

# COST-UTILITY OF DRONEDARONE COMPARED WITH ANTI-ARRHYTHMIC DRUGS AND STANDARD OF CARE IN TREATMENT OF ATRIAL FIBRILLATION IN POLAND

## Summary

**Objectives:** To evaluate cost-utility of dronedarone on top of standard care compared with amiodarone, propafenone, sotalol and standard of care (SOC: including beta-blockers, calcium antagonists, digoxin, ACE inhibitors, statins, vitamin K antagonists, aspirin, in placebo arm of the ATHENA trial).

**Methods:** A cost-utility analysis was performed based on the Markov model with states that capture crucial events associated with atrial fibrillation (AF): symptomatic AF, acute coronary syndrome, stroke, congestive heart failure, death. Results were obtained by conducting microsimulations in a lifetime horizon. Cycle length is one month. The clinical data were obtained from clinical trials included in the systematic review (2010) conducted according to HTA guidelines in Poland (2009). A mixed treatment comparison was conducted for comparison of dronedarone against other drugs. Costs were calculated from perspective of public payer and patients (in case of co-payment) on the basis of Ministry of Health data, Polish registries, surveys and relevant literature.

Cost per QALY gained and cost per life year gained were calculated. Discounting according to HTA guidelines was applied: 5% for costs and 3.5% for outcomes. One-way and probabilistic sensitivity analysis were performed.

**Results:** Dronedarone yielded 7.2 QALY which was 1.9 more QALY than amiodarone and propafenone, 2.5 more than sotalol and 0.2 more than SOC in life time horizon. Dronedarone was associated with higher total costs: 4.0k Euro more than amiodarone and sotalol, 3.9k Euro more than propafenone and 3.5k Euro more than SOC. The cost-effectiveness threshold in Poland is 25,011 Euro. Incremental cost per QALY gained (ICUR) for dronedarone was 2,154 Euro, 2,090 Euro, 1,636 Euro and 16,233 Euro in comparison with amiodarone, propafenone, sotalol and SOC, respectively.

**Conclusion:** Dronedarone is a new option for treatment of patients with non-permanent AF and is highly cost-effective as compared to amiodarone, propafenone and sotalol in Polish clinical settings.

## Objectives

The aim of this economic analysis was to compare costs and effectiveness of dronedarone (Multaq®) in treatment of atrial fibrillation (AF) and to determine whether it is a cost-effective option for AF patients in Poland.

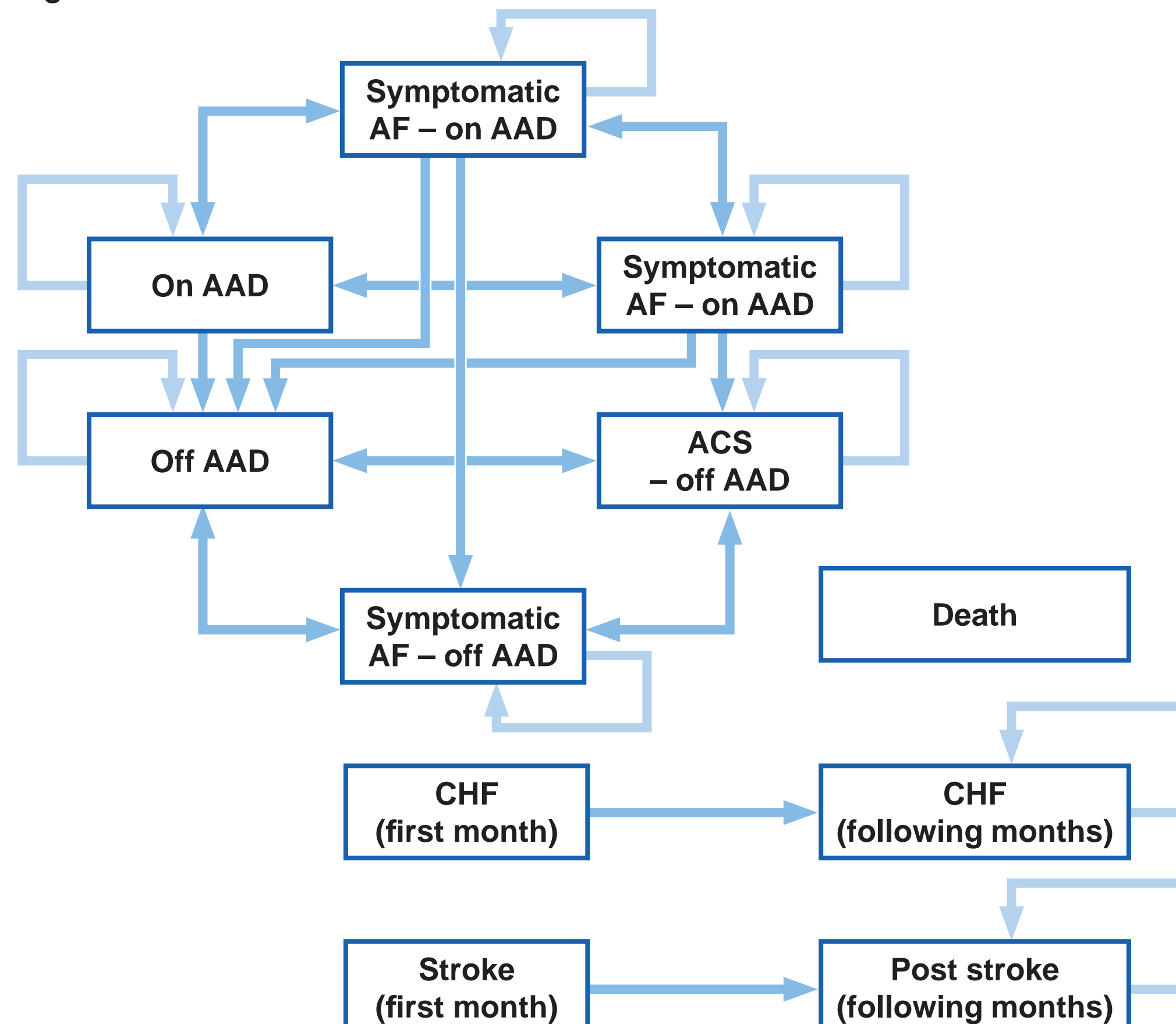
## Methods

- Comparators for dronedarone (DRO) in Polish setting are: amiodarone (AMIO), propafenone (PROP), sotalol (SOT) and standard of care (SOC).
- Cost-effectiveness was analyzed in subpopulation corresponding to the group of patients included in the ATHENA trial [1].
- The analysis was conducted by adapting to the Polish settings 2 economic models: ATHENA lifetime model and ATHENA comparative model (detailed below).
- Efficacy and safety of interventions were assessed based on the results of clinical trials identified by means of a systematic review. The ATHENA trial was a main data source for the analysis. A mixed treatment comparison (MTC) was conducted to estimate relative effectiveness of comparators. MTC methodology was based on Freemantle et al [2].
- Utilities for health states included in the model were derived from the AFTER cohort which was part of the Euro Heart Survey on AF undertaken by the European Society of Cardiology [3].
- The perspective adopted was that of the public payer (Polish Ministry of Health and National Health Fund) and patients (in case of co-payment). Costs were calculated on the basis of Ministry of Health data, Polish registries, surveys and literature. The following cost categories were taken into account in the analysis: 1) costs of drugs—dronedarone, other AAD drugs; 2) costs of AF complications—acute coronary syndrome (ACS), congestive heart failure (CHF), stroke, adverse events, and 3) other costs—AF recurrence, treatment initiation and monitoring.
- The main outcome measures used in the economic analysis were quality-adjusted life years (QALYs) and life years (LYs). Incremental cost-utility ratios (ICURs) were calculated and compared to Polish acceptability threshold (25,011 Euro, 3xGDP per capita).
- A lifetime horizon was adopted.
- Discounting rates for costs and outcomes were applied according to Polish HTA guidelines. The discount rates used were 5% for costs and 3.5% for health outcomes.
- One-way sensitivity analyses were conducted in order to assess the influence of assumptions regarding input parameters on final results. The following parameters were included in one-way sensitivity analysis: discount rates (5% for both costs and outcomes, 0% for both costs and outcomes, 5% for costs and 0% for health outcomes), costs parameters (minimal costs, maximal costs), time horizon (according to ATHENA study), discontinuation of treatment in patients with permanent AF. In addition to one-way sensitivity analysis a probabilistic sensitivity analysis (PSA) was conducted in order to estimate uncertainty for main outcomes of the analysis.
- Analysis was conducted according to Polish HTA Agency (AHTA-Pol) guidelines [4].

## Model

In ATHENA models, treatment with dronedarone 400 mg bid on top of standard of care is compared to either standard of care alone (the ATHENA lifetime model) or active treatment with amiodarone, propafenone or sotalol (the ATHENA comparative model). The models' structure and principles of calculations were based on Markov model theory. Monte Carlo simulations were implemented to assess uncertainty. The following events were modelled: recurrence of atrial fibrillation, acute coronary syndrome (ACS), stroke, congestive heart failure (CHF), death, treatment discontinuation, progressing to permanent atrial fibrillation. The cycle length is one month. Structure of models and rules of transitions are presented on Figure 1. Additionally, from each state except for CHF, CHF (following months), stroke, post stroke (following months) and death it is possible to move to CHF or stroke state.

Figure 1. Model structure



## Results

Benefits associated with dronedarone surpass those for other interventions: the difference in QALY is 1.9-2.5 QALY in comparison with anti-arrhythmic drugs and 0.2 QALY for standard of care (Table 1).

Difference in total costs in a life-time horizon between dronedarone on top of SOC and standard of care alone is 3.5k Euro, and between dronedarone and other anti-arrhythmic drugs is 3.9-4.0k Euro (Table 2).

ICUR range for comparisons with AADs is 1.6-2.2k Euro, in comparison with SOC ICUR equals to 16.2k Euro. Incremental cost-utility ratios infer that additional costs that have to be incurred in order to gain additional QALY are well below the acceptability threshold.

Results of probabilistic sensitivity analysis were presented on Figure 2-5.

## Conclusions

**Dronedarone is a new option for treatment of patients with non-permanent AF and is highly cost-effective as compared to amiodarone, propafenone and sotalol. It is also cost-effective as compared to standard of care in non-permanent AF patients in Poland.**

## References

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Table 1. Clinical outcomes

| Parameter        | QALY  |             | LY    |             |
|------------------|-------|-------------|-------|-------------|
|                  | Value | Difference* | Value | Difference* |
| Dronedarone      | 7.2   | -           | 9.5   | -           |
| Standard of care | 7.0   | 0.2         | 9.2   | 0.3         |
| Amiodarone       | 5.3   | 1.9         | 7.0   | 2.5         |
| Propafenone      | 5.3   | 1.9         | 7.0   | 2.5         |
| Sotalol          | 4.7   | 2.5         | 6.3   | 3.2         |

\* Dronedarone vs. comparator

Table 2. Economic outcomes in Euro

| Treatment        | Treatment costs   | Difference vs. dronedarone | ICUR*  |
|------------------|---|----------------------------|--------|
| Dronedarone      | 5.6k in comparison with SOC<br>5.9k in comparison with AADs | -                          | -      |
| Standard of care | 2.1k  | 3.5k                       | 16,233 |
| Amiodarone       | 1.9k  | 4.0k                       | 2,154  |
| Propafenone      | 2.0k  | 3.9k                       | 2,090  |
| Sotalol          | 1.9k  | 4.0k                       | 1,636  |

Differences between costs of DRO in comparison with standard of care and anti-arrhythmic drugs are due to differences in assumptions in ATHENA comparative and lifetime models. The cost-effectiveness threshold in Poland is 25,011 Euro.

Figure 2. Scatter plot, dronedarone vs. amiodarone

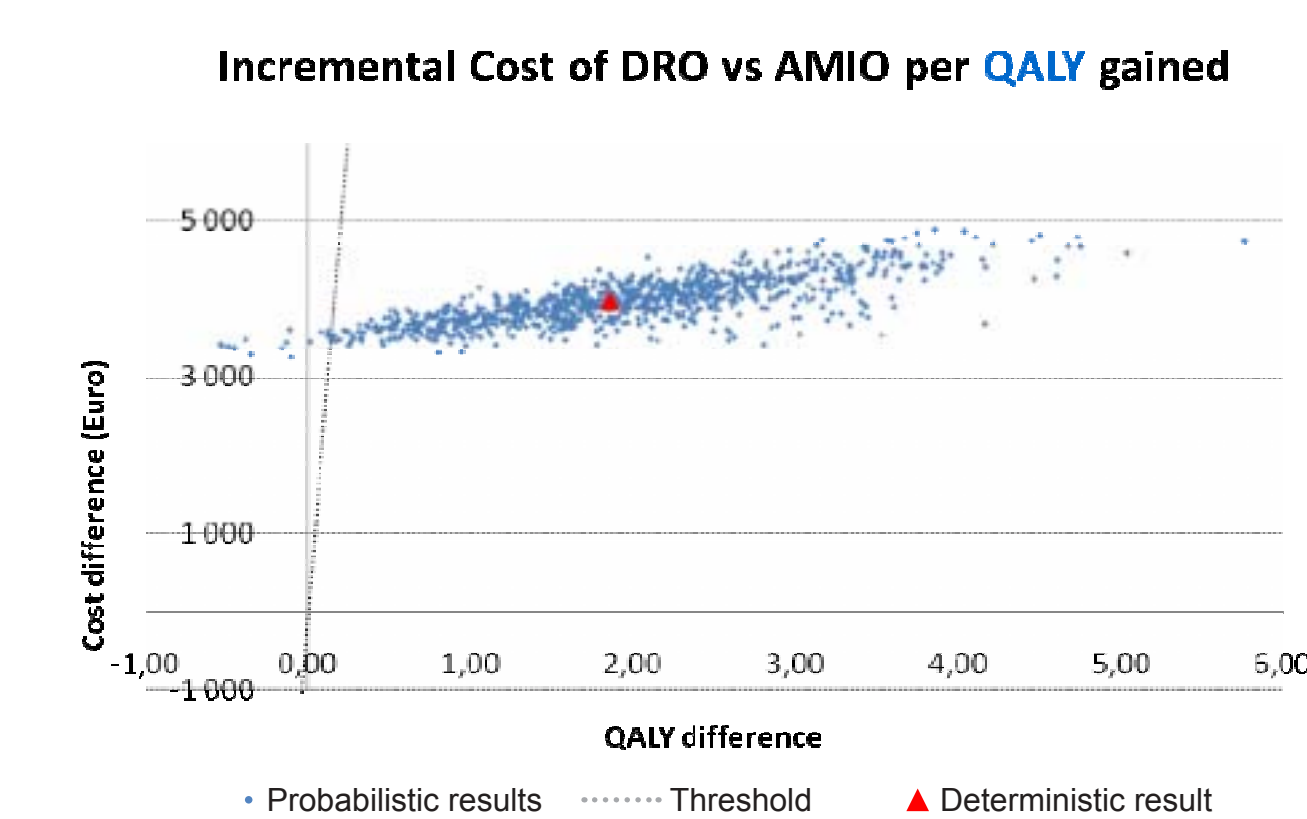


Figure 3. Scatter plot, dronedarone vs. sotalol

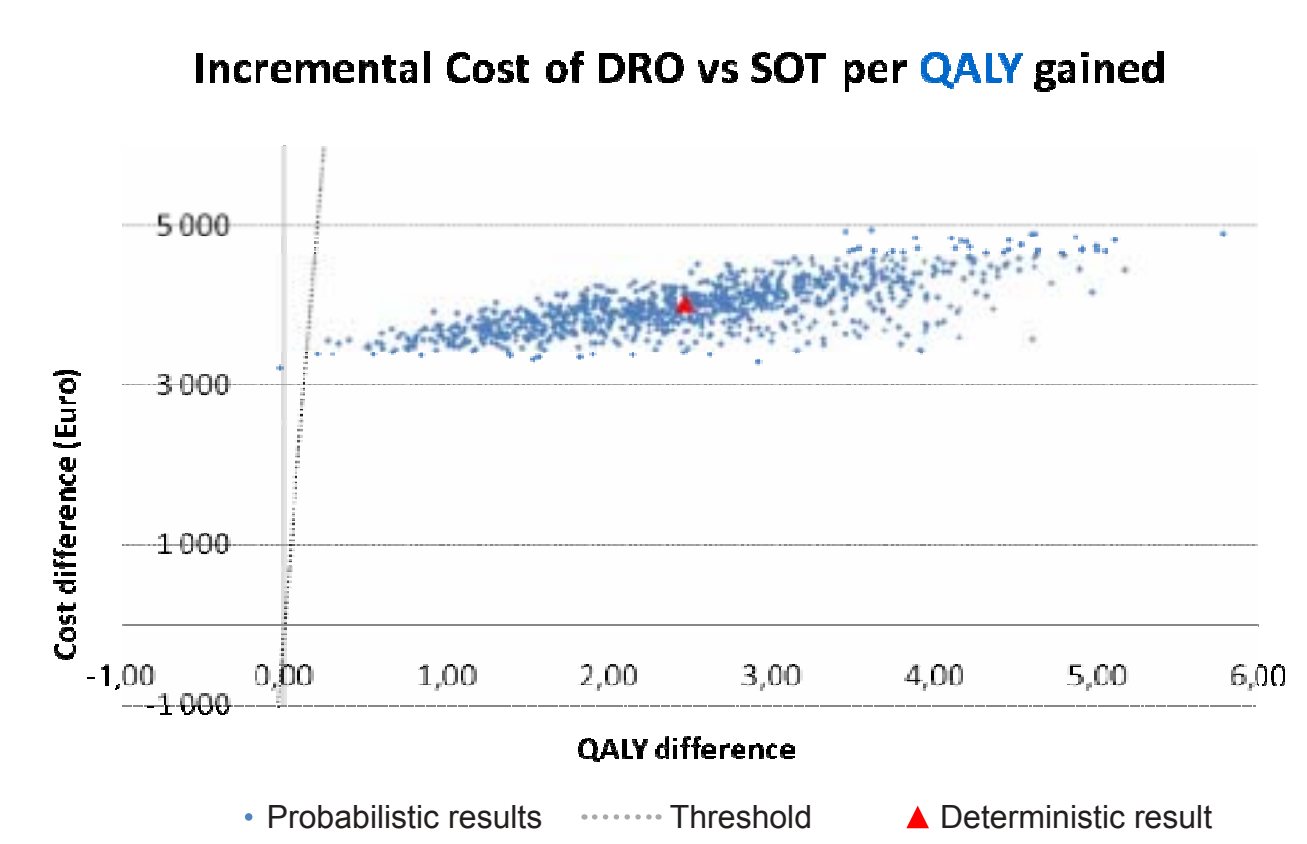


Figure 4. Scatter plot, dronedarone vs. propafenone

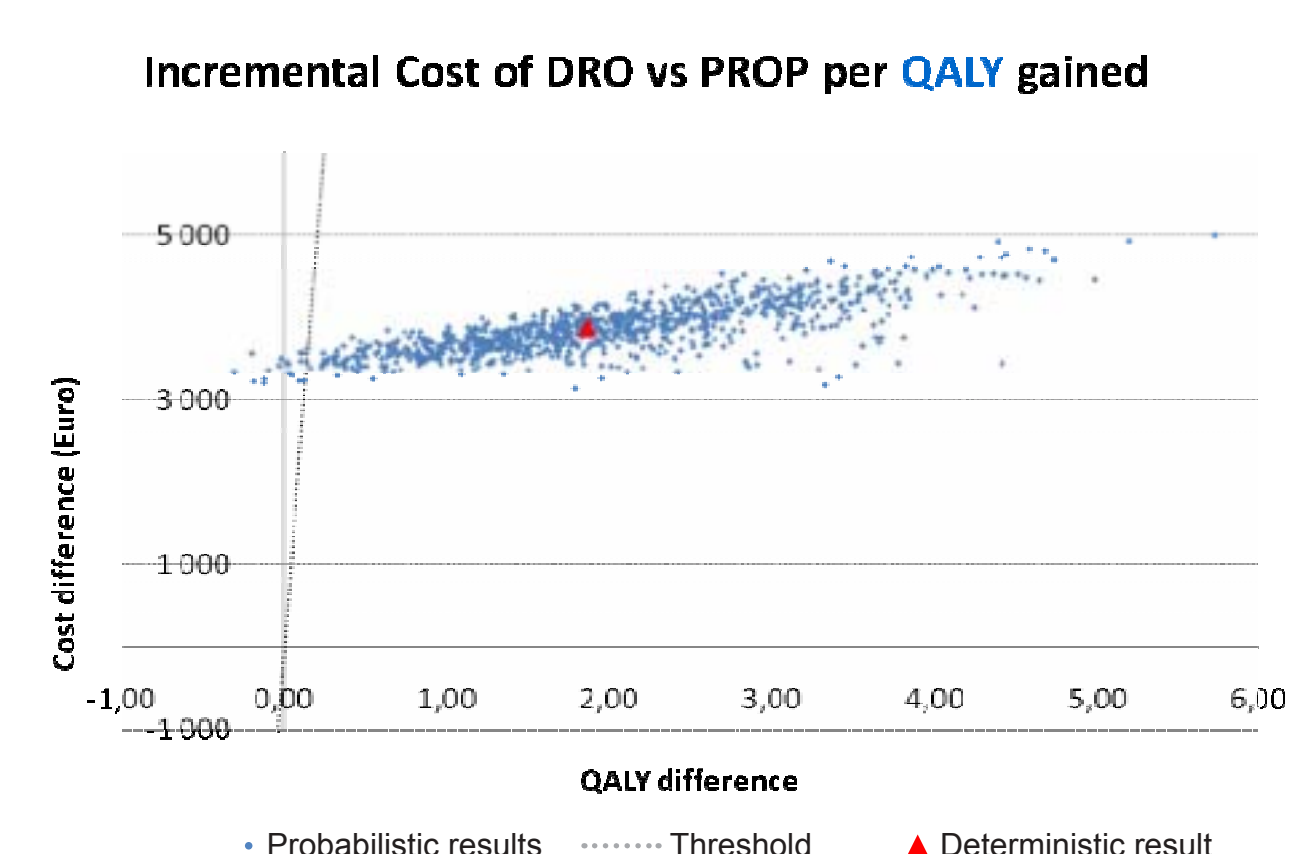


Figure 5. Scatter plot, dronedarone vs. standard of care

