A Markov model was developed to assess the cost-effectiveness of LAAC with the WATCHMAN Device relative to warfarin for stroke risk reduction in non-valvular atrial fibrillation in CMS Patients. The objective of this analysis was to assess the cost-effectiveness of LAAC versus warfarin for stroke prevention in non-valvular atrial fibrillation from the perspective of the US Centers for Medicare & Medicaid Services (CMS).

BACKGROUND

Medical care expenditures are estimated $354 billion annually to manage beneficiaries with atrial fibrillation (AF), nearly half of this spend is AF-related stroke.

AF affects almost 9% of all Medicare beneficiaries putting them at time greater risk of stroke.1,2 Strokes is considered the most severe and debilitating consequence of AF, with many patients ranking the resultant disability worse than death.3

To fully understand the burden of stroke, stroke severity and the resultant impact on patient quality of life (QoL) need also be considered. Warfarin has been the long established treatment for stroke prevention in AF; it is effective at reducing the risk of stroke, but leads to increased risk of bleeding, reduced overall quality of life, and poor patient acceptance.4

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Lafrance and the WATCHMAN Device was recently approved by the FDA to reduce the risk of thromboembolism from the LAA in patients with non-valvular AF who are at increased risk for stroke, warfarin, and suitable, and seeking a non-pharmacological alternative to warfarin.

In light of ever increasing cost pressures, healthcare policy makers are increasingly in need of evidence of value in addition to evidence of clinical efficacy. Other analyses have evaluated the life expectancy of LAAC and stroke risk reduction in AF, but none have incorporated PROTECT AF stroke severity and QoL data, variables which impact both effectiveness and patient acceptance therapy.5

METHODS

The model was populated with data from a cohort of 10,000 75-85-year-old patients with a mean CHADS2 score of 2 and a bleeding risk reflective of the PROTECT AF population.6

Clinical event probabilities and QoL data were obtained from the PROTECT AF trial at 4 years of follow-up.7

Table 1. Markov model states

- No neurological impairment (MRS 0-2)
- Moderate disability (MRS 3-4)
- Severe disability (MRS 5-6)
- Moderate hemorrhagic stroke
- Severe hemorrhagic stroke

RESULTS

- A cohort of 10,000 AF patients, LAAC avoided 1,252 strokes over the 10 year time horizon, representing a 35% reduction relative to warfarin.
- LAAC patients, on average, lived 1.1 quality adjusted life years.
- Sensitivity analyses were conducted on clinical variables and LAAC procedure cost by varying inputs across 95% confidence intervals, where available and +/- 20% was not available.
- As the US reimbursement specific to this procedure is being revalued, a separate sensitivity analysis examined the impact of procedure cost with values up to $28,000.
- Patients who were successfully implanted with the WATCHMAN Device were assumed to remain on warfarin therapy; otherwise there was no LAAC treatment decision.
- Compliance with warfarin therapy was assumed to be equal to that observed in the PROTECT AF at 4 year ITT; no additional discontinuation was assumed.
- SF-12 data for PROTECT AF patients who did not have a stroke were used to inform the QoL utilities for well treated patients with either LAAC or warfarin.

Table 3. Cost inputs

<table>
<thead>
<tr>
<th>Event</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe ischemic stroke</td>
<td>$48,189</td>
<td>DRG: 451, 452, 453, 454</td>
</tr>
<tr>
<td>Severe hemorrhagic stroke</td>
<td>$42,362</td>
<td>DRG: 464, 465, 466, 467</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>$9,504</td>
<td>DRG: 467</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>$5,877</td>
<td>DRG: 370</td>
</tr>
<tr>
<td>LAAC procedure</td>
<td>$134,451</td>
<td>DRG: 250, 251, 252</td>
</tr>
<tr>
<td>Warfarin + INR monitoring</td>
<td>$285</td>
<td>CPT: 99364, 99365, 99366</td>
</tr>
<tr>
<td>No neurological impact post stroke</td>
<td>$157</td>
<td>CPT: 92481</td>
</tr>
</tbody>
</table>

Table 3. Cost inputs

- The Markov model weighs 0.16 per QALY.
- 20 years horizon.

Figure 3. Scatter plot of cost effectiveness plane at 10 years

- The 95% confidence interval for the cost-effectiveness ratio is $5,211 to $19,411 per QALY gained.

Table 5. Model results

<table>
<thead>
<tr>
<th>Year</th>
<th>Incremental cost per life year gained</th>
<th>Incremental quality-adjusted life years gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 yrs</td>
<td>$45,610</td>
<td>0.17 years</td>
</tr>
<tr>
<td>10 yrs</td>
<td>Dominant</td>
<td>0.43 years</td>
</tr>
<tr>
<td>20 yrs</td>
<td>Dominant</td>
<td>1.1 years</td>
</tr>
</tbody>
</table>

Figure 4. Total number of strokes by severity and therapy at 20 years

- In a cohort of 10,000 AF patients, LAAC avoided 1,252 strokes over the 20 year time horizon, representing a 35% reduction relative to warfarin.
- LAAC patients, on average, lived 1.1 quality-adjusted life years longer than their warfarin counterparts.
- By year 10, mean cumulative patient costs were lower for LAAC than warfarin ($24,516, 95% CI: $18,479 to $30,553, respectively).
- On average, LAAC used an average of $13,089 per patient relative to warfarin.
- LAAC was cost effective (less than $50,000 per QALY) compared to warfarin by year 5 and dominant (less expensive and more effective) compared to warfarin by year 10.
- In a probabilistic sensitivity analysis, LAAC was shown in greater life expectancy at 20 years (8.26 years, 95% CI: 7.88 to 8.64 years) than warfarin (7.88 years, 95% CI: 7.54 to 8.11) at 100% of simulations.
- LAAC was cost saving relative to warfarin in 35% of simulations at 10 years.

Figure 5. Mean cumulative cost per patient

- The mean 10-year cost per QALY was $2,208 (95% CI: $1,534 to $3,016).
- Probability of cost effectiveness at 10 years was greater than 95% given a willingness to pay threshold of $100,000 per QALY.
- In a secondary sensitivity analysis, LAAC remained cost effective versus both lifetime ($8,305 per QALY) and 10-year ($45,318 per QALY) time horizons despite increased procedure costs.

Figure 6. Scatter plot of cost effectiveness plane at 10 years

- This economic analysis does not capture the full clinical impact of discontinuation of warfarin therapy. Since drug withdrawal is generally substantially less of a major clinical trials than in real world practice, it is difficult to quantify the impact of therapy persistence on clinical event rates.

CONCLUSIONS

- Four years of the PROTECT AF trial found LAAC to be superior to warfarin for reduction of strokes/systemic embolism/cardiovascular death.
- This analysis indicates that LAAC with the WATCHMAN Device is cost effective compared to warfarin at 6 years and less expensive than warfarin at 10 years.
- LAAC remains cost effective relative to warfarin even when procedure costs are increased substantially.
- LAAC with the WATCHMAN Device for stroke prevention in AF provides improved clinical and quality of life outcomes and offers better value to CMS over a patient’s lifetime.
- The results of this analysis should be considered when formulating policy and practice guidelines for stroke prevention in AF.