The Alemtuzumab MS Safety Systems (AMS3) study
Clinical outcomes

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Background & Aim

The AMS3 study tracked the development of an automated clinical decision support system (CDSS) for patients treated with alemtuzumab for MS. The CDSS used electronic pathology transmission, reminder and alerting algorithms, and automatic communication with neurologists, their teams and the patients to efficiently improve safety and compliance with the risk management program. The development of the system included 10 alemtuzumab treated patients who participated in beta-testing the system. These patients were able to access alemtuzumab a year before general availability in Australia. The 2 year clinical & MRI outcomes of these 10 patients with very active relapsing remitting MS is reported.

Methods

Ten patients selected by rank order of need from 30 nominated by neurologists from near Sydney, Australia, with highly active MS and failure or unsuitability for other therapies. Relapses, EDSS and MRI outcomes were collected. MRI analysis but not clinical measures were blinded. Treatment with alemtuzumab followed CAMMS 03409 protocols with 12mg/d x5 at year 0 and x 3 at year 1.

Baseline Characteristics

- Age = 36 (24 – 57),
- Disease duration = 5.3y (2 – 10)
- EDSS entry = 3.05 (2 – 4)
- Average relapses last 12/12 = 2.3 (1-5)
- *n* prior MS Rx = 2.9 (1-6 – all had prior natalizumab)

Reason for alemtuzumab

- Relapse fingolimod (6) or DMF(2), JC+
- Relapse on natalizumab, JC- (1)
- Relapse while pregnant, JC+ (1)

Demographics and lesion load

ID	Gender	Age at baseline	No. T2 lesions	No. GAD+ lesions	
AMS3-001	Female	56	29	0	Tysabri Switch
AMS3-002	Female	29	25	15	
AMS3-003	Female	25	108	26	
AMS3-004	Female	31	46	2	
AMS3-005	Female	33	69	0	Tysabri Switch
AMS3-006	Female	24	44	3	
AMS3-007	Female	45	86	15	
AMS3-008	Male	40	76	25	
AMS3-009	Male	35	6	2	
AMS3-010	Male	37	42	4	
		Mean 53.1 ± 31.1 SD		Mean 9.2 ± 10.2 SD	

Clinical results

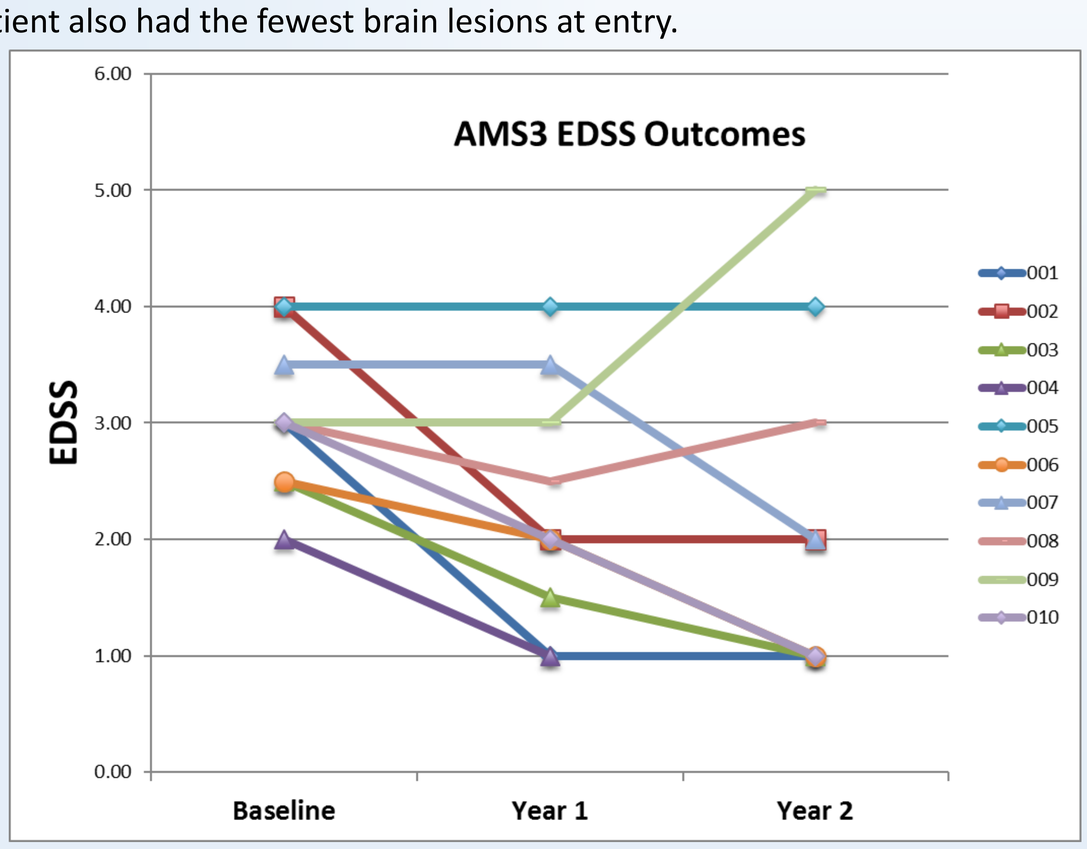
Relapses: 7/10 patients free of clinical disease activity

3/10 patients had relapses (one patient reported 4 without objective change, 2 each in two patients with new symptoms, signs and/or MRI Δ)

- annualised relapse rate 0.4 (from 2.9 year prior)
- 86% ARR reduction

EDSS mean declined from **3.05** at baseline, to **2.25** at Y1, and **2.22** at Y2.

Seven patients had confirmed disability improvement, 2 unchanged, 1 confirmed disability worsening. That patient (#9) had cord relapses with pial spinal cord enhancement and cerebral Gd+ lesions unchanged over 2 years suggesting a non-MS disease such as neurosarcoidosis (MRI figure). That patient also had the fewest brain lesions at entry.



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MRI outcomes

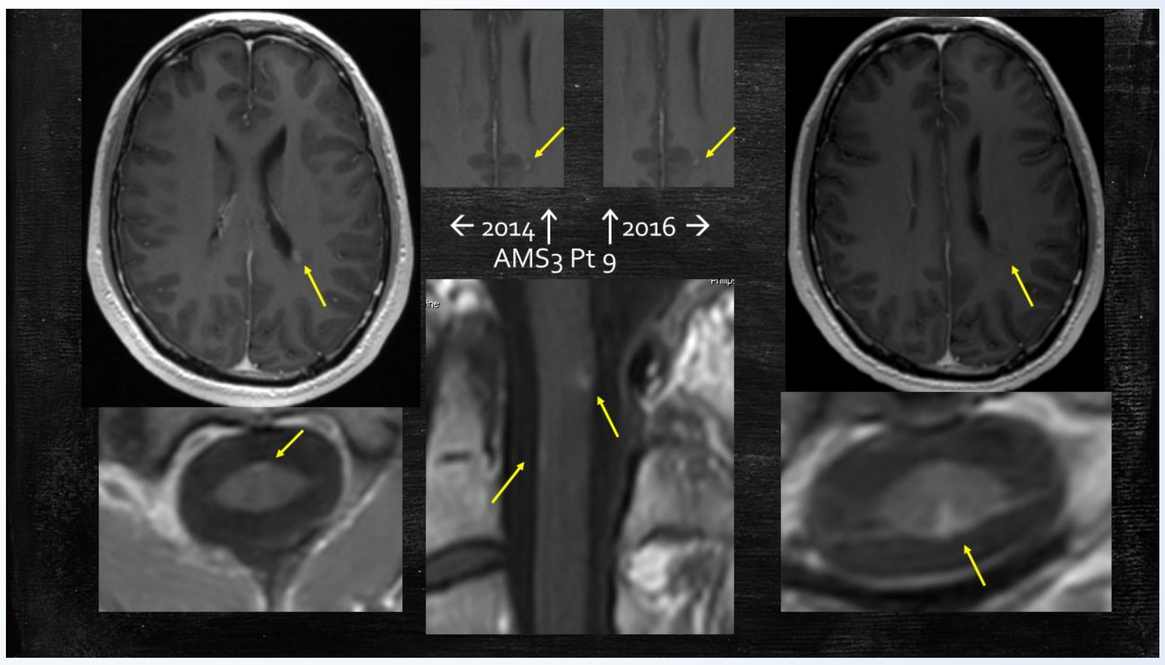
- Mean Gd lesion number at entry was 9.2 (0-26), Y1 1.9 (0-13), Y2 0.11 (0-1).
- Conversion of enhancing lesions to T1-black holes: 4 patients at BL (n lesions = 1,1,2,2), no Y1 Gd lesions converted to black holes.
- On year end imaging, mean MRI-T2-hyperintense lesion volume increased 3.6% BL-Y1, then declined -3.1% Y1 – Y2.
- Atrophy (SIENA): average -0.97% (SD 0.68%) brain atrophy BL-Y1 and -0.29% (SD 0.53%) Y1-Y2.

Both volume measures suggest a contribution of active disease and subsequent pseudoatrophy in the first year with brain volume changes approximately in the normal range in the second year

Gad lesion n	Mean	Range
BL	9.2	0-26
Y1	1.9	0-13
Y2	0.11	0-1

Δ Volumes	T2 lesion	SIENA
BL	-	-
Y1	3.6%	-0.97%
Y2	-3.1%	-0.29%

MRI figure: Pt 9 had persisting enhancement of brain lesions for two years and pial cord lesions suggesting neurosarcoidosis rather than MS



Conclusions

Alemtuzumab is a highly effective treatment for MS, even in this highly active cohort with considerably more pre-treatment than patients in the pivotal trials. Careful review of the diagnosis is needed in atypical cases before alemtuzumab treatment. Marked improvement in relapse rates, new gadolinium lesions, and second year brain atrophy occurred. Most patients with clinical and radiological disease activity had confirmed disability improvement after switching to alemtuzumab.

Disclosures
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