8. Davis ID, Martin AJ, Stockler MR, Stephen Begbie, Kim N. Chi, Simon Chowdhury, et al.: Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. N Engl J Med 381 (2): 121-131, 2019.
9. Kyriakopoulos CE, Chen YH, Carducci MA, Liu G, Jarrard DF, Hahn NM, et al.: Chemohormonal Therapy in Metastatic Hormone-Sensitive Prostate Cancer: Long-Term Survival Analysis of the Randomized Phase III E3805 CHAARTED Trial. J Clin Oncol 36 (11): 1080-1087, 2018.
10. A. Oliver Sartor, Michael J. Morris, Richard Messman, Bernd J. Krause,: VISION: An International, Prospective, Open Label, Multicenter, Randomized Phase 3 Study of 177Lu-PSMA-617 in the Treatment of Patients With Progressive PSMA-positive Metastatic Castration-resistant Prostate Cancer (mCRPC), DOI: 10.1200/JCO.2021.39.15_-suppl.LBA4 Journal of Clinical Oncology 39, no. 18_suppl
11. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GA, Tomaszewski JE, Renshaw AA, Kaplan I, Beard CJ, Wein A.: Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA. 1998 Sep 16; 280(11):969-74.
12. Mi Jung Rho, Jihwan Park, Hyong Woo Moon, Chanjung Lee, Sejin Nam, Dongbum Kim, et al. Dr. Answer AI for prostate cancer: clinical outcome prediction model and service. August 2020 PLOS ONE - Article

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Sp02

GENERIC IMATINIB VS GLEEVEC

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The tyrosine kinase inhibitors (TKI) used in chronic myeloid leukemia (CML) treatment have dramatically changed the disease outcome. Glivec/Gleevec (branded imatinib) was the first TKI developed and has proven to be effective and safe in the long term (Hochhaus et al., 2017).

After the Glivec patent expired, many countries approved generic imatinib for CML treatment. Generic formulations are less expensive and, therefore, more affordable and available for limited resources countries.

Generic formulations of imatinib are used in India since the early 2000s (Parikh et al. 2002) and in most countries since 2016. In Brazil, generics replaced Glivec in 2013 in the first-line treatment patients with CML treated at the Public Health System.

There are still conflicting results about safety and efficacy in the published studies. Regarding pharmacological properties and bioequivalence, several studies compared branded with generic imatinib showing similarity (Malhotra et al., 2014; Arora et al., 2016, Natarajan et al., 2019).

Switching from branded to generic imatinib appears to maintain efficacy and safety (Skazan et al., 2019; Scalzulli et al., 2019; Dalle et al., 2019; Gemelli et al., 2020). However, some studies showed that patients reported new or worsening side effects after switching, primarily mild and moderate, such as nausea, edema, diarrhea, and fatigue (Abudalli et al., 2019, Scalzulli et al., 2020).

In the first-line setting, retrospective and prospective studies compared branded with generic imatinib. A recent study from China compared 236 pts treated with generic with 206 pts treated in first line with branded imatinib and did not find differences in toxicity, responses and overall survival (OS) and progression-free survival in 4 years (Dou, 2020). An updated analysis of a Brazilian study compared the outcomes of a retrospective cohort treated with Glivec with a prospective cohort treated with generics. There was a similar rate of major molecular responses and toxicity at 12 months, OS and PFS survival. (personnal communication).

In terms of health care costs, real-life studies demonstrated that generics use reduced the cost of CML treatment and are more cost-effective than branded imatinib. In the last ELN 2020 recommendations, generic imatinib is indicated as one of the options for first-line treatment in CML, if the drug has quality control of production, similar bioavailability, and efficacy (Hochaus 2020). Monitoring of the short and long-term efficacy and safety is essential.

References

1. Abou Dalle I, Kantarjian H, Burger J, et al. Efficacy and safety of generic imatinib after switching from original imatinib in patients treated for chronic myeloid leukemia in the United States. Cancer Med. 2019 Nov;8(15):6559-6565.
2. Arora R, Sharma M, Monif T, Iyer S. A Multi-centric Bioequivalence Trial in Ph+ Chronic Myeloid Leukemia Patients to Assess Bioequivalence and Safety Evaluation of Generic Imatinib Mesylate 400 mg Tablets. Cancer Res Treat. 2016 Jul;48(3):1120-9. doi: 10.4143/crt.2015.436. Epub 2016 Feb 12.
3. Eskazan AE, Elverdi T, Yalniz FF, et al. The efficacy of generic formulations of imatinib mesylate in the treatment of chronic myeloid leukemia. Leuk Lymphoma.
4. Gemelli M, Elli EM, Elena C, Iurlo A, et al. Use of generic imatinib as first-line treatment in patients with chronic myeloid leukemia (CML): the GIMS (Glivec to Imatinib Switch) study. Blood Res. 2020 Sep 30;55(3):139-145.
5. Hochhaus A, Larson RA, Guilhot F, et al (2017) Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. N Engl J Med 376:. https://doi.org/10.1056/NEJMoa1609324
6. Hochhaus, A., Baccarani, M., Silver, R.T. *et al.* European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia* **34,** 966–984 (2020). https://doi.org/10.1038/s41375-020-0776-2
7. Malhotra H, Sharma P, Bhargava S, et al. Correlation of plasma trough levels of imatinib with molecular response

in patients with chronic myeloid leukemia. Leuk Lymphoma. 2014 Nov;55(11):2614-9.
8. Natarajan H, Kumar L, Bakhshi S, et al. Imatinib trough levels: a potential biomarker to predict cytogenetic and molecular response in newly diagnosed patients with chronic myeloid leukemia. Leuk Lymphoma. 2019 Feb;60 (2):418-425.
9. Parikh P. Report of chronic myeloid leukemia in chronic phase from Tata Memorial Hospital, Mumbai, 2002-2008. Indian J Med Paediatr Oncol. 2013 Jul;34(3):164-7.
10. Scalzulli, E., Colafigli, G., Latagliata, R. *et al.* Switch from branded to generic imatinib: impact on molecular responses and safety in chronic-phase chronic myeloid leukemia patients. *Ann Hematol* **99,** 2773–2777 (2020).
11. Xuelin Dou, Yazhen Qin, Yueyun Lai, et al. Comparable Efficacy and Safety of Generic Imatinib and Branded Imatinib in Patients With Newly Diagnosed Chronic Myeloid Leukemia With a Consideration of Socioeconomic Characteristics: A Retrospective Study From a Single Center, Clinical Lymphoma Myeloma and Leukemia, Volume 20, Issue 6,2020,Pages e304-e315.

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Sp03

REVIEW OF NEW INDICATIONS – JOURNAL OF CLINICAL APHERESIS PERSPECTIVE

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Therapeutic apheresis is used to treat various types of disorders. The American Society for Apheresis (ASFA) publishes evidence-based guidelines every 3 years to assist apheresis practitioners in the rationale and management of apheresis patients and outlines basic technical specifications for procedures. However, the ASFA guidelines on the use of therapeutic apheresis published by the Journal of Clinical Apheresis only include indications that have enough evidence in the medical literature to provide apheresis recommendations. The guidelines do not include all the diseases that were reported in the medical literature or the ones that may be potentially treated by apheresis in the future. For new factsheet development, the committee responsible for developing the ASFA guidelines review requests from apheresis practitioners. One or more committee members will evaluate the available literature for evidence for the use of therapeutic apheresis in the disease or indication. A minimum of 10 cases, preferably by at least 2 groups, published in the last decade in peer-reviewed journals. In the current version of the ASFA guidelines (2019), the committee considered several potential new indications; however, none of them had enough evidence to be included in the current guidelines as new factsheets. Of note, the committee will review and issue interim factsheets for new indications if necessary before the release of the next version of the guidelines. Furthermore, due to COVID-19 pandemic, the next version of the ASFA Guidelines will be released in 2023.

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Sp04

HOW I TREAT NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS?

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Although Multiple Myeloma (MM) remains as a potential incurable disease, important advances are occurring in the knowledge of the disease as well as in the treatment and management and as result, the overall survival is significantly improving. This benefit is applicable along the course of the disease, but the first line of therapy is crucial because almost 100% of patients will receive the first line of therapy and this is the place where patients will get the maximum benefit.

The deeper the response, the longer the progression free and overall survival and patients therefore should receive the combinations of therapies resulting in the highest rates of complete response or undetectable measurable residual disease using sensitive techniques for its detection inside and outside of the bone marrow. This is applicable to both transplant and non-transplant eligible patients and this distinction should be based on biological age together with comorbidities more than in the classical chronological age.

For transplant eligible newly diagnosed MM patients, the treatment should include induction followed by high-dose therapy and autologous stem cell transplantation and maintenance. Induction should include three-drugs based combinations (proteasome inhibitor plus immunomodulatory drug and dexamethasone) and now it is possible to add the monoclonal antibodies targeting CD38 daratumumab to the combination of VTd. Melphalan at high doses followed by transplant has demonstrated to upgrade the response and it results as a complementary rather than an alternative strategy, although in the future risk cytogenetic together with the depth of response will be introduced in the algorithm and some patients could not need transplant. Consolidation might be considered if the response previously achieved could be upgraded and maintenance will be able to maintain the response achieved and under the lenalidomide platform, new combinations are emerging like lenalidomide plus either daratumumab or carfilzomib.

In the setting of transplant ineligible patients, the old standards of care bortezomib, melphalan and prednisone and continuous therapy with lenalidomide and dexamethasone have been replaced by daratumumab plus either VMP or Rd because the addition of daratumumab significantly improved the responses rate including complete responses and undetectable measurable disease but also the outcomes in terms of progression free and overall survival. Bortezomib, lenalidomide and dexamethasone is another combination maybe of choice for fit patients and the platform to which monoclonal antibodies anti CD38 are going to be added.

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