Patterns of Pharmacotherapy Changes and Switches Suggest Unmet Need in US Patients with Acromegaly

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BACKGROUND

- Acromegaly is a slowly progressive disorder due to growth hormone (GH) excess that is managed primarily with surgery, followed by medical therapy or radiotherapy if GH levels continue being elevated.[1]
- About 50% of acromegaly patients require adjuvant therapy after surgery, which may include multiple medications.[2]
- Guidelines suggest a sequence of medical therapy, but treatment choices are usually individualized and actual treatment practices are unknown.[3-5]

OBJECTIVE

- To assess patterns of pharmacotherapy in patients with acromegaly

METHODS

Study Design and Data Source

- Retrospective cohort study using two HIPAA-compliant commercial claims databases, Truven Health Analytics MarketScan and IMS Health PharMetrics, from 1/1/2002 to 12/31/2013 (ID period).

Patient Population

- Included patients had ≥2 medical claims with acromegaly (ICD-9-CM code 253.0) and ≥1 pharmacotherapy claim during the ID period.
  - Pharmacotherapy (bromocriptine, cabergoline, octreotide SA, octreotide LAR, lanreotide, pegvisomant) were identified in pharmacy and medical claims using National Drug Codes (NDC) and Healthcare Common Procedure Coding System (HCPCS) codes.

Measure Definitions

- Course of treatment: duration from the first treatment claim to the last claim plus the days of supply remaining (calculated for patients enrolled ≥90 days after the end of treatment).
- Combination treatment: ≥2 medications with overlap of ≥90 days (excludes short-term octreotide SA use).
- Treatment change/switch: subsequent pharmacologic treatment different from the prior treatment. For combination therapy, a change in any of the medications or addition of a new one was considered a switch.
- Treatment stop: no subsequent pharmacotherapy occurred for ≥90 days.

Statistical Analysis

- Descriptive analyses were done for varying patient cohorts to report on pharmacologic switch rates and stops, and subsequent pharmacotherapy among initial switchers who switched after 2007. All statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC).

RESULTS

- Depending on the year, 7.4-10.6% of all pharmacologically treated patients switched to a new treatment and 4.1-9.3% stopped treatment.

Table 1. Annual switch and stop rates in all pharmacotherapy users

	2008	2009	2010	2011	2012	2013
No. of users	874	1,029	1,110	1,127	1,079	846
Switch, n (%)	89 (10.2%)	76 (7.4%)	118 (10.6%)	95 (8.4%)	98 (9.1%)	70 (8.3%)
Stop, n (%)	36 (4.1%)	57 (5.5%)	80 (7.2%)	75 (6.7%)	87 (8.1%)	79 (9.3%)

RESULTS

- For all patients who either stopped or switched therapy, 63.6% changed to a different treatment and 36.4% stopped pharmacologic treatment completely.
- Combination treatments were the least likely to end in cessation (10.0%) and treatment with bromocriptine and cabergoline were most likely to end with cessation of all pharmacotherapy (50.6% and 47.4%, respectively).

Table 2. Stopping status by treatment[a]

Pharmacologic Treatment, n (%)	Stop Status	
	Stop[b]	Change
Octreotide LAR 814 (28.8%)	312 (38.3%)	502 (61.7%)
Octreotide SA 419 (14.8%)	101 (24.1%)	318 (75.9%)
Lanreotide 254 (9.0%)	90 (35.4%)	164 (64.6%)
Cabergoline 589 (20.9%)	279 (47.4%)	310 (52.6%)
Bromocriptine 249 (8.8%)	126 (50.6%)	123 (49.4%)
Pegvisomant 260 (9.2%)	95 (36.5%)	165 (63.5%)
Combination 240 (8.5%)	24 (10.0%)	216 (90.0%)
All N=2,825	1,027 (36.4%)	1,798 (63.6%)

[a] Among all pharmacotherapy treatment courses (not necessarily first line treatment).
[b] No claim of other pharmacologic treatment occurred after the stop date (at least 90 days.

- Among patients who switched pharmacotherapy, 23.2% switched to a combination pharmacotherapy, followed by octreotide-LAR (19.1%), lanreotide (17%), cabergoline (16.3%), pegvisomant (14.2%), octreotide-SA (6.7%) and bromocriptine (3.4%).

LIMITATIONS

- We were unable to follow individuals longer than 2-3 years because of disenrollment, making it impossible to draw conclusions about treatment duration over the longer term.
- Most patients likely had surgery as their initial intervention but were only followed beginning with their first observed pharmacologic treatment.
- Results may not be generalizable to populations that are not commercially insured.

CONCLUSIONS

- **Among acromegaly patients who use medical therapy, more than 80% continue on the same pharmacotherapy from year to year.**
- **Patients who change their medical treatment generally switch to a new regimen (47%-71.2%), rather than stopping treatment completely.**
- **Changes may be due to lack of response to therapy, disease progression, or other reasons.**
- **Nearly a quarter of patients change initial monotherapy to combination therapy, suggesting inadequate disease control is a significant reason for treatment modification.**
- **Dopamine agonists are stopped more commonly than other pharmacotherapies, consistent with evidence that they are less efficacious than other therapies, or that they are used in patients with minimal symptomatology, and therefore are more readily discontinued.[3]**
- **Overall, our findings suggest an unmet need in the medical treatment of acromegaly.**
- **These results reflect patient care over more than a decade but only until 2013. The 2014 approval of pasireotide patients for patients who have had an inadequate response to (or who cannot have) surgery may change these patterns of treatment**

References

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Table 3. Initial and subsequent treatments used by switchers[a]

Change from	Change to						
	Octreotide LAR	Octreotide SA	Lanreotide	Cabergoline	Bromocriptine	Pegvisomant	Combination[d]
Octreotide LAR n=361	--	27 (7.5%)	105 (29.1%)	56 (15.5%)	6 (1.7%)	62 (17.2%)	105 (29.1%)
Octreotide SA n=203	113 (55.7%)	--	40 (19.7%)	19 (9.4%)	3 (1.5%)	20 (9.9%)	8 (3.9%)
Lanreotide n=164	16 (9.8%)	7 (4.3%)	--	49 (29.9%)	3 (1.8%)	37 (22.6%)	52 (31.7%)
Cabergoline n=219	52 (23.7%)	30 (13.7%)	31 (14.2%)	--	21 (9.6%)	24 (11.0%)	61 (27.9%)
Bromocriptine n=79	8 (10.1%)	11 (13.9%)	3 (3.8%)	47 (59.5%)	--	1 (1.3%)	9 (11.4%)
Pegvisomant n=127	23 (18.1%)	9 (7.1%)	23 (18.1%)	17 (13.4%)	4 (3.1%)	--	51 (40.2%)
Combination=167	40 (24.0%)	5 (3.0%)	23 (13.8%)	27 (16.2%)	8 (4.8%)	44 (26.3%)	20 (12.0%)
Total Switchers N=1,320	252 (19.1%)	89 (6.7%)	225 (17.0%)	215 (16.3%)	45 (3.4%)	188 (14.2%)	306 (23.2%)

[c] Patients who switched after 2007 (year of lanreotide approval for acromegaly), had 2 different courses of different treatments, and were continuously enrolled for ≥90 days after the end of the 2nd treatment. [d] Changed to different combination treatment.

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