

LEUPROLIDE ACETATE PERSISTENCE VARIES BY AGE IN PATIENTS WITH PROSTATE CANCER

M.J. Fuldeore, BScPharm, MBA, PhD,¹ R.A. Brook, MS, MBA,² J.E. Smeeding, RPh, MBA,³ O.H. Dabbous, MD, MPH¹

¹TAP Pharmaceutical Products Inc., Lake Forest, IL; ²The JeSTARx Group, Newfoundland, NJ; ³The JeSTARx Group, Dallas, Tx

Introduction:

- In 2003, 186,000 men were diagnosed with prostate cancer:¹
 - Within those diagnosed, the incidence increased with age.
 - Prostate cancer ranks as one of the most commonly diagnosed cancers in the United States.
 - Nearly 30,000 men died from the disease that same year.¹
- Leutinizing hormone-releasing hormone [LH-RH] is one of the treatment options for prostate cancer.²
- Medication adherence is typically poor across chronic conditions despite clear evidence that improved adherence results in better long-term health outcomes for patients with conditions typically managed through medications.³
- Medication compliance from claims data has been shown to be more reliable than self-report⁴ and is widely used to assess both compliance and persistence with therapies.
- Many previous prostate cancer persistence and compliance studies have used patient- or partner-reported surveys,⁵⁻⁸ and some reported changing outcomes based on subject age.⁹
- Understanding the factors that drive non-compliance may target programs to improve it.

Objective:

The objectives of this retrospective study of prostate cancer subjects naive to therapy with leuprolide acetate depot were to examine, overall and by age group:

- Persistence (duration of therapy) with leuprolide acetate depot, and
- Compliance with leuprolide acetate depot.

Methods:

- Utilized the Medstat MarketScan database which:
 - Includes medical and pharmacy claims and covering more than 56 million commercial patient lives from a variety of health plans and insurers, and more than 250,000 Medicare lives.
 - Has been used in prior oncology and claims-based analysis.⁹
 - Is Health Insurance Portability and Accountability Act (HIPAA) compliant.
- Males subjects with prostate cancer were identified based on the presence of *International Classification of Diseases*, 9th Revision (ICD-9) diagnostic codes of (185.xx) and were considered eligible if they had one or more claims in 2002 claims for leuprolide acetate depot.
- Claims for leuprolide acetate were identified by claims processed through:
 - Medical claims for outpatient services with J-codes of J9217 or
 - Pharmacy claims for leuprolide acetate (Lupron) depot.
- The date of first leuprolide acetate use or purchase was assigned as the index date

- Subjects were excluded if they did not have continuous eligibility for
 - 36 months after their index date and
 - 12 months prior to their index date (48 months total eligibility were required)
- Subjects were excluded if they had any leuprolide acetate utilization during the 12 months prior to their index date.
- Because leuprolide acetate is available in multiple formulations that act for differing lengths of time, a “depot length” was determined for each claim.
 - Medical benefit and identified by outpatient service claims for J-code J9217 do not differentiate among different dosage strengths and intervals. For these claims, a proxy for the depot length was determined by the cost of the product administered such that claims costing:

Cost of Procedure	≤ \$1000	\$1000 < and ≤ \$2000	< \$2000
Depot-Length (months)	1	3	4

- Pharmacy benefit claims were assigned a depot length based on the strength associated with the NDC processed such that a strength of:

Strength	7.5 mg	22.5 mg	30 mg	45 mg
Depot-Length (months)	1	3	4	6

- Subjects were stratified into age-range groups based on their age at their index dates. The age groups were defined as those no older than 40 years, 41–50, 51–60, 61–70, and 71–80, and those at least 81 years old.

Outcomes Metrics

- Compliance** was measured in patients with more than one administration of leuprolide acetate using the medication possession ratio (MPR), defined as:

$$\text{MPR} = \frac{\text{total months supply obtained}}{\text{months in the time period (36)}}$$

- An MPR of 1.0 indicates perfect compliance.

- Persistence** is defined as the length of time between the index leuprolide acetate usage date and the start of the first gap in medication supply measured by the number of days or months the patient was receiving therapy. The last observed date of a leuprolide acetate depot fill was used to determine the discontinuation date.

$$\text{Duration of Therapy} = (\text{Last fill date} + \text{Last fill supply}) - \text{Start date}$$

Statistical Analysis

- Subjects were followed from their initial use of leuprolide acetate until the end of the three-year study or discontinuation. The time until discontinuation of therapy were assessed through a survival analysis and a Kaplan–Meier plot.
- Differences were considered statistically significant if $P < 0.05$.
- All data was analyzed by using SAS, Cary, NC

Results:

- 1541 men with prostate cancer receiving leuprolide acetate were included in the study.
- For patients with more than one administration of leuprolide acetate, the average MPR for all ages was 0.70 (SD, 0.15) and did not change significantly by age (Table 1).
- Average persistence with leuprolide acetate was 15.9 months (SD, 11.8) and increased with age from 10.6 months (< 51) to 19.8 months (> 80) (Table 2).
- More than one-third of patients discontinued by six months of therapy (Figure 1).
- There was a trend towards earlier discontinuations in the younger age groups (Figure 2)

Limitations:

- This study did not compare cost of prostate cancer therapy nor did it evaluate the effectiveness of the therapy.
- The depot lengths for administrations received in the doctors’ office were estimated, while the administrations of leuprolide acetate for acquired through the pharmacy were assumed.
- This study did not evaluate reasons for discontinuation such as changes in treatment strategy (ie, radiation or surgical procedures) or patient expiration (death).

Conclusions:

- Leuprolide acetate therapy persistence increased with age.
- Persistence improvement efforts in younger patients and during the first six months of therapy may result in better outcomes.

Table 1: Compliance (MPR) with Leuprolide Acetate Depot Stratified by Age Groups For patients with more than one administration of leuprolide acetate

Age Group	N	Mean MPR	Std Dev
18-50	40	0.73	0.30
51-60	128	0.76	0.23
61-70	201	0.73	0.23
71-80	587	0.71	0.24
>80	237	0.63	0.24
Overall	1,193	0.70	0.24

Table 2. Average persistency with of leuprolide acetate by age

Age Group	N	Persistence: Mean Duration (Months)	Std Dev
18-50	59	10.6	12.4
51-60	188	14.8	13.5
61-70	302	12.5	11.2
71-80	718	16.7	11.4
>80	274	19.8	10.4
Overall	1,541	15.9	11.8

Figure 1: Discontinuation of Leuprolide Acetate Over Time

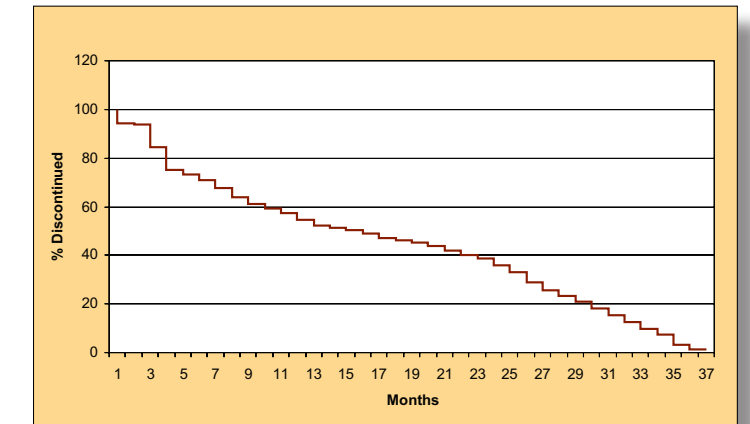
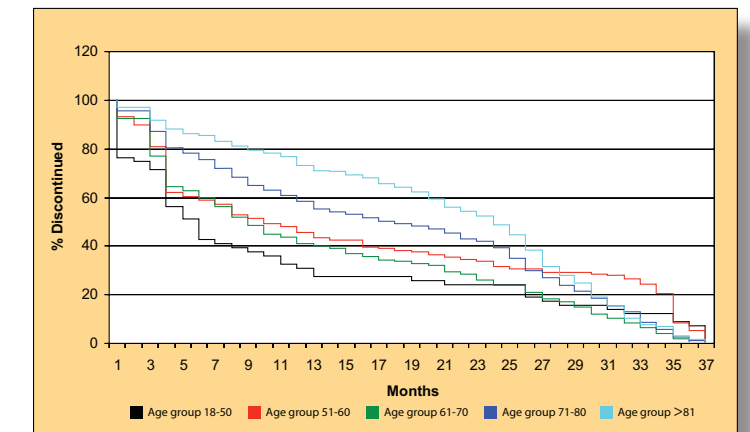


Figure 2: Discontinuation of Leuprolide Acetate by Age Group



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NOTES

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ABSTRACT

BACKGROUND: The prevalence of prostate cancer increases with age. Leuprolide acetate is an efficacious therapy in patients with prostate cancer. Therapy persistence is essential for desirable clinical outcomes.

METHODS: A retrospective analysis was conducted using the Medstat MarketScan database on a commercially and Medicare aged insured population from 2001-2005. The MarketScan database collects medical claims, pharmacy claims, cost, and demographics data. Subjects new to leuprolide acetate (identified by J-Code of J9217) in 2002 and no codes in 2001 were followed for 3 years. Compliance was calculated using the medication possession ratio (MPR=total days supply obtained/days on therapy). Persistence was characterized by the number of fills and the days on therapy (start plus estimated discontinuation date). Subjects were stratified into age-range groups, by those > 18 and < 51 yr, those > 81 yr, and 10- year age ranges in between (51-60, 61-70, 71-80). Survival rate was calculated using Kaplan-Meier survival curves.

RESULTS: 1541 men with prostate cancer receiving leuprolide acetate were included in the study. The average MPR for all ages was 0.70 (SD, 0.15) and did not change significantly by age. Average persistence was 15.9 months (SD, 11.8) and increased with age from 10.6 months (< 51) to 19.8 months (> 80). More than one-third of patients discontinued by six months of therapy.

CONCLUSIONS: Leuprolide acetate therapy persistence increased with age. Persistency improvement efforts in younger patients and during the first six months of therapy may result in better outcomes