resposta parcial. Após 5 meses do término do tratamento, evoluiu com acentuada dor em membro inferior esquerdo e dificuldade para deambular. PET-CT com recaída do linfoma, iniciado quimioterapia de resgate (R-GDP). Porém, pós o quarto ciclo, evoluiu com progressão de doença. Confirmado diagnóstico de LDGCB com nova biópsia da lesão. O paciente evoluiu com piora importante da dor, impossibilitando deambulação e atividades básicas diárias. Além disso, apresentou abscesso tumoral perineal com progressão para osteomielite. Foi realizada drenagem do abscesso tumoral, antibioticoterapia guiado por antibiograma e sessões de hiperbárica. Diante do caso de um paciente idoso, frágil e com infecção grave, foi optado por realizar a terapia de terceira linha com o protocolo Tafasitamabe 12 mg/kg e Lenalidomida 25 mg/dia. O paciente não apresentou reação alérgica ou outros efeitos adversos após infusão do tafasitamabe. Porém, após início do segundo ciclo, o mesmo evoluiu com náuseas grau 3, além de perda de apetite e edema em membros inferiores. Portanto, foi optado por reduzir a dose de Lenalidomida para 15 mg/dia, com melhora de todos os sintomas. O PET-CT após o segundo ciclo, demonstrou resposta parcial, com redução significativa da massa tumoral. Atualmente, encontra-se sem infecção ativa, deambulando sem apoio e sem dor, além de retorno as suas atividades diárias. **Discussão:** Este caso ilustra o potencial da combinação tafasitamabe + lenalidomida como uma opção terapêutica eficaz para pacientes adultos com LDGCB recidivado ou refratário, que não são elegíveis para TACT. A resposta observada no paciente, juntamente com a tolerabilidade do tratamento, destaca a importância de terapias direcionadas e imunomoduladoras no manejo de linfomas agressivos.

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LEUCEMIA LINFOIDE CRÔNICA E OUTRAS DOENÇAS LINFOPROLIFERATIVAS CRÔNICAS

SYSTEMATIC REVIEW AND META-ANALYSIS OF PHASE I AND II CLINICAL TRIALS: SAFETY AND EFFICACY OF ANTI-CD19 CAR-T CELL THERAPY IN COMBINATION WITH BRUTON'S TYROSINE KINASE INHIBITORS (BTKI) FOR CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

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Objective: Chronic lymphocytic leukemia (CLL) presents a variable evolution history, resulting in different treatment outcomes due to disease progression in lymph nodes, organs, or bone marrow. Complete Remission (CR) is rare, and the majority of patients experience disease recurrence after standard treatment. Recent studies portray the use of chimeric antigen receptor T (CAR-T) cells as promising in this area. Thus, the aim of the present study is to conduct a systematic review and meta-analysis evaluating the safety and efficacy of CAR-T cell immunotherapy concomitant with the use of Bruton tyrosine kinase inhibitors (BTKi) in relapsed/refractory (R/R) CLL. **Methods:** PubMed, Embase, Web of Science, and Cochrane databases were searched for trials published up to January 9, 2024. We included studies that reported outcomes from patients with R/R CLL who underwent CD19 CAR T-cell immunotherapy and received ibrutinib before, during, and after infusion. We used single proportion analysis with 95% confidence intervals under a random-effects model and heterogeneity was examined with the Cochran Q test and I(2) statistics. Endpoints were related to safety (prevalence of adverse events) and efficacy of the treatment (complete response rate, minimal residual disease, overall survival and progression-free survival). **Results:** Four studies were included, comprising phase I and II clinical trials, involving 62 patients aged between 40 and 77 years with R/R CLL who underwent CAR-T cell immunotherapy targeting CD19 concurrently with ibrutinib. The prevalence of Cytokine Release Syndrome (CRS) grades III and IV was 5.12% (95% CI 0.00 -12.54; $p = 0.25$), while that of neurotoxicity was 37.13% (95% CI 17.22-57.05; $p = 0.05$), with a predominance of grade III cases. The Complete Remission (CR) rate was 36.8% (95% CI 22.32-51.29; $p = 0.34$), and the prevalence of undetectable Minimal Residual Disease (MRD) was 68.2% (95% CI 41.87-94.52; $p < 0.01$). In studies reporting patients' overall survival (OS) rate at 1 year, it was 82.76% (95% CI 63.47-100.00; $p = 0.06$), and the progression-free survival (PFS) rate at 1 year was 64.2% (95% CI; 31.42 - 96.99; $p < 0.01$). Significant results were revealed in the analyses of PFS, MRD, and OS, suggesting a potential real efficacy in improving the survival of CLL patients. **Discussion:** The safety profile of CAR-T cell therapy with BTK inhibitors in R/R CLL patients appears manageable, with a low prevalence of severe CRS but a relatively higher occurrence of grade III neurotoxicity. However, the efficacy outcomes are promising, with a significant CR rate of 36.8% and a high prevalence of undetectable MRD at 68.2%. Additionally, the one-year OS and PFS rates of 82.76% and 64.2%, respectively, highlight the potential clinical benefit of this combination therapy. While acknowledging the study's limitations, including sample size, heterogeneity, and phase 1 and 2 trials, these promising findings support the potential feasibility of CAR-T cell therapy with BTK inhibitors in R/R CLL. **Conclusion:** These findings indicate a reduction in disease progression, highlighting the potential clinical benefit of this approach. They suggest that CAR-T cell therapy in combination with BTK inhibitors is well tolerated and may increase survival and prevent disease progression in patients with R/R CLL. However, continuing current clinical trials with larger samples is necessary to further validate the results presented in this study with greater reliability.

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