

Introduction

- Allogeneic hematopoietic stem cell transplant can result in acute graft versus host disease (aGVHD)
- First line therapy for aGVHD is steroids
- Steroid-refractory (SR) aGVHD has >90% mortality risk
- Wharton's Jelly Mesenchymal Stem Cells (WJMSCs), umbilical cord-derived mesenchymal stromal cells, have potent immunosuppressive effects

Patient Population

- Patients aged 18-75
- Previous allogeneic stem cell transplant
- Developed high-risk (Figure 1) and/or SR aGVHD
- Steroid-refractory: progression of disease within 3 days or no improvement within 7 days of consecutive treatment with 1.6 mg/kg/d of methylprednisolone/equivalent

Investigational Agent

- MSCTC-0010: a suspension of WJMSCs
- Umbilical cords from healthy donors undergoing cesarean section
- ≥95% of cells expressed characteristic MSC markers (CD105, CD73, CD90, and CD44)

Results

- 26 patients screened for inclusion, 24 patients enrolled and treated with MSCTC-0010
- Twenty-three (96%) of patients had no treatment-related adverse events
- Ten (42%) patients achieved complete response by Day 28
- Seventeen (71% all patients, 89% at risk) patients had some improvement by Day 28
- Thirteen (54% all patients, 100% at risk) patient had some improvement by Day 90
- Eight (33%) patient had additional immunosuppressive therapy added on within 90 days
- Zero patients had development of any ectopic tissue foci via CT scan on Day 90.
- Fig 4 shows GvHD biomarker data

Figure 1. Minnesota Criteria for Standard vs High Risk GVHD

GVHD Risk Score	GVHD Risk Definition by Organ Stage at Onset [20]		
	One Organ (n)	Two Organs (n)	Three Organs (n)
Standard risk (n = 1454, 84%)	Stage 1-3 Skin (901) Stage 1-2 GI (279)	Stage 1-3 skin plus stage 1 GI (223)* Stage 1-3 skin plus stage 1-4 liver (51)	-- --
High risk* (n = 269, 16%)	Stage 4 Skin (13) Stage 3-4 GI (74) [§] Stage 1-4 Liver (25) [¶]	Stage 1-3 skin plus stage 2 GI (54) Stage 1-2 lower GI plus stage 1-3 liver (12) Stage 3-4 GI plus stage 1-3 skin (45) Stage 3-4 GI plus stage 1-4 liver (10)	Stage 1-3 skin plus stage 1-2 GI plus stage 1-3 liver (23) Stage 1-3 skin plus stage 3-4 GI plus stage 1-4 liver (13)

GI = gastrointestinal; GVHD = graft versus host disease; UGI = upper gastrointestinal.
 * Stage 1-3 skin plus stage 1 GI includes stage 1-3 skin plus UGI (n ¼ 90), stage 1-3 skin plus stage 1 lower GI (n ¼ 71), or stage 1-3 skin plus UGI plus stage 1 lower GI (n ¼ 62).
[†] Stage 1-2 GI includes UGI alone (n ¼ 115), stage 1-2 lower GI alone (n ¼ 100), or UGI or stage 1 lower GI (n ¼ 64).
[‡] For high risk disease, the degree of organ involvement is the minimum necessary to be deemed high risk. Patients with higher stage of GVHD than observed in the high risk group should also be considered high risk.
[§] Stage 3-4 GI includes stage 3 lower GI alone (n ¼ 65), or stage 4 lower GI alone (n ¼ 9).
[¶] Stage 1-4 liver includes Stage 1 liver alone (n ¼ 7), stage 2 liver alone (n ¼ 10), stage 3 liver alone (n ¼ 5), or stage 4 liver alone (n ¼ 3). UGI plus lower GI considered as single-organ disease.

Figure 3. Patient Responses at Day 28

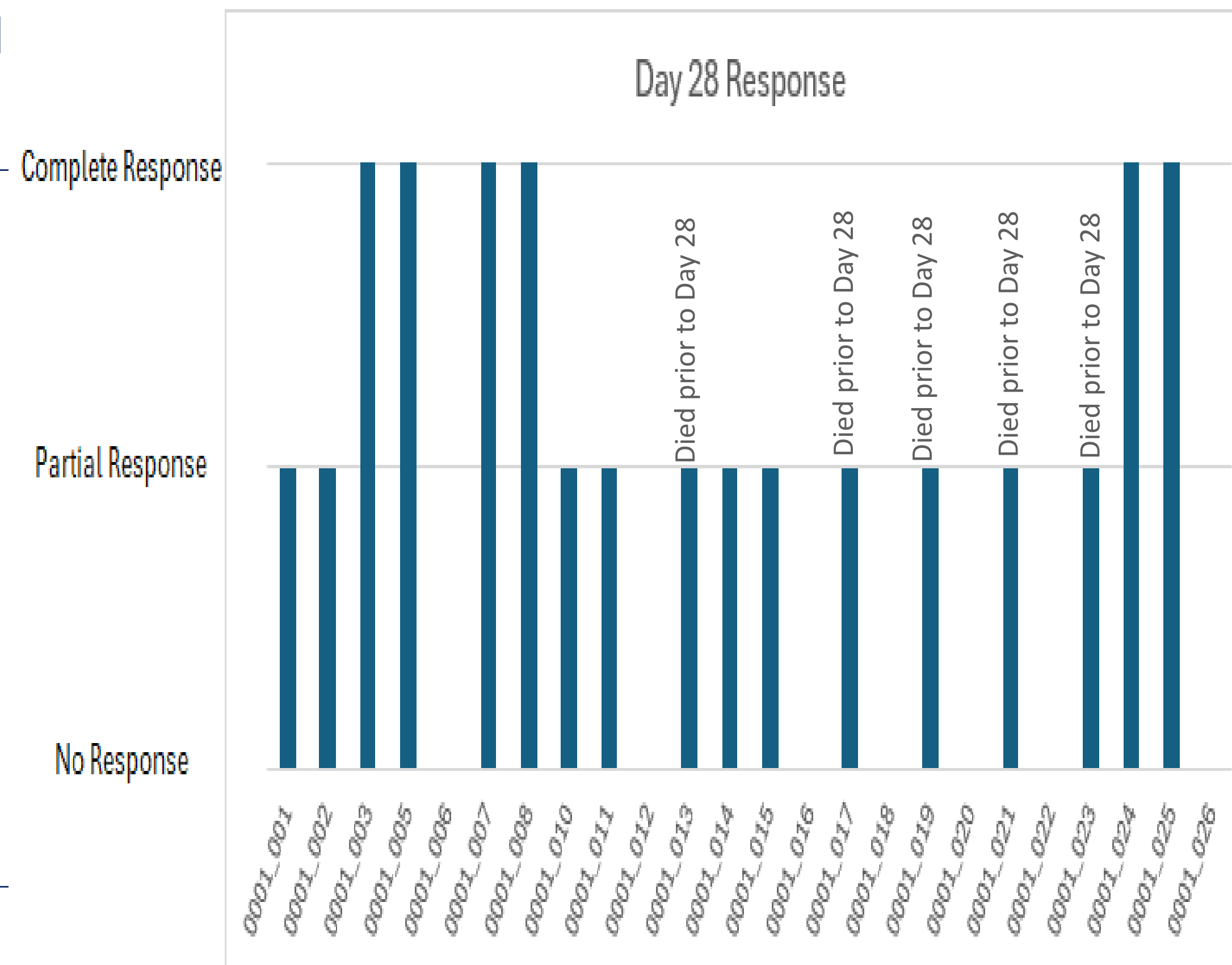


Figure 2. Patient Overall Survival

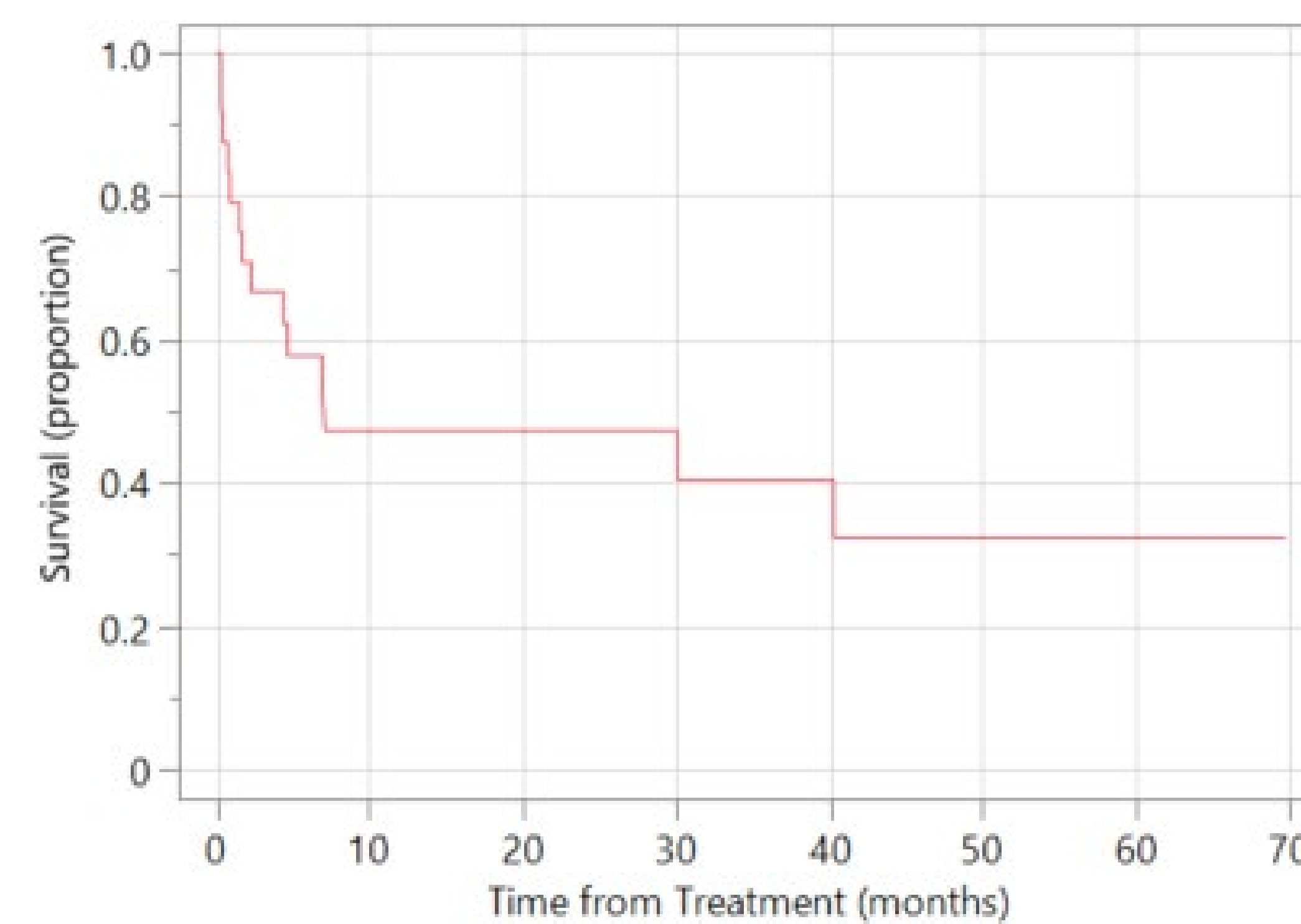
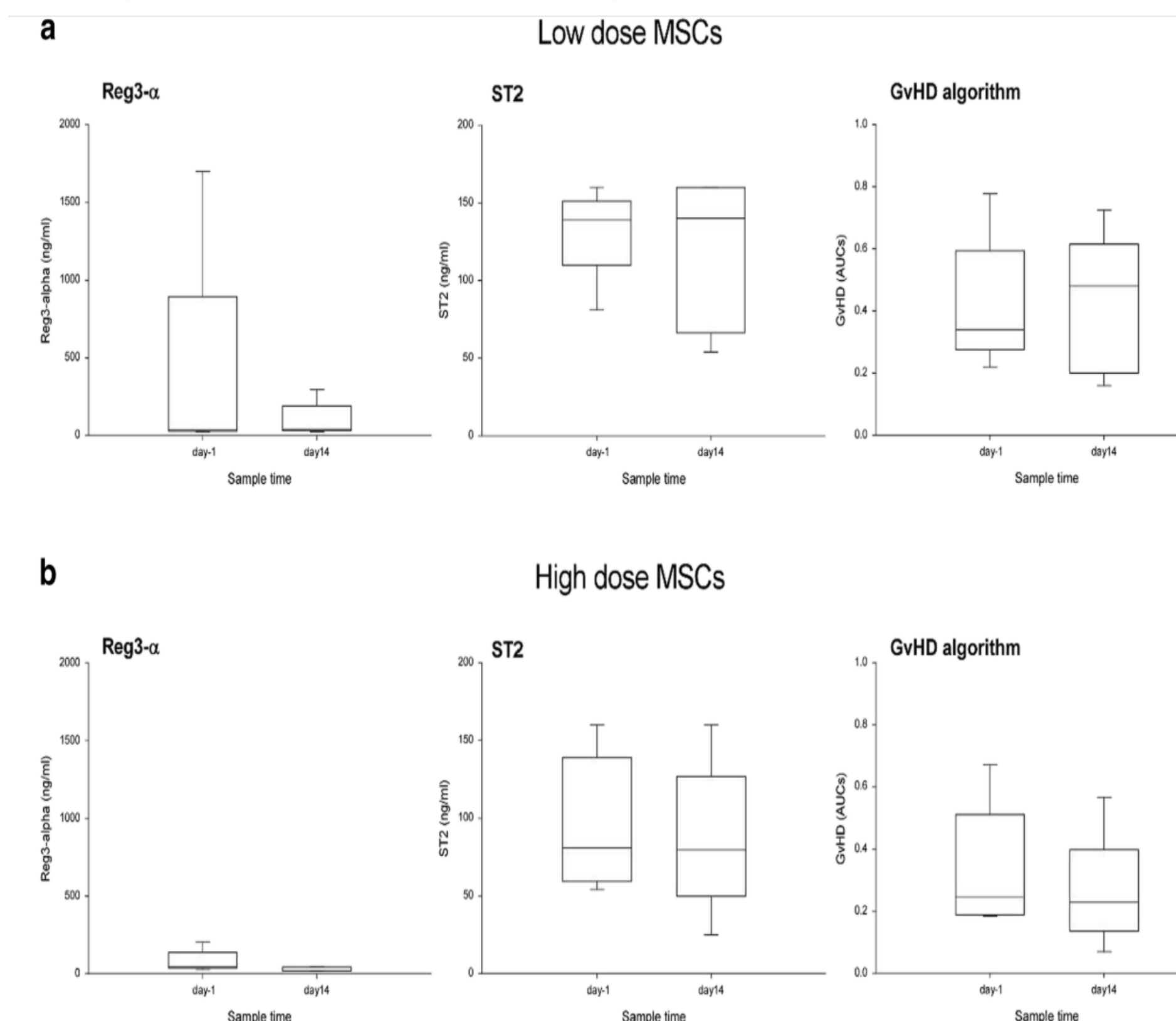


Figure 4. GvHD Biomarkers and Algorithm



Conclusions

- Thirteen (54%) patients at baseline were steroid-refractory, two (8%) were high risk, and nine (38%) were both.
- MSCTC-0010 appears to be safe and well-tolerated in this population

Future Directions

- Clinical trials expanding on the efficacy of MSCTC-0010 in high risk and SR aGVHD are warranted to find novel efficacious solutions for an extremely at-risk population

Funding Sources

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Fig 4: Reg3-α and ST2 concentrations and GvHD predictive algorithm on one day prior to infusion and at day 14 post infusion. Panel A shows results from low dose MSCT-0010 cohort. Panel B shows patients in the high dose MSCT-0010 cohort. There was a stronger trend for Reg3-α to decrease after high dose MSC infusions than low dose MSC cohort. *Stem Cell rev and Reports Sept 2020*