do enfermeiro quanto às emergências oncológicas, aos sinais e sintomas para uma identificação precoce iniciando os cuidados adequados (Toneti et al, 2020). A SLT é uma emergência onco-hematológica grave, com grande morbimortalidade, que requer intervenções especificas, eficazes e rápidas. Para o diagnóstico da SLT o paciente pode apresentar alterações biológicas e clínicas, levando a um risco elevado de complicações neurológicas, cardíacas, renais e risco iminente de morte. Tal complicação se deve a deposição da degradação das micropartículas liberadas na corrente sanguínea, provenientes das células tumorais, depositando-se então, nos túbulos renais. A doença oncológica é a segunda enfermidade que mais mata no mundo, segundo o Instituto Nacional de Câncer (INCA). A SLT pode ocorrer de forma espontânea ou horas após o início do tratamento quimioterápico, causando uma desordem metabólica, caracterizada por hiperuricemia, hipercalemia, hiperfosfatemia, hipocalcemia e acidose metabólica, colaborando para o desenvolvimento de insuficiência renal aguda, ou até mesmo outras disfunções, podendo levar à morte (Santos et al, 2022). O manejo principal para profilaxia é com alopurinol e hidratação vigorosa e para tratamento utiliza-se além desses, hidratação endovenosa, rasburicase, cuidados intensivos e em casos selecionados diálise. Nesse sentido a qualificação, conhecimento e manejo adequado do profissional da enfermagem diante de uma emergência oncológica se torna primordial para uma assistência ideal ao paciente. O departamento de Hematologia realiza várias intervenções de acordo com a criticidade de cada paciente e por isso avaliamos diariamente os exames laboratoriais, realizamos hidratação endovenosa, monitorização dos sinais vitais e balanço hídrico rigoroso. Além desses cuidados administramos medicamentos de profilaxia e tratamento (Alopurinol e Rasburicase). **Conclusão:** Na nossa realidade evidenciamos a importância de ações de educação específica para melhor capacitação e atualização de conhecimentos dos enfermeiros referentes à SLT para um cuidado integral e eficaz do paciente.

https://doi.org/10.1016/j.htct.2023.09.357

GENOMIC EVOLUTION AND RESISTANCE TO PIRTOBRUTINIB IN COVALENT BTK-INHIBITOR PRE-TREATED CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS: RESULTS FROM THE PHASE I/II BRUIN STUDY

JR Brown [a], JA Woyach [b], K Patel [c], TA Eyre [d], Cy Cheah [e,f], P Ghia [g], W Jurczak [h], P Abada [i], WG Wierda [j], GFPN Presenter [k]

[a] *Dana-Farber Cancer Institute and Harvard Medical School, Boston, United States*
[b] *The Ohio State University Comprehensive Cancer Center, Columbus, United States*
[c] *Swedish Cancer Institute, Seattle, United States*
[d] *Churchill Cancer Center, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom*
[e] *Linear Clinical Research, Perth, Australia*
[f] *Sir Charles Gairdner Hospital, Perth, Australia*
[g] *Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milano, Italy*
[h] *Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland*
[i] *Loxo@Lilly, Indianapolis, United States*
[j] *University of Texas MD Anderson Cancer Center, Houston, United States*
[k] *Hospital Israelita Albert Einstein (HIAE), São Paulo, Brazil*

Objectives: Pirtobrutinib, a highly selective, non-covalent (reversible) BTKi, demonstrated efficacy in patients (pts) with CLL/SLL who were resistant to cBTKi. Mechanisms of resistance to pirtobrutinib have not been systematically analyzed. We explore the genomic evolution of pirtobrutinib resistance in cBTKi pre-treated CLL/SLL pts. **Materials and methods:** cBTKi pre-treated CLL pts treated with pirtobrutinib monotherapy in phase 1/2 BRUIN (NCT03740529) who subsequently developed disease progression (PD) were included. Targeted next-generation sequencing (NGS) of 74 relevant genes was centrally performed on peripheral blood mononuclear cells collected at baseline and at or near PD. Somatic mutations were reported with a limit of detection (LoD) of 5% variant allele frequency (VAF). Manual inspection of *BTK* exons with a LoD of 1% was performed to detect whether *BTK* mutations identified at PD were present at baseline at <5% VAF. **Results:** As of 29 July 2022, 49 cBTKi pre-treated CLL pts who progressed on pirtobrutinib had paired NGS data at baseline and PD. The median age was 69 y (36-86), median number of prior lines was 4 (1-10) and 41 pts (84%) had discontinued prior cBTKi due to PD. Pts received 1 or more cBTKi: ibrutinib (n = 44, 90%), acalabrutinib (n = 10, 20%) or zanubrutinib (n = 1, 2%). The ORR to pirtobrutinib (including PR-L) was 80%. The most common alterations at baseline were mutations in *BTK* (51%), *TP53* (49%), *ATM* (27%), *NOTCH1* (20%), *SF3B1* (18%), and *PLCG2* (10%). Among the 25 pts with ≥1 *BTK* mutation detected at baseline, *BTK* mutations included C481S (n = 23), C481R (n = 4), C481Y (n = 2), C481F (n = 1), T474I (n = 1). *BTK* C481 VAF decrease or complete clearance was observed at PD in nearly all pts (92%, 22/24, median VAF decrease=100%). At PD, 71% (35/49) of pts acquired ≥1 mutation, 55% (27/49) acquiring ≥1 *BTK* mutation. Among these 27 pts 36 acquired *BTK* mutations were identified; including gatekeeper mutations (T474I/F/L/Y, 17/49, 35%), kinase-impaired (L528W, 9/49, 18%) and variants of unknown significance (VUS) proximal to the ATP-binding pocket (6/49, 12%; V416L (n = 2), A428D (n = 2), D539G/H (n = 1), Y545N (n = 1)). Manual inspection for acquired *BTK* mutations at PD in baseline samples revealed that 9 mutations (8 pts) pre-existed at baseline at low VAFs (1-4%): 6 gatekeeper T474I/L, 2 kinase impaired L528W, 1 VUS A428D. These pts responded to pirtobrutinib (6/8, 75% ORR) and had received prior ibrutinib (n = 5) and acalabrutinib (n = 4). The most commonly acquired non-*BTK* mutations were *TP53* (7/49, 14%) and *PLCG2* (4/49, 8%). **Conclusions and discussion:** Pts who progressed on pirtobrutinib showed clearance of *BTK* C481 clones and the emergence or outgrowth of non-C481 clones, particularly gatekeeper T474 and kinase-impaired L528W mutations and other VUS. Many acquired *BTK* mutations were shown to pre-exist at baseline at low VAF, reflecting emergence on prior cBTKi. Importantly, these baseline kinase domain *BTK*

mutations did not preclude pirtobrutinib efficacy. Approximately half of pts did not acquire *BTK* mutations and 29% did not acquire any mutations in this targeted panel, suggesting alternate resistance mechanisms. Whether similar patterns of resistance would manifest if pirtobrutinib was utilized in earlier lines of therapy or prior to cBTKi treatment remains uncertain. This abstract was accepted and previously presented at EHA2023.

https://doi.org/10.1016/j.htct.2023.09.358

COMPARISON OF BLEEDING-RELATED EVENTS IN PATIENTS WHO RECEIVED PIRTOBRUTINIB WITH AND WITHOUT ANTITHROMBOTIC AGENTS

N Lamanna [a], CS Tam [b,c], W Jurczak [d], A Kontos [e], H Konig [f], AS Ruppert [f], DE Tsai [e], AAS Scheliga [g]

[a] *Herbert Irving Comprehensive Cancer Center, Columbia University, New York, United States*
[b] *Alfred Health, Melbourne, Victoria, Australia*
[c] *Monash University, Melbourne, Victoria, Australia*
[d] *Maria Sklodowska-Curie National Research Institute of Oncology, Krakow, Poland*
[e] *Loxo@Lilly, Indianapolis, United States*
[f] *Eli Lilly and Company, Indianapolis, United States*
[g] *Grupo Oncoclínicas, Rio de Janeiro, Brazil*

Objectives: Bruton tyrosine kinase inhibitors (BTKi) are associated with an increased risk of bleeding events. Pirtobrutinib, a non-covalent (reversible) BTKi FDA approved for treatment of R/R MCL after 2 lines of therapy including a BTKi, demonstrated efficacy and tolerability across multiple B-cell malignancies. The incidence of bleeding events in pts treated with pirtobrutinib and concomitant antithrombotic therapy have not been specifically reported. We analyze bleeding events in pts from BRUIN who received pirtobrutinib with antithrombotic therapy. **Material and methods:** Pts with B-cell malignancies (317 CLL, 166 MCL, 290 other) who enrolled in the open-label, multicenter Phase 1/2 BRUIN study (NCT03740529) were analyzed. Concomitant antithrombotic therapy (direct factor XA inhibitors, heparin anticoagulants, platelet aggregation inhibitors) at time of enrolment was permitted (excluding warfarin). Pirtobrutinib was administered once daily in 28-day cycles) until disease progression or discontinuation due to toxicity. Common Terminology Criteria for Adverse Events V5.0 were used to determine grade and type of bleeding events. Descriptive analyses were performed. **Results:** As of 29 July 2022, 773 pts received at least 1 pirtobrutinib dose of pirtobrutinib monotherapy, including 216 with concomitant antithrombotic therapy (median age: 72 years [IQR 65-77]and the proportion who were ≥75 years: 34%). Median time on pirtobrutinib with and without antithrombotic therapy was 10.6 (IQR 4.0-19.9) and 9.3 months (IQR 3.1-17.3). Any-grade bleeding events were reported in 44.9% (97/216) pts with antithrombotic therapy vs 32.5% (181/557) without. Most bleeding events (>90%) in both groups were grade ≤2. The most common bleeding events (≥3%) in pts with antithrombotic therapy were contusion (22.7%), hematuria (5.6%), epistaxis (5.1%), petechiae (3.7%), and hematoma (3.2%). Of the 6 (2.8%) pts on antithrombotic therapy with a grade3 bleeding event, 2 (0.9%) were deemed related to pirtobrutinib by investigators: an upper GI bleeding with anemia and a hemarthrosis from a knee injury (1each). Grade≥3 bleeding events occurred in 11 (2%) pts not taking antithrombotics. Any-grade hemorrhage/hematoma occurred in 13/79 (16.5%) pts who received direct factor XA inhibitors, 10/39 (25.6%) who received heparins and 18/112 (16.1%) who received platelet aggregation inhibitors (some received >1 class). Among pts with antithrombotic therapy, median time to onset of any-grade bleeding event was 8.1 weeks (IQR 2.6-24) and median duration of a bleeding event was 2.1 weeks (IQR 0.6-4.3). Among pts who received antithrombotic therapy, bleeding events required dose interruption of pirtobrutinib in 5 pts (2.3%) and no bleeding events led to dose reduction or permanent discontinuation of pirtobrutinib. **Conclusion and discussion:** Concomitant antithrombotic therapy with pirtobrutinib was associated with an increased rate of bleeding events relative to pirtobrutinib alone, though most events were grade ≤2. High-grade bleeding events were infrequent (<2%). This supports the safety of pirtobrutinib administration in pts requiring antithrombotic therapies. Previously presented at EHA 2023.

https://doi.org/10.1016/j.htct.2023.09.359

LEUCEMIA LINFOCÍTICA CRÔNICA ASSOCIADA A ANEMIA HEMOLÍTICA AUTOIMUNE COM RESPOSTA SOMENTE APÓS INTRODUÇÃO DE IBRUTINIBE

ASH Gallotti, SLBG Oliveira, ERM Neri, MM Garcia, NN Kloster, CM Freitas, ACP Silva, CE Gonçalves, VLP Figueiredo

Serviço de Hematologia, Hospital do Servidor Público do Estado de São Paulo (HSPE), Instituto de Assistência Médica ao Servidor Público Estadual (IAMSPE), São Paulo, SP, Brasil

Objetivo: Relatar caso de paciente com diagnóstico de leucemia linfocítica crônica (LLC) associada a anemia hemolítica autoimune (AHAI) por anticorpos quentes refratária a várias terapias, com resposta após início de ibrutinibe. **Metodologia:** Descrição de caso clínico realizado através da coleta de dados em sistema digital do HSPE. **Relato de caso:** Homem, 62 anos, com diagnóstico de LLC em 2013. Indicado tratamento com fludarabina, ciclofosfamida e rituximabe (FCR) devido anemia, com remissão da doença até o segundo semestre de 2022, quando iniciou acompanhamento no HSPE. Evoluiu com cansaço, linfonodomegalias, esplenomegalia, hemoglobina (Hb) 4,8 g/dL, leucócitos (Lt) 202 mil/mm^3 com 197 mil linfócitos, plaquetas 42 mil/mm^3, aumento de DHL e bilirrubina indireta, testes de Coombs direto e indireto positivos. Realizado tratamento com corticoide, seguido de imunoglobulina e rituximabe, porém sem melhora clínica e laboratorial. O mielograma evidenciou ausência de displasias e presença de 93% de linfócitos morfologicamente maduros,