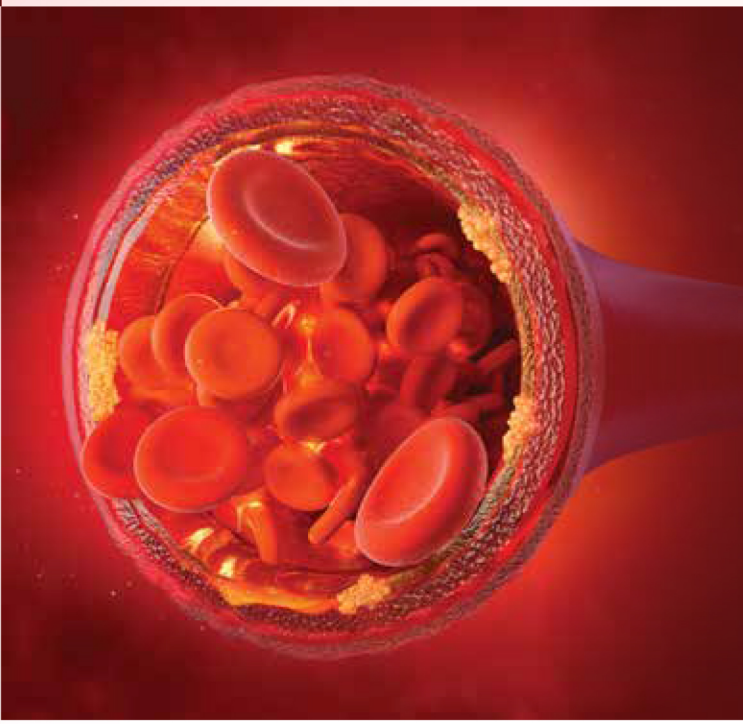


Dear Doctor,

Did you know, the current weight-based r-ATG dosing is empiric at its best and has significant limitations

Challenges in weight-based r-ATG dosing[1–4]

- Poor T-cell reconstitution
- Reduced graft vs. leukemia effect and increased relapse and nonrelapse mortality

Emerging evidence suggests that individualizing r-ATG dosing may be the key to:[5,6]

- Overcome the drawbacks of current weight-based r-ATG dosing strategies
- Produce optimal r-ATG exposure (AUC)

EMA and USFDA guidelines:[7]

Recommend

Population pharmacokinetics modeling for optimum individual r-ATG exposure

AUC: Area under the curve; EMA: European medicines agency; r-ATG: Rabbit anti-thymocyte globulin; USFDA: United States Food and Drug Administration.

Association between r-ATG exposure and CD4+ immune reconstitution[8]

Study Design[8]

Retrospective analysis of pediatric aHSCT patients; **n=251**

Outcome[8]

Reduced chance of successful immune reconstitution with increasing r-ATG AUC after aHSCT (odds ratio 0.991; p<0.0001)

Conclusion[8]

Achieved effective immune reconstitution **that resulted in:**

- Relapsed and non-relapsed mortality
- Overall survival

aHSCT: Allogenic hematopoietic stem cell transplantation; AUC: Area under the curve; CD4+: Cluster of differentiation 4+; r-ATG: Rabbit anti-thymocyte globulin.

Association between r-ATG exposure and the 5-year overall survival outcome[7]

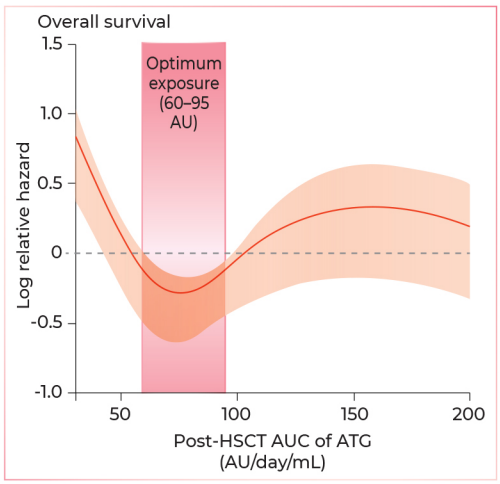
Study Design

Retrospective analysis of ALL, AML, and MDS patients;
n=146

The optimal post-transplantation r-ATG exposure =60–95 AU/day/mL[7]

ALC-based dosing is better than weight-based dosing.[7]

For optimal target exposure of r-ATG (>50 kg)



r-ATG exposure after aHSCT—Best predictor of 5-year survival[7]

Cumulative dose of intravenous r-ATG =400+350×lymphocyte count (in 10^9/L)[7]

aHSCT: Allogenic hematopoietic stem cell transplantation; ALC: Absolute lymphocyte count; ATG: Anti-thymocyte globulin; AU: Arbitrary unit; AML: Acute myeloid leukemia; ALL: Acute lymphoid leukemia; AUC: Area under the curve; HSCT: Hematopoietic stem cell transplantation; MDS: Myelodysplastic syndrome; r-ATG: Rabbit anti-thymocyte globulin.

Prospective clinical evidences on individualization of r-ATG dose and aHSCT outcomes: PARACHUTE Study[9]

Prospective analysis of aHSCT pediatric patients[9]

Intervention

Individualized dosing regimen based on:

▸ Body weight ▸ ALC at the time of r-ATG initiation

Primary Endpoint

T-cell reconstitution >0.05×10^9 $CD4^+$ T cells/L twice within 100 days [±3] after transplantation

Conclusion

80% of the subjects met the primary endpoint within 100 days.

The model reveals—The optimum r-ATG exposure is:

Achieved in 97% patients receiving r-ATG doses based on ALC[9]

VS.

Achieved in 30%–53% of patients receiving r-ATG doses based on weight alone[9]

Conclusion

Emerging clinical outcomes from attempts at individualizing r-ATG dose based on ALC +/- weight-guided r-ATG exposure are quite encouraging and lend credence to further evaluation attempts in the form of large-scale RCTs.

aHSCT: Allogenic hematopoietic stem cell transplantation; ALC: Absolute lymphocyte count; CD4+: Cluster of differentiation 4+; r-ATG: Rabbit anti-thymocyte globulin; r-ATG: Rabbit anti-thymocyte globulin; RCTs: Randomized clinical trials.

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