South Tees Hospitals NHS
NHS Foundation Trust

6446 – Audit of use of alemtuzumab in relapsing remitting MS

***1st* audit cycle**

Neurology Department

Date: **December 2018**

Audit Report By: **Viv Horton, Advanced Clinical Pharmacist Neurosciences**
Trust Staff Lead: **Viv Horton, Advanced Clinical Pharmacist Neurosciences**
Project Team Members: **Adrienn Petreczky, Consultant Neurologist**
Michael Osei-Bonsu, Consultant Neurologist
Karen Little, MS Nurse Specialist
Fiona Tait, MS Nurse Specialist
Claire Naisbitt, MS Nurse Specialist
Sam Hewson, MS Nurse Secretary

Clinical Audit Facilitator: **Joanne Miller**
Clinical Audit Officer: **Chris Moonie**

1. Background and Aims

The aim of this audit compare current practice of prescribing alemtuzumab in accordance with NICE guidance TA312, NHS commissioning and local guidelines developed from the product SPC.

Alemtuzumab is licensed for treating active relapsing remitting multiple sclerosis defined by clinical or imaging features. The treatment schedule is 12mg daily for days 1-5 of year 1 and 12mg daily for days 1-3 of year 2. Recent NHS England commissioning has included further treatment 12mg daily for days 1-3 of the third year if the patient's MS continues to be active.

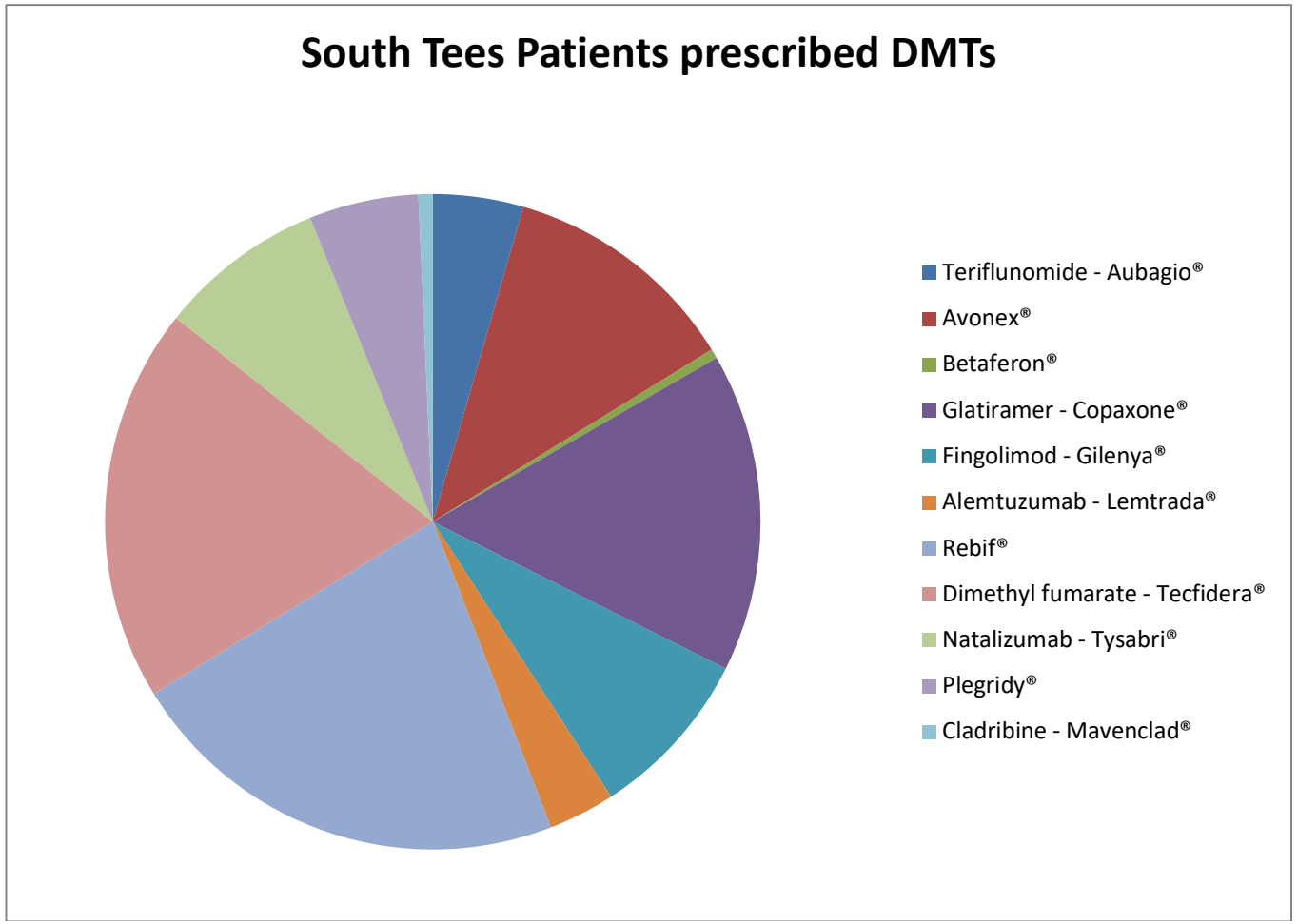
Alemtuzumab is a monoclonal antibody that is administered intraveneously, it's full mechanism of action in multiple sclerosis is not yet fully elucidated. It binds to CD52 antigen present at high levels on the surface of T and B lymphocytes and this is believed to reduce the activity of relapsing remitting multiple scelrosis. Patients need to commit to 4 years of follow up following their last infusion of alemtuzumab in order to minimise potential risks and side effects.

Risks associated with alemtuzumab include:

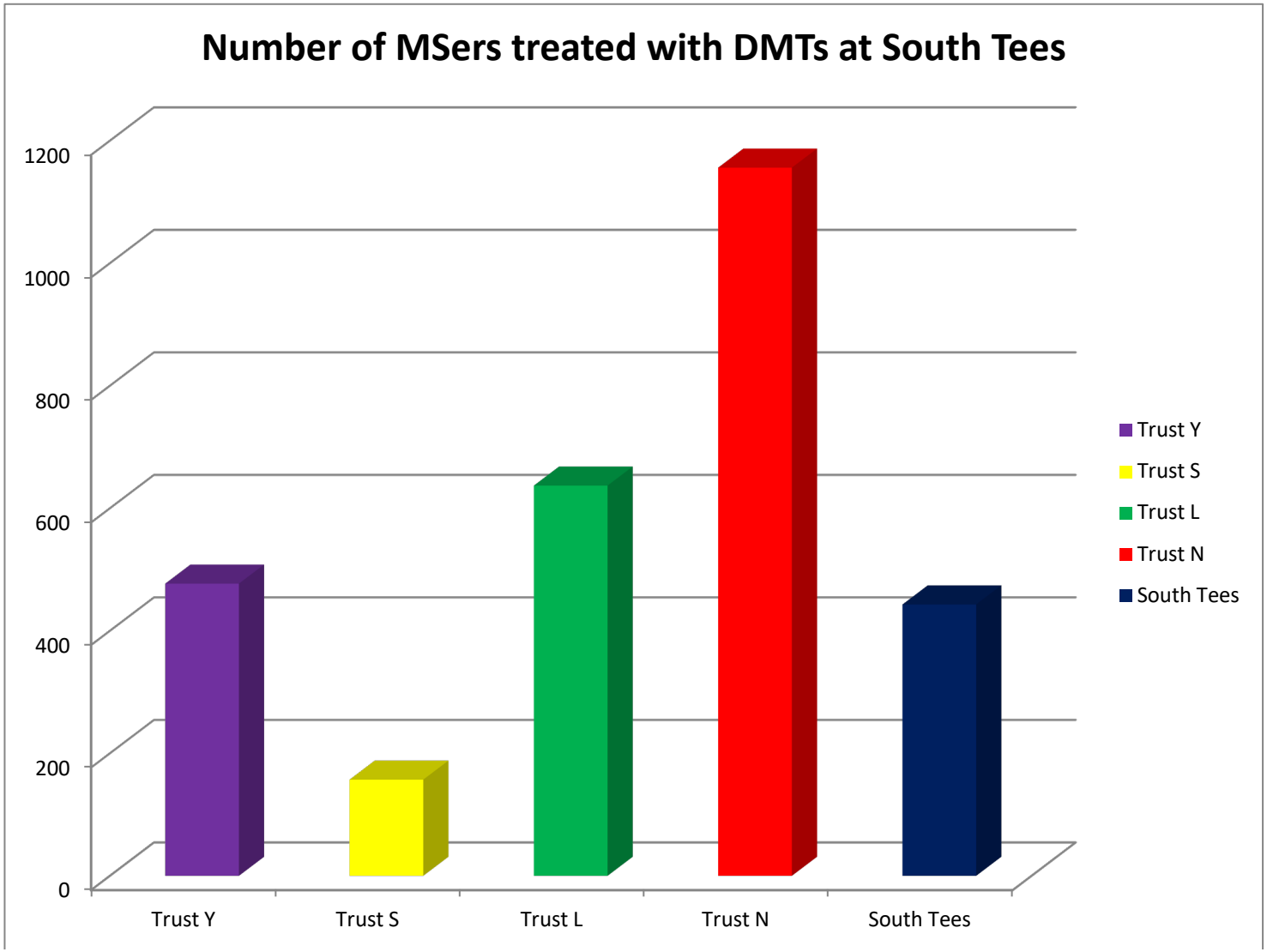
- Serious infection
- Autoimmune conditions – thyroid disorders, ITP (idiopathic thrombocytopenic purura), nephropathies including anti-GBM disease

Careful monitoring of blood tests and vigilance for signs and symptoms is therefore of high importance. Since infusion reactions are also possible, patients are closely monitored during the course of each infusion.

South Tees care for 2000 patients with multiple sclerosis (all types) and have 426 patients prescribed disease modifying treatments (DMTs) (Jul 2018). Alemtuzumab represents a small fraction of the DMTs used at South Tees.


South Tees Patients prescribed DMTs
Teriflunomide - Aubagio®
Avonex®
Betaferon®
Glatiramer - Copaxone®
Fingolimod - Gilenya®
Alemtuzumab - Lemtrada®
Rebif®
Dimethyl fumarate - Tecfidera®
Natalizumab - Tysabri®
Plegridy®
Cladribine - Mavenclad®

It can be seen that the use of disease modifying treatment is reasonably modest when compared to other trusts



2. Objective of Audit

As of October 2018 there had been 26 patients treated with alemtuzumab by the MS (multiple sclerosis) team at South Tees, this has been shown to be an effective treatment for relapsing remitting MS but requires close supervision and monitoring pre, during and post treatment to ensure patient safety and minimise potentially serious side effects. The aim of this audit was to measure how safely we are using this treatment at South Tees Hospitals NHS Foundation Trust.

3. Method

Alemtuzumab has been available to prescribe for relapsing remitting MS since 2014. In October 2018 26 patients were identified via the national Blueteq system and verified with local pharmacy system. Unfortunately it soon became evident that the local trust MS database was not currently fit for this purpose as there had been a lack of investment in properly resourcing the update and upkeep of this system. WebICE was used to view blood results and patients notes were requested for data collection.

NICE TA312 describes the situations in which alemtuzumab may be used and the Blueteq system requires the prescriber to confirm that the clinical condition meets the NHS England commissioning standards. The manufacturer has made recommendations for safe use of alemtuzumab via the SPC and product checklists, additionally the MS team have developed local guidelines for alemtuzumab use. All of these were collated to form the audit standards.

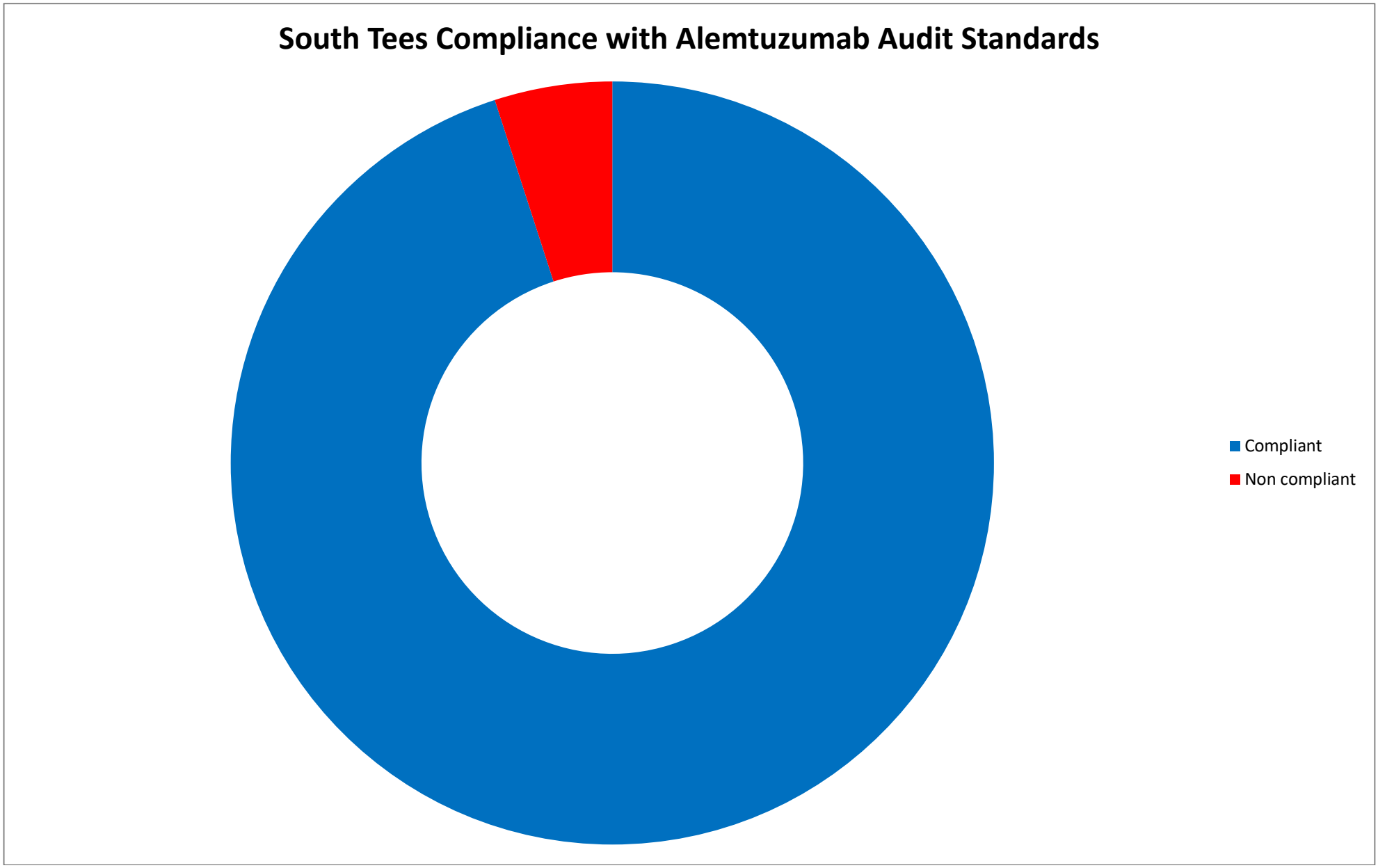
4. Results

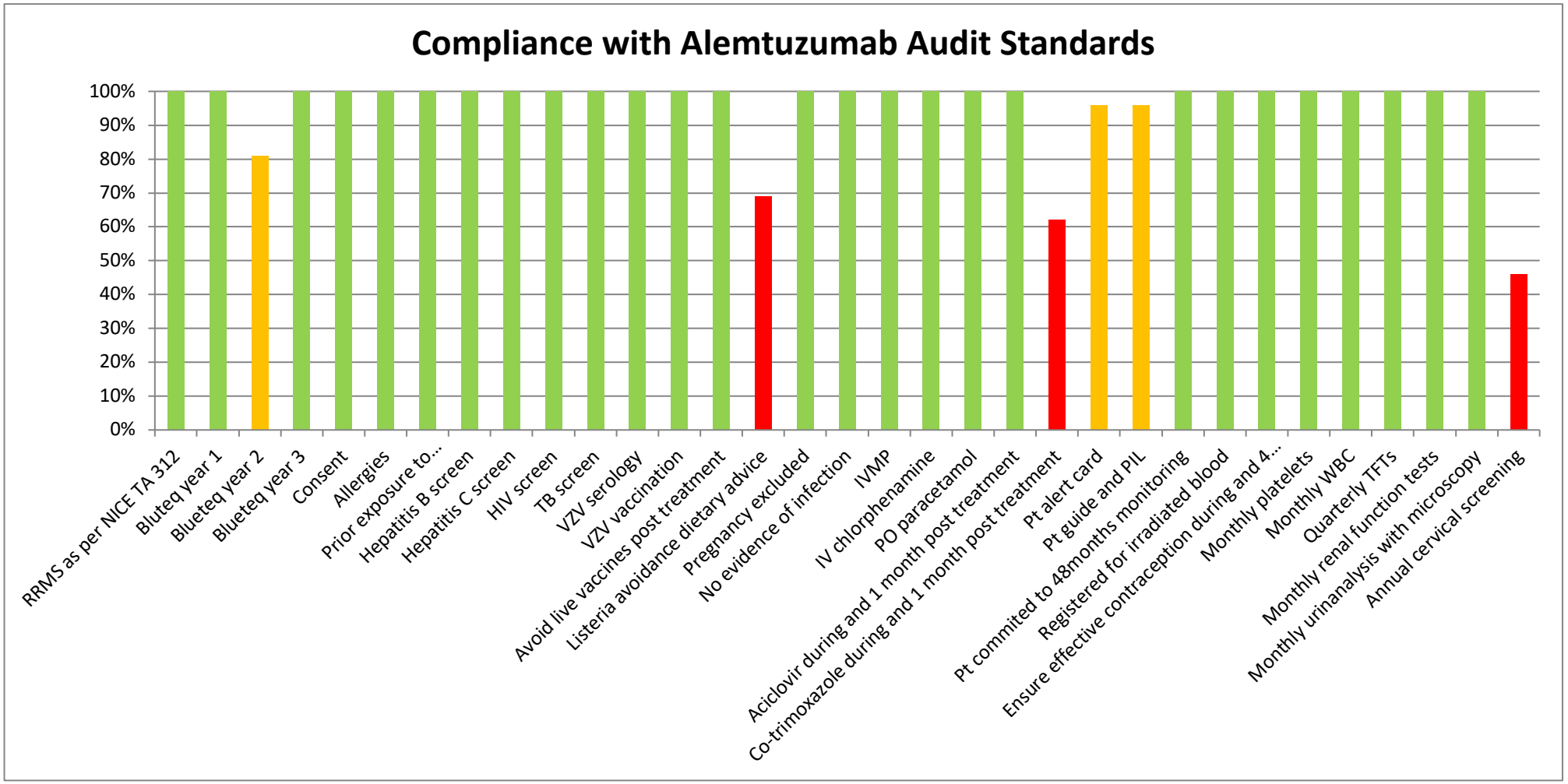
26 patients have been prescribed alemtuzumab since it was approved for use within the trust.

Measure of quality	**Standard**	**Exceptions**	**Cycle 1 Date: 12/2018**
Alemtuzumab used for adults with active relapsing-remitting multiple sclerosis	100%	None	100%
The patient has been informed about and understands the risks of serious autoimmune disorders, infections and malignancies and the measures to minimise risk	100%	None	100%
Blueteq confirms funding	100%	None	100% year 1 81% for year 2
No hypersensitivity to alemtuzumab/excipients	100%	None	100%
No prior exposure to antineoplastic/immunosuppressant therapy	100%	None	100%
Hepatitis B screen prior to treatment	100%	None	100%
Hepatitis C screen prior to treatment	100%	None	100%
HIV screen negative	100%	None	100%
No evidence of active/latent TB	100%	None	100%
Positive VZV serology	100%	None	100%
VZV vaccination in antibody negative patients (6 weeks prior to treatment)	100% if applicable	None	NA
Avoid live vaccines post treatment	100%	None	100%
Listeria avoidance dietary advice	100%	None	69%
Pregnancy excluded for female patients	100%	None	100%

No evidence of active infection	100%	None	100%
Pre treatment with corticosteroids each day of treatment	100%	None	100%
Pre treatment with anti-histamine each day of treatment	100%	None	100%
Pre treatment with anti-pyretic each day of treatment	100%	None	100%
Aciclovir prophylaxis during and for at least a month following each treatment course	100%	None	100%
Co-trimoxazole prophylaxis during and for at least a month following each treatment cycle	100%	None	62%
Pt given alert card	100%	None	96%
Pt given patient guide	100%	None	96%
Pt committed to at least 48months of monitoring	100%	None	100%
Patient has been registered as requiring irradiated blood products and provided with the patient information leaflet and alert card	100%	None	100%
Ensure women of childbearing age are using effective contraception during treatment and for 4months after	100%	Male patients	100%
Monthly platelet counts for 4 years after last treatment	100%	None	100%
Monthly WBC counts for 4 years after last treatment	100%	None	100%
Quarterly thyroid function for 4 years after last treatment	100%	None	100%
Monthly renal function tests for 4 years after last treatment	100%	None	100%

Urinanalysis with microscopy monthly for 4 years after last treatment	100%	None	100%
Annual cervical screening for female patient	100%	Male patients	46%


South Tees Compliance with Alemtuzumab Audit Standards
Compliant
Non compliant


Compliance with Alemtuzumab Audit Standards
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
RRMS as per NICE TA 312
Bluteq year 1
Bluteq year 2
Bluteq year 3
Consent
Allergies
Prior exposure to...
Hepatitis B screen
Hepatitis C screen
HIV screen
TB screen
VZV serology
VZV vaccination
Avoid live vaccines post treatment
Listeria avoidance dietary advice
Pregnancy excluded
No evidence of infection
IVMP
IV chlorphenamine
PO paracetamol
Aciclovir during and 1 month post treatment
Co-trimoxazole during and 1 month post treatment
Pt alert card
Pt guide and PIL
Pt commited to 48months monitoring
Registered for irradiated blood
Ensure effective contraception during and 4...
Monthly platelets
Monthly WBC
Quarterly TFTs
Monthly renal function tests
Monthly urinanalysis with microscopy
Annual cervical screening

5. Discussion

It can be seen that there was a high level of compliance with the audit criteria with 25 out of 31 criteria achieving 100% compliance. It seems highly likely that this is testament to the dedication of the MS team and the effective use of checklists.

The standard for Blueteq completion for year 2 of alemtuzumab reached only 81%, this is explained by the lack of continuation Blueteq form at the time of treatment for 5 patients. 69% of patients were initially counselled re dietary advice to avoid listeria since this advice was published after 8 patients had commenced treatment. 10 patients were not given co-trimoxazole during and for 1 month after treatment since their treatment was initiated prior to this updated guidance, (advised in May 2017). One patient did not appear to have been given the patient alert card and patient guide as documented in his notes, the reason for this was unclear. Female patients are advised to have annual cervical screening, however this has not been possible in this region and therefore patients could only be advised to participate in routine screening.

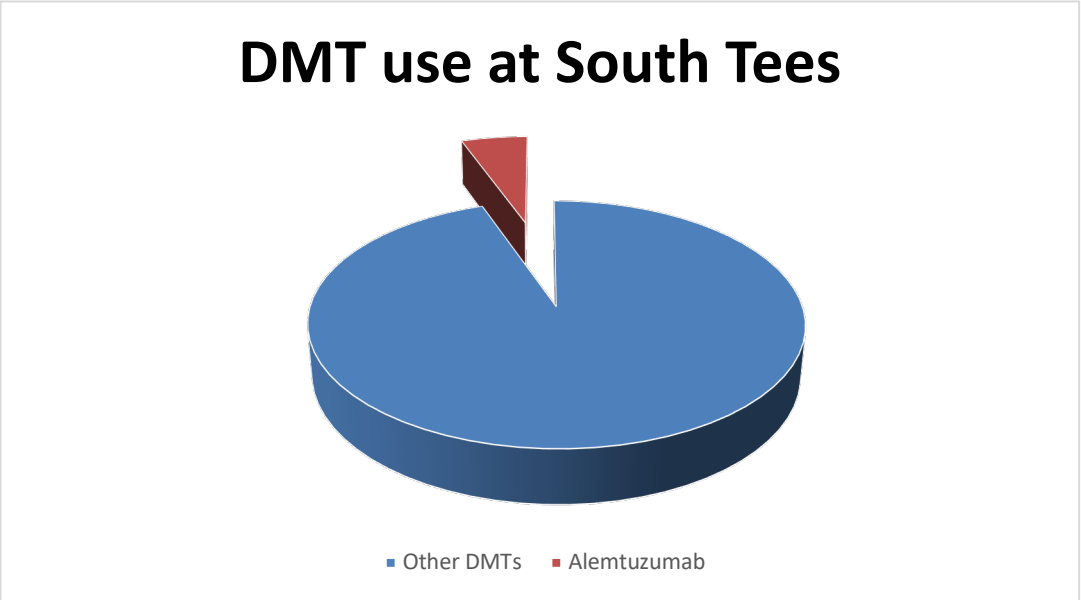
It was unfortunate that the trust does not currently have electronic noting linked to electronic prescribing since this would have significantly aided the audit process. Even the process of tracking down and viewing 26 sets of paper notes was very time consuming. Additionally it was clear that there would need to be significant investment in the MS database for this to be a usable resource. Having a real time updated electronic and searchable record would be invaluable in terms of data collection and aid the safe monitoring of this treatment.

5a. Key Successes

I believe the high compliance with these audit standards is largely due to the dedication of the MS team and the effective use of checklists. Special mention must be made of the MS nurses who undertake the majority of this monitoring and the MS nurse secretary who coordinates this process and requests all of the monthly bloods.

5b. Key concerns

The main concern is that of the sustainability of the high level of compliance with the audit standards. It is of the upmost importance that this treatment if carefully monitored however alemtuzumab is only a small fraction of the disease modifying treatment (DMTs) prescribed by the MS team to their patients; there are around 2000 patients with MS cared for by the team and 426 patients prescribed DMTs. This is summarised in the chart below.



If one considers that each of the patients prescribed alemtuzumab needs monthly review, this is a huge resource pressure for the MS nurses. They have 30 minute appointments and if there were 25 patients needing monitoring at any one time, this represents 12.5 hours per month of MS nurses' time or 150 hours/300 clinic slots per year. It is conceivable that these numbers could increase to 50 patients in the following year which would require 300hours/600 clinic slots. There are now 3 nurses in post but this can be seen to be quite a commitment, considering that many of the other DMTs also require close monitoring and around 75% of the patients under their care do not qualify for DMTs.

I think this audit raises questions around capacity within the MS team. It is also important to consider that some of these patients are able to work because of the effectiveness of this treatment and therefore require appointments outside of normal clinic hours. It is possible to consider patients having their bloods taken by their GP, in an outpatient setting, but the MS team would still need time allotted to review the results. It is unclear if compliance with this ongoing monitoring would be so high if patients were not seen by their MS nurse at these appointments.

6. Actions

This audit has therefore been presented to the MS team and the neurology directorate in order to begin discussions about how to change working practices to ensure sustainability of this excellent service.