

**Table 1: Patients' characteristics**

| No   | WAS score/<br>WAS protein | WAS<br>mutation                                     | Significant Pre-<br>transplant<br>morbidity  | Year<br>of transplant | Age at<br>diagnosis | Age at<br>transplant<br>(months) | Time<br>from<br>Diagnosis<br>to<br>transplan<br>t | Donor/cel<br>l source | Conditioning         | GvHD<br>Prophylaxis | Engraftment<br>Day Post-D0<br>(Neutrophil <sup>+</sup><br>) | GvHD<br>(Grade)                          | Post-transplant<br>complications   | Outcome/<br>Last Follow<br>Up (months)  | Last<br>Chimerism     |
|------|---------------------------|---|--|-----------------------|---------------------|----------------------------------|---|-----------------------|----------------------|---------------------|---|--|--|---|-----------------------|
| P1   | 2/absent                  | Null<br>mutation<br>exon 4                          | None   | 2009                  | 5m                  | 44m                              | 39m   | MUD<br>BM             | Alemtuzumab/Flu/Treo | CSA/MMF             | 15  | None                                     | None   | Off Ig<br>72 m  | 100%                  |
| P2   | 5/absent                  | del ex 1,7,12                                       | AIHA<br>(Steroid/Rituximab/<br><b>Splenectomy</b> ).<br>Fungal Pneumonia   | 2008                  | 2m                  | 33m                              | 31m   | MSD<br>BM             | Bu/Cyc               | CSA/MTX             | 21  | Grade I<br>(skin)                        | None   | Off Ig<br>68 m  | 100%                  |
| P3Q  | 2/absent                  | 27bp del<br>exon2/intron<br>2.2                     | None   | 2007                  | 4m                  | 19m                              | 15m   | MUD<br>PBSCs          | Alemtuzumab/Flu/Treo | CSA/MMF             | 12  | Grade I<br>(skin)                        | None   | Off Ig<br>92 m  | 100%                  |
| P4   | 5/absent                  | E133K   | AIHA/ITP<br>(Steroids/Rituximab/<br><b>Splenectomy</b> )<br><br>Retinal/CNS<br>haemorrhage<br>(frontal lobectomy)      | 2007                  | 10m                 | 21m                              | 11m   | mMUD<br>(1A)<br>PBSCs | Alemtuzumab/Flu/Treo | CSA/MMF             | 12  | None                                     | None   | Off Ig<br>60 m<br><br>Partial<br>blindness  | 100%T<br>50%M<br>90%B |
| P5   | 2/absent                  | c.100C>T,<br>(R34X)                                 | None   | 2007                  | 11m                 | 32m                              | 21m   | MUD<br>BM             | Alemtuzumab/Flu/Treo | CSA                 | 12  | None                                     | None   | Off Ig<br>98 m.   | 100%                  |
| P6Q  | 3/absent                  | c.177delT<br>detectable<br>10% somatic<br>reversion | None   | 2006                  | 17m                 | 47m                              | 30m   | MUD<br>BM             | Alemtuzumab/Flu/Treo | CSA/MMF             | 10  | None                                     | Low grade CMV<br>urine → No TTT<br>Accidental<br>discovery of old<br>CMV retinitis<br>(school<br>screen;18m post-<br>HSCT) | Off Ig<br>Poor vision.<br>106m  | 100%                  |
| P7Q  | 5/absent                  | c.150-<br>151insT                                   | AIHA<br>(steroids/IVIG/<br>Rituximab)<br><br>Severe chicken pox,<br>fungal lung infection,<br>Severe RSV<br>bronchitis | 2006                  | 2m                  | 15m                              | 13m   | MUD<br>BM             | Alemtuzumab/Flu/Treo | CSA                 | 14  | None                                     | Early<br>adenoviraemia/<br>Pneumatoxis<br>intestinalis.<br><br>Post-transplant<br>splenectomy                              | Off Ig<br>105m  | 83%T 0%M              |
| P8   | 2/absent                  | c.100C>T(R3<br>4X)                                  | Refractory<br>thrombocytopenia<br><b>Pre-HSCT<br/>splenectomy</b>  | 2005                  | birth-FH            | 11m                              | 11m   | MUD<br>PBSCs          | Alemtuzumab/Bu/Cyc   | CSA/MMF             | 17  | Grade II<br>(skin/gut)                   | None   | Off Ig<br>105m  | 80%T 7%M<br>56%B      |
| P9   | 3/Absent                  | R34X  | None   | 2004                  | 14m                 | 22m                              | 8m  | MUD<br>BM             | Alemtuzumab/Flu/Mel  | CSA/MP              | 12  | Grade II<br>(skin)                       | None   | Off Ig<br>96m   | 100%T<br>89%M<br>99%B |
| P10Q | 2/absent                  | c.469-<br>473del, and<br>ins18bp in<br>exon 5       | None   | 2004                  | 36m                 | 44m                              | 8m  | MSD<br>BM             | Alemtuzumab/Bu/Cyc   | CSA/MTX             | 38  | None                                     | EBV LPD +MV<br>Atypical<br>Mycobacterium<br>(encephalopathy)   | Off Ig<br>133m  | 100%                  |
| P11Q | 2/absent                  | L126P   | Severe respiratory<br>infection (MV)   | 2004                  | 4m                  | 15m                              | 11m   | MSD<br>BM             | Alemtuzumab/Bu/Cyc   | CSA                 | 28  | Grade I<br>aGvHD                         | Adenoviraemia/<br>pneumonia  | Off Ig<br>36m   | 100%                  |
| P12  | 2/absent                  | IVS6+2t>c   |  | 2004                  | 2m                  | 24m                              | 22m   | MUD<br>BM             | Alemtuzumab/Flu/Mel  | CSA                 | 14  | Grade IV<br>skin (steroid<br>refractory) | Adenoviral<br>enteritis/recurren<br>t pneumonia.<br>Recurrent<br>AIHA/ITP/AIN<br>(AB)<br><br>Post-transplant               | <b>On Ig</b> (low T<br>and B counts:<br>late effect of<br>prolonged<br>steroid<br>therapy).<br>bronchiectasi<br>s | 74% T0% M             |

|       |                 |  |  |      |          |     |     |   |                      |                        |    |                     |  |   |                 |
|-------|-----------------|--|--|------|----------|-----|-----|---|----------------------|------------------------|----|---------------------|--|---|-----------------|
|       |                 |  |  |      |          |     |     |   |                      |                        |    |                     | splenectomy  | 138m  |                 |
| P13   | 5/absent        | c777+1 G>A splice site mutation          | CMV pneumonitis (MV)<br><br>ALL<br><br>Post-chemo fungal disease.<br><br>AIN (Rituximab)   | 2013 | 4m       | 14m | 10m | TCR alpha beta/B celldeplet edhaplo<br><br>PBSCs  | ATG/Flu/Treo/TT      | CSA                    | 15 | None                | CMV viraemia D+3 followed by CMV retinitis after 2m. AIHA, ITP (AB)                              | Off Ig<br>Drop of vision 21m                          | 100%            |
| P14   | 5/absent        | c777+1 G>A splice site mutation          | CMV pneumonitis (no MV)  | 2014 | 4m       | 21m | 17m | TCR alpha beta/B cell depleted haplo<br><br>PBSCs | ATG/Flu/Treo/TT      | None                   | 21 | Grade II (skin/gut) | CMV viraemia D+7 followed by CMV retinitis after 1m.<br><br>Atypical ITP                         | <b>On Ig</b> (low IgM with normal B cell counts). 19m | 100%T<br>94%M   |
| P15Ω  | 5/low           | c.961C>T                                 | AIHA/AIN (Rituximab)   | 2013 | 5m       | 14m | 9m  | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF                | 15 | None                |  | Off Ig<br>21m   | 100%            |
| P16   | 5/absent        | whole gene del                           | AIHA/ITP   | 2014 | 14m      | 19m | 5m  | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF                | 21 | None                |  | Off Ig<br>36m   | 93%T 17%M       |
| P17 Ω | 2/Absent        | c687del (p.Lys230Arg fsX31)              | CMV viraemia   | 2011 | 1m       | 11m | 10m | mMUD (1B/1C) cord                                 | Treo/Flu             | CSA/MMF                | 45 | Grade II (skin/gut) | Low grade CMV reactivation D+27 followed by detection of retinal scars at 12m post-transplant.   | Off Ig<br>52m   | 100%            |
| P18   | 2/low           | c.37C>T (PArg13*)                        | CMV viraemia   | 2013 | 3m       | 14m | 11m | MSD<br>BM   | rATG/ Bu (RIC)/Flu   | CSA/MMF                | 30 | Grade I skin        | Parafllu III pneumonitis followed by CMV viraemia  | Off Ig<br>28m   | 100%            |
| P19Ω  | 3-4/absent      | c687del (p.Lys230Arg fsX31)              | CMV viraemia. severe perianal/oral thrush, severe respiratory infection(CPAP).<br><br>Refractory thrombocytopenia<br><br><b>Pre-transplant splenectomy</b> | 2012 | 1m       | 19m | 18m | mMUD 8/10 cord                                    | Treo/Flu             | CSA/MMF                | 17 | Grade II skin       | CMV retinitis 2m post-transplant   | Off Ig<br>Slight drop of vision 44m                   | 100%            |
| P20   | 2/Absent        | stop mutation - c.763del C               | None   | 2013 | 5m       | 14m | 11m | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF                | 19 | Grade I skin        | None   | Off Ig<br>24m   | 100%            |
| P21   | 2/Absent        | c.121C>T (p.Arg41X)                      | RSV bronchitis   | 2012 | 3m       | 17m | 14m | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF                | 16 | None                | Adenoviral reactivation Parafllu III pneumonitis Late disseminated varicella 18m post-transplant | 24m   | 100%            |
| P22Ω  | 2/Absent (FACS) | Exon10c.126 3-1266dup (pGLY423CYS fsX73) | None   | 2010 | 2m       | 22m | 20m | mMUD 9/10 1C cord                                 | Treo/flu             | CSA/MMF                | 20 | Grade I skin        | Chronic warts for 2 years post-transplant (resolved)   | Off Ig<br>17m   | 100% T<br>66% M |
| P23   | 5/Low           | c.143C>T[pT HR48lle]                     | AIHA/ITP (Rituximab)   | 2010 | 9m       | 23m | 14m | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF/M P (0.5mg/kg) | 19 | None                | Refractory AIHA/ITP (Rituximab)  | Off Ig<br>63 m  | 100%T<br>98%M   |
| P24   | 5/ Absent       | c.100 C>T (R34X)c.100C >T ( R34X)        | AIHA/anti-HLA (Rituximab)/Steroids/ <b>Pre-transplant splenectomy</b>  | 2010 | Birth-FH | 13m | 13m | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF/M P (0.5mg/kg) | 16 | Grade I skin        |  | Off Ig<br>60m   | 100%            |
| P25Ω  | 3/Absent        | 273G>T in intron 2                       | Chronic periorbital inflammation (no specific organism retrieved)  | 2010 | 9m       | 18m | 9m  | MUD<br>PBSCs                                      | Alemtuzumab/Flu/Treo | CSA/MMF                | 17 | Grade II (skin/gut) | Recurrent AIHA; positive cold agglutinin (Rituximab)   | <b>On Ig</b> (delayed B cell recovery post-           | 100%            |

|      |          |  |  |      |     |   |      |   |  |                 |   |   |   |  |              |
|------|----------|--|--|------|-----|---|------|---|--|-----------------|---|---|---|--|--------------|
|      |          |  |  |      |     |   |      |   |  |                 |   |   |   | Rituximab).<br>63m   |              |
| P26  | 3/NA     | IVS7-2a>g  | None<br>Refractory<br>thrombocytopenia<br><br><b>Pre-transplant<br/>splenectomy</b>  | 1996 | NA  | 36m   | NA   | MUD<br>BM   | Bu/Cyc   | CSA/MTX         | 30  | Grade IV<br>skin (steroid<br>dependent) |   | Off Ig<br>172m   | >99% (WB)    |
| P27  | 3/absent | (NA)   | CMV viraemia   | 1998 | NA  | 23m   | NA   | MSD<br>BM   | Alemtuzumab/Bu/Cyc   | CSA/MTX         | 28  | Grade I skin                            | CMV enteritis<br>Chronic perineal<br>warts.   | Off Ig<br>6m (No<br>further<br>Follow-up in<br>London).                      | 100%         |
| P28  | 3/Absent | Q20X   | Chronic otitis media<br><br>Perianal abscesses<br>Repeated cellulitis  | 1998 | 7m  | 1 <sup>st</sup> TX: 12m.<br><br>2 <sup>nd</sup> : 25m | 5m   | CD34 +<br>selected<br>Haplo<br>(father)<br>BM<br><br>CD34<br>+selected<br>Haplo<br>(father)<br>BM/PBSC<br>s | rATG/Flu/Mel<br><br>Alemtuzumab 0.6<br>mg/kg/Cyc<br>150mg/kg/methylprednis<br>olone 12 mg/kg | CSA<br><br>None | Failed<br>engraftment<br>D+30<br><br>22m              | NA<br><br>None                          | CMV viraemia<br>Fungal lung   | Off Ig<br>150m   | 100%         |
| P29  | 5/Absent | T284C single<br>nucleotide<br>substitution<br>(F84L) | Vasculitis/arthritis<br>Refractory<br>thrombocytopenia<br><b>Pre-TX splenectomy</b>  | 2001 | NA  | 144m  | NA   | MUD<br>BM   | Alemtuzumab/Flu/Mel  | CSA             | 21  | Grade II<br>skin/gut/live<br>r          | RSV pneumonitis<br>EBV viraemia, no<br>PTLD   | Off Ig<br>64m  | 100%         |
| P30  | 5/Absent | Q20X   | Vasculitis   | 2001 | 3m  | 1st Tx:144m<br><br>2 <sup>nd</sup> Tx: 150m           | 141m | MSD BM<br>(P28)<br><br>Combine<br>d MSD/<br>CD34+sel<br>ected<br>haplo(fat<br>her)<br>PBSCs                 | Alemtuzumab/Flu/Mel<br><br>rATG/Bu/Cyc   | CSA<br><br>CSA  | PB (3m) 10%<br>donorT<br>cells,0%<br>donorM<br><br>14 | NA<br><br>Grade I skin                  | Vasculitis<br>controlled by<br>steroid therapy  | Off Ig<br>149 m  | 100%         |
| P31Q | 5/Low    | c.271C>T   | ITP/Vasculitis<br>(Steroids/Rituximab/<br>IVIg)  | 2012 | 5m  | 55m   | 50m  | MSD<br>BM   | Bu (RIC)/Flu   | CSA/MTX         | 20  | Grade I skin                            | None  | Off Ig<br>36 m   | 100%         |
| P32  | 5/Absent | T284C single<br>nucleotide<br>substitution<br>(F84L) | Arthritis<br><br>Recurrent<br>Candida infection<br><br>Refractory<br>thrombocytopenia<br><b>Pre-transplant<br/>splenectomy</b>   | 2000 | 9m  | 108m  | 99m  | MUD<br>BM   | Alemtuzumab /Flu/Mel   | CSA/MP          | 23  | None                                    | Intermittent joint<br>swelling<br>(on/off Ibuprofen)  | Off Ig<br>81 m   | 74% T<br>0%M |
| P33Q | 5/NA     | G405fX495  | AI colitis with severe<br>failure to thrive.<br><br>Localised cutaneous<br>EBV<br>LPD of the thigh<br><br>Cryptosporidium<br>cholangiopathy<br><br>Refractory<br>thrombocytopenia<br><b>Pre-transplant<br/>splenectomy</b><br><br>Recurrent<br>Molluscum/skin<br>warts | 2001 | 42m | 204m  | 162m | MUD<br>BM   | Alemtuzumab/Flu/Mel  | CSA             | 31  | None                                    | SCC at<br>gastrostomy site<br>at 3m post-<br>Transplant.<br><br>Cryptosporidium<br>enteritis<br>EBV viraemia<br>(Rituximab) | <b>On Ig</b><br>60 m<br>(Post-<br>Rituximab;<br>normal B, low<br>serum IgM). | 100%         |

|      |                        |                                    |   |      |    |    |    |              |                      |         |    |              |  |               |  |
|------|------------------------|------------------------------------|---|------|----|----|----|--------------|----------------------|---------|----|--------------|--|---------------|--|
| P34Ω | 5/Absent<br>4% By flow | premature<br>stop codon<br>exon 10 | Neonatal<br>enteocolitis.<br><br>Lymphoid<br>hyperplasia<br><br>Carrier of FMF gene<br>Autoinflammatory<br>phenomenon.<br>Coomb's positive<br>(steroids/Anakinra) | 2013 | 4m | 9m | 8m | MUD<br>PBSCs | Alemtuzumab/Treo/Flu | CSA/MMF | 19 | Grade I skin | Recurrent auto-<br>inflammatory<br>phenomenon<br>with poor donor<br>myeloid<br>engraftment (DLI<br>X3 started 6<br>months post-<br>transplant).<br><br>Gut malrotation<br>with Ladd<br>operation at 22<br>months post-<br>transplant.<br><br>Patchy<br>granulomas of the<br>gut at 24 months<br>post-transplant<br>(Sulfasalazine) | On Ig<br>44 m |  |
|------|------------------------|------------------------------------|---|------|----|----|----|--------------|----------------------|---------|----|--------------|--|---------------|--|

**Abbreviations:** Bu:Busulfan,Cyc:Cyclophosphamide ,rATG-rabbit ATG, Treo:Treosulfan, TT:Thiotepa, Mel:Melphalan, MP::methylprednisolone, BP: peripheral blood, T: T cell, M: myeloid,CMV:Cytomegalovirus, Flu:Fludarabine, GvHD- Graft versus Host Disease, , mMUD- mismatched unrelated donor, AIN:autoimmune neutropenia, AIHA:-Autoimmune haemolyticaemia, Al:autoimmune, MSD:matched sibling donor, MUD:matched unrelated donor, Haplo:haploidentical transplant, mMUD:mismatched unrelated donor, BM:bonemarrow, PBSCs:peripheral blood stem cells , MV-mechanical ventilation, LPD-lymphoproliferative disease. DLI-donor lymphocyte infusion, SCC:squamous cell carcinoma, Haplo:haploidentical, RIC: reduced intensity conditioning.FH: family history.

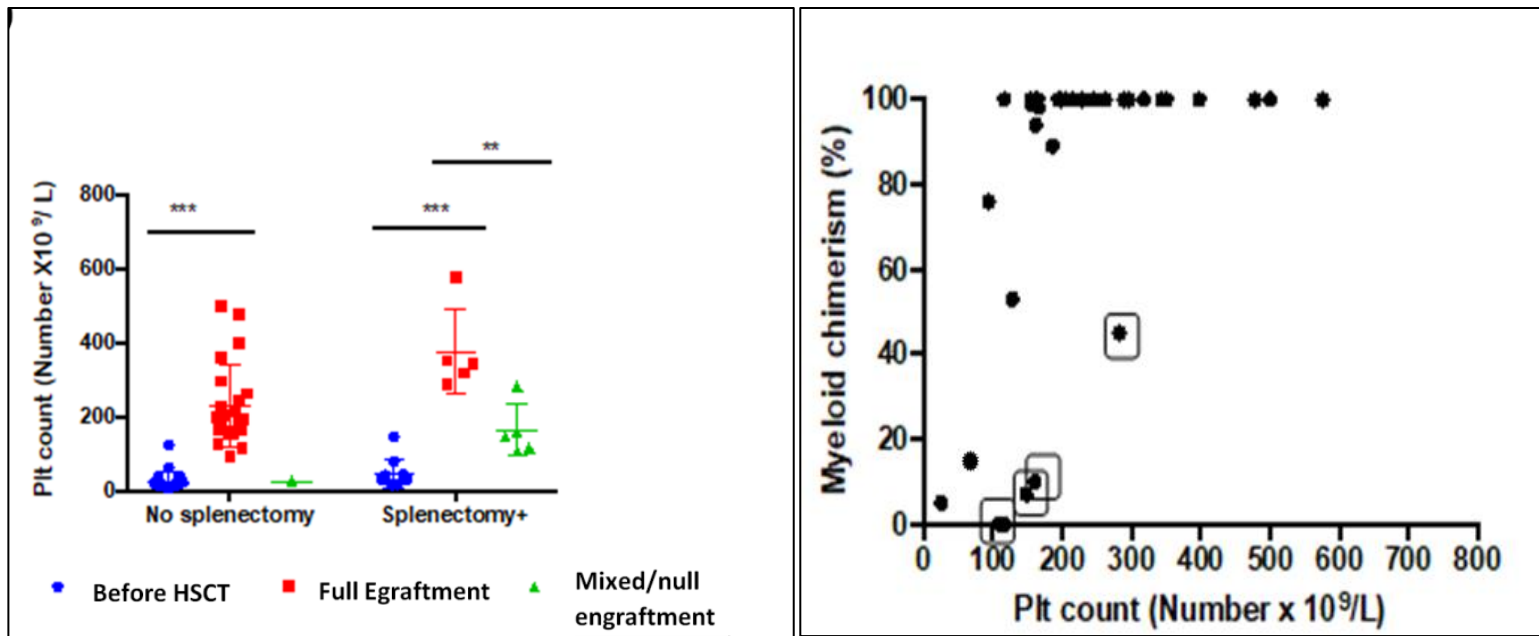
Ω Denotes patients who had novel mutations. P17 and P19 are brothers who share the same novel mutation.

† Neutrophil engraftment: ANC >0.5x10<sup>9</sup>/L for 3 consecutive days. P26-P28received their transplant beforethe year 2000.

Figure 1: Platelet recovery post-transplant

1a)

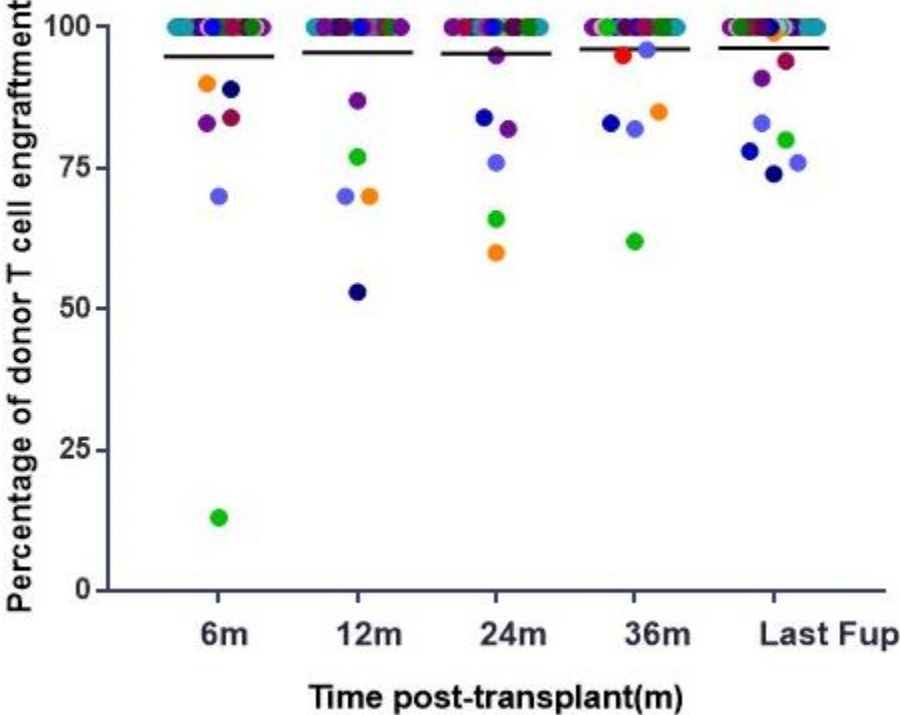
1b)



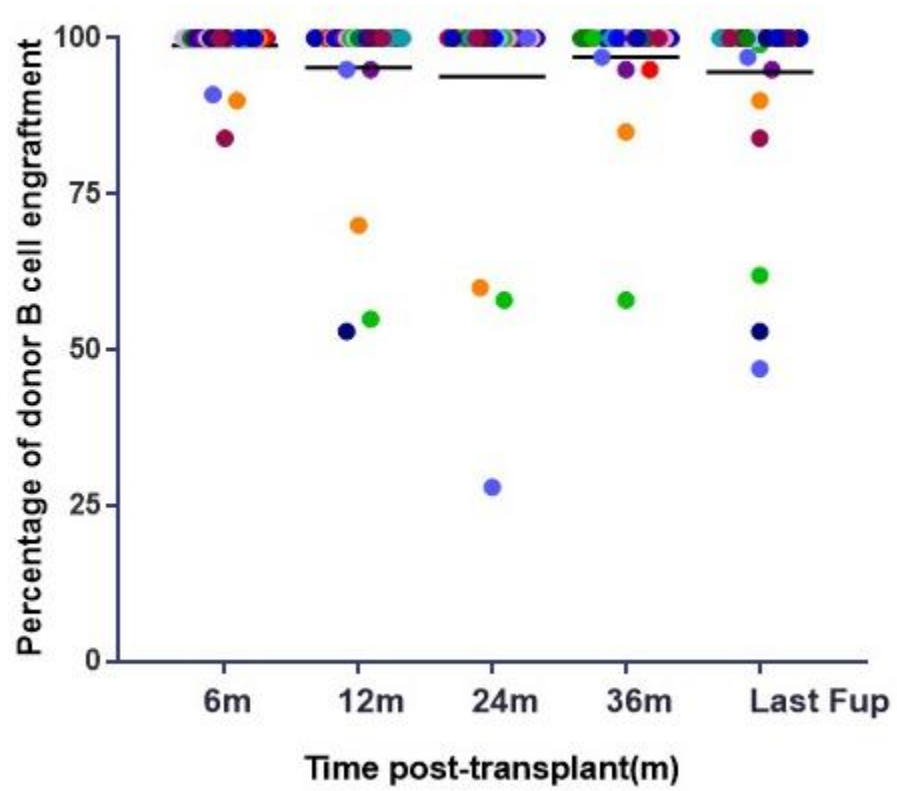
In Figure 1b: Boxes represent patients who had donor myeloid engraftment below 50% and were splenectomized.

Figure2: Kinetics of donor engraftment

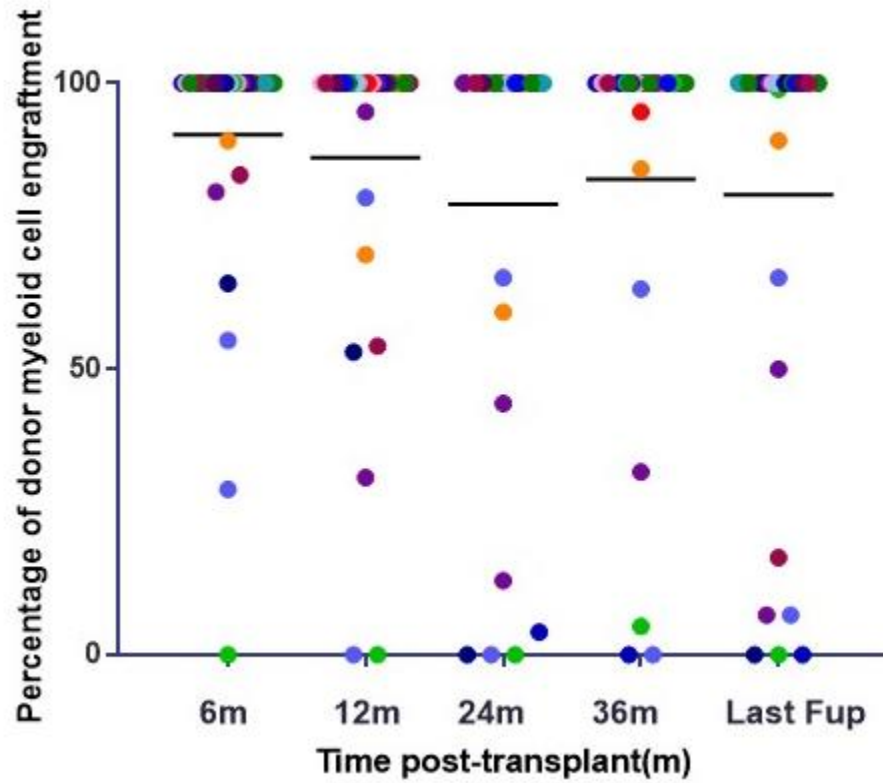
2a) Donor T cell engraftment



2b) Donor B cell engraftment



## 2c) Donor myeloid cell engraftment



Abbreviations:Fup: follow-up.

P8 had a drop in donor T cell engraftment to 13% at 6 months post-transplant this was followed by a sustained higher donor T cell engraftment above 70% from 1 year post-transplant till last follow-up.





