

Cost-Utility Analysis of Ustekinumab vs Vedolizumab in Crohn's Disease in Italy

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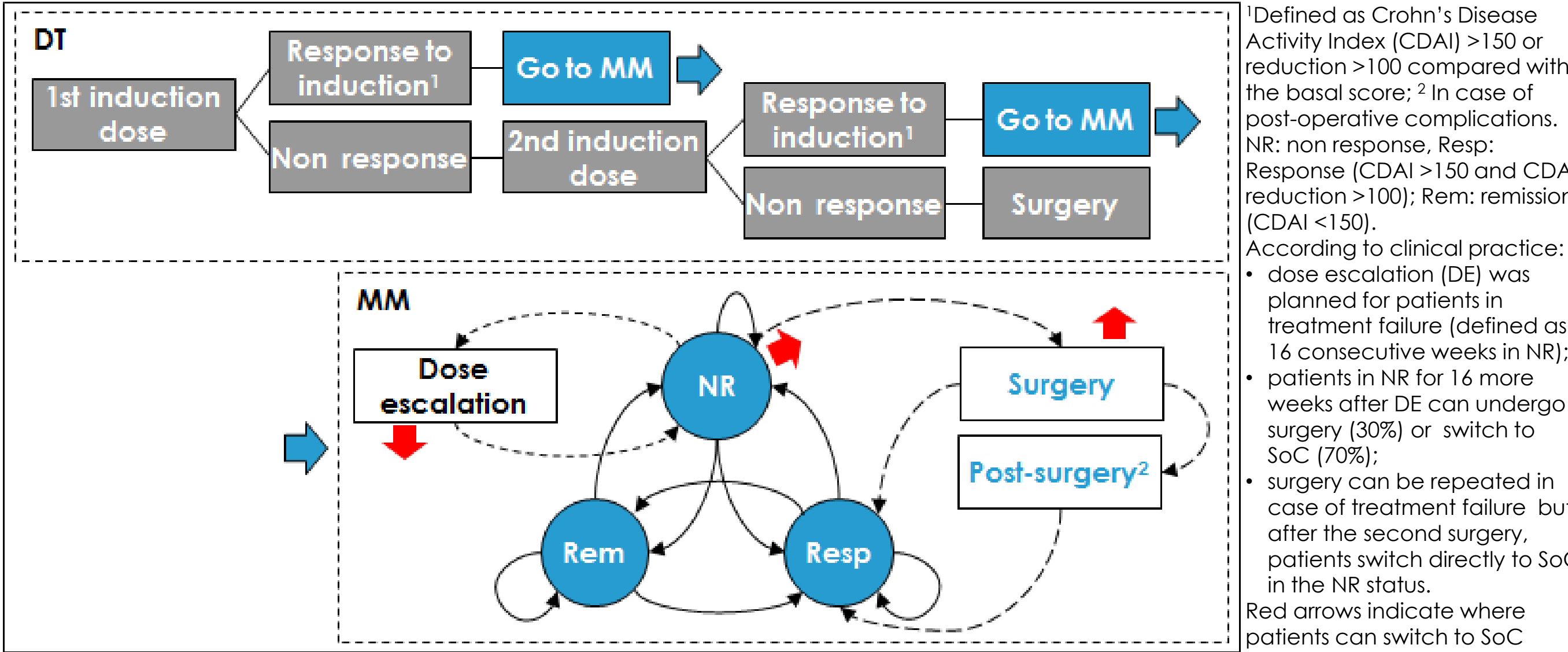
Objective

- ◆ Ustekinumab (UST), an IL 12/23 p40 inhibitor, and vedolizumab (VEDO), a selective α4β7 inhibitor, have provided the much-awaited out-of-class alternatives for patients who have failed (experienced) or who are intolerant (naïve) to anti-Tumor Necrosis Factor (anti-TNFα) therapy [1]
- ◆ A cost-utility analysis was developed to compare UST versus VEDO in both anti-TNFα naïve and experienced patients with moderate-to-severe Crohn's disease (CD) in Italy.

Methods

- ◆ A decision tree and 28-days Markov model cycles (Figure 1) is used to model the induction (IND) and maintenance (MAIN) phase, respectively, of a cohort of patients starting UST every 12 weeks (q12w) or VEDO every 8 weeks (q8w).
- ◆ 5.4% (range 1.4–23.9%) of the patients are anti-TNFα-naïve and represents those patients for which anti-TNFα are contraindicated [2-5]. Naïve and experienced patients are modeled separately due to the different disease evolution.
- ◆ Response rates after the first induction dose are obtained applying odds ratios [7] to the placebo rates observed in UNIT1/2 trials [8]. Response after the second induction dose comes directly from UNIT1/2 (for UST) and GEMINI II [9] (for VEDO).
- ◆ According to NICE guidelines [10], during the maintenance phase the same transition probabilities were applied to both treatments; UNIT1/2 source were used as reference: UST q12w for standard dose, UST q8w for dose escalation, placebo for standard of care (SoC).

Figure 1. Model scheme use to evaluate the cost-utility of ustekinumab vs vedolizumab: decision tree (DT) to model induction phase in the top box and Markov model (MM) for the maintenance phase in the bottom box



- ◆ Utilities are detailed for disease status according to a logistic regression model [11] on 500 patients affected by CD (Italian tariffs applied):
 - ◆ Remission: 0.915 for anti-TNFα-naïve and 0.909 for anti-TNFα-experienced
 - ◆ Response: 0.850 for anti-TNFα-naïve and 0.839 for anti-TNFα-experienced
 - ◆ Non response: 0.765 for anti-TNFα-naïve and 0.751 for anti-TNFα-experiencedThe utility in case of surgery is assumed to be equal to that of non-response status [12], while patients in post-surgery are supposed to turn into responders.

Lifetime cost included in the analysis are drugs, administration, surgery, post-surgery complications, and management of adverse events, in the perspective of Italian National Health Service

- ◆ Drug costs per cycle, administration cost included, are reported in Table I:
 - ◆ Each drug is valorized using the maximum selling price excluding VAT and compulsory discounts per pack and the posology of the IND and MAIN phases.
 - ◆ The cost of administration of intravenous drugs is considered equal to € 135 [13].
 - ◆ SoC is valorized according to drugs consumption observed in a recent analysis enrolled 509 CD patients in 36 Italian hospitals [14]
- ◆ Disease management costs are calculated by valorizing the main tests/visits/hospitalizations according to the relevant monthly frequencies [7] for health state (remission € 32.51, response € 54.96, non response € 268.28 per cycle, 6 months pre-surgery € 493.48, and 6 months post surgery € 342.25). A 1.3 factor is applied to anti-TNF-experienced patients to take into account the greater disease severity.
- ◆ Cost of surgery (€ 7,358.52) is calculated weighting the DRGs concerning gastrointestinal surgeries by the number of ordinary hospitalizations (70%) and day-hospital admissions (30%) [15] plus the cost of 6 months pre and post surgery (the last adjusted for 1.5% mortality [16]). An additional € 3,853.11 was added in 21.1% of surgery episode due to post-operative complications (infections, bleeding requiring re-intervention and anastomotic loss) [17].
- ◆ Adverse events are estimated using DRGs weighted by the number of hospitalizations and day-hospital admissions: gastrointestinal infections (€ 3,400), respiratory infections (€ 5,819), and reactions to the infusion site (€ 2,028). 28-days rates come from [10].

Table I. Drug cost per cycle including administration cost

Drugs	Ex-factory price	Posology		Cost per cycle	
		IND	MAIN	IND	MAIN
Ustekinumab ¹	€ 2,842.88	6 mg/kg (week 0) ²	90 mg q12w	€ 8,211.62	€ 2,842.88
Vedolizumab (300 mg)	€ 2,036.04	300 mg (weeks 0,2,6,10)	300 mg q8w	€ 8,684.16	€ 2,171.04
Standard of care				€ 32.82	€ 29.66
Steroids	22.18%	20-60 mg daily	10-15 mg daily	€ 26.04	€ 11.76
Immunosuppressors	28.49%	1-4 mg/kg daily		€ 24.64	€ 24.64
Mesalamine	49.33%	3 tablets daily		€ 40.60	€ 40.60

¹The 130 ml/mg vial is used in induction (intravenous administration) while the 90 mg package is used in maintenance (subcutaneous administration); ²According to UNIT1/2, it was assumed 2.89 vials per patient; IND: induction, MAIN: maintenance

Results

- ◆ Treatment with UST is associated with higher quality of life (+0.72 QALY) than VEDO, with an incremental cost of € 2,102 per patient. The Incremental cost-utility ratio (ICUR) results less than € 3,000 per QALY (Table II)
- ◆ Drugs and disease management represents the main cost drivers (Figure 2); surgery and post-operative complication accounts only for 3–4% of the total cost.
- ◆ The main drivers of cost are the response and remission rates during the induction phase while the increase in QALY is sensitive to the increase in utility due to the lower frequency of ustekinumab administration (Figure 3). Even for more conservative assumptions on efficacy of ustekinumab versus vedolizumab, the ICUR remains small (lower than € 8,000 per QALY).
- ◆ UST has 40% of probability to be dominant versus VEDO, 70% to be more cost-effective at a willingness to pay (WTP) of € 10,000 per QALY, 90% at a WTP of € 20,000; finally UST reaches almost 100% at a WTP of € 30,000 per QALY (Figure 4).

Table II. Incremental cost analysis ustekinumab versus vedolizumab; results are expressed as mean value (95% CI resulting from probabilistic sensitivity analysis)

Ustekinumab	
QALY	20.79 (17.93–23.43)
Total cost	€ 157,720 (136,822–178,018)
Vedolizumab	
QALY	20.07 (17.33–22.68)
Total cost	€ 155,619 (133,761–177,635)
delta (ustekinumab vs vedolizumab)	
QALY	0.72 (0.18–1.17)
Total cost	€ 2,102 (-15,757–19,201)
ICUR	€ 2,931 (dominant up to € 42,641)

Figure 3. Tornado charts (dashed bar represents the case in which UST is dominant)

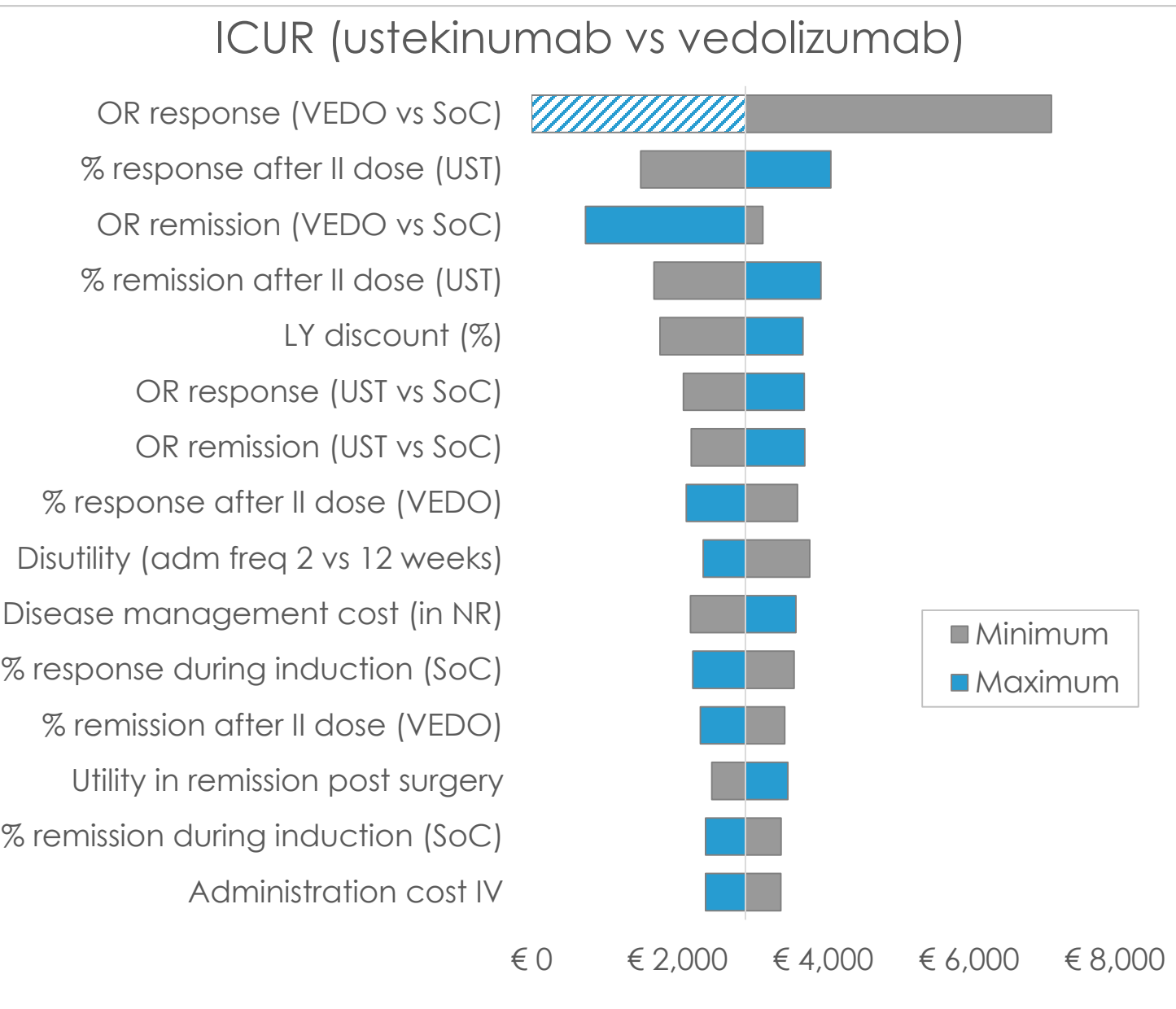


Figure 2. Cost composition, comparison between ustekinumab and vedolizumab treatment

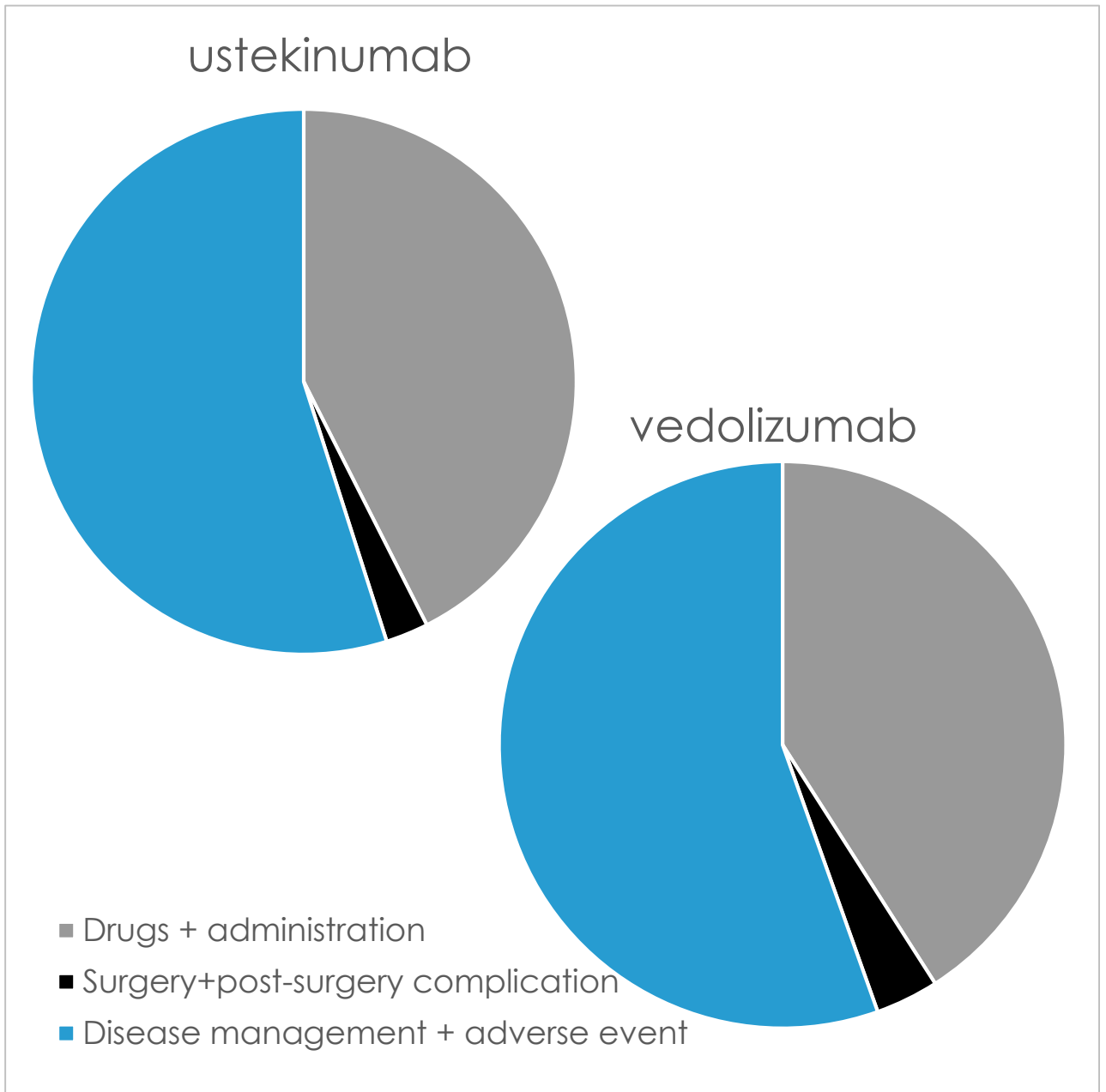
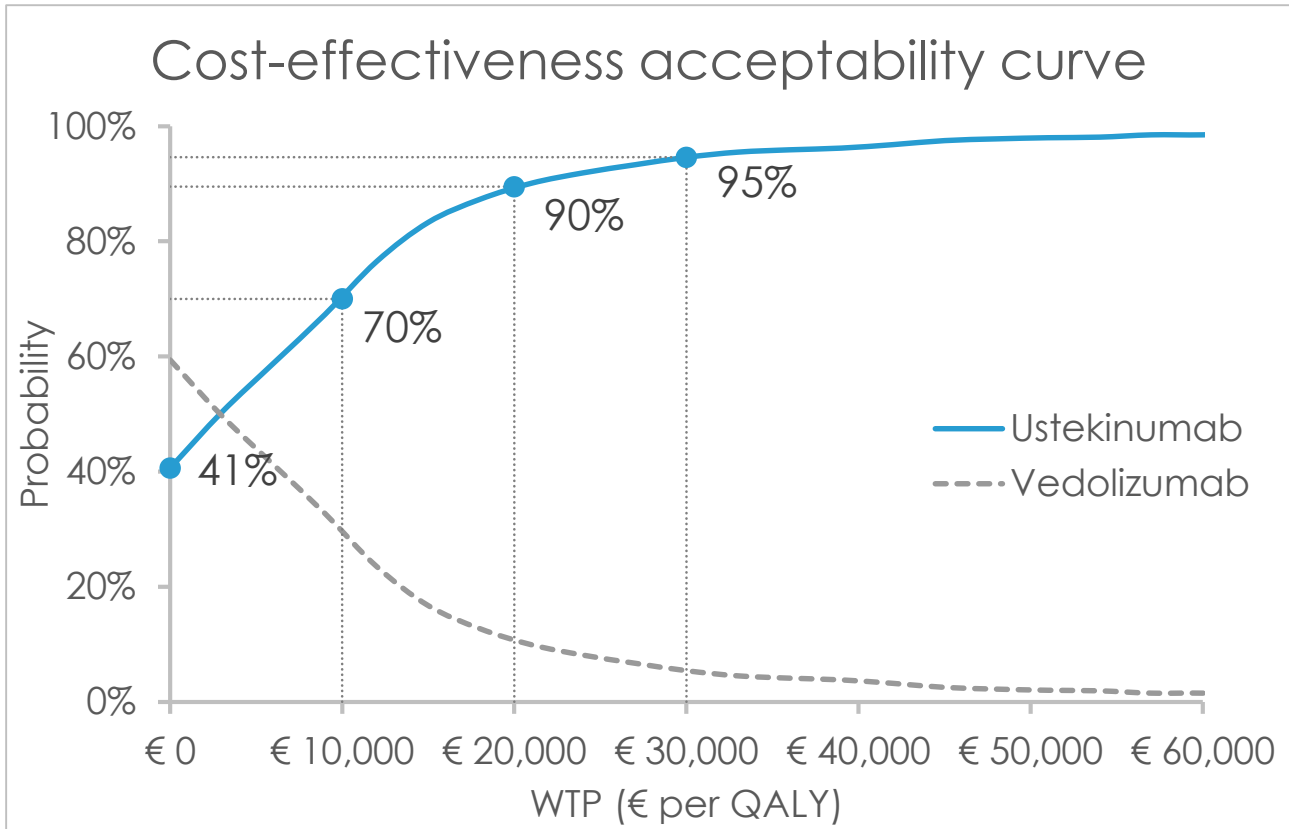


Figure 4. Cost-effectiveness acceptability curves



Conclusions

The results indicate that ustekinumab is cost-effective versus vedolizumab in a representative cohort of moderate-to-severe CD patients in Italy.

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