

## **BAB 5**

### **KESIMPULAN DAN SARAN**

#### **5.1. Kesimpulan**

Berdasarkan hasil penelitian yang dilakukan dengan metode *literature review* dengan judul *Literature review* efektivitas dan keamanan penggunaan filgrastim pada pasien kanker payudara yang menjalani kemoterapi diperoleh kesimpulan sebagai berikut:

1. Terapi filgrastim terbukti efektif dalam menurunkan insiden demam neutropenia bila dilihat melalui tingkat ANC pasien dengan ANC *recovery* 2 hari.
2. Efek samping yang sering terjadi pada penggunaan terapi filgrastim dan pegfilgrastim adalah nyeri pada tulang (2,8-32%), sakit kepala (3,13-31,25%), nyeri otot (1,5-11%) dan kelelahan (12,3-23%).
3. Dosis pemberian terapi filgrastim yang efektif untuk mencegah neutropenia yang diakibatkan penggunaan obat kemoterapi myelosuppresan adalah 5 µg/kg/hari selama 7/10 hari yang diberikan 24 jam setelah pemberian obat kemoterapi sedangkan dosis pegfilgrastim yang efektif adalah 6 mg/ siklus kemoterapi

#### **5.2. Saran**

1. Diperlukan penelitian yang lebih lanjut mengenai toksisitas G-CSF sehingga dapat menurunkan efek samping yang sering terjadi pada pasien kanker payudara yang menerima terapi filgrastim atau pegfilgrastim.

2. Diharapkan farmasis dapat memberikan edukasi dan informasi mengenai efek samping yang sering terjadi akibat penggunaan G-csf sehingga dapat meningkatkan kualitas hidup pasien dan efektivitas terapi dapat dicapai secara maksimal.

## DAFTAR PUSTAKA

- Al-Tawiq, J. A., Hinedi, K., Khairallah, H., Saadeh, B., Abbasi, S., Noureen, M., Raza, S., Alkhatti, A. 2018, Epidemiology and Source of Infection in Patients with Fibrile Neutropenia : A Ten-year Longitudinal Study, *Journal of Infection and Public Health*, **12**: 364-366.
- Albrand, H., Kamioner, D., Leprêtre, S. 2016, 'Biosimilar Filgrastim In The Treatment Of Patients with Breast Cancer Undergoing Neutropenia-induced Chemotherapy: A Subanalysis Of The Next Study', American Association For Cancer Research. *Proceeding Of The Thirty-Eighth Annual CTRC-AACR San Antonio Breast Cancer*, San Antonio, Philadelphia, pp. 03-10.
- American Society of Clinical Oncology. 2019. Breast Cancer: Types of Treatment. Di akses pada tanggal 19 Oktober 2019, <http://cancer.net/cancer-types/breast-cancer/types-treatment>.
- American Cancer Society. 2019. *Breast cancer fact & figure 2017-2018*, Atlanta: American Cancer Society.
- American Cancer Society. 2019. About Breast Cancer. Diakses pada tanggal 5 Oktober 2019, <http://www.cancer.org/content/dam/CRC/PDF/Public/8577.00.pdf>.
- British Pharmacopoeia Commission, 2019, *British Pharmacopoeia 2019*, London: Stationary Office.
- Badan Pengawas Obat dan Makanan RI. 2016. Neukine. Diakses tanggal 19 Oktober 2019, <http://pionas.pom.go.id/obat-baru/neukine-cairan-injeksi-300-mcgml>.
- Barnett, C.M., Boster, B.L. dan Michaud, L.B. 2017, 'Breast Cancer', in Dipiro, J.T., Talbert, R.L., Yee, G.C., Matzke, G.R., Wells, B.G. and Posey L.M., *Pharmacotherapy: A Pathophysiologic Approach*, 10<sup>th</sup> ed., Mc-Graw Hill Companies, New York, pp 5703-5794.

- British Columbia Cancer Agency, 2019, *BC Cancer Manual Drug*, Vancouver: British Columbia Cancer Agency.
- Budiana, N. dan Febiani, M. 2017, Febrile Neutropenia pada Pasien Pasca-kemoterapi, *Indonesian Journal of Cancer*, **11(2)**: 77-82.
- Brayfield, A. (eds). 2018, *Martindale The Complete Drug Reference 38<sup>th</sup> edition Vol. 2*, Pharmaceutical Press, London, United Kingdom.
- Brito, M., Esteves, S., Andre, R., Isidoro, M., Moreira, A. 2015, Comparison Of Effectiveness Of Biosimiliar Filgrstim (Nivestim™) Reference Amgen Filgrastim And Pegfilgrastim In Febrile Neutropenia Primary Prevention In Breast Cancer Patients Treated With Neo(Adjuvant) TAC: a Non-interventional Cohort Study, *Support Care Cancer*, **24(2)**: 597-603.
- Celkan, T. dan Koc, B.S. 2015, 'Approach to the patient with neutropenia in childhood, *Turk Pediatri Ars* 2015, **50**: 136-44 diakses pada tanggal 19 Oktober 2019, <http://www.turkpediatriarsivi.com>.
- Chu, E., and Sartorelli, A.L. 2015, 'Cancer Chemotherapy' in Katzung, B.G. and Trevor, A.J., *Basic & Clinical Pharmacology*, 13<sup>th</sup> ed, McGraw-Hill Education, San Francisco, United States, pp 1242-1248.
- Clemons, M., Fergusson, D., Simos, D., Mates, M., Robinson, A., Califaretti, N., Zibdaw, L., Bahl, M., Raphael, J., Ibrahim, M., Fernandes, R., Pitre, L., Aseyev, O., Stober, C., Vandermeer, L., Saunders, D., Hutton, B., Mallick, R., Pond, G., Awan, A., Hilton, J. 2020. A Multicenter, Randomized Trial Comparing Schedules Of G-CSF (Filgrastim) Administration For Primary Prophylaxis Of Chemotherapy-induced Febrile Neutropenia In Early Stage Breast Cancer. *Annals of Oncology*, **31(7)**: 951-957
- Departemen Kesehatan RI. 2018. Profil Kesehatan Indonesia Tahun 2017. Diakses pada tanggal 2 Oktober 2019, [http://depkes.go.id<download<pusdatin](http://depkes.go.id/download<pusdatin).

- Dinas Kesehatan Provinsi Jawa Timur, 2017, *Profil Kesehatan Provinsi Jawa Timur 2016*, Surabaya: Dinas Kesehatan Provinsi Jawa Timur.
- Drugbank. 2019. Filgrastim Monograph. Diakses pada tanggal 19 Oktober 2019, <http://www.drugbank.ca/drug/DB00099>.
- European Cancer Information System. 2019. Breast Cancer Research. Diakses pada 2 oktober 2019, <http://www.ecis.jrc.ec.europa.eu>.
- Furuya, Y., 2019, Early Neutropenia On Day 8 Treatment With Adjuvant Docetaxel-based Chemoterapy In Early Breast Cancer Patient: Putative Mechanisms Within The Neutrophil Pool System, *Plos One Journal*, **14(4)**: e215576.
- Geredeli, C., Yasar, N., and Sakin, A. 2019, Germline Mutation in BRCA1 and BRCA2 in Breast Cancer Patient with High Genetic Risk in Turkish Population, *International Journal Of Breast Cancer*, **19**: 43-49.
- Garcia-Estevez, L., dan Moreno-Bueno, G. 2019, Updating The Role of Obesity And Cholesterol In Breast Cancer, *Breast Cancer Research*, **21**: 35-43.
- Hassan, B., Yussof, Z., dan Othman, S., 2015, ‘A Close Look At Neutropenia Among Cancer Patients-Risk Factor And Management’, in Rangel, L.B. and Silva, V., *Update On Cancer Treatment*, 1<sup>st</sup> ed., Intech Open, Kuala Lumpur, pp 1-23.
- Hima, N. A., Andrajati, R., Radji, M., 2021, Kejadian Demam Neutropenia pada Pasien Kanker Payudara setelah Menerima Regimen Kemoterapi TAC-G-CSF dan FAC di RSUP Dr. Hasan Sadikin Bandung, *Jurnal Farmasi Klinik Indonesia*, **10(1)**: 1-9.
- Ikatan Apoteker Indonesia, 2019, *ISO: Informasi Spesialit Obat Indonesia*, Jakarta: PT Isfi Penerbitan.
- Kementrian Kesehatan RI, 2016, *Formularium Nasional*, Jakarta: Departemen Kesehatan Republik Indonesia.
- Klustersky, J., deNaurois, J., Rolston, K., Rapoport, B., Maschmeyer, G. Aapro, M., Herrstedt, J. 2016, Management of Febrile Neutropenia: ESMO Clinical Practice Guidelines, *Annals of Oncology*, **27(5)**:111-118.

- Klastersky, J., Paesmans, M. 2013, The Multinational Association for Supportive Care in Cancer (MASCC) Risk Index Score: 10 Years Of Use for Identifying Low-risk Febrile Neutropenic Cancer Patients, *Support Care Cancer*, **21**: 1487-1495.
- Lucas, A.J., Olin, J.L. and Coleman, M.D. 2018, Management and Preventive Measure for Febrile Neutropenia, *Pharmacy and Therapeutics*, **43(4)**: 228-232.
- Lundqvist, E.A., Fujiwara, K. and Seoud, M. 2015, Principles of Chemotherapy, *International Journal of Gynecology and Obstetrics*, **131(2015)**: 146-149.
- Lyman, G. H., Abella, E., Pettengell, R. 2014, Risk Factor For Febrile Neutropenia Among Patients With Cancer Receiving Chemotherapy: A Systematic Review, *Critical Review in Oncology Hematology*, **90(3)**: 190-199.
- Mehta, H., Malandra, M., Corey, J. 2019, 'G-CSF and GM-CSF In Neutropenia', *The Journal Of Immunology*, **195(4)**: 1341-1349 diakses pada tanggal 4 Desember 2019.
- Najafi, S., Ansari, M., Kaveh, V., Haghghat, S. 2021, Comparing The Efficacy Side-effect Of PDLasta® (Pegfilgrastim) With PDGrastim® In Breast Cancer Patients: A Non-inferiority Randomized Clinical Trial, *BioMedical Central Cancer*, **21(1)**: 454-466.
- National Comprehensive Cancer Network. 2017, 'Myeloid Growth Factor version 2', *NCCN Clinical Practiced Guideline In Oncology*, **15(12)**: 1520-1541 diakses pada tanggal 5 Oktober 2019, [http://nccn.org/professionals/physician\\_gls/pdf/myeloid\\_growth.pdf](http://nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf).
- National Breast and Ovarian Cancer Center, 2009, Breast Cancer Risk Factor: A Review Evidence, Sydney: National Breast Cancer Center.
- Ramdhani, A., Ramdhani, M.A., Amin, A.S. 2014, Writing a Literature Review Research Paper: A Step-By-Step Approach, *International Journal of Basics and Applied Sciences*, **1(3)**: 47-56.

- Rajan, SS., Stearns, S.C., Lyman, G.H., Carpenter, W.R. 2011. Effect Of Primary Prophylactic G-CSF Use On Systemic Therapy For Elderly Breast Cancer Patients, *Breast Cancer Research and Treatment*, **130(1)**: 255-66
- Rasmy, A., Amal, A., Fotih, S., Selwi, W. 2016, Febrile Neutropenia in Cancer Patient: Epidemiology, Microbiology, Pathophysiology and Management, *Journal Cancer Prevention & Current Research*, **5(3)**: 165-173.
- Rastogi, S., Kalaiselvan, V., Ali, S., Guru, S.A., Sarwat, M., 2021, Efficacy And Safety Of Filgrastim And Its Biosimilar To Prevent Febrile Neutropenia In Cancer Patients: A Prospective Study And Meta-Analysis, *Multidisciplinary Digital Publishing Institute*, **10(10)**: 1069-1091.
- Rout, A., Parida, P., Das, P., Nayak, J., Mohanty, S. 2019, Comparison Of Pegfilgrastim In Management Of Chemotherapy Induced Neutropenia In Breast Cancer Patients, *Journal Of Medical Science And Clinical Research*, **7(1)**: 992-1003.
- Sachdeva, P.D., Patel, B.G., 2010, Drug Utilization Studies - Scope And Future Perspectives, *International Journal On Pharmaceutical And Biologcal Research*, **1(1)**: 11-17.
- Smith, T., Bohkle, K., Lyman, G., Carson, K., Crawford, J., Cross, S., Goldberg, J., Khatcheressian, J., Leighl, N., Perkins, C., Somlo, G., Wade, J., Wozniak, A., Armitage, J., 2015, Recommendation For The Use Of WBC Growth Factor: American Society Of Clinical Oncology Clinical Practice Guideline Update, *Journal Of Clinical Oncology*, **33(28)**: 3199-3212.
- Takuwa, H., Tsuji, W., Goto, T., Otsuji, T., Yotsumoto, F. 2019, Pegfilgrastim-induced Fatigue And Leukocytosis Following Dose Reduction In A Young Patients With Breast Cancer: A Case Report, *Molecular and Clinical Oncology*, **11(4)**: 371-375.
- Territo, M. 2018 Neutropenia (Agranulocytosis; Granulocytopenia), Diakses pada 2 Oktober 2019, <http://www.msmanuals.com/professional/hematogy-and-oncology/leukopenias/neutropenia.pdf>.

- The United States Pharmacopoeial Convention, 2018, *United States Pharmacopeia 41- National Formulary 36*, United Book Press, Rockville.
- Utomo, A., Widyati., Supono, A., Susilo, D.H., 2020, Efektivitas Profilaksis Primer Filgrastim Pada Pasien Kanker Payudara Terhadap Insiden Neutropenia, *Media Pharmaceutica Indonesiana (MPI)*, **3(1)**: 52-60.
- Widya, R.A., Nugroho, S., Winarsih, S., dan Yulistiani, 2019, Analysis Of ANC Levels After Filgrastim Therapy In Acute Leukimia Children With Neutropenia, *Folia Medica Indonesia*, **55(1)**: 10-16.
- Weddle, K.J. 2018, 'Breast Cancer', in Zeind, C.S. and Carvalho, M.G., *Applied Therapeutics The Clinical Use of Drugs*, 11<sup>th</sup> ed., Lipincott Williams and Wilkins, Philadelphia, pp 2044-2058.
- World Health Organization. 2019. Breast Cancer, Diakses pada 2 oktober 2019, <http://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en>.
- World Health Organization. 2017. Fact sheet about cancer, Diakses pada 2 Oktober 2019, <http://www.who.int/news-room/fact-sheet/detail/cancer>.
- Xu, F., Zhang, Y., Miao, Z., Zeng, X., Wu, B., Cai, L., Liu, J., Wang, S., Hu, X., Chen, Z., Yang, Q., Jiang, Z. 2019, Efficacy And Safety Mecapegfilgrastim For Prophylaxis Of Chemotherapy-induced Neutropenia In Patients With Breast Cancer: A Randomized, Multicenter, Active-controlled Phase III Trial, *Annals of Translatate Medicine*, **7(18)**: 482-493.
- Zehnder, J.L. 2018, 'Agent Use In Cytopenia; Hematopoietic Growth Factor', in Katzung, B.G. & Trevor, A.J., *Basic & Clinical Pharmacology*, 14<sup>th</sup> edn, McGraw-Hill Education, San Francisco United States.
- Zhang, W., Jiang, Z., Wang, L., Li, C., Xia, J. 2015, An Open-label, Randomized, Multicenter Dose-finding Study of Once-per-cycle Pegfilgrastim Versus Daily Filgrastim In Chinese Breast Cancer Patients Receiving TAC Chemotherapy, *Medical Oncology*, **(32)**: 147.