Characteristics of Mast Cells in the Bone Marrows of Patients Following CAR -T Therapy

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Introduction

- Chimeric antigen receptor T-cell (CAR-T) therapy was initially approved in 2017
- Steadily increasing number of indications for CAR-T therapy
- CAR-T therapy triggers inflammatory cytokines which may result in activation of mast cells (MC) [1-2]
- The physiologic effects of CAR-T therapy continue to be researched
- **The aim of this study is to evaluate the morphologic and immunophenotypic characteristics of mast cells in bone marrow biopsies from patients who underwent CAR-T therapy**

Materials and Methods

- 5 patients with pre- and post-CAR-T (0-24 months) marrow biopsies at the University of Utah from Jan. 1st, 2020, to Dec. 31st, 2021
- Studied parameters:
  - Number, morphology, and localization/distribution of MCs
  - Immunophenotype: CD117 (EP10, Leica), tryptase (AA1, Dako), CD25 (4C9, Leica), and CD30 (Ber-H2, Bio SB0)
  - Morphometric assessment: MCs per sq mm were used to compare MC counts
  - Fibrosis (reticulin and collagen) by special stains

Results

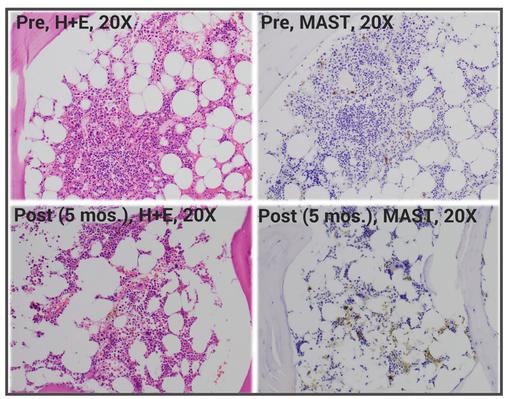

Figure 1: Pre- and post CAR-T marrow biopsies, Patient 1

Patient	Diagnosis	CAR-T status	MCs per sq mm	Round/spindled MCs in core, %	% MC in clusters	Comments
1	CLL/SLL	Pre	5.6	74/26	0	
		Post, 5 months	3	89/11	0	
2	PCM	Pre	0	N/A	N/A	Hematopoietic marrow is replaced by neoplasm
		Post, 3 months	13	71/29	0	
3	MCL	Pre	18.3	81/19	0	
		Post, 3 months	7	86/14	0	
4	PCM	Pre	16.4	77/23	6	
		Post, 3 months	15.5	74/26	0	
		Post, 5 months	4.8	90/10	0	
5	DLBCL	Pre	2.3	88/12	0	Cellularity <1%
		Post, 2 months	15	72/28	2	

Table 1: Clinical and morphologic characteristics of bone marrow biopsies. Abbreviations: CLL/SLL chronic lymphocytic leukemia/small lymphocytic lymphoma; DLBCL diffuse large B-cell lymphoma; MC mast cells; MCL mantle cell lymphoma; PCM plasma cell myeloma

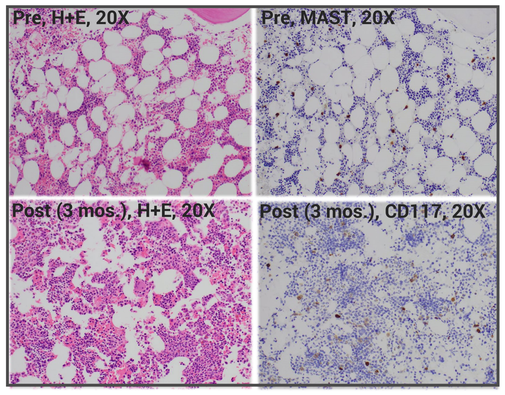

Figure 2: Pre- and post CAR-T marrow biopsies, Patient 3

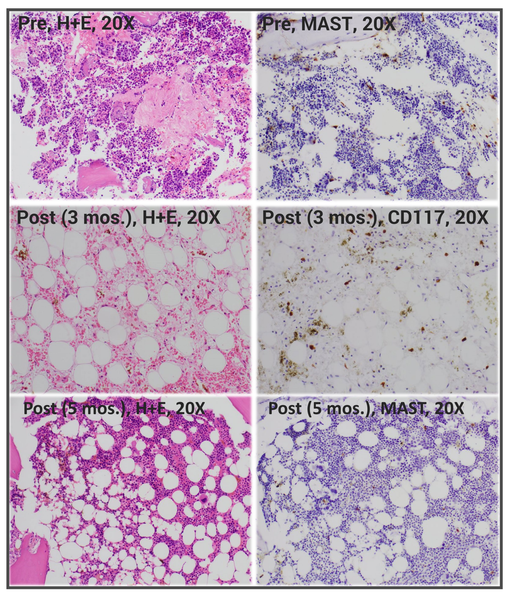

Figure 3: Pre- and post CAR-T marrow biopsies, Patient 4

Discussion

- All patients' marrow specimens after CAR-T therapy (up to 5 months follow-up) showed no evidence of residual disease
- Prior to CAR-T therapy , three patients' biopsies demonstrated an increased number of mast cells; the baseline assessment of the other two patients' biopsies was limited
  - In these three patients, a decrease in overall MC numbers was observed
  - There was no detectable difference in mast cell distribution or cluster formation. However, a relative decrease in spindle-shaped MCs was noted
- No immunophenotypic abnormalities, other than a mild loss of tryptase expression in patient 1, were observed

Conclusion

- CAR-T therapy may be associated with normalization of MC numbers in patients who experience remission
- Further studies with longer-term follow-up and a greater number of patients may be needed to better understand the long-term effects of CAR-T therapy on marrow MCs

References

1. Caraffa A, Gallenga CE, Kritas SK, Ronconi G, Di Emidio P, Conti P. CAR-T cell therapy causes inflammation by IL-1 which activates inflammatory cytokine mast cells: anti-inflammatory role of IL-37. J Biol Regul Homeost Agents. 2019 Nov-Dec;33(6):1981-1985.

2. Maus M et al. T cells expressing chimeric antigen receptors can cause anaphylaxis in humans. Cancer Immunol Res 2013; 1(1):26-31

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