Pre-transfusion testing for patients on anti-CD38/CD47: Genotyping and matching vs screening for underlying antibodies

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SNBTS

- 5 Patient Testing sites
- Blood Bank and RCI
- Clinical activity differs – WoSCC in Glasgow, RCI Lab for 15 HTLs
- Aim is consistency across all 5 sites
- Good progress in all aspects
- ..... Then along came DARA

Blood Provision – The Challenge

- DARA – IgG human monoclonal antibody, specifically targets CD38
- CD38 – relatively high expression on all malignant cells in MM patients
- CD38 – low expression on ALL red cells
- Panreactivity with reagent screening / ID panel cells and donor red cells
- Inability to exclude allo-antibodies

First Patient

- WoSCC December 2015
- Treatment with DARA had commenced!
- Alerted by clinician to problems in antibody screening / matching
- Required transfusion so quick decision to be made
- Phenotyped units readily available
- Pre-treatment sample available

Ongoing Blood Provision – Glasgow

- Clinical trial – “Unlikely to be approved”
- Patients unlikely to form allo-antibodies
- Minimal blood requirement in Myeloma patients (rarely urgent)
- Genotype patients fully pre-treatment
- Continue with phenotype matched units
- Further patients added to trial
- Strategy not suitable on other sites

DTT – Resolving the Issue?

- BSH Guideline addendum recommended use
- SNBTS Policy required
- Method not in SNBTS Technical Manual
- Validation required – Dundee site
- X10 antibodies tested
- Better strategy for this site √
- Better strategy for both sites?

Patients Treated to Date – Glasgow

- Total patients = 5
- Number transfused = 4
- Units transfused = 1-16
- Urgent requirement = 0
- Difficulty in providing suitable units = 0
- DAT + = 5

Patients Treated to Date – Dundee

- Total patients = 5
- Number transfused = 5
- Units transfused = 6-30
- Urgent requirement = 0
- Difficulty in providing suitable units = 0
- DAT + = 5
- Allo-antibodies found = 0

Phenotyped Units Issued

- All irradiated
- Pat 1: O R1R1, K-, Jka-, s-, Leb-
- Pat 2: A R1R1, K-, Jka-, S-
- Pat 3: O rr, K-, S-, M-, P1
- Pat 4: O R1r, K-, s-, N-

Phenotyped Units vs Antibody Screening

Phenotyped Units

Advantages: Fast, compatible with patient type , ability to irradiate

Disadvantages: Expensive, irradiated wastage, patient may have allo-antibodies

Antibody Screening

Advantages: Detects allo-antibodies, inexpensive

Disadvantages: Length of time to provide units

So What's the Strategy Now?

- SNBTS Policy approved August
- In line with BSH guideline addendum
- Preferred is DTT treatment of reagent cells for AST and donor cells for XM
- Carryover noted in automated systems – new LIMS code to flag DARA patients
- Pre-treatment: Baseline pheno / geno typing + G&S
- Priority order for unit selection where DTT method not possible

Future – SMC Approval

- 09/10/17 – 4th line treatment
- Any DGH with Oncology Unit can administer
- Potentially 125 new patients p.a. in Scotland
- Increased workload for RCI section of lab
- Out of core hours testing
- “Special requirements” form to be amended
- Patient-held record

Anti-CD47 Trial Experience

- CD47 highly expressed on red cells
- Tioma (Ti-061)
- Solid tumours
- 2 sites Scotland, 1 site Holland
- Can interfere with blood grouping as well as antibody screening and DAT
- Small trial, May 2017

Anti-CD47 Trial Experience

- Plasma gives moderate to strong panreactivity with all red cells
- Reactivity remains after DTT treatment
- Reactivity remains after trypsin / ficin / chymotrypsin treatment
- Can only be eliminated by adsorption of Ti-061 with His – CD47 coated beads
- Can only test with specific anti-IgG

Anti-CD47 Trial Experience

- Pre-therapy: ABO/Rh and antibody screen
- Pre-therapy: Genotype / extended phenotype
- During therapy: Treat plasma using provided method, reagents, equipment
- Validation of method required – insufficient reagent sent!
- First patient enrolled and pre-therapy testing completed
- Trial stopped after 1st transfusion

Anti-CD47 Trial Experience

- Method is time–consuming and very different to other serological testing techniques
- Estimated **3 hours** minimum to prepare adsorbed plasma
- Interference > 3 months after therapy discontinued

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