Cost-effectiveness analysis of indacaterol/glycopyrronium (QVA149) fixed combination as a maintenance bronchodilator treatment in adult patients with chronic obstructive pulmonary disease in Spain

Meritxell Granell[1], María Giovanna Ferrario[2], Silvia Paz[2], Isabel Betoret[1]

[1] Novartis Farmacéutica, Barcelona, Spain

[2] Outcomes'10, Castellón, Spain

Background

- Chronic Obstructive Pulmonary Disease (COPD) is a chronic condition affecting 10.2% of adults between 40 and 80 years old in Spain, accounting for a burden of €0.75-1.00 billions per year.[1] No fixed-dose combination of a long-acting β2-agonist (LABA) and a long-acting muscarinic antagonist (LAMA) are currently commercialized in Spain. QVA149 is an inhaled fixed combination of indacaterol, a LABA, and glycopyrronium, a LAMA, which is being developed for the once daily treatment of COPD.

Objective

- To assess the cost-effectiveness (CE) of indacaterol/glycopyrronium (QVA149; 85μg/43μg) as a maintenance bronchodilator treatment of adult patients with Chronic Obstructive Pulmonary Disease (COPD) versus salmeterol/fluticasone (SFC; 50μg/500μg).

Materials and methods

- A CE model of micro-simulation over a 3-, 5-, 10-year and lifetime horizon was developed from the perspective of the Spanish National Healthcare System (Figure 1).

- Patients progress through subsequent COPD stages based on their baseline characteristics[2,3,4] and considering the natural decline of Forced Expiratory Volume in 1 second (FEV1) and exacerbation rate[3] (Table 1).

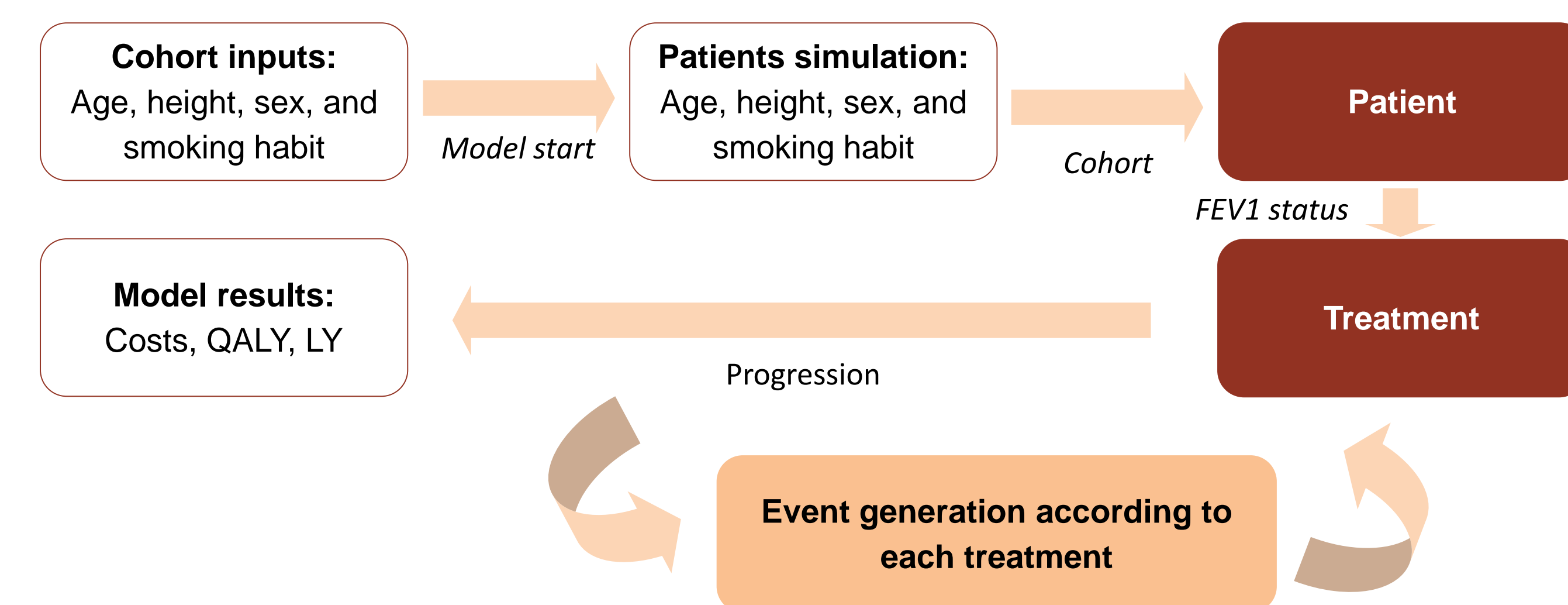**Figure 1.** Model schematic [adapted from Asukai et al., 2013[5]]

Table 1. Baseline characteristics of simulated patients

Baseline characteristics	Value	Source
Age [mean (SD)]	64 (10.2) years	2
Heigh men/women [mean (SD)]	177(7)/164(6) cm	3
% Men	70.5%	2
BMI [mean]	28.0	2
% Mild disease	38%	4
% Moderate disease	40%	4
% Severe disease	22%	4
FEV1 status in mild [mean (SE)]	87.39 (21.2)	4
FEV1 status in moderate [mean (SE)]	66.62 (50.8)	4
FEV1 status in severe [mean (SE)]	43.99 (90.7)	4

- In the model this is counteracted by treatment-associated FEV1 improvement from baseline and exacerbation rate reduction associated to each treatment vs. placebo, which were obtained by direct and indirect comparison of primary data from TORCH[6] (SFC vs. placebo), SHINE[7] (QVA149 vs. placebo) and ILLUMINATE[8] (QVA149 vs. SFC) clinical trials (Table 2).

Table 2. Efficacy inputs

Efficacy inputs	
FEV1 improvement [mean (95% CI) difference vs. placebo]	
QVA149	0.33 (0.25-0.42)
SFC	0.19 (0.17-0.21)
Exacerbations risk (95% CI)	
QVA149	0.54 (0.48-0.59)
SFC	0.74 (0.69-0.80)

CI: confidence interval

- The proportion of patients with severe (requiring hospitalization) and non-severe exacerbations depends on disease severity group (Table 3), combining the data from three indacaterol clinical trials (INVOLVE[9], INHANCE[10] and INLIGHT[11]).

Table 3. Proportion of severe/non-severe exacerbations by disease severity

	Mild	Moderate	Severe
% Non-severe exacerbations	100%	94%	92%
% Severe exacerbations	0%	6%	8%

- Cost estimates (Euros 2014) include drugs, disease management and non-severe/severe exacerbation expenditures from Spanish healthcare cost databases[12] and publications[13] with a discount rate of 3% for costs and benefits (Table 4).

Table 4. Costs inputs

Cost inputs	
Daily pharmacy costs	
QVA149	€1.84
SFC	€1.77
Annual maintenance costs	
Mild disease	€511.27
Moderate disease	€697.94
Severe disease	€972.60
Exacerbation costs	
Non-severe exacerbation	€98.69
Severe exacerbation	€2,539.70

- Mortality rates according to disease severity were obtained from Hoogendoorn et al (2011)[14] and from the Spanish Statistical Office mortality tables[15].

- Utility values were based on the regression model published by Rutten van Mölken et al. (2006)[16].

- One-way and probabilistic sensitivity analyses were carried out to assess uncertainty.

Results

- QVA149 has shown to be less costly and more effective than the fixed combination of SFC with respect to both Life Years (LY) and Quality-Adjusted Life Years (QALYs) gained (Table 5).

Table 5. LYs and QALYs gained for each time horizon

Time horizon	LYs			QALYs		
	QVA	SFC	Incremental	QVA	SFC	Incremental
3 years	2.765	2.761	0.004	1.655	1.648	0.007
5 years	4.408	4.396	0.012	2.642	2.627	0.015
10 years	7.844	7.797	0.047	4.706	4.663	0.043
Lifetime	12.385	12.204	0.181	7.422	7.292	0.130

- The cost per patient treated with QVA149 over a 3-, 5-, 10-year and lifetime period was estimated to be €108, €182, €305, and €467 lower than with SFC, which resulted from avoiding exacerbation costs and decreasing maintenance cost in relation to slowing COPD progression (Table 6).

Table 6. Total cost results for each time horizon

Time horizon	Total Costs (€)		
	QVA149	SFC	Incremental
3 years	€2,585.94	€2,694.39	€-108.45
5 years	€4,186.54	€4,368.10	€-181.56
10 years	€7,595.80	€7,900.75	€-304.95
Lifetime	€12,336.03	€12,802.59	€-466.56

- Therefore, QVA149 was estimated to be dominant over SFC with respect to both cost-effectiveness and cost-utility.

- OWSA shows that the variable that has the greatest impact on the QVA149 vs. salmeterol/fluticasone ICER is the COPD stage of the population (Figure 2).

Figure 2. One-way sensitivity analysis results
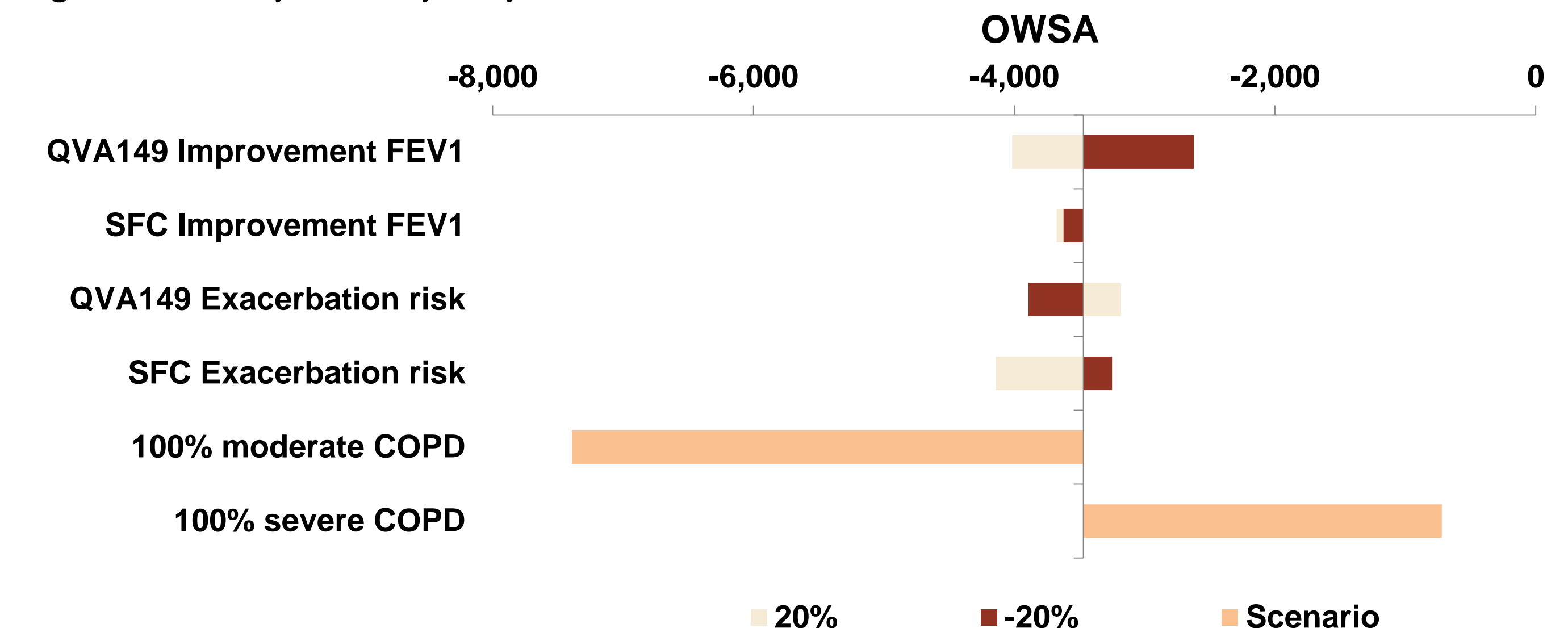
- The PSA cost-effectiveness plane (Figure 3) and acceptability curve (Figure 4) show that QVA149 is always cost-effective (cost-effectiveness threshold in Spain[17] being €30,000/QALY) and most of times dominant (more effective and less costly) than salmeterol/fluticasone in the treatment of COPD in Spain.
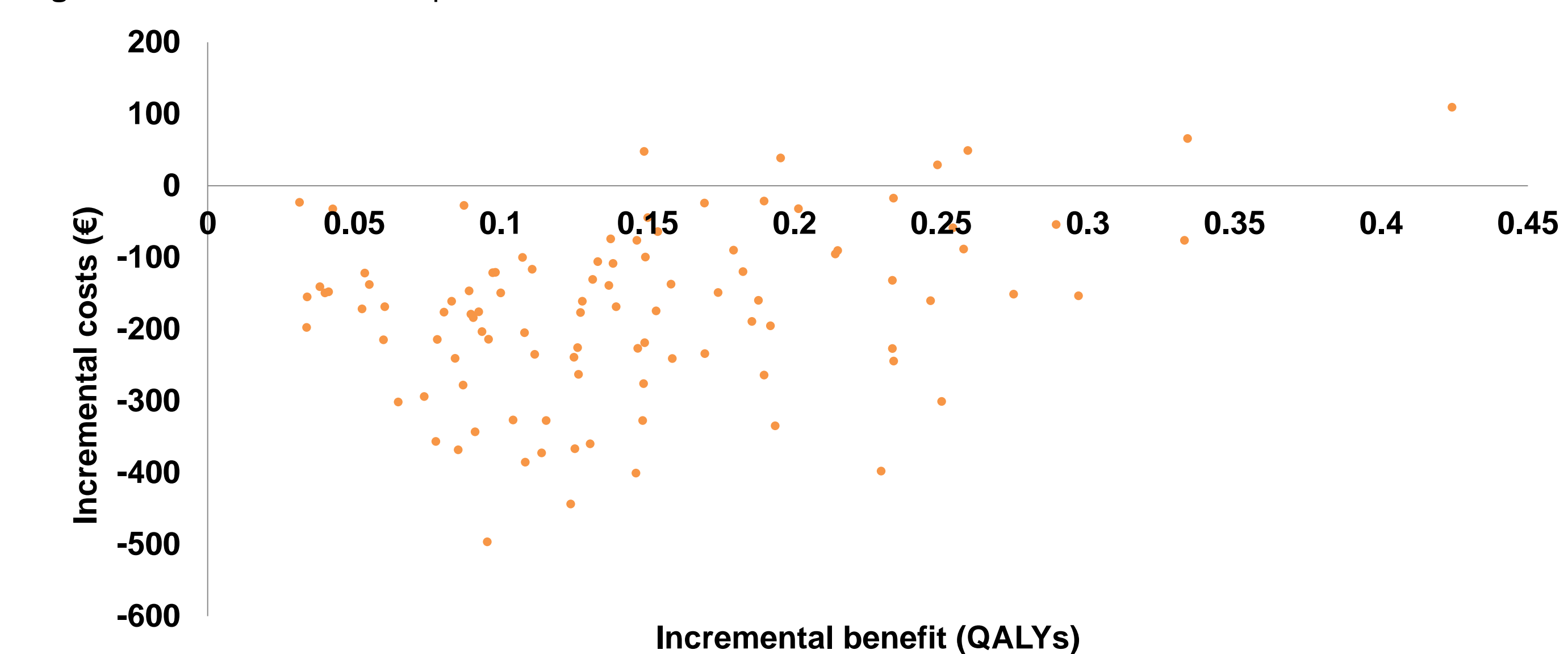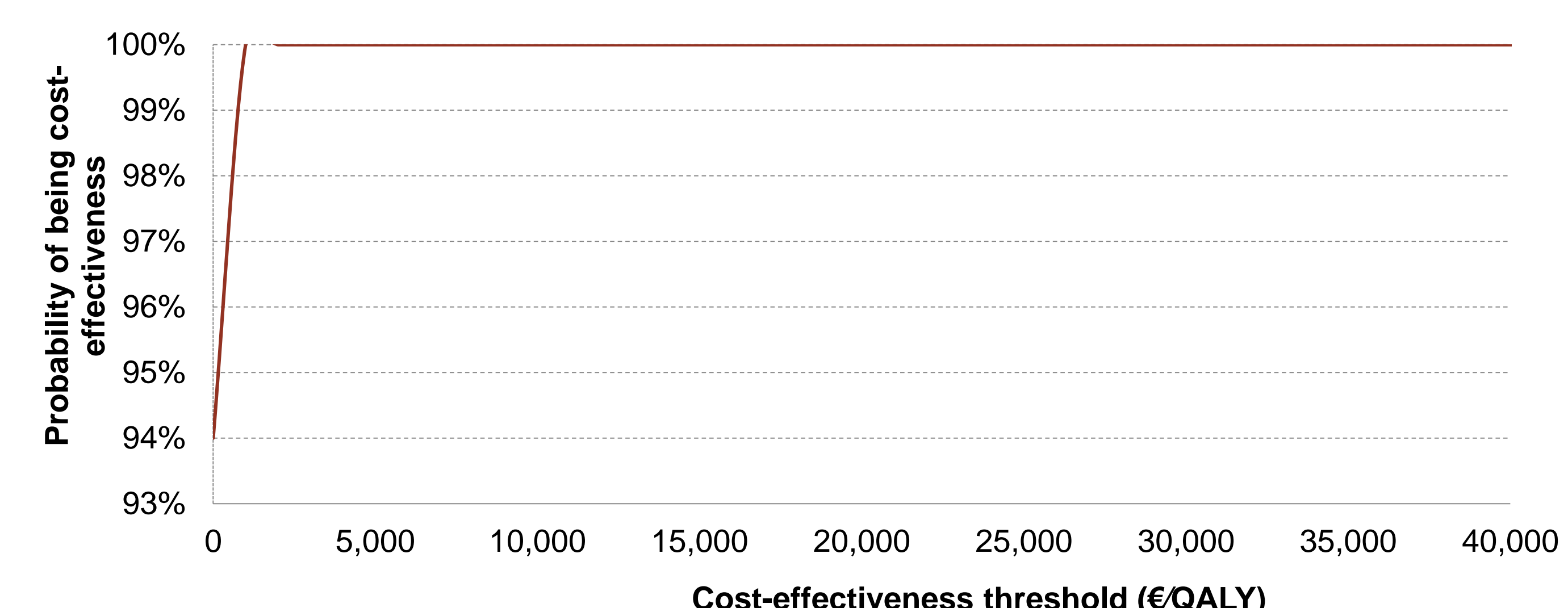
Figure 3. Cost-effectiveness plane

Figure 4. Acceptability curve

Conclusions

Despite the higher daily drug cost, QVA149 higher efficacy in improving FEV1 and reducing COPD exacerbations allows decreasing exacerbation and maintenance costs, resulting in higher cost-effectiveness compared to SFC.

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