

Cardiovascular Adverse Effects in CAR T Cell Therapies

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INTRODUCTION

CD19-specific chimeric antigen receptor (CAR) T cell therapies have seen substantial promise in highly refractory haematological malignancies. Cytokine release syndrome (CRS) and neurotoxicity are the most widely appreciated adverse effects, but the extent and characteristics of cardiovascular involvement remain poorly defined.

Retrospect Studies in Paediatric Populations of CAR T Cell Therapy Cardiovascular Toxicity

	Profound ↓BP or LVSD	In patients with profound ↓BP:			
		LVSD	ACEI	B-Blockers	ECG changes
Fitzgerald et al, 2017 ¹	36% (14/39)	-	-	-	-
Burstein et al, 2018 ²	24% (24/98)	41% (10/24)	21% (5/24)	17% (4/21)	18% (6/24)

DISCUSSION

Cardiovascular problems range from sinus tachycardia and other arrhythmias, to left ventricular systolic dysfunction (LVSD), profound hypotension, and shock requiring intensive therapy unit (ITU) admission and inotropic support. Their extent has only been assessed in two retrospective studies in paediatric populations by The Children's Hospital of Philadelphia. Fitzgerald et al analysis of 39 patients in 2017 demonstrated cardiotoxicity in 36% (14 patients) as defined by either fluid-refractory vasoplegic shock treated with inotropic agents or LVSD. This was further supported by the analysis of 93 patients by Burstein et al in 2018, where 24% (24 patients) met the primary endpoint of hypotension requiring inotropic support. Of those, 41% (10 patients) had LVSD, and 18% (6 patients) had ST-segment abnormalities on ECG. LVSD persisted at discharge in 7% (7 patients), and 1% (1 patient) at six months. Both studies demonstrated dramatic clinical improvement with use of tocilizumab.

CONCLUSION

Ability to counteract on-target, off-tumour toxicities will allow us to optimally utilize the life-saving potential of CAR T cell therapies. Subsequently, prospective studies defining the cardiac safety of CAR T cell therapies are needed. Surveillance must encompass biomarkers and advanced cardiac imaging that have informed other areas of cardio-oncology, including global longitudinal strain and diastolic assessment on echocardiography, and magnetic resonance imaging.

1. Fitzgerald JCMPD, Weiss SLMDM, Maude SLMDP, Barrett DMMDD, Lacey SFP, Melenhorst JJP, et al. Cytokine Release Syndrome After Chimeric Antigen Receptor T Cell Therapy for Acute Lymphoblastic Leukemia. *Critical Care Medicine*. 2017;45(2):e124-e31.

2. Burstein DS, Maude S, Grupp S, Griffis H, Rossano J, Lin K. Cardiac Profile of Chimeric Antigen Receptor T Cell Therapy in Children: A Single-Institution Experience. *Biology of Blood and Marrow Transplantation*. 2018;24(8):1590-5.

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