Clinical and Cost Outcomes From Different Hyaluronic Acid Treatments in Patients With Knee Osteoarthritis

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**Background**

Hyaluronic acid (HA) injections are a safe and effective treatment to alleviate pain and improve joint function in patients with knee osteoarthritis (OA). It acts by supplementing synovial fluid in joints affected by knee OA and can also induce direct anti-inflammatory and chondroprotective effects\textsuperscript{1,2}. Therefore, HA has the potential to lessen the need for invasive and costly surgical treatments such as total knee replacement (TKR).

Recent research using a large U.S. health plan claims database has demonstrated that HA can successfully delay TKR\textsuperscript{3,4}. However, little is known about the relative differences in clinical and economic outcomes among different HA products.

**Objectives**

Compare OA-related costs and risk of TKR among patients receiving different HA treatments in a commercially-insured cohort of patients with knee OA

**Methods**

**Study Design**
Retrospective cohort analysis was conducted using IMS Health’s PharMetrics Plus Health Plan Claims Database.

**Inclusion Criteria**
- An outpatient claim indicating the initiation of HA drugs of interest during the selection period (2007-2010). The date of the first such claim for the patient within the selection period was defined as their index date.
- Patients ≥ 18 years of age in the year of their index date.
- At least one clinical diagnosis for OA of the knee at any point in the 12 month pre-index period.
- Continuous enrollment during the study period (12 months pre-index and 36 months post-index).

**Exclusion Criteria**
- Evidence of HA therapy in the pre-index period.
- Evidence of another HA product use (in addition to/instead of the original HA product that was considered as the index medication) in the post-index period.
- Evidence of TKR within 30 days of the index event (post-index).
- Evidence of two index medications on the index date.
- Evidence of diagnosis of hip OA, fibromyalgia, rheumatoid arthritis, lupus or gout during the pre-index period.

**Statistical Analysis**
The 12-month pre-index baseline period was used to measure patient baseline characteristics. The 36-month post-index period was used for outcomes measurement.

A generalized linear model (GLM) with a gamma distribution and log-link function was fit to model aggregate patient-based changes in OA-related costs.

A Cox proportional hazards model (PHM) was fit to model risk of TKR. Both multivariate models included covariates such as age, gender, comorbidities, and pre-index healthcare costs.

**Results**

**Patient Cohorts**
- 50,389 patients with HA treatment for knee OA were identified.
- 6,263 (12.4%) received Euflexxa, 5,391 (10.7%) received Orthovisc, 18,217 (36.2%) patients received Supartz/Hyalgan (shared HCPCS code), and 20,518 (40.7%) received Synvisc.

**OA-Related Costs**
- Estimates from the covariate-adjusted generalized linear model showed that Synvisc and Orthovisc patients had greater changes in OA-related costs compared to Supartz/Hyalgan (8.9% (p=0.0001) and 6.8% (p=0.0048) increase respectively) whereas Euflexxa’s cost was comparable to that of Supartz.
- If users of Synvisc and Orthovisc with average OA-related costs of $14,959 and $14,224 switch to Supartz/Hyalgan, they could potentially save $1,223 and $906 over 3 years.

**Survival Analysis of Time to TKR**

<table>
<thead>
<tr>
<th>Cohorts</th>
<th>% Patients without TKR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyalgan/Hyalgan (J code)</td>
<td>80.1%</td>
</tr>
<tr>
<td>Euflexxa</td>
<td>66.4%</td>
</tr>
<tr>
<td>Synvisc</td>
<td>64.4%</td>
</tr>
<tr>
<td>Orthovisc</td>
<td>61.4%</td>
</tr>
</tbody>
</table>

Hazard ratios derived from the covariate-adjusted Cox proportional hazards model showed a significantly higher risk of TKR for patients receiving Synvisc compared to Supartz/Hyalgan (6.9% increase in hazard (p=0.0009)). Patients treated with Supartz/Hyalgan, Euflexxa and Orthovisc experienced longer delays of TKR than Synvisc.

**Conclusion**

Multivariate statistical modeling showed that Supartz/Hyalgan represents a cost-effective alternative for providers. Both HAs reduced OA-related costs and delay TKR when compared to other products.

**References**