LETTER TO THE EDITOR
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Defying the Odds: Successful Rescue with Teclistamab in a Case of Ultra-High-Risk Relapsed/Refractory Multiple Myeloma Transforming to Secondary Plasma Cell Leukemia Post-BCMA CAR T Failure

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To the editor,

A 67-year-old male with a known diagnosis of IgG Kappa multiple myeloma (MM) and high-risk cytogenetic abnormalities—deletion 17p and gain of 1q—presented with biochemical and clinical relapse. The patient was initially diagnosed with MM in February 2017. He received induction chemotherapy comprising four cycles of Bortezomib, Cyclophosphamide, and Dexamethasone (VCd regimen). The post-induction response assessment demonstrated complete remission (CR). Subsequently, he underwent consolidation with autologous hematopoietic stem cell transplantation (ASCT) in July 2017. Following ASCT, the patient was commenced on lenalidomide maintenance therapy.

He remained in sustained CR until March 2022, when he experienced his first relapse. At that time, treatment was initiated with a regimen of Bortezomib, Pomalidomide, and Dexamethasone (VPd), resulting in re-establishment of CR, which was maintained until August 2023. The patient then experienced a second relapse and was commenced on Daratumumab, Carfilzomib, and Dexamethasone (DKd regimen). He again achieved CR, which was sustained for one year.

In August 2024, the patient had a third relapse and was subsequently referred to our institute for consideration of B-cell maturation antigen (BCMA)-directed chimeric antigen receptor T-cell (CAR T-cell) therapy.

Prior to CAR T-cell infusion, the patient received one cycle of bridging chemotherapy with the oral Melphalan, Thalidomide, and Prednisolone (MPT) regimen. The patient was subsequently administered BCMA-directed CAR T-cell therapy, manufactured by Abgentil Biomedical (Malaysia) in collaboration with ProMab Biotechnologies Inc. (USA), at a dose of 5.87 million CAR T cells per kilogram of body weight. Vein-to-vein time, defined as the duration from apheresis to CAR T-cell infusion, was 21 days. On Day +30 post-infusion, biochemical progression was noted: M protein 0.38 g/dL, serum kappa light chains 1593 mg/L, lambda 1.37 mg/L, with an abnormal kappa: lambda ratio of 1171:1. Flow cytometry revealed CAR T cell expansion (Fig 1), indicating adequate cellular proliferation. Despite the progression of the disease markers, the absence of clinical deterioration warrants continued observation.

However, by Day +45, further biochemical progression was evident with worsening myeloma markers (M-protein 0.36 g/dL, kappa 2696 mg/L, lambda 1.74 mg/L, kappa: lambda ratio 1549:1). The patient reported a new-onset myalgia and back pain. Bone marrow aspiration and biopsy confirmed a 95% plasma cell infiltration. FISH analysis confirmed the persistence of del(17p) and gain(1q). A peripheral blood smear showed 9% circulating plasma cells (Fig 2), and cytopenia was notable: hemoglobin 80 g/L, TLC 3.4 × 10^9/L, platelet count 53 × 10^9/L—findings consistent with transformation to secondary plasma cell leukemia (sPCL).

To investigate CAR T refractoriness, BCMA expression was evaluated via immunophenotyping, which revealed sustained expression (64.79%) in plasma cells (Fig 3), ruling out antigen escape/downregulation.
Given the aggressive disease phenotype and refractoriness to CAR T, the patient was initiated on teclistamab monotherapy, a BCMA × CD3 bispecific T cell engager. A step-up dosing regimen was followed: 0.06 mg/kg (Day 1), 0.3 mg/kg (Day 4), and culminating in the initial full treatment dose of 1.5 mg/kg on Day 7. Within 48 hours of receiving the full dose, the patient developed a high-grade fever (Tmax 102 °F), which was unresponsive to broad-spectrum antimicrobials. An extensive infectious workup returned negative, and a clinical diagnosis of grade 1 cytokine release syndrome (CRS) was established. CRS persisted for a total of four days and was effectively managed with a single intravenous dose of Tocilizumab at 8 mg/kg, resulting in complete resolution of symptoms. Importantly, the patient did not develop any features of immune effector cell-associated neurotoxicity syndrome (ICANS) during the post-infusion course.
The second treatment dose (1.5 mg/kg) was administered on day 14 without CRS recurrence. The patient continued to receive weekly maintenance therapy with teclistamab.
Following six weekly doses of teclistamab, the patient achieved a profound hematologic response and a CR. Hemoglobin level improved to 120 g/L, total leukocyte count rose to 4 × 10^9/L, and platelet count normalized to 190 × 10^9/L. Peripheral blood analysis showed complete clearance of plasma cells. Serum immunofixation electrophoresis (SIFE) revealed no detectable M-protein. Bone marrow aspiration and biopsy demonstrated less than 5% plasma cells. Additionally, the serum free light chain assay showed a marked reduction, with kappa at 11.6 mg/L, lambda at 0.506 mg/L, and a kappa: lambda ratio of 23:1.
At the 4-month follow-up, after receiving 16 weekly doses of teclistamab, the patient continues to maintain CR.

Discussion:

CAR T-cell therapy has reshaped the treatment approach for relapsed and refractory multiple myeloma (RRMM). With broader use, CAR T-cell treatment failure has become evident, as ~50% of patients relapse within a year of infusion [1,2]. In the pivotal phase 1 trial evaluating the BCMA-targeted CAR T-cell therapy bb2121, over half of the patients experienced disease progression within one year of infusion, even among those who initially responded, including patients who achieved undetectable minimal residual disease. Outcomes after BCMA CAR T relapse are significantly influenced by both the timing and nature of the relapse. In particular, early relapse (within three months post-infusion) and relapse involving extramedullary disease (EMD), including sPL, are associated with poor overall survival (OS). Currently, there is no universally accepted standard of care for patients who relapse after CAR-T cell therapy.
One study reported an overall response rate (ORR) of 43% among 76 patients who received post–CAR T-cell salvage therapy, with a notably higher ORR of 91% observed in patients treated with T-cell–engaging agents [3]. Among these, bispecific antibodies (e.g., Teclistamab) have shown the most promise, demonstrating improved response rates and survival outcomes compared with other treatment modalities. They appear especially capable of overcoming the poor prognosis associated with early relapse and EMD including sPL [4].
A key area of ongoing debate is the optimal timing for introducing bispecific antibodies following CAR T-cell therapy. Two major hypotheses are central to this discussion: antigen loss and immune cell exhaustion. The former is supported by findings of heterogeneous BCMA expression within tumor populations, suggesting that relapse may be driven by the emergence of BCMA-negative clones [5]. T-cell exhaustion, a major barrier to sustained responses, has also emerged as a critical factor, particularly in patients whose T cells were harvested after multiple lines of prior treatment [6]. Consequently, administering additional immunotherapies soon after CAR T cell infusion may be suboptimal. However, emerging data have identified teclistamab as a particularly effective post-relapse option, delivering excellent median OS, even in patients who relapsed early—within three months of CAR T-cell therapy [4].
In our case, the patient was refractory to BCMA CAR-T cell therapy and experienced early progression to sPCL. To investigate the etiology of this resistance, BCMA expression was assessed using flow cytometry, which demonstrated persistently high expression (64.79%) in plasma cells. Subsequently, the patient was treated with teclistamab using a standard step-up dosing regimen. Initial grade 1 CRS promptly resolved with a single dose of tocilizumab. Importantly, no further CRS episodes occurred after the subsequent administration.
The hematological and biochemical responses to teclistamab were both rapid and profound. Within six weeks, peripheral blood plasma cells were cleared, cytopenia was resolved, and free light chain levels showed a marked reduction. This striking response despite prior BCMA-targeted CAR T-cell therapy highlights the continued efficacy of teclistamab in this setting. These findings support its use as sequential or salvage therapy for relapsed/refractory disease post-BCMA treatment.
Treatment with EMD continues to represent a significant unmet clinical need as conventional therapies have yielded disappointing results in terms of both response and survival. Although CAR T-cell therapy has generated impressive

clinical responses overall, patients with EMD at the time of infusion consistently fare worse than those without [7]. Until recently, data on the outcomes of patients who relapsed with EMD post-CAR T-cell therapy were limited. Our latest findings highlight that EMD at relapse is a strong predictor of poor prognosis; however, bispecific antibodies may offer a path forward, producing comparable efficacy and survival irrespective of EMD status.

Conclusion:

This case highlights the potential of teclistamab as an effective salvage therapy following BCMA CAR T cell failure, even in aggressive disease with sPCL and high-risk cytogenetics. Despite early progression, the patient achieved a rapid and deep response, with normalization of hematological parameters and clearance of circulating plasma cells. The efficacy of Teclistamab in this setting supports its role as a viable post–CAR T option, particularly in patients with early relapse or extramedullary disease. These findings reinforce the emerging paradigm of sequential immunotherapy in relapsed/refractory multiple myeloma.

Key words: Multiple Myeloma, Secondary Plasma cell Leukemia, BCMA CAR T, Teclistamab
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Authorship Contributions

Surgical and Medical Practices: A.A, K.B, P.V, T.P, R.I; **Concept:** A.A, K.B, P.V, R.I; **Design:** A.A, K.B, P.V, R.I, K-C.M; **Data Collection or Processing:** A.A, K.B, T.P, R.I, K-C. M; **Analysis or Interpretation:** K.B, P.V, T.P; **Literature Search:** K.B, R.I, K-C. M; **Writing:** A.A, K.B, R.I, K-C. M.

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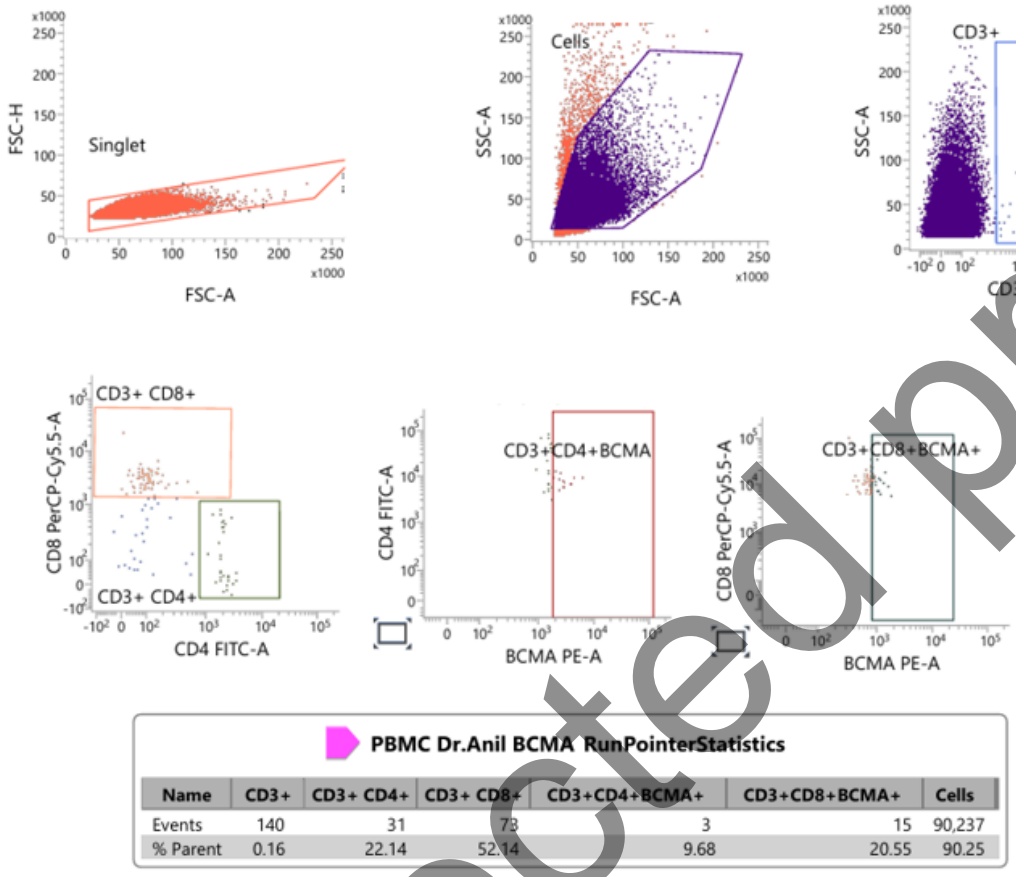

PBMC Dr.Anil BCMA RunPointerStatistics

Name	CD3+	CD3+ CD4+	CD3+ CD8+	CD3+CD4+BCMA+	CD3+CD8+BCMA+	Cells
Events	140	31	73	3	15	90,237
% Parent	0.16	22.14	52.14	9.68	20.55	90.25

Fig 1: BCMA CAR T expansion by flow cytometry

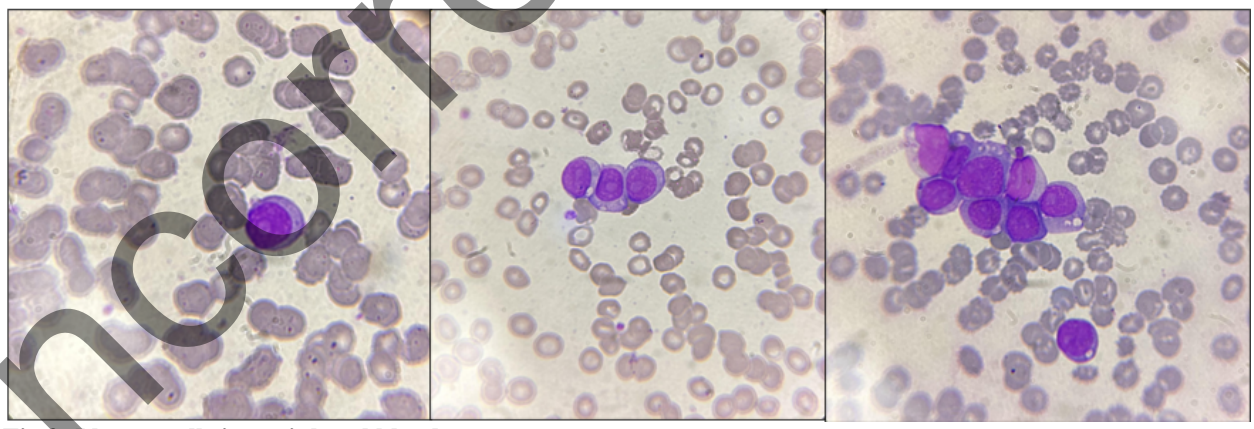

Fig 2: Plasma cells in peripheral blood

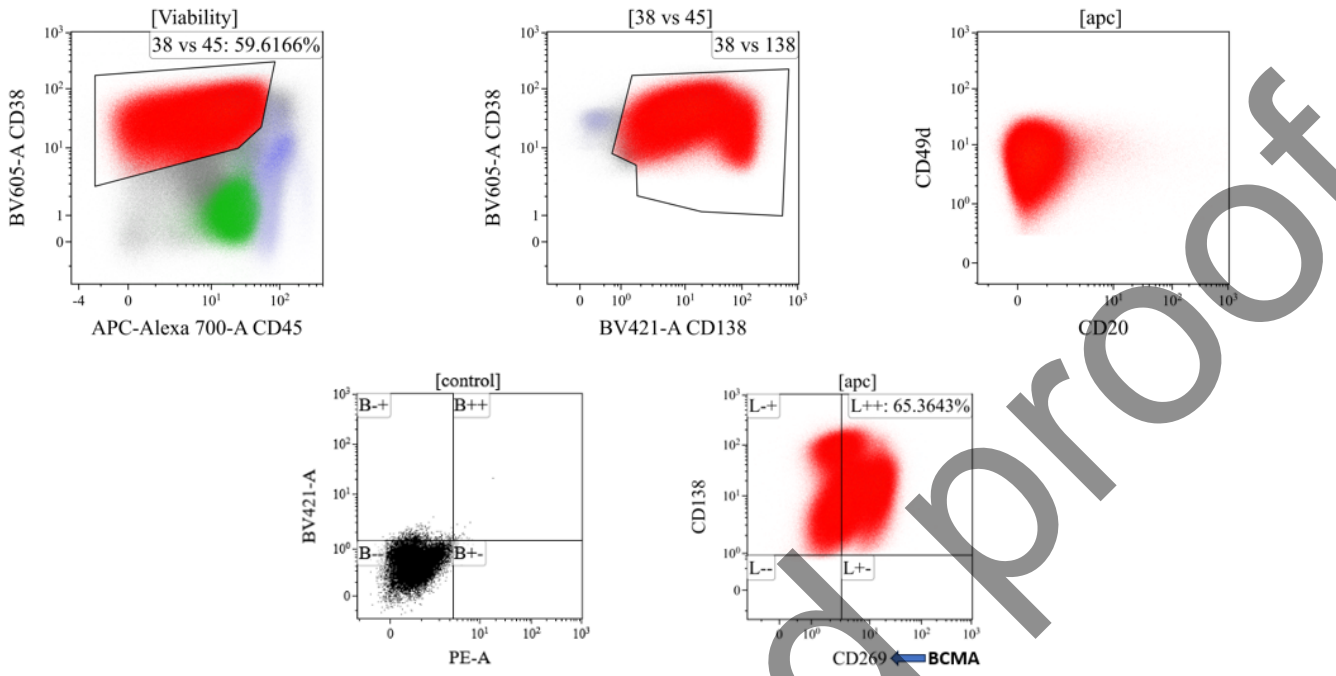

Fig 3: BCMA expression testing on plasma cells by Flow cytometry