

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

Berdasarkan dari *literature review* pada 11 artikel ilmiah terkait efektivitas dan keamanan penggunaan kombinasi tenofovir disoproxil fumarate (TDF) pada pasien HIV- AIDS yang dilaksanakan mulai dari bulan Oktober 2021 – November 2021 dapat disimpulkan bahwa:

Penggunaan tenofovir disoproxil fumarate efektif digunakan untuk penekanan virus berkelanjutan untuk orang dewasa atau untuk odha yang akan memulai terapi ARV, dan dapat ditoleransi dengan baik. Efek samping yang perlu diwaspadai selama penggunaan regimen terapi tenofovir disoproxil fumarate adalah gangguan gastrointestinal yang berupa mual, muntah, diare, serta kemungkinan adanya gangguan ginjal, dan kepadatan tulang.

5.2 Saran

1. Perlu dilaksanakan penelitian lebih lanjut untuk mengetahui faktor resiko yang dapat memicu gangguan gastrointestinal, ginjal dan kepadatan tulang. Informasi tersebut dapat menjadi bekal penting bagi Dokter dan Farmasi dalam monitoring terapi tenofovir disoproxil fumarate.
2. Perlu dilaksanakan kajian *literature* dengan memperluas database yang digunakan sehingga artikel ilmiah yang digunakan dapat semakin banyak.
3. Perlu dilaksanakan meta analisa untuk melihat signifikansi hasil dari beberapa penelitian dengan karakteristik maupun luaran hasil yang sama untuk mendapatkan kesimpulan lebih objektif mengenai profil efektivitas dan keamanan penggunaan tenofovir disoproxil fumarate.

DAFTAR PUSTAKA

- Achhra, A. C., Nugent, M., Mocroft, A., Ryom, L., and Wyatt, C. M. 2016. Chronic kidney Disease and Antiretroviral Therapy in HIV-Positive Individuals: Recent Developments, *Current HIV/AIDS Reports*, **12(3)**: 149–157.
- Anderson, P. L., Kakuda, T. N. and Fletcher, C. V. 2017. 'Human Immunodeficiency Virus Infection', in *Pharmacotherapy: A Pathophysiologic Approach*, 10e. New York: McGraw-Hill Education.
- Arts, E. J. and Hazuda, D. J. 2012. HIV-1 Antiretroviral Drug Therapy, *Cold Spring Harbor Perspectives in Medicine*, **2(4)**: a007161.
- Avihingsanon, A., Gatechompol, S., Sapsirisavat, V., Thiansanguankul, W., Sophonphan, J., Thammajaruk, N., and Ruxrungtham, K. 2017. Efficacy and Safety of A Once-Daily Single Tablet Regimen of Tenofovir, Lamivudine, and Efavirenz Assessed at 144 Weeks Among Antiretroviral-Naïve And Experienced HIV-1 Infected Thai Adults, *International Journal of Infectious Diseases*, **61**: 89–96.
- Blunt, C. 2015. *Hierarchies of Evidence in Evidence-Based Medicine*.
- Bowen, L. N., Smith, B., Reich, D., Quezado, M., and Nath, A. 2016. HIV Associated Opportunistic CNS Infections: Pathophysiology, Diagnosis and Treatment, *Nature Reviews Neurology*, **12(11)**: 662–674.
- Chapman, D., McGovern, R. A., Thielen, A., Mo, T., Dong, W., Woods, C. K., and Harrigan, P. R. 2010. Population-Based V3 Genotypic Tropism Assay: A Retrospective Analysis Using Screening Samples From The A4001029 and MOTIVATE Studies, *Aids*, **24(16)**: 2517–2525.
- Chen, J., Chen, R., Shen, Y., Wei, H., Wang, X., Zhang, R., Hu, Z., Xie, R., Huang, Q., Wang, J., Liu, L., Qi, T., Wang, Z., Song, W., Tang, Y., Sun, J., and Lu, H. 2020. Efficacy and Safety Of Lower Dose Tenofovir Disoproxil Fumarate And Efavirenz Versus Standard Dose In HIV-Infected, Antiretroviral-Naïve Adults: A Multicentre, Randomized, Noninferiority Trial, *Emerging Microbes and Infections*, **9(1)**: 843–850.

- Cirincione, L. R. and Scarsi, Kimberly K. 2018. 'Drug Interactions in HIV: Nucleoside, Nucleotide, and Nonnucleoside Reverse Transcriptase Inhibitors and Entry Inhibitors'. In *Drug Interactions in Infectious Diseases: Antimicrobial Drug Interactions*. 4th edition. Humana Press.
- Cronin, P., Ryan, F. and Coughlan, M. 2008, Undertaking A Literature Review: A Step-by-step Approach, *British journal of nursing*, **17(1)**: 38–43.
- DiPiro, Joseph T. and PharmD, F. 2020. *Pharmacotherapy: A Pathophysiologic Approach*. 11th edition. Dipro.
- Donnell, D., Baeten, J. M., Kiarie, J., Thomas, K. K., Stevens, W., Cohen, C. R., McIntyre, J., Lingappa, J. R., Celum, C., and Partners in Prevention HSV/HIV Transmission Study Team. (2010). Heterosexual HIV-1 Transmission After Initiation Of Antiretroviral Therapy: A Prospective Cohort Analysis. *The Lancet*, 375(9731): 2092-2098.
- Flexner, C. 2014. *Simplification of Antiretroviral Therapy: A Necessary Step in The Public Health Response to HIV/AIDS in Resource-Limited Settings*, *Antivir Ther*, **19(3)**: 31–37.
- Eron, J., Hung, C. C., Baril, J. G., Slim, J., Falcó, V., Bogner, J., Maggiolo, F., Mills, A., Sievers, J., Man, C. Y., Urbaityte, R., Underwood, M., Tenorio, A. R. Pappa, K. A., Wynne, B., Koteff, J., Gartland, M., Smith, K. Y., and Boud, M. 2020. Brief Report: Virologic Response by Baseline Viral Load With Dolutegravir Plus Lamivudine vs Dolutegravir Plus Tenofovir Disoproxil Fumarate/Emtricitabine: Pooled Analysis, *Journal of Acquired Immune Deficiency syndromes* (1999), **84(1)**: 60–65.
- Feeney, E. R., & Mallon, P. W. (2011). HIV and HAART-Associated Dyslipidemia. *The Open Cardiovascular Medicine Journal*, **5**: 49.
- Gafni, R. I., Hazra, R., Reynolds, J. C., Maldarelli, F., Tullio, A. N., DeCarlo, E., and Zeichner, S. L. 2006. Enofovir Disoproxil Fumarate and An Optimized Background Regimen of Antiretroviral Agents As Salvage Therapy: Impact on Bone Mineral Density in HIV-Infected Children, *Pediatrics*, **118(3)**: e711–e718.
- Johnson, M., Kumar, P., Molina, J. M., Rizzardini, G., Cahn, P., Bickel, M., Mallolas, J., Zhou, Y., Morais, C., Kumar, S., Sklar, P., Hanna, G. J. Hwang, C., and Greaves, W. 2019. Switching to

- Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF) Maintains HIV-1 Virologic Suppression through 48 Weeks: Results of the DRIVE-SHIFT Trial, *Journal of Acquired Immune Deficiency Syndromes*, **81(4)**: 463–472.
- Jotwani, V., Atta, M. G. and Estrella, M. M. 2017. Kidney Disease in HIV: Moving Beyond HIV-Associated Nephropathy, *Journal of the American Society of Nephrology*, **28(11)**: 3142-3154.
- Katzung, B. G. and Trevor, A. J. 2015. '*Basic and Clinical Pharmacology*'. 13th Edition, McGraw Hill Education LANGE.
- Kemenkes RI. 2020. Pusat Data dan Informasi Kementerian Kesehatan RI.
- Kementerian Kesehatan Republik Indonesia. 2011. '*Pedoman Nasional Tatalaksana Klinis Infeksi HIV dan Terapi Antiretroviral Pada Orang Dewasa*'.
- Kementrian Kesehatan Republik Indonesia. 2012. *Pedoman Nasional Tatalaksana Klinis Infeksi HIV dan Terapi Antiretroviral pada Orang Dewasa dan Remaja*. Jakarta. Indonesia. Kementerian Kesehatan RI. Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan.
- Kementerian Kesehatan RI. 2014. *Rencana Aksi Nasional Pengendalian HIV-AIDS Tahun 2015-2019*.
- Kementerian Kesehatan Republik Indonesia. 2015. '*Program Pengendalian HIV AIDS dan PIMS Fasilitas Kesehatan Tingkat Pertama*'. Jakarta.
- Kemenkes RI. 2016. '*Program Pengendalian HIV AIDS dan PIMS di Fasilitas Kesehatan Tingkat Pertama: Petunjuk Teknis*', Direktorat Jenderal Pencegahan dan Pengendalian Penyakit.
- Kementerian Kesehatan Republik Indonesia. 2019. '*Profil Kesehatan Indonesia 2018*'. Jakarta: Kementerian Kesehatan Republik Indonesia.
- Kemenkes RI. 2020. '*Pusat Data dan Informasi Kementerian Kesehatan RI*'.
- Luo, W., Hong, H., Wang, X., McGoogan, J. M., Rou, K., & Wu, Z. (2018). Synthetic Drug Use And HIV Infection Among Men Who Have Sex with Men in China: A Sixteen-City, Cross-Sectional Survey. *PLoS ONE*, **13(7)**: e0200816.

- Maggiolo, F., Rizzardini, G., Raffi, F., Pulido, F., Mateo-Garcia, M. G., Molina, J. M., Ong, E., Shao, Y., Piontkowsky, D., Das, M., McNicholl, I., and Haubrich, R. 2019. Bone Mineral Density In Virologically Suppressed People Aged 60 Years Or Older With HIV-1 Switching From A Regimen Containing Tenofovir Disoproxil Fumarate To An Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Single-Tablet Regimen: A M, *The Lancet HIV*, **6(10)**: e655-e666.
- Mala, E. and Oberoi, A. 2015. Opportunistic Infections in Relation to CD4 Counts in Human Immunodeficiency Virus Seropositive Patients in A Tertiary Care Hospital in North India, *CHRISMED Journal of Health and Research*, **2(3)**: 99–202.
- Mayer, K. H., Molina, J. M., Thompson, M. A., Anderson, P. L., Mounzer, K. C., De Wet, J. J., DeJesus, E., Jessen, H., Grant, R. M., Ruane, P. J., Wong, P., Ebrahimi, R., Zhong, L., Mathias, A., Callebaut, C., Collins, S. E., Das, M., McCallister, S., Brainard, D. M., Brinson, C., Clarke, A., and Coll, P. 2020. Emtricitabine and Tenofovir Alafenamide Vs Emtricitabine and Tenofovir Disoproxil Fumarate For HIV Pre-Exposure Prophylaxis (DISCOVER): Primary Results From A Randomised, Double-Blind, Multicentre, Active-Controlled, Phase 3, Non-Inferiority Trial, *Lancet (London, England)*. **396(10246)**: 239-254.
- Meintjes, G., Moorhouse, M. A., Carmona, S., Davies, N., Dlamini, S., Van Vuuren, C., Manzini, T., Mathe, M., Moosa, Y., Nash, J., Nel, J., Pakade, Y., Woods, J., Van Zyl, G., Conradie, F., and Venter, F. 2017. Adult Antiretroviral Therapy Guidelines 2017, *Southern African Journal of HIV Medicine*, **18(1)**.
- Menteri Kesehatan RI. 2019. ‘Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MENKES/90/2019 Tentang ‘Pedoman Nasional Pelayanan Kedokteran Tata Laksana HIV’, *Sustainability (Switzerland)*, **11(1)**.
- Nasronudin. 2014. ‘HIV & AIDS Pendekatan Biologi Molekuler, Klinis, dan Sosial’. 2th Edition. Surabaya: Airlangga University Press.
- NCBI. 2021. Chemical Structure, National Center for Biotechnology Information.
- Ng, H. H., Stock, H., Rausch, L., Bunin, D., Wang, A., Brill, S., Gow, J., and Mirsalis, J. C. 2015. Tenofovir Disoproxil Fumarate: Toxicity, Toxicokinetics, and Toxicogenomics Analysis After 13 Weeks of

Oral Administration in Mice, *International Journal of Toxicology*, **34(1)**: 4–10.

- Nurmawati T, Sari Y.K, Hidayat A.P. 2020. ‘Evaluasi Jumlah CD4 Pada Penderita HIV/AIDS yang Menjalankan Program Pengobatan Antiretroviral (ARV)’. Blitar STIKes Patria Husada Blitar.
- Orkin, C., DeJesus, E., Sax, P. E., Arribas, J. R., Gupta, S. K., Martorell, C., Stephens, J. L., Stellbrink, H. J., Wohl, D., Maggiolo, F., Thompson, M. A., Podzamczar, D., Hagins, D., Flamm, J. A., Brinson, C., Clarke, A., Huang, H., Acosta, R., Brainard, D. M., Collins, S. E., and Martin, H. 2020. Fixed-Dose Combination Bictegravir, Emtricitabine, And Tenofovir Alafenamide Versus Dolutegravir-Containing Regimens For Initial Treatment Of HIV-1 Infection: Week 144 Results From Two Randomised, Double-Blind, Multicentre, Phase 3, Non-Inferiority Trials, *The Lancet HIV*, **7(6)**: e389-e400.
- Orkin, C., Squires, K. E., Molina, J. M., Sax, P. E., Sussmann, O., Lin, G., Kumar, S., Hanna, G. J., Hwang, C., Martin, E., and Teppler, H. 2021. Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (TDF) Versus Efavirenz/Emtricitabine/TDF in Treatment-naïve Adults with Human Immunodeficiency Virus Type 1 Infection: Week 96 Results of the Randomized, Double-Blind, Phase 3 DRIVE-AHEAD Noninferiority, *Clinical Infectious Diseases*, **73(1)**: 33–42.
- Pinsky, L. and Douglas, P. H. 2009. *The Columbia University Handbook on HIV and AIDS*. Columbia: Columbia University.
- Prazuck, T., Verdon, R., Le Moal, G., Ajana, F., Bernard, L., Sunder, S., Roncato-Saberan, M., Ponscarne, D., Etienne, M., Viard, J. P., Padeloup, T., Darasteanu, I., Pialoux, G., De La Blanchardière, A., Avettand-Fènoël, V., Parienti, J. J., and Hocqueloux, L. 2021. Tenofovir Disoproxil Fumarate And Emtricitabine Maintenance Strategy In Virologically Controlled Adults With Low HIV-1 DNA: 48 Week Results From A Randomized, Open- Label, Non-Inferiority Trial, *Journal of Antimicrobial Chemotherapy*, **76(6)**: 1564–1572.
- Qiao, Y. C., Xu, Y., Jiang, D. X., Wang, X., Wang, F., Yang, J., and Wei, Y. S. 2019. Epidemiological Analyses of Regional and Age Differences of HIV/AIDS Prevalence in China, *International Journal of Infectious Diseases*, **81**: 216–220.

- Sadaf, D. and Ahmad, Z. 2019. 'A Protocol on Antimicrobial Effectiveness of Adjunctive Disinfection Techniques During Root Canal Therapy in Patients with Pulp Necrosis and Apical Periodontitis, A Systematic Review & Meta-Analysis'.
- Samad, F., Saeed, Z., Hasan, Z., and Fahim, M. F. 2018. Evidence Based Medicine, *The Professional Medical Journal*, **25(6)**: 896–902.
- Sharon, M., Kesarkar, R., Oza, G., Pandey, S., Dahake, R., Mukherjee, S., and Chowdhary, A. 2012. Gold Nanoparticles: Effective As Both Entry Inhibitors And Virus Neutralizing Agents Against HIV, *J Microbiol Biotech Res*, **2(2)**: 276–283.
- Sörstedt, E., Carlander, C., Flamholc, L., Hejdeman, B., Svedhem, V., Sönnernborg, A., and Yilmaz, A. 2018. 'Effect of Dolutegravir in Combination with Nucleoside Reverse Transcriptase Inhibitors (NRTIs) on People Living with HIV Who Have Pre-Existing NRTI Mutations', *International journal of antimicrobial agents*, **51(5)**: 733–738.
- Steglitz, J., Warnick, J. L., Hoffman, S. A., Johnston, W., and Spring, B. 2015. Evidence-Based Practice, *International Encyclopedia of the Social & Behavioral Sciences*, **8**: 332–338.
- Suardana, I. B. K. 2017. Diktat Immunologi Dasar Sistem Imun, Universitas Udayana Denpasar.
- Suciati, R., Mujiati, M., and Novianti, N. 2018. Kendala Organisasi Berbasis Komunitas dalam Program Pencegahan dan Penanggulangan HIV/AIDS: Studi Kasus pada Dua LSM Peduli AIDS di Jakarta, *Jurnal Penelitian dan Pengembangan Pelayanan Kesehatan*, pp. 163–174.
- Oduola, T., Akinbolade, A. A., Oladokun, L. O., Adeosun, O. G., Bello, I. S., & Ipadeola, T. I. 2009. Lipid profiles in people living with HIV/AIDS on ARV therapy in an urban area of Osun State, Nigeria. *World Journal of Medical Sciences*, **4(1)**: 18-21.
- Tungsiripat, M., Kitch, D., Glesby, M. J., Gupta, S. K., Mellors, J. W., Moran, L., Jones, L., Alston, S. B. Rooney, J.F and Aberg, J. 2010. A Pilot Study to Determine The Impact on Dyslipidemia of Adding Tenofovir to Stable Background Antiretroviral Therapy: ACTG 5206, *AIDS*, **24(11)**: 1781–1784
- Toklu, H. Z. 2015. 'Promoting Evidence-Based Practice In Pharmacies, Integrated Pharmacy Research & Practice', p. 127.

- Wasey, J. O. 2019. PRISMA statement: *Plot Flow Charts According To The "PRISMA" Statement*.
- Wassner, C., Bradley, N. and Lee, Y. 2020. A Review and Clinical Understanding of Tenofovir: Tenofovir Disoproxil Fumarate Versus Tenofovir Alafenamide, *Journal of the International Association of Providers of AIDS Care (JIAPAC)*, **19**, p. 2325958220919231.
- World Health Organization. 2013. '*Consolidated guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection Summary of Key Features and Recommendations*'. Switzerland: World Health Organization.
- World Health Organization. 2015. '*Guideline on When to Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis For HIV*'. Switzerland: World Health Organization.
- World Health Organization. 2016. Global Health Sector Strategy on HIV 2016-2021 Towards Ending AIDS. Available at: <https://apps.who.int/iris/bitstream/handle/10665/246178/WHO-HIV-2016.05-eng.pdf>.
- Wong, A., Goldstein, D., Mallolas, J., DeJesus, E., Johnson, M., Molina, J. M., Pozniak, A., Rodgers, A., Teal, V., Hepler, D., Kumar, S., Sklar, P., Hanna, G. J., Hwang, C., Badshah, C., and Teppler, H. 2019. Efficacy and Safety of Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate (DOR/3TC/TDF) in Treatment-Naïve Adults With HIV-1 and Transmitted Nonnucleoside Reverse Transcriptase Inhibitor Resistance Mutations. *Journal of acquired immune deficiency syndromes* (1999). vol. **82(4)**: e47-e49.
- Wyatt, C. M. and Klotman, P. E. 2019. '*Overview of Kidney Disease in HIV-Positive Patients*'. Alphen aan den Rijn, South Holland: Up To Date, Wolters Kluwer.
- Yayasan Spiritia. 2017. Statistik Kasus HIV/AIDS di Indonesia. Retrieved September 25, 2017, from <http://spiritia.or.id/Stats/Statistik.php>.