achados confirmados em biópsia de medula óssea. A imunofenotipagem confirmou LLC e o estudo citogenético não mostrou alterações. Após resultado destes exames foi optado pelo tratamento com protocolo FCR, porém sem resposta depois de 2 ciclos, sendo substituído por ibrutinibe 420 mg ao dia. Em dez dias deste tratamento evoluiu com Hb acima de 7 g/dL, e após seis meses com Hb 12,7 g/dL, Lt 12.330/mm^3, linfócitos 7400/mm^3 e plaquetas 123 mil/mm^3. Segue em tratamento e assintomático. **Discussão:** A AHAI é um evento autoimune comum em pacientes com LLC, geralmente por produção de anticorpos do tipo IgG quentes direcionados contra as hemácias. Envolve células apresentadoras de antígenos, linfócitos B e T, citocinas pró-inflamatórias e produção dos autoanticorpos. O tratamento de condições autoimune associada a LLC é semelhante ao empregado caso ocorresse de forma espontânea. Diante da refratariedade aos tratamentos, deve ser considerado terapia direcionada para a LLC. Novos agentes terapêuticos vêm sendo estudados nesses casos, como os inibidores da tirosina quinase de Bruton (BTK). Esses atuam na inativação dos linfócitos B / plasmócitos, complemento, monócitos e macrófagos no baço e assim impedindo a destruição do eritrócito por citotoxicidade celular ou fagocitose no baço. Os dados mais extensos disponíveis até o momento são baseados em relatos de casos e em uma subanálise do estudo RESONATE de fase III (ibrutinibe vs. ofatumumabe em pacientes com LLC R/R) avaliando os efeitos desse agente em pacientes com AHAI e/ou PTI concomitantes. Nesses estudos, foi evidenciado melhora do quadro e manutenção da resposta durante um acompanhamento médio de 17,5 meses, corroborando com o caso clínico apresentado acima. **Conclusão:** A presença de AHAI é um evento autoimune comum em pacientes com LLC, com o uso de inibidor de BTK em relatos de estudos clínicos e neste caso apresentado demonstrando bons resultados e com a necessidade de seguimento para avaliação de permanência de resposta.

https://doi.org/10.1016/j.htct.2023.09.360

MATCHING-ADJUSTED INDIRECT COMPARISON OF PIRTOBRUTINIB VS VENETOCLAX CONTINUOUS MONOTHERAPY IN PATIENTS WITH RELAPSED/REFRACTORY CLL PREVIOUSLY TREATED WITH A COVALENT BTK INHIBITOR

O Al-Sawaf [a], M Jen [b], LM Hess [b], J Zhang [c], B Goebel [b], JM Pagel [d], TA Eyre [e], LYCGN Presenter [f]

[a] *University Hospital, Cologne, Germany*
[b] *Eli Lilly and Company, Indianapolis, United States*
[c] *TechData Services LLC, United States*
[d] *Swedish Cancer Institute, United States*
[e] *Churchill Cancer Center, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom*
[f] *Eli Lilly and Company, Brazil*

Objectives: Venetoclax-based therapy is a standard option for pts with relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) previously treated with a covalent BTK inhibitor (cBTKi). Pirtobrutinib is a highly selective, noncovalent (reversible) BTKi designed to overcome the pharmacologic limitations of cBTKi and restore BTK inhibition. Pirtobrutinib has demonstrated marked efficacy and a favorable safety profile. This unanchored MAIC was designed to estimate the treatment effect of pirtobrutinib (BRUIN, NCT03740529) vs venetoclax continuous monotherapy (NCT02141282) in pts with R/R CLL previously treated with a cBTKi. **Materials and methods:** Data from pts with R/R CLL previously treated with at least 1 cBTKi and without prior venetoclax exposure who received pirtobrutinib were analyzed (n = 146). Only 1 prospective trial of venetoclax (administered as a continuous monotherapy) for pts previously treated with a cBTKi (n = 91) was identified. Progression-free survival (PFS), overall survival (OS), investigator-assessed overall response rate (ORR), and grade≥3 treatment-emergent adverse events (TEAEs) regardless of attribution were evaluated. Pt-level data from the pirtobrutinib cohort were re-weighted to match the venetoclax cohort using method of moments approach, adjusting for well-established prognostic factors reported in both studies (age, IGHV mutation status, *TP53* aberrancy, del(17p), del(11q); number of prior lines of therapy, and reason for prior cBTKi discontinuation). KaplanMeier PFS and OS curves from the venetoclax trial were digitized (using WebPlotDigitizer) for time-to-event analyses. Fishers exact test was used to compare proportional outcomes (ORR, TEAEs); time-to-event outcomes (PFS, OS) were compared using Cox regression model and log-rank test. **Results:** The median age in pirtobrutinib and venetoclax cohorts was 66.5 and 66.0 years; all other prognostic factors were well matched in both cohorts. Median follow-up was 21.3 months and 14 months for the pirtobrutinib and venetoclax cohorts, respectively. PFS and OS were comparable with no significant differences noted for pirtobrutinib versus venetoclax (both $p > 0.05$). ORR was 80% for pirtobrutinib (inclusive of PR-L) vs 65% for venetoclax ($p = 0.01$). Grade ≥3 TEAEs reported in both trials indicated that febrile neutropenia, neutropenia, anemia, and thrombocytopenia were significantly lower for pirtobrutinib vs venetoclax in adjusted analyses (all $p < 0.01$). No differences were observed for pneumonia ($p = 0.06$) or for discontinuation due to TEAEs (3% vs 7%, $p = 0.32$) in adjusted analyses. Unadjusted results were consistent with the adjusted analyses. **Conclusions and discussion:** The efficacy of pirtobrutinib was comparable to continuously administered venetoclax monotherapy in pts with R/R CLL previously treated with a cBTKi. Pirtobrutinib was associated with improved ORR and favorable overall safety profile for most TEAEs vs venetoclax. This study raises questions regarding optimal treatment sequencing of pirtobrutinib and venetoclax in cBTKi-treated CLL, but the lack of prospective direct comparisons and limited long-term follow-up preclude definitive conclusions. Randomized Phase 3 studies of pirtobrutinib in pts with CLL are ongoing. Previously presented at EHA 2023.

https://doi.org/10.1016/j.htct.2023.09.361