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COST-EFFECTIVENESS OF BEZLOTOXUMAB FOR THE PREVENTION OF RECURRENCE OF *CLOSTRIDIUM DIFFICILE* INFECTION IN HIGH RISK PATIENTS IN SPAIN

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INTRODUCTION

- *Clostridium difficile* infection (CDI) is a type of infectious diarrhea that can recur repeatedly after antibiotic therapy and is associated with considerable morbidity, mortality and healthcare resource utilization[1,2].
- Bezlotoxumab is a new antitoxin agent that, used in combination with standard of care (SoC) antibiotic therapy, prevents recurrent CDI[3].

OBJECTIVE

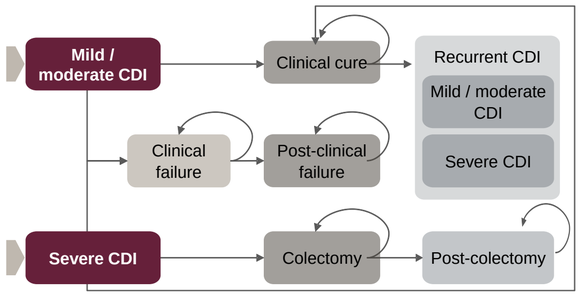
- To estimate the cost-effectiveness of bezlotoxumab added to SoC (metronidazole, vancomycin and/or fidaxomicin) vs. SoC alone in patients with CDI in Spain.

MATERIAL AND METHODS

Model structure

- A Markov model was developed to simulate the natural history of CDI using the Spanish Healthcare System perspective and a lifetime horizon (***Figure 1***). The cycle length was 15 days for the first 180 days and annual thereafter.

Figure 1. Markov model structure



Patients

- The analysis was conducted in five populations of patients at high risk of CDI recurrence according to MODIFY trials (***Figure 2, Table 1***)

Figure 2. Five populations at high risk of CDI recurrence

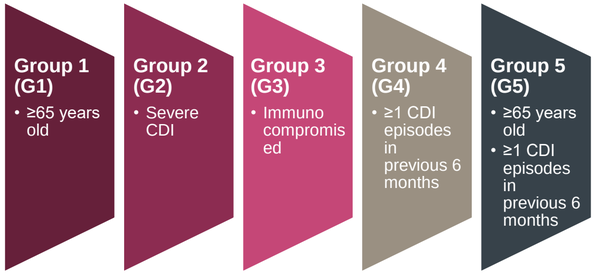


Table 1. Patient baseline characteristics by population

	G1	G2	G3	G4	G5
Age, median (years)	76.58	70.99	60.7	66.11	77.00
Female (%)	57.86	53.44	49.24	54.94	55.50
Patients entering the model with severe CDI (%)	25.4	100	18.79	12.29	17.60

Clinical inputs

- First recurrence rate was obtained from MODIFY trials[3]. Second and third recurrence rate (45%) were obtained from literature[4] and experts opinion. The proportion of severe recurrences were extracted from MODIFY trials[5] (***Table 2***).
- The efficacy of SoC was based on clinical cure rates of the MODIFY trials[5] (***Table 2***).
- The risk of colectomy and the mortality risk in patients requiring colectomy was assumed to be 1.8% and 40.0%, respectively[6].
- The risk of mortality (180-days after CDI) was assumed to be 25.7% for patients without recurrence and 36.3% for those with a recurrence[1]. From 180 days after CDI, the mortality risk was assumed the same as general population[7].

Cost inputs

- The cost inputs (€, 2017) considered were bezlotoxumab drug acquisition (€2,950) and CDI costs (first recurrence: €5,006.63; subsequent recurrences: €6,075.73)[8].

Table 2. Clinical inputs for each population of patients (%)

	G1	G2	G3	G4	G5
Recurrence rate (first) on Bezlotoxumab+SoC	15.38	10.66	14.61	25.00	19.38
Recurrence rate (first) on SoC	31.36	22.40	27.45	41.10	43.38
Proportion of severe recurrence	15.63	41.67	15.52	4.72	8.33
SoC efficacy for index case	81.26	71.67	83.72	80.67	77.70
SoC efficacy for first recurrence	76.74	62.16	71.67	80.67	77.70
SoC efficacy for subsequent recurrences	80.77	66.67	76.47	82.14	80.34

Utilities

- Utility values were considered for mild/moderate and severe CDI, colectomy, clinical failure (0.42)[9] and post-colectomy heath states (0.79)[10]. General population utility values were considered for clinical cure and post-clinical failure health states according to gender and age[11].

Outputs

- The model estimated total recurrences, life years (LY), quality-adjusted life years (QALY), costs and incremental cost-effectiveness ratio (ICER).
- Costs and benefits were discounted at 3%[12].

Sensitivity analysis

- One-way (OWSA) and probabilistic sensitivity analysis (PSA) were performed to test the impact of uncertainty on the model.
- A willingness-to-pay threshold of €21,000/QALY with a range varying between €11,000 and €30,000/QALY was considered[13].

RESULTS

- Bezlotoxumab added to SoC reduced CDI recurrence and increased LY and QALY. The ICER were below the threshold of €21,000/QALY in all groups (***Table 3***).

Table 3. Cost-effectiveness results

	Incremental cost (€)	Avoided recurrence (%)	LY gained	QALY gained	Cost per avoided recurrence (€)	ICER (€/QALY gained)
G1	1,515.50	26.4	0.15	0.12	5,735.97	12,723.68
G2	1,889.67	19.5	0.13	0.11	9,681.41	17,494.70
G3	1,797.33	21.2	0.22	0.19	8,465.27	9,544.72
G4	1,504.85	26.6	0.24	0.2	5,653.53	7,386.38
G5	794.57	39.7	0.22	0.18	2,001.46	4,378.20

- OWSA showed that ICER was most sensitive to recurrence rates, 180-day mortality rate and utilities associated with clinical cure health state. In groups 4 and 5, all analysis were below €21,000/QALY threshold.
- PSA results showed that bezlotoxumab was cost-effective at the €21,000/QALY threshold for most of the simulations performed (***Table 4***).

Table 4. PSA results. Probability of bezlotoxumab being cost-effective at different thresholds (%)

	G1	G2	G3	G4	G5
€11,000 /QALY	34.47	23.08	55.74	72.13	97.10
€21,000/QALY	85.51	54.14	86.01	94.51	99.60
€30,000/QALY	95.80	74.53	93.71	98.10	100.00

CONCLUSIONS

- **The analysis suggested that bezlotoxumab added to SoC is a cost-effective treatment to prevent the recurrence of CDI in high-risk patients in Spain.**

References

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