Poster 004

Substantial Burden of Illness and Mortality in Men with Adrenomyeloneuropathy

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INTRODUCTION

- X-linked adrenoleukodystrophy (X-ALD) is a genetic, metabolic condition with an incidence of 1:16,800 caused by a *ABCD1* gene mutation.[1,2]
- Males with the mutation develop adrenomyeloneuropathy (AMN) in adulthood. Symptom onset is typically observed around the late 20s to 30s. Women may also develop symptoms, though onset is observed later in life.[3-5]
- AMN is neurodegenerative – characterized by progressive myeloneuropathy that causes spastic paraparesis, sensory ataxia, incontinence, and sexual dysfunction. Eventually walking is severely affected and mobility is impaired.[3,6-8]
- There are currently no effective treatments in stabilizing or reversing the progression of AMN. Moreover, suggested and practiced care varies based on the symptoms experienced by each person.[9]
- AMN's impact on healthcare resource utilization (HRU) and mortality is unknown.

Objective

- To quantify healthcare resource use (HRU) and mortality associated with AMN in men with ALD.

Methods

Study Design

- HRU was assessed using commercial insurance claims from IQVIA's PharMetrics Plus database (1/01/2006-6/30/2021) via a retrospective cohort study. Mortality rates and age at death were assessed in the Medicare Limited Dataset (1/1/2016-12/31/2020).
  - HRU, including inpatient (IP) admissions with and without Intensive Care Unit (ICU) stays, outpatient (OP) services, and prescription medication fills, was measured as the average number of healthcare encounters per patient per year (PPPY) and average pharmacy fills PPPY.
    - *Medications were categorized based on the Generic Product Identifier code (GPI) medication class.*
  - Mortality was measured as the proportion of patients who died in a 5-year period among those with Medicare coverage and as the average age at death among those who died with Medicare coverage.
- Patient selection: Male individuals with ≥1 inpatient or ≥2 outpatient claims with an AMN diagnosis (ICD-10-CM: E71.52x; ICD-9-CM 277.86), no evidence of childhood cerebral adrenoleukodystrophy or other peroxisomal disorders. To assess for adult cerebral adrenoleukodystrophy, the distribution of utilization and costs was examined for potential associations–however, this did not lead to any further exclusions.
  - Commercially insured AMN study patients were limited to those aged 18-64y and were 1:4 propensity score matched on demographic characteristics and enrollment time to individuals without AMN.
  - No age restrictions were applied to study patients with Medicare coverage.
- Study period: Commercially insured patients were observed from the month of their first observed AMN diagnosis and followed until disenrollment from their insurance plan. Medicare patients were observed for the 5-year study period.
- Analyses: Descriptive univariate analyses (mean ± standard deviation and counts [percentages]) and bivariate analyses (Mann-Whitney U/ Student's t-test and Fisher's Exact/Chi-squared tests) were used to assess for differences between cases and controls. All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC) and R 2022.02, assuming a two-tailed test of significance and an alpha level set a-priori at 0.05.

Figure 1: Patient Attrition

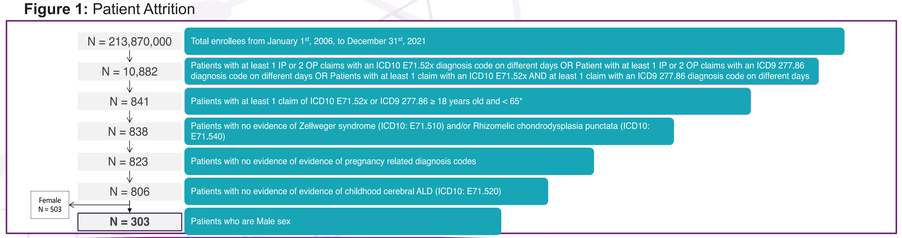


Table 1: Patient Characteristics

Table 1A. Patient Demographics– number and proportion of patients with 1+ characteristic during observation

Characteristics	Cases (AMN) N = 303	Controls (Non-AMN) N = 1,037
Demographics, n (%)		
Follow-up months, mean ± SD	29.0 ± 27.7	30.1 ± 25.3
Age, mean ± SD	35.1 ± 13.8	35.2 ± 13.3
Age 18-35	56.4% (171)	56.4% (585)
Age 36-51	26.7% (81)	26.5% (275)
Age 52-64	16.8% (51)	17.1% (177)
Geographic Region, n (%)		
East	15.2% (46)	15.5% (161)
Midwest	30.4% (92)	29.8% (309)
Other	4.0% (12)	6.7% (69)
South	34.3% (104)	31.4% (326)
West	16.2% (49)	16.6% (172)

Measures containing less than 5 patients are masked to protect patient confidentiality

Table 1B. Patient Clinical Characteristics – number and proportion of patients with 1+ characteristic during observation

Characteristics	Cases (AMN) N = 303	Controls (Non-AMN) N = 1,037	P value
Comorbid Conditions, n (%)			
Non-Diabetic Neuropathy	10.9% (33)	0.6% (6)	<.001
Hemiplegia or Paraplegia	10.9% (33)	<5	<.001
Chronic Pulmonary Disease	6.3% (19)	2.6% (27)	<.01
Diabetes	5.9% (18)	5.2% (54)	0.6
Liver Disease	5.6% (17)	0.8% (8)	<.001
Peripheral Vascular Disease	4.6% (14)	0.9% (9)	<.001
Cerebrovascular Disease	4.3% (13)	0.6% (6)	<.001
Cancer	4.3% (13)	1.4% (14)	<.01
Renal Disease	3.0% (9)	0.6% (6)	<.001
Congestive Heart Failure	2.3% (7)	<5	<.001
Diabetic Neuropathy	<5	0.6% (6)	0.2

Measures containing less than 5 patients are masked to protect patient confidentiality

Results

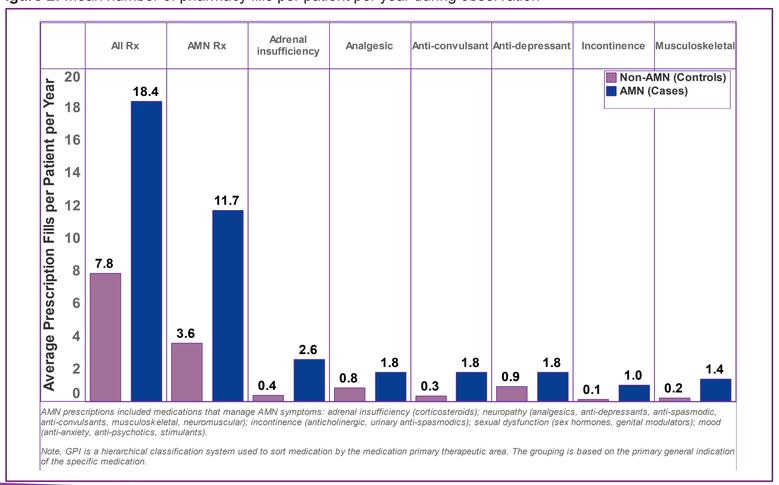
Comorbidities

- A total of 303 men met study inclusion requirements (**Figure 1**) and were propensity score matched to 1,037 non-AMN controls (**Table 1a**)
- Compared to controls, AMN men had a greater comorbidity burden as measured by the CCI (0.67 ± 1.33 vs. 0.19 ± 0.68; p <0.001). Hemiplegia/paraplegia, Myasthenia Gravis and other AI/neuro conditions, including non-diabetic neuropathy, were expected comorbid conditions within the AMN cohort (**Table 1b**).

Prescription medications

- Prescription medication use differed significantly between AMN men and controls at p <0.001 (**Figure 2**).
- Medications with less than 1 fill PPPY (not shown) also differed significantly at p <0.001. This included: anti-anxiety, anti-psychotic, anti-spasmodic, neuromuscular, sexual dysfunction, and stimulants.

Figure 2: Mean number of pharmacy fills per patient per year during observation



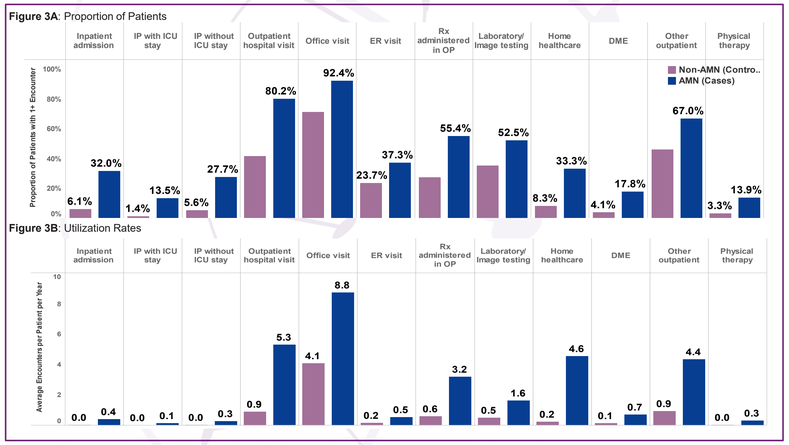
AMN prescriptions included medications that manage AMN symptoms: adrenal insufficiency (corticosteroids); neuropathy (analgesics, anti-depressants, anti-spasmodic, anti-convulsants, musculoskeletal, neuromuscular); incontinence (antichlolinergic, urinary anti-spasmodics); sexual dysfunction (sex hormones, genital modulators); mood (anti-anxiety, anti-psychotics, stimulants).

Note, GPI is a hierarchical classification system used to sort medication by the medication primary therapeutic area. The grouping is based on the primary general indication of the specific medication.

Healthcare Resource Utilization

- AMN men had longer lengths of stay (LOS) vs. controls for IP w/ ICU (8.7 vs. 5.1 days) and IP w/o ICU (9.2 vs. 4.3 days); p <0.05
- All HRU (proportion of patients and rates PPPY) differed significantly between AMN men and controls, p <.05 (**Figure 2**).

Figure 3: HRU

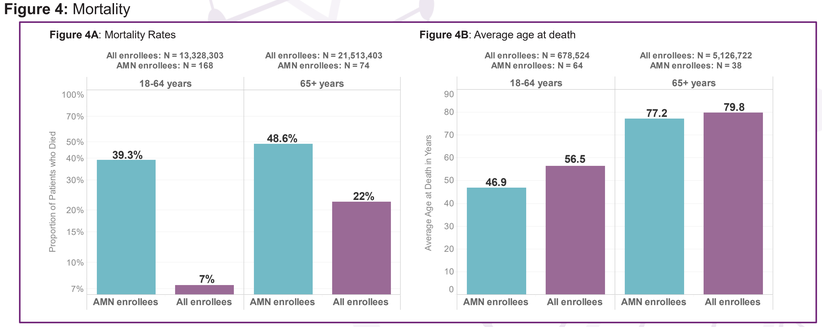


IP: Inpatient; ICU: Intensive Care Unit; ER: Emergency Room; Rx: Prescription Medication; OP: Outpatient; DME: Durable Medical Equipment

Mortality

- Patients may be age-eligible for Medicare coverage (aged ≥65 years old) or disability-eligible (aged <65 years old). The generalizability of these findings is limited to AMN patients with Medicare coverage.
- Mortality rates (aged 18-64y and ≥ 65y) and the average age at death (18-64y) differed significantly between AMN enrollees and all enrollees, p <.001 (**Figure 4**).

Figure 4: Mortality



CONCLUSIONS

- AMN confers a high burden of illness including higher HRU and, in some patient segments, higher mortality rates and earlier age at death
- Better understanding of comorbidity and mortality drivers in AMN is needed to improve health outcomes.

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Author contributions: JB, BH, NS, RM, PC, ES, CS, and FE contributed to the design and implementation of the study, and to the interpretation of results.

Disclosures: JB has received consultant fees from Bluebird bio, Neurogene, Passage Bio,Takeda, and Autobahn; owns stock in Orchard; received research support from NIH. RM, BH, NS, and PC received employee salary from PrecisionHEOR. ES received employee salary from and owns stock in uniQure Inc; received research support from Sanofi and NIH. CS has received consultant fees from SwanBio; received research support from Sanofi. FE has received consultant fees from SwanBio, Alnylam, Origin Biosciences, Orchard, Autobahn, Bluebird; received fees from UpToDate; received research support from Bluebird, Minoryx, and Sio; owns stock in SwanBio.

Poster presented at AAN 2023, Boston, MA, April 26, 2023

This study was sponsored by SwanBio Therapeutics Ltd