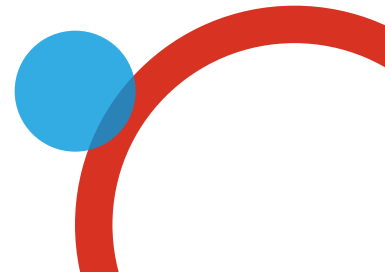


**Pre-transfusion
testing for patients
on anti-CD38/CD47:
Genotyping and
matching vs
screening for
underlying
antibodies**

Marie McQuade
Senior Clinical Laboratory Manager, SNBTS

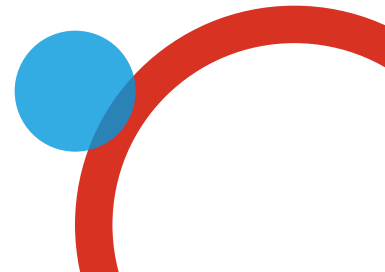
SNBTS

- 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



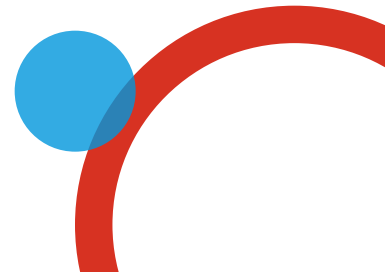
Blood Provision – The Challenge

- 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



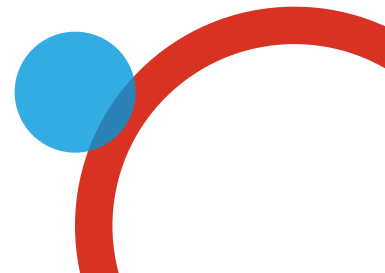
First Patient

- 🔥 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



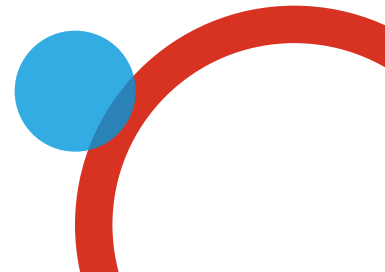
Ongoing Blood Provision – Glasgow

- 🔴 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



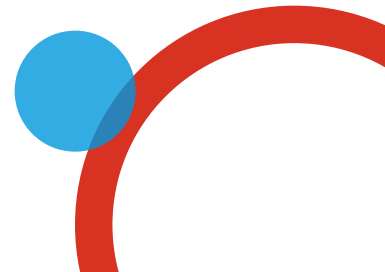
DTT – Resolving the Issue?

- 🔥 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?

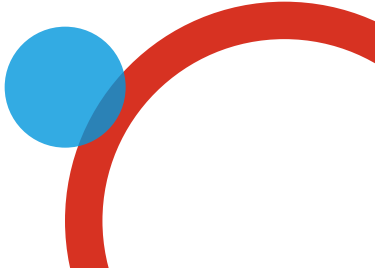


Patients Treated to Date – Glasgow

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

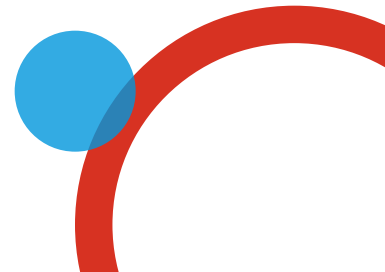


Patients Treated to Date – Dundee

- 🔥 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

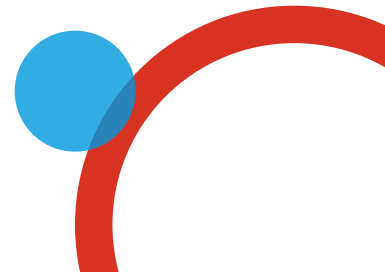
Advantages: Fast, compatible with patient type , ability to irradiate

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

Antibody Screening

Advantages: Detects allo-antibodies, inexpensive

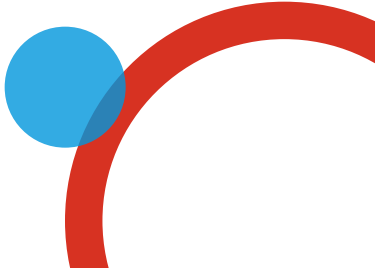
Disadvantages: Length of time to provide units



So What's the Strategy Now?

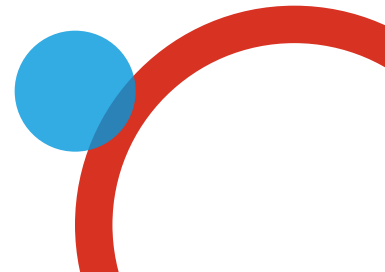
- 🔥 SNBTS Policy approved August
- 🔥 In line with BSH guideline addendum
- 🔥 Preferred is DTT treatment of reagent cells for AST and donor cells for XM
- 🔥 Carryover noted in automated systems – new LIMS code to flag DARA patients
- 🔥 Pre-treatment: Baseline pheno / geno typing + G&S
- 🔥 Priority order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

Future – SMC Approval

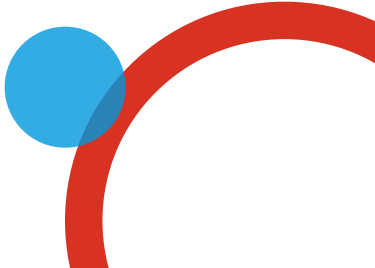
- 🔥 09/10/17 – 4th line treatment
 - 🔥 Any DGH with Oncology Unit can administer
 - 🔥 Potentially 125 new patients p.a. in Scotland
 - 🔥 Increased workload for RCI section of lab
 - 🔥 Out of core hours testing
 - 🔥 “Special requirements” form to be amended
 - 🔥 Patient-held record
- 

Anti-CD47 Trial Experience

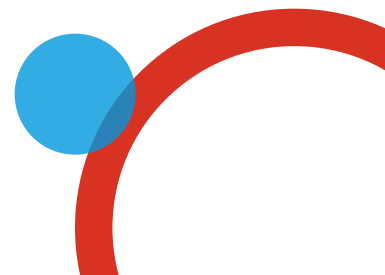
- 🔴 CD47 highly expressed on red cells
- 🔴 Tioma (Ti-061)
- 🔴 Solid tumours
- 🔴 2 sites Scotland, 1 site Holland
- 🔴 Can interfere with blood grouping as well as antibody screening and DAT
- 🔴 Small trial, May 2017



Anti-CD47 Trial Experience

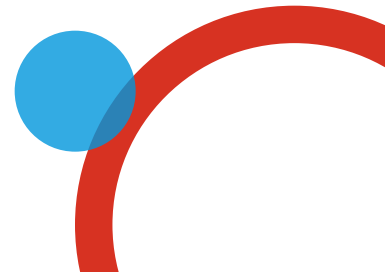
- 🔥 Plasma gives moderate to strong panreactivity with all red cells
 - 🔥 Reactivity remains after DTT treatment
 - 🔥 Reactivity remains after trypsin / ficin / chymotrypsin treatment
 - 🔥 Can only be eliminated by adsorption of Ti-061 with His – CD47 coated beads
 - 🔥 Can only test with specific anti-IgG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

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



Acknowledgements

- 🔴 Eve McLaughlin, SNBTS Glasgow
- 🔴 Mark Bonar, SNBTS Dundee
- 🔴 Dr Karen Bailie, SNBTS Glasgow
- 🔴 Dr Richard Soutar, WoSCC / SNBTS Glasgow
- 🔴 Dr Megan Rowley, SNBTS Edinburgh

