Design and implementation of an automated platform supporting the Alemtuzumab risk management plan: The Alemtuzumab MS Safety Systems (AMS3) study.

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Background

Alemtuzumab is an effective treatment for MS, but pathology monitoring for late adverse effects is difficult to implement. In the real world, patients may miss tests, and pathology reports might not be received or reviewed. Risk management theory suggests that in addition to education and training of staff and patients to improve human factors, safety can also be improved by adding organisational layers of defense, with distinct characteristics that have different non-overlapping points of weakness (Reason, 2000). We proposed that a computerised monitoring clinical decision support system (CDSS) would have different strengths and weaknesses to traditional human-based clinical care and would complement safety as an additional layer.

Aims

To improve the benefit:risk ratio of alemtuzumab for MS by developing:

- an efficient automated CDSS to prompt and track pathology
- providing customisable alerts for abnormalities in identified risks
- an app based education module
- a systematic approach to pre-treatment screening.

Dataflow timeline for communicating an ITP result

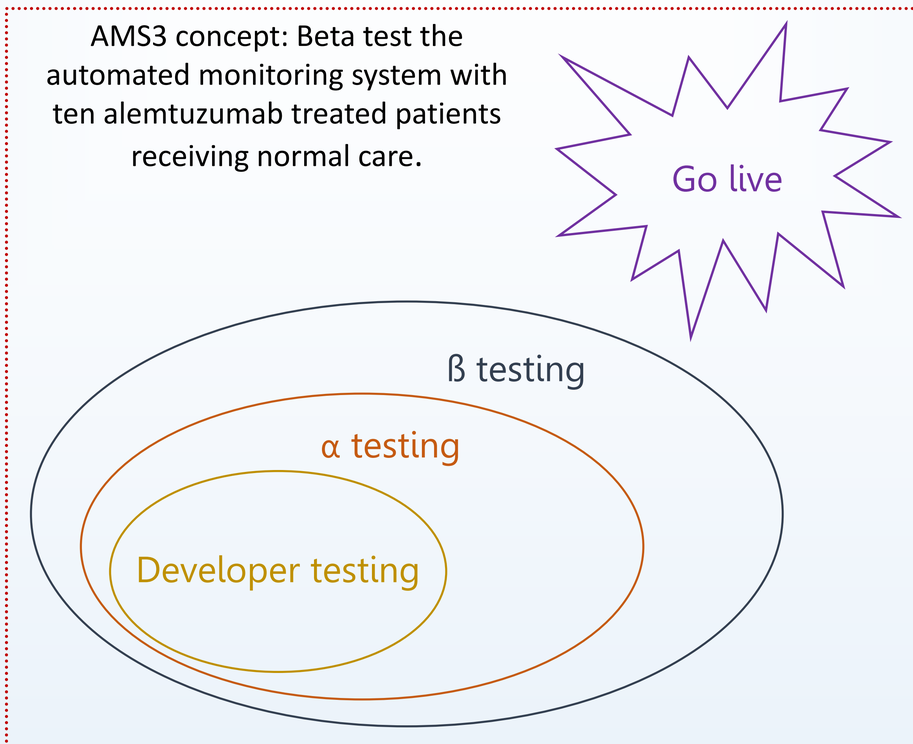
Time Stamp	Time elapsed	Event
11/07/2016 08:30	Collected	Pathology collected
12/07/2016 14:04	Result +29H 26m	Released to Pathology company server
12/07/2016 14:12	+8m	Received by RiskMx™ server
12/07/2016 14:16	+12m	Alert sent
12/07/2016 14:18	+14m	Alert acknowledged by patient
12/07/2016 14:51	+47m	Alert acknowledged by neurologist's delegate
12/07/2016 15:08	+64m	Alert Acknowledged by neurologist (from Germany)

Methods

Ten patients with active MS treated with alemtuzumab and followed for 2 years served as beta-testing patients for the CDSS. Pathology monitoring was performed by a networked pathology provider and hardcopy reports reviewed. Electronic results in HL7 format were also sent to CDSS project software (RiskMx™), once operational. We developed electronic alerts for abnormal results and patient reminders that were sent as required to neurologists, their teams, and/or to patients. Compliance, time to receipt, time to alerting, and clinical consequences of alerts were evaluated.

Inclusion and exclusion criteria mirrored those of the CAMMS03409 study (Coles et al., 2008) including amendments 1 and 2, amended to include email and cell phone. The study was approved in 2013 by the Sydney Local Health District Ethics committee (CH62-6-2013-180). The study was registered with the Australian New Zealand Clinical Trials Registry, ACTRN12613001027707, Universal Trial Number: U1111-1147-9190.

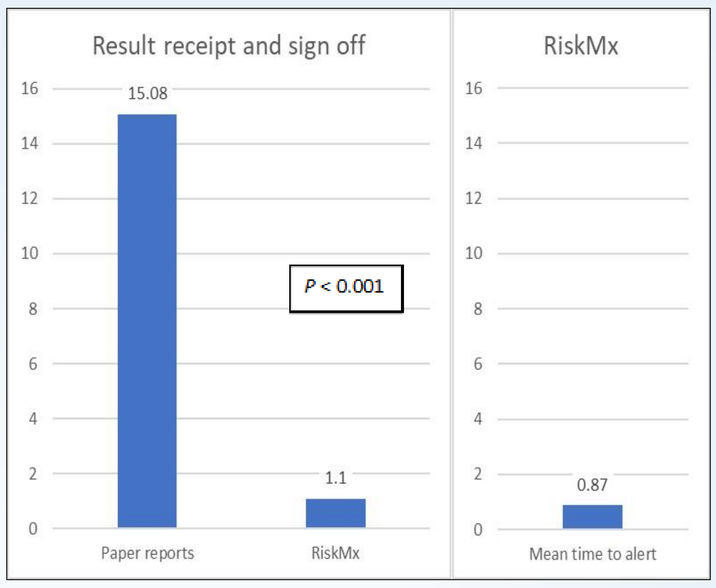
AMS3 concept: Beta test the automated monitoring system with ten alemtuzumab treated patients receiving normal care.



Results

The study successfully met the combined endpoint of design and implementation of the monitoring CDSS, educational app and prescreening tool. Other results are as follows:

- Compliance with monthly monitoring **96.7%** (146/151 test groups).
- HL7 results received by RiskMx = 151 (all), hardcopy 143 (8 lost).
- Final HL7 receipt 1.10 days +/-1.57 (0-15), final hardcopy = 15.08 days +/-15.99 (0-106), p<0.001.
- Alerts when abnormal were sent in 0.87 days +/-0.45 (0-2).



Performance of the RiskMx CDSS as measured by (A) comparison between standard care and RiskMx platform in time from specimen collection to result sign off by the neurologist, in days post collection; **p = 1.24007E-18** by two tailed paired Student's t-test.
(B) mean time for alerts to be sent where alerts were required, in days post collection.

The study was powered to test the accuracy and speed of electronic versus hardcopy transmission of results, but few actual autoimmune adverse effects of alemtuzumab were anticipated given the study size and duration. Nevertheless, three patients had 5 autoimmune conditions: 2 with hyperthyroidism only, 1 with ITP, neutropenia and hyperthyroidism. All were alerted correctly by RiskMx prior to hardcopy receipt.

The neurologist received and acknowledged the ITP alert (platelets=77 (<150x10^9, subsequent nadir = 12 with gum bleeding) while travelling internationally 64 minutes after release of the electronic HL7 pathology report (see Dataflow Timeline). The patient commenced treatment for ITP *that day*. The paper report and urgent fax were reviewed *7 days later*.

Subsequently we made the RiskMx system fully available throughout Australia for use with alemtuzumab outside the AMS3 study, following national reimbursement. Australia is the 6th largest country at 7,617,930 km^2 and has an estimated population of 24,678,000. To date, this national application (Bloodwatch™) monitors >1000 patients, is used by 100% of prescribing neurologists and >99% of patients in Australia.

National Pathology Compliance

Apr 2015 – Jan 2017 – 98.7% (9777/9908)

Feb 2017 – Aug 2017 – 97.8% (6896/7052)

Conclusions

The RiskMx platform effectively supported the risk management plan implementation, demonstrated impressive compliance with monitoring, and timely receipt of abnormalities, without requiring extra clinical staff. Not surprisingly, the AMS3 study also demonstrated significantly faster review of pathology results by electronic means than standard practice.

The largely automated service was delivered nationally in Australia with >99% uptake and excellent ongoing compliance with laboratory monitoring for the risk management program. The RiskMx platform, customised to specification, has potential value in supporting many medical therapies that require pathology monitoring, both in MS and in other clinical settings.

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Disclosures

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