Results from an expanded access program of the anti-CD3/CD7 immunotoxin combination (T-Guard®) for the treatment of steroid-refractory acute GVHD

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BACKGROUND

More effective therapies for steroid-refractory acute graft-versus-host disease (SR-aGVHD) are urgently needed.[1] In a phase I/II study the anti-CD3/CD7 immunotoxin (IT) combination (T-Guard) proved to be safe and well tolerated, and resulted in a high CR rate and a promising 6-month OS in high-risk patients. After the study patients with SR-aGVHD were able to receive T-Guard in the expanded access program (EAP).

OBJECTIVES

1. Evaluation of the EAP efficacy (ORR and OS) with the IT-combination for SR-aGVHD.
2. Correlate the change in citrulline (biomarker of enterocyte mass) and response in those with SR-aGVHD of the gastrointestinal (GI) tract.

METHODS

- Adult patients (≥ 18 years) with grade II-IV SR-aGVHD received the IT-combination as second- or third-line treatment for aGVHD.
- Exclusion criteria: uncontrolled infections, moderate/severe chronic GVHD, and severe renal impairment.
- IT-combination 4-hour i.v. infusion every 48 hours, for a total of four doses at 4 mg/m^2.
- Citrulline levels measured at baseline and weekly thereafter.
- Citrulline levels <10 µmol/L reflect severe acute GI-GVHD (stage 1-4).

CHARACTERISTICS

Number of Subjects	12
Age, years - Median (range)	54 (20-70)
Gender - Male : Female	8 : 4
SR-aGVHD, grade	
- Grade II	1 (8%)
- Grade III-IV	11 (92%)

Organ involvement	
- GI	75%
- Liver	17%
- Skin	50%
Baseline albumin levels g/L - Median (range)	23 (13-32)
Baseline citrulline levels µmol/L - Median (range)	4.3 (2.9-17.9)

RESULTS

- ORR (CR + PR) day 28: **9/12 (75%)**. CR day 28: **5/12 (42%)**
- OS 6-months and 1-year: **9/12 (75%)** and **7/12 (58%)** *(Figure 1)*
- In T-Guard treated patients with GI involvement the course of citrulline corresponded to the day 28 response. The significant increase in citrulline levels in the CR group indicates gut mucosal recovery *(Figure 2)*.

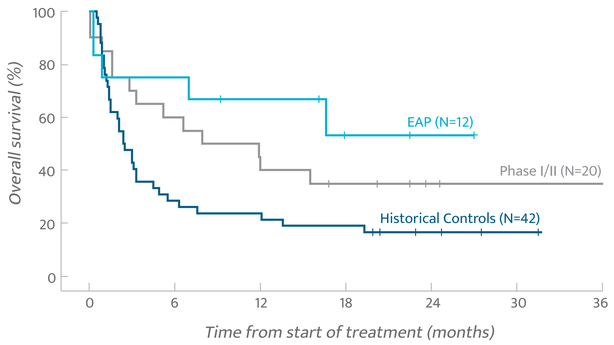

Figure 1
Kaplan-Meier curves of OS of the patients treated with T-Guard in the EAP, phase I/II study and historical controls; Cox regression analysis comparing T-Guard with historical controls P=0.01.

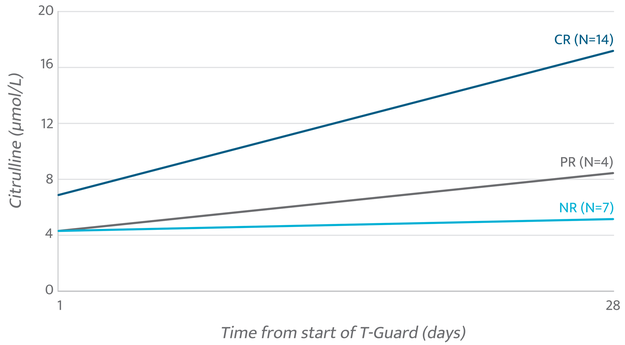

Figure 2
The increase in citrulline is correlated with the complete response achieved with T-Guard at day 28 in SR-GI-aGVHD (independent *t*-test P<0.01)

CONCLUSIONS

In a real-life cohort consisting of 12 patients with high-risk SR-aGVHD we could confirm the efficacy and safety of T-Guard for SR-aGVHD. Outcomes were similar to those reported in the phase I/II trial[1]. Additional studies are required to determine the possible value of measuring citrulline as a prognostic marker following GVHD treatment.

[1]Groth C, van Groningen LFJ et al. Phase I/II trial of a combination of Anti-CD3/CD7 immunotoxins for SR-aGVHD. BBMT 2019; 25(4): 712-719.

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