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

L.F.J. van Groningen¹, C. Groth², M.E.J. Bremmers¹, H.G. van Hooren³, YV.J.M. van Oosterhout³, M. Stelljes², N.M.A. Blijlevens¹, W.J.F.M. van der Velden¹

¹Radboudumc Nijmegen, the Netherlands; ²University Hospital of Muenster, Muenster, Germany; ³Xenikos B.V., Nijmegen, the Netherlands

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/m².
- Citrulline levels measured at baseline and weekly thereafter.
- Citrulline levels <10 µmol/L reflect severe acute GI-GVHD (stage 1-4).

RESULTS
- ORR (CR + PR) day 28: 9/12 (75%). CR day 28: 5/12 (42%) (Figure 1)
- 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).

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 trial¹. Additional studies are required to determine the possible value of measuring citrulline as a prognostic marker following GVHD treatment.


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