***Supplementary Table 1: Hematologic responses of the study population based on hATG formulation***

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|  | **ATGAM;n(%)** | **Thymogam; n(%)** | **P value**  |
| **Low dose ATG**  | **n=39**  | **n=23** |  |
| Overall Response\* (PR+CR)At 3 monthsAt 6 monthsAt 12 months | 19(48.7)23(63.9)27(75.0) | 12(52.2)14(63.6)12(60.0) | 0.7900.9810.242 |
| **Standard dose ATG** |  **n=12** |  **n=19** |  |
| Overall Response\* (PR+CR)At 3 monthsAt 6 monthsAt 12 months | 6(50)8(72.7)9(81.8) | 9(47.4)12(70.6)10(76.9) | 0.8870.9040.768 |
| **Standard and Low dose ATG (combined)** | **n=51** | **n=42** |  |
| Overall Response\* (PR+CR)At 3 months At 6 monthsAt 12 months | 25(49)31(66)36(76.6) | 21(50)26(66.7)22(66.7) | 0.9230.9640.328 |

\*Number of surviving patients on follow up at each time point were denominators for

calculation of response rates

***Supplementary Table 2: Details of deaths in study population***

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|   | **Total patients****(n = 93)** | **Low dose ATG** **(n = 62)** | **Standard dose ATG** **(n = 31)** | **P value**  |
| Overall deaths after hATGTotal, n/N (%)Among responders, n/N (%)Among non-responders, n/N (%) | 15/93 (16.1)5/72 (6.9)10/21(47.6) | 9/62 (14.5)2/47 (4.2)7/15 (46.7) | 6/31 (19.4)3/25 (12.0)3/6 (50.0) | 0.550.220.89 |
| Deaths according to response at 3 monthsAmong responders, n/N (%)Among non-responders, n/N (%) | 2/46 (4.3)13/47 (27.6) | 0/31 (0)9/31 (29.0) | 2/15 (13.3)4/16 (25.0) | 0.040.77 |
| Deaths according to response at 6 monthsAmong responders, n/N (%)Among non-responders, n/N (%) | 4/57 (7.0)9/29 (31.0) | 1/37 (2.7)7/21 (33.3) | 3/20 (14.3)2/8 (25.0) | 0.090.66 |
| Deaths according to response at 12 monthsAmong responders, n/N (%)Among non-responders, n/N (%) | 5/58 (8.6)7/22 (31.8) | 2/39 (5.1)6/17 (35.3) | 3/19 (15.8)1/5 (20.0) | 0.170.52 |

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| **Author, Year*****Supplementary Table 3. Key studies using alternative\* dosing strategies of various ATG formulations for treatment of Aplastic Anemia*** | **Study** **design** | **Antithymocyte Globulin(ATG) preparation** | **ATG Dose** | **n** | **Outcomes and Comments** |
| 1. Young et al (1988) (1) | Randomized controlled trial  | ATGAM (Upjohn, Kalamazoo) | ATGAM 15mg/kg/d x 10 days (Total dose 150 mg/kg)ATGAM 15mg/kg/d x 14 days followed by alternate day doses for 14 days (Total dose 315 mg/kg) | 4136 | Comparable outcomes between two groups at 3 months in acute severe aplastic anemia ATG was administered without cyclosporineNo added benefit of higher cumulative dose of eATG |
| 2. Killick et al (2006)(2) | Retrospective | Lymphoglobuline (Genzyme, Cambridge, USA)  | Lymphoglobuline 5mg/kg x 5 days (Total 25 mg/kg) | 12 | 1/12 patients responded (Age >60 years) to low dose eATGMedian age of study population 71 years |
| 3.Atta et al (2010)(3) | Retrospective  | Lymphoglobulin (Lymphoglobuline®, Genzyme, Cambridge, MA, USA)Thymoglobuline®, Genzyme, Cambridge, MA, USA | Lymphoglobulin 15 mg/kg/d x 5 days (Total 75 mg/kgThymoglobuline 2.5 mg/kg/d x 5 days (Total 12.5 mg/kg) | 4229 | Overall response rate at 6 months was 59.5% for eATG (Lymphoglobulin)and 34% for rATG (Thymoglobuline);similar response rates of rATG as compared to historical controls despite lower dose |
| 4. Yoshimi et al (2013)(4) | Retrospective  | Lymphoglobulin (Lymphoglobuline®, Genzyme, Cambridge, USA)Thymoglobuline®, (Genzyme, Cambridge, MA, USA)  | Lymphoglobulin 15 mg/kg x 8 days (Total 120 mg/kg)Thymoglobulin 3.75 mg/kg/d x 5 days (Total 18.75 mg/kg) | 9632 | ORR at 6 months was 65% for eATG (Lymphoglobulin) and 34% for rATG (Thymoglobuline); no added benefit of higher cumulative dose of eATG as compared to other published studies on eATG  |
| 5. Vallejo et al (2013)(5) | Retrospective  | Thymoglobuline® (Genzyme, Cambridge, USA) Lymphoglobuline (Genzyme, Cambridge, USA)ATGAM (Upjohn, Kalamazoo) | Thymoglobuline dose range from 2.5 mg/kg – 4 mg/kg x 5 days (Total 12.5 – 20 mg/kg) Lymphoglobulin 15 mg/kg/days x 5 days (Total 75 mg/kg)ATGAM 40mg/kg x 4 days (Total 160 mg/kg) | 1694616 | ORR at 3 months was 73.2% for rATG (Thymoglobuline),75.4% for eATG (Lymphoglobulin and ATGAM combined)Similar response rates as compared to historical controls of rATG despite lower cumulative dose used in a fraction of patients. |
| 6. Kulagin et al (2013)(6) | Retrospective  | ATGAM (Pfizer, USA) | ATGAM 40 mg/kg x 4 days (Total 160mg/kg)ATGAM 20 mg/kg x 5 days (Total 100mg/kg) | 7481 | Overall response rate was 69% in higher dose eATG arm group and was 51% in lower dose arm(p = 0.023); results reported only in abstract form with limited follow up  |
| 7.Kulaginet al(2014) (7) | Prospective | ATGAM (Pfizer, USA)Thymoglobuline, Genzyme, Cambridge, MA, USA  | ATGAM40 mg/kg/d x 4 days(Total 160mg/kg)ATGAM 20 mg/kg/d x 5 days (Total 100mg/kg)Thymoglobuline 3.75mg/kg x 5 days | 555218 | Overall response rate was 69% in higher dose eATG arm and 53% in lower dose eATG arm, eATG dose had borderline significance for response on univariate analysis, dose was not significant predictor of response on multivariate analysis |
| 8.Scott et al(2016)(8) | Retrospective | ATGAM (Pfizer, USA) | ATGAM40 mg/kg/d x 4 days(Total 160mg/kg)ATGAM 15mg/kg x 5 days(Total dose 75mg/kg)  | 1417 | Overall response rate (64 vs 71%, *P* = 1.0), relapse (33 vs 33%, *P* = 1.0), transformation (14 vs 24%, *P* = 0.66) infection (43 vs 47%, *P* = 1.0), overall and event free survival were comparable between standard and lower-dose cohorts.  |
| 9. Malhotra et al (2015)(9) | Retrospective | ATGAM(Pfizer,USA)Thymogam(Bharat Serums and Vaccines,India) | ATGAM25 mg/kg/d x 4 days(Total 100 mg/kg)Thymogam 40mg/kg/d x 4 days(Total 160mg/kg)  | 2316 | Overall response rate was 77% at 6 months and was similar in lower dose ATGAM and standard dose Thymogam  |
| 10.Diego V Cle et al (2018)(10) | Retrospective  | Lymphoglobuline (Genzyme, Cambridge, USA) Thymoglobulin®, Genzyme, Cambridge, MA, USA)  | LymphoglobulineDose:30mg/kg/d x 5 days(total dose 150 mg)Dose:15mg/kg/d x 5 days(Total dose 75 mgThymoglobulineDose:1-2.5mg/kg/day x 5 daysDose:2.6-3.0mg/kg/day x 5 daysDose:3.1-3.5mg/kg/day x 5 daysDose:3.6-5.0mg/kg/day x 5 days  | 8556294638 | Overall response rate at 6 months was 59% and 31% for eATG and rATG respectively, dose-based responses for different eATG doses were not reported,dose of rATG did not influence response or survival  |
| 11.Narita et al (2019)(11) | Prospective randomized trial  | Thymoglobulin®, Genzyme, Cambridge, MA, USA)  | ThymoglobulineDose:2.5mg/kg/d x 5 days(Total dose 12.5mg/kg)Dose:3.5mg/kg/d x 5 days(Total dose 17.5mg/kg) | 112110 | Overall response rate at 6 months was 49% for lower dose and 48% for higher dose rATG with no difference in efficacy and safety of low-dose versus higher-dose |
| 12. Gyi et al (2020)(12) | Retrospective | Thymogam (Bharat Serums and Vaccines, India) | Thymogam 40-60 mg/kgThymogam 60-80 mg/kgThymogam 160 mg/kg | 955 | Overall response rate was 78.9% and response was attained even with 40mg/kg total dose |
| 12. Current study | Retrospective  | ATGAM(Pfizer,USA)Thymogam(Bharat Serums and Vaccines,India) | ATGAM 25mg/kg x 4 days(Total 100 mg/kg) 40 mg/kg x 4 days(Total 160mg/kg) Thymogam  25mg/kg x 4 days(Total 100mg/kg) 40mg/kg/d x 4 days(Total 160mg/kg)  | 39122319 | Overall response rate was 66.3% and 72.5% with no statistical difference in low dose and standard dose group, with comparable 10 year overall and event free survival |

\*Standard cumulative dose for the treatment of AA in combination with cyclosporine is ATGAM: 160 mg/kg;Lymphoglobuline:75 mg/kg,Thymoglobuline:17.5 - 18.75 mg/kg; dosing strategies other than standard were termed as alternative dosing strategies

1. Young N, Griffith P, Brittain E, Elfenbein G, Gardner F, Huang A, et al. A multicenter trial of antithymocyte globulin in aplastic anemia and related diseases. Blood. 1988;72(6):1861-9.

2. Killick SB, Cavenagh JD, Davies JK, Marsh JC. Low dose antithymocyte globulin for the treatment of older patients with aplastic anaemia. Leuk Res. 2006;30(12):1517-20.

3. Atta EH, Dias DS, Marra VL, de Azevedo AM. Comparison between horse and rabbit antithymocyte globulin as first-line treatment for patients with severe aplastic anemia: a single-center retrospective study. Ann Hematol. 2010;89(9):851-9.

4. Yoshimi A, Niemeyer CM, Führer MM, Strahm B. Comparison of the efficacy of rabbit and horse antithymocyte globulin for the treatment of severe aplastic anemia in children. Blood. 2013;121(5):860-1.

5. Vallejo C, Montesinos P, Polo M, Cuevas B, Morado M, Rosell A, et al. Rabbit antithymocyte globulin versus horse antithymocyte globulin for treatment of acquired aplastic anemia: a retrospective analysis. Ann Hematol. 2015;94(6):947-54.

6. Kulagin A, Ivanova, M., Golubovskaya, I., Babenko, E., Kruchkova, I., Pronkina, N., Bond- arenko, S., Vavilov, V., Stancheva, N., Lisukov, I., Kozlov, V. & Afanasyev, B. . The horse ATG (ATGAM) total dose of 160 mg/kg as compared with 100 mg/kg is superior in achieving haematologic response in aplastic anaemia patients. . Bone Marrow Transplantation. 2013;48(2):S43.

7. Kulagin A, Lisukov I, Ivanova M, Golubovskaya I, Kruchkova I, Bondarenko S, et al. Prognostic value of paroxysmal nocturnal haemoglobinuria clone presence in aplastic anaemia patients treated with combined immunosuppression: results of two-centre prospective study. British Journal of Haematology. 2014;164(4):546-54.

8. Scott A, Morris K, Butler J, Mills AK, Kennedy GA. Treatment of aplastic anaemia with lower-dose anti-thymocyte globulin produces similar response rates and survival as per standard dose anti-thymocyte globulin schedules. Internal Medicine Journal. 2016;46(10):1198-203.

9. Malhotra P, Bodh V, Guru Murthy GS, Datta AK, Varma N, Varma S. Outcomes of immunosuppressant therapy with lower dose of antithymocyte globulin and cyclosporine in aplastic anemia. Hematology. 2015;20(4):239-44.

10. Clé DV, Atta EH, Dias DSP, Lima CBL, Bonduel M, Sciuccati G, et al. Rabbit antithymocyte globulin dose does not affect response or survival as first-line therapy for acquired aplastic anemia: a multicenter retrospective study. Ann Hematol. 2018;97(11):2039-46.

11. Narita A, Zhu X, Muramatsu H, Chen X, Guo Y, Yang W, et al. Prospective randomized trial comparing two doses of rabbit anti-thymocyte globulin in patients with severe aplastic anaemia. Br J Haematol. 2019;187(2):227-37.

12. Gyi AA, Htut KT, Han YN, Khine MM, Thandar HM, Thant YM. Outcome of Severe Aplastic Anemia Treated with Low Dose Immunosuppression in Resource Limited World during Pandemic: Single Center Experience from Myanmar. Blood. 2020;136(Supplement 1):27-.