An oral drug for chronic lymphocytic leukemia.

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An oral drug for chronic lymphocytic leukemia.
JAAPA. 2020 Feb;33(2):51–53
Authors: Koehler A

Abstract
Ibrutinib is a new first-line drug for treating chronic lymphocytic leukemia (CLL), and could change frontline treatment of CLL from traditional IV chemotherapy to oral targeted therapy. Lymphocytosis often worsens with initiation of ibrutinib, but typically resolves over 6 to 18 months. Though patients generally tolerate ibrutinib well, the drug can cause adverse reactions including hypertension, atrial fibrillation, bleeding, and infections such as fungal pneumonia.

PMID: 31990837 [PubMed — in process]

High efficacy of venetoclax plus obinutuzumab in patients with complex karyotype and chronic lymphocytic leukemia.

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High efficacy of venetoclax plus obinutuzumab in patients with complex karyotype and chronic lymphocytic leukemia.
Blood. 2020 Jan 27::

PMID: 31990291 [PubMed — as supplied by publisher]

Cell Death Pathways in Lymphoid Malignancies.

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Cell Death Pathways in Lymphoid Malignancies.
Authors: Fletcher L, Nahinsky E, Liu T, Danilov A

Abstract
PURPOSE OF REVIEW: This review highlights the importance of the Bcl-2 family members in lymphoma cell survival and discusses the approaches to modulate their function, directly or indirectly, to advance lymphoma therapeutics.

RECENT FINDINGS: The balance of cell death versus survival is ultimately leveraged at the mitochondria. Mitochondrial outer membrane permeabilization (MOMP) is the critical event that governs the release of pro-apoptotic molecules from the intermembrane mitochondrial space. MOMP is achieved through the coordinated actions of pro- and anti-apoptotic Bcl-2 family member proteins. Recognition of functional alterations among the Bcl-2 family member proteins led to identification of tractable targets to combat hematologic malignancies. A new class of drugs, termed BH3 mimetics, was introduced in the clinic. Venetoclax, a Bcl-2 inhibitor, received regulatory approvals in therapy of chronic lymphocytic leukemia and acute myeloid leukemia. Alternative pro-survival Bcl-2 family proteins, in particular Mcl-1, have been successfully targeted in preclinical studies using novel-specific BH3 mimetics. Finally, anti-apoptotic Bcl-2 family members may be targeted indirectly, via interference with the pro-survival signaling pathways, e.g., phosphoinotiside-3 kinase, B-cell receptor signaling, and NF-κB.

PMID: 31989308 [PubMed — in process]
Application of a sequential multiple assignment randomized trial (SMART) design in older patients with chronic lymphocytic leukemia.

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Application of a sequential multiple assignment randomized trial (SMART) design in older patients with chronic lymphocytic leukemia.


Authors: Ruppert AS, Yin J, Davidian M, Tsiatis AA, Byrd JC, Woyach JA, Mandrekar SJ

Abstract

BACKGROUND: Ibrutinib therapy is safe and effective in patients with chronic lymphocytic leukemia (CLL). Currently, ibrutinib is administered continuously until disease progression. Combination regimens with ibrutinib are being developed to deepen response which could allow for ibrutinib maintenance (IM) discontinuation. Among untreated older patients with CLL, clinical investigators had the following questions: (i) does ibrutinib + venetoclax + obinutuzumab (IVO) with IM have superior progression-free survival (PFS) compared with ibrutinib + obinutuzumab (IO) with IM, and (ii) does the treatment strategy of IVO + IM for patients without minimal residual disease complete response (MRD– CR) or IVO + IM discontinuation for patients with MRD– CR have superior PFS compared with IO + IM.

DESIGN: Conventional designs randomize patients to IO with IM or IVO with IM to address the first objective, or randomize patients to each treatment strategy to address the second objective. A sequential multiple assignment randomized trial (SMART) design and analysis is proposed to address both objectives.

RESULTS: A SMART design strategy is appropriate when comparing adaptive interventions, which are defined by an individual’s sequence of treatment decisions and guided by intermediate outcomes, such as response to therapy. A review of common applications of SMART design strategies is provided. Specific to the SMART design previously considered for Alliance study A041702, the general structure of the SMART is presented, an approach to sample size and power calculations when comparing adaptive interventions embedded in the SMART with a time-to-event end point is fully described, and analyses plans are outlined.

CONCLUSION: SMART design strategies can be used in cancer clinical trials with adaptive interventions to identify optimal treatment strategies. Further, standard software exists to provide sample size, power calculations, and data analysis for a SMART design.

PMID: 31987270 [PubMed — in process]

Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies.

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Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies.


Authors: Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, Aune D, Greenwood DC, Chan DSM, Norat T

Abstract

BACKGROUND: To summarise the evidence on the associations between body mass index (BMI) and BMI in early adulthood, height, waist circumference (WC) and waist-to-hip ratio (WHR), and risk of lympho-haematopoietic cancers.

METHOD: We conducted a meta-analysis of prospective studies and identified relevant studies published up to December 2017 by searching PubMed. A random-effects model was used to calculate dose-response summary relative risks (RRs).

RESULTS: Our findings showed BMI, and BMI in early adulthood (aged 18-21years) is associated with the risk of Hodgkin’s and non-Hodgkin’s lymphoma (HL and NHL), diffuse large beta-cell lymphoma (DLBCL), Leukaemia including acute and chronic myeloid lymphoma (AML and CML), and chronic lymphocytic leukaemia (CLL) and multiple myeloma (MM). The summary RR per 5kg/m2 increase in BMI were 1.12 [95% confidence interval (CI): 1.05–1.20] for HL, 1.05 (95% CI: 1.03−1.08) for NHL, 1.11 (95% CI: 1.05–1.16) for DLBCL, 1.06 (95% CI: 1.03−1.09) for ML, 1.09 (95% CI: 1.03−1.15) for leukaemia, 1.13 (95% CI: 1.04−1.24) for AML, 1.13 (95% CI: 1.05−1.22) for CML and 1.04 (95% CI: 1.00−1.09) for CLL, and were1.12 (95% CI: 1.05–1.19) for NHL, 1.22 (95% CI: 1.09–1.37) for DLBCL, and 1.19 (95% CI: 1.03–1.38) for FL for BMI in early adulthood analysis. Results on mortality showed a 15%, 16% and 17% increased risk of NHL, MM and Leukaemia, respectively. Greater height increased the risk of NHL by 7%, DLBCL by 10%, FL by 9%, MM by 5% and Leukaemia by 7%. WHR was associated with increased risk of DLBCL by 12%. No association was found between higher WC and risk of MM.

CONCLUSION: Our results revealed that general adiposity in adulthood and early adulthood, and greater height may increase the risk of almost all types of lympho-haematopoietic cancers and this adds to a growing body of evidence linking body fatness to several types of cancers.

PMID: 31987269 [PubMed — in process]
This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of chronic lymphocytic leukemia. It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions. This summary is reviewed regularly and updated as necessary by the PDQ Adult Treatment Editorial Board, which is editorially independent of the National Cancer Institute (NCI). The summary reflects an independent review of the literature and does not represent a policy statement of NCI or the National Institutes of Health (NIH).

PMID: 26389470