D1 No.5
3	dr. John Sammy Leids Alfawim Pieter, SpB, Subsp.Onk(K)	Jl. Datumuseng No.3
4	dr. Salman Ardi Syamsu, SpB, Subsp.Onk(K)	Jl. Mapala A4 No.1
5	dr. Nilam Smaradhania, SpB, Subsp.Onk(K), M.Kes	Jl. Toddopuli Raya Timur, Komp Villa Surya Mas Blok J No. 21
6	Dr. dr. Berti Julian Nelwan, DFM, M.Kes, SpPA (K), SpF	Komp. Baruga Antang



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*has received Travel Award
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2024 the Japanese Society of
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Kiruj. Inst.

Hiroji Iwata, M.D., Ph.D.
Congress President
2024 the Japanese Society of Medical Oncology
Annual Meeting (JSMO2024)

JSM02024

President Hiroshi Iwata, M.D., Ph.D. Vice director and chief of Breast Oncology

Date **February 22 (Thu)–24 (Sat), 2024** Venue **Nagoya Congress Center**

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