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Infectious Complications of High Efficacy Therapies in Multiple Sclerosis: Pre-treatment screening and risk mitigation

Introduction

- There is no gold standard for baseline screening and risk mitigation of infectious complications prior to initiating multiple sclerosis (MS) disease modifying therapies (DMTs).
- Baseline screening is often based on recommendations from the summary of product characteristics (SPC).
- These recommendations are based on adverse effects reported during clinical trials, often excluding known class adverse effects that have been reported in other disease areas.
- Clinical trials involve a finite number of patients over an average period of 24 months and patients with known risk factors are often excluded from participating in clinical trials.
- Consequently some serious adverse effects are only identified during real world practice. Any new risks identified during post marketing authorisation pharmacovigilance are added to the SPC as they become known.
- JCV/ PML risk stratification in natalizumab treated patients is out of the scope of this report.

Objectives

- To develop local standards for baseline infection screening prior to starting high efficacy DMTs in MS
- To evaluate infection screening and risk mitigation of infectious complications prior to initiating high efficacy DMTs

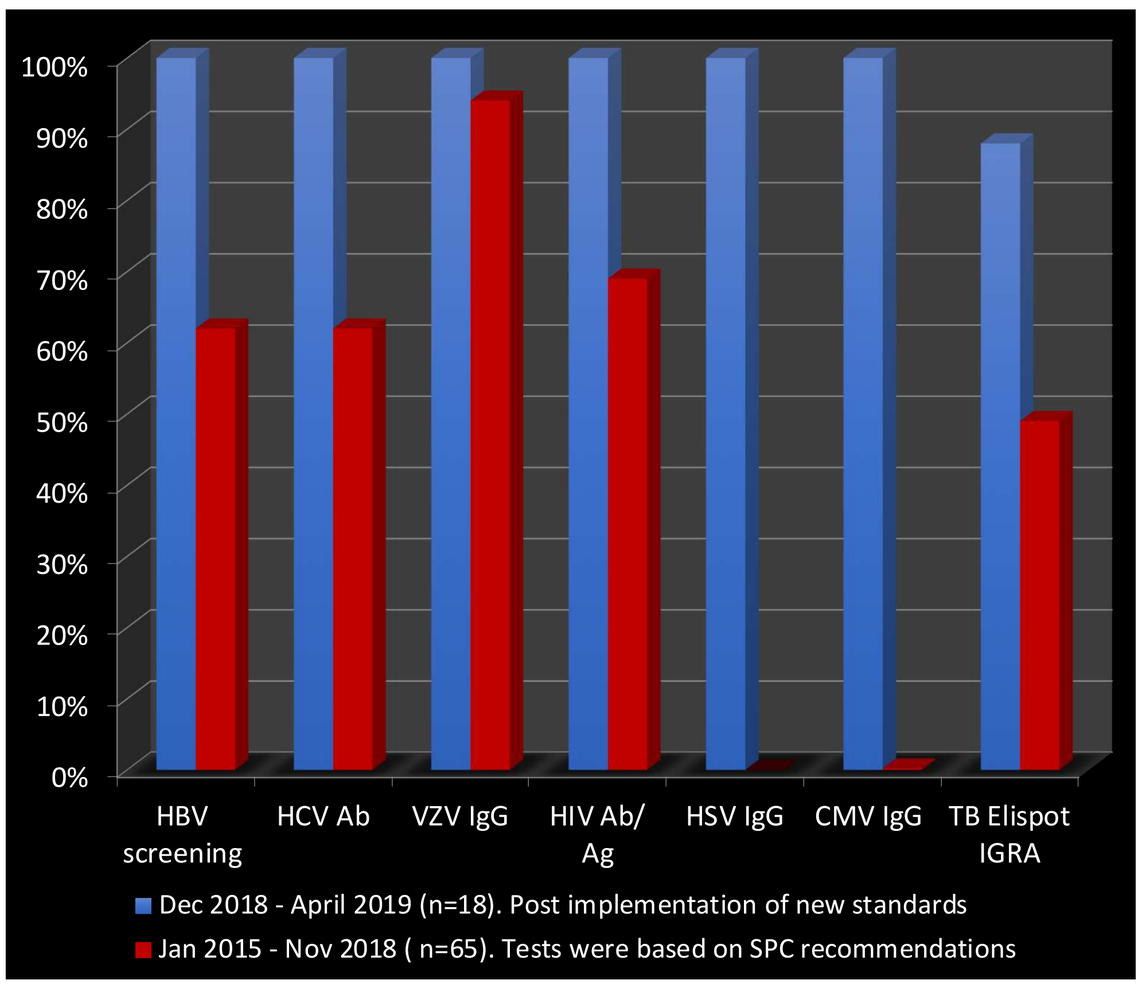
Methods

- In 2018 the local MS and infectious diseases (ID) teams developed standards for baseline infection screening prior to starting high efficacy DMTs in MS.
- An audit of baseline infection screening to determine pre - alemtuzumab, cladribine, fingolimod, natalizumab and ocrelizumab screening compliance with the new standards was undertaken. Data was obtained from available electronic records.
- Exclusion criteria: Treatment initiated during clinical trials, treatment initiated by another MS centre and incomplete electronic records from local district general hospitals or out of area.

Results: Agreed local standards

- We agreed on a standard set of tests: HBV screening (including core antibody), HCV Ab, VZV IgG, HIV Ab/ Ag, HSV IgG, CMV IgG and TB Elispot IGRA.
- The recommended tests were based on known risks and risks that can be predicted from mechanisms of action of DMTs.
- We acknowledge that not all of the high efficacy DMTs carry the same level of risk for the above infections, however standardising tests makes it more likely that infection screening will be performed consistently. Moreover screening for multiple infections regardless of planned treatment aids decision making during treatment switching.
- We recommend immunisation with Pneumococcal 23 valent and Hib prior to initiating long term immunosuppression with ocrelizumab. For those with incomplete immunisation records, we recommend MMR IgG and VZV IgG serology and immunisation with DTP, MenACWY, influenza, and Men B vaccines.

Figure 1 : Pre- high efficacy DMT infection serology screening



Risk mitigation

- Complete vaccine status check lists were not available to audit from clinical electronic records. Measles IgG, Mumps IgG and Rubella IgG screening was completed on the two occasions when immunisation records were not available.
- 2 out of 48 samples tested positive for latent TB. In both cases treatment with isoniazid 300mg was initiated pre-ocrelizumab / natalizumab.
- 6 HSV and 4 CMV IgG positive samples from the 18 tested. Reactivation risk awareness and prompt treatment if symptoms develop. Regular CMV viral load tests for n=1 on ocrelizumab plus acute steroids.
- Multiple positive viral screening tests identified in one case could be attributed to antibody and immunoglobulin acquisition from prior IVIg infusion.

Conclusions

Infection screening was more complete following implementation of new standards.

Pre- treatment screening checklists that are integrated with the electronic patient record will help ensure consistency.

Going forward, collaboration between MS specialists and other specialties such as infectious diseases to develop a toolkit and a consensus statement on managing infection risks associated with MS DMTs will improve the care quality of care for people on MS DMTs.

References

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Multiple Sclerosis Academy *Raising the Bar*

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