Post Bone Marrow Transplant Monitoring of Host/Donor Chimerism

Background
Single nucleotide polymorphisms (SNP) are normal variations in the DNA sequence within the population. Real Time PCR (qPCR) is a quantitative PCR method whereby the amount of target sequence can be determined. qPCR of SNPs is an informative and sensitive method for assessing donor engraftment after conventional or reduced intensity (RIC) conditioning bone marrow transplant. We currently identify recipient and donor specific SNPs from a panel of 34 markers. The sensitivity of the test (% recipient detected in a background of donor) is at least 0.1%. qPCR of SNPs is applicable to both sex-matched and mismatched transplantation. However, if leukaemia specific markers for the detection of minimal residue disease are available (i.e. fusion genes), these are generally more sensitive than SNP analysis.

Peripheral blood analysis is generally more useful than bone marrow and lineage specific chimerism should be considered the assay of choice in the non-myeloablative setting, especially when combined with donor lymphocyte infusions (DLI) as early patterns of cell specific chimerism may not only predict relapse but also graft-versus-host disease (GVHD).

Samples
Pre transplant
Send 4mls EDTA peripheral blood with an EPR haematology request, from both host and donor at the time of work up.

Post transplant
PERIPHERAL BLOOD MONITORING OF CD3 CHIMERISM
This is mandatory in all patients receiving conditioning regimens containing ATG or Alemtuzumab. Results are used to guide withdrawal of immunosuppression because mixed CD3 chimerism can commonly occur with this protocol. With patients with falling donor CD3 chimerism (<80%), more than 100 days post transplant, then immunosuppression should be rapidly tailed over a few weeks if possible (not possible in the presence of GvHD). If this fails to improve CD3 chimerism then DLIs may be given, although these should generally only be given more than 12 months post-transplant, except for selected patients at high risk of relapse.

PERIPHERAL BLOOD MONITORING OF WHOLE BLOOD CHIMERISM
In most patients this may alert to possible disease relapse, although some patients may develop mixed whole blood chimerism in the absence of relapse. Patients should be assessed for disease relapse according to standard methods. In the absence of relapse, donor lymphocytes infusions may be considered as for cases of mixed CD3 chimerism.

Send 10mls EDTA (3 bottles) peripheral blood with a haematology EPR request at 1, 3, 6, 9 12, and 24 months as indicated on Investigations Post BMT B.15 attached to the front cover of BMT patient’s medical notes. Request chimerism for CD3 and Whole Blood.

BONE MARROW CHIMERISM
Bone marrow chimerism is a useful technique for monitoring for disease relapse. It is not necessary if there is a molecular marker for monitoring disease e.g. BCR-ABL monitoring for Ph+ ALL and CML. It may be performed on CD34 subsets.
Bone marrow 2mls EDTA should also be sent at 1, 3, 6 and 12 if BM aspirate is being performed. For cell specific chimerism, samples should not be more than 72 hours old.

**Send samples to:**
Thames Valley Haemato Molecular Diagnostics Service (TVHMDS)
Level 4, John Radcliffe Hospital
Oxford
The results should be available in 2 weeks on the hospital haematology result system.

**Enquiries:** Tel: 01865 572769 molhaem@ouh.nhs.uk

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**Review**

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
<th>Date</th>
<th>Version</th>
<th>Review date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Andy Peniket</td>
<td>Update</td>
<td>July 2012</td>
<td>V.2.0</td>
<td>July 2014</td>
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<td>Jan 2016</td>
<td>V.2.1</td>
<td>January 2018</td>
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