Targeted Substitution of Omadacycline in Place of Standard of Care for CABP Treatment is Associated with a Risk Reduction of *Clostridioides difficile* Infection and Financial Cost Savings in the Acute Care Setting

Mauricio Rodriguez PharmD, BCPS, BCCCP, BCIDP,[1] Surya Chitra PhD,[1] Kelly Wright PharmD[1], Thomas Lodise PhD, PharmD[2]

[1]Paratek Pharmaceuticals, Inc., King of Prussia, PA; [2]Albany College of Pharmacy and Health Sciences, Albany, NY

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BACKGROUND

- To aid in reducing the impact of *Clostridioides difficile* Infections (CDI) in acute care facilities, the CDC encourages institutions to develop facility-specific antibiotic stewardship programs and consider restricting the use of antibiotics that have the highest risk for CDI, such as fluoroquinolones (FQ) and 3rd generation cephalosporins (3GC).[1,2]
- Despite their increased propensity to cause CDIs, FQ and 3GC continue to be the guideline recommended first-line agents for hospitalized patients with suspected or documented community-acquired bacterial pneumonia (CABP).
- Omadacycline (OMC), approved by the FDA in 2018 for the treatment of CABP, has demonstrated a low propensity to induce CDI in preclinical and clinical studies.[3,4]
- In the phase 3 OPTIC study, 2% of CABP patients who received moxifloxacin developed CDI vs 0% for OMC[4]
- Among patients in the phase 3 OPTIC study with a Davis risk score (DRS) ≥ 6, 14% of CABP patients treated with moxifloxacin developed CDI compared with no patients in the OMC-treated group, despite balanced CDI risk between treatment groups.[4,5]
  - The DRS is one of the most well-described predictive indices for 30-day risk of healthcare-associated CDI using readily available and clinically useful variables.[6]
  - Davis Risk Index Scoring:[6]
    - Number of high-risk antibiotics received = 1 point each (maximum 5 points)
    - Receipt of proton-pump inhibitors = 1 point
    - Age 40 – 55 years = 1 point; > 55 years = 2 points
    - Charlson Comorbidity Index: 1 comorbidity = 1 point; > 1 comorbidity = 2 points

OBJECTIVE

To assess the economic impact of substituting current guideline-concordant CABP treatments (i.e., FQ and 3GC) with OMC in hospitalized patients at high risk for CDI (Davis Risk Score ≥ 6[6]).

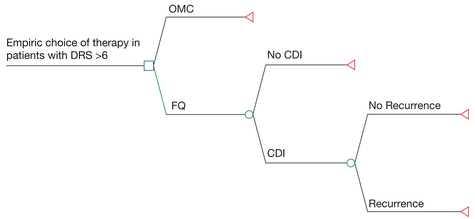
METHODS

Model Description and Structure

- A deterministic framework from the US hospital perspective was used to develop the conceptual healthcare-decision analytic model that replaced the use of guideline-concordant CABP treatments with high risk for CDI (i.e., FQ and 3GC) with OMC in hospitalized adult CABP patients with a DRS ≥ 6 (**Figure 1**).

METHODS

Figure 1. Structural healthcare-Decision Analytic Model



Model structure, input and assumptions

- The underlying model assumption was that OMC treatment has a lower propensity to induce CDI relative to current guideline-concordant CABP treatments in high-risk CDI patients and has the potential to avoid CDI events and associated costs.
- Based on the US prevalence of CAP admissions per year, it was estimated that 100,000 patients had a DRS ≥ 6 (**Table 1**).
- Base-case scenario:
  - For the current guideline-concordant CABP treatment scenario, 14,000 were assumed to develop CDI, based on the 14% rate in patients with DRS ≥ 6 from the OPTIC study (**Figure 2**).[4,5]
    - Mean (SD) moxifloxacin treatment duration was 7.25 days (SD 2.49) in CDI patients vs. 9.60 (SD 2.94) in the overall study.
    - Two patients developed CDI after completion of treatment, whereas CDI occurred on Days 4–8 of treatment in the other six patients.
  - For the OMC scenario, no patients were assumed to develop CDI, based on 0% rate in patients with DRS ≥ 6 from the OPTIC study.[4]
- Only excess costs associated with each treatment were considered in the model.
- Cost per episode of hospital-onset CDI, CDI recurrence rate, and cost per episode recurrent CDI were derived from a real-world data analyses of healthcare resource utilization and direct medical costs associated with index and recurrent CDI (**Table 1**).
- OMC acquisition costs for 5 days of therapy was assumed to be $2070.

METHODS

Figure 2. Predicted individual CDI risk scores for observed CDI cases in the phase 3 OPTIC randomized clinical trial. No cases were observed in the OMC group.[5]

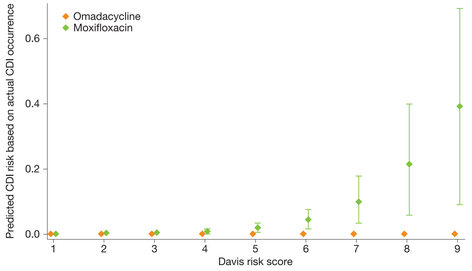


Table 1. Input parameters used in the deterministic healthcare-decision analytic model.

Factor	Parameter
Number of CAP admissions per year [7]	1,000,000
Percentage of CAP patients with DRS ≥ 6 [4,6]	10%
Percentage of DRS ≥ 6 patients who developed CDI [4]	14%
Cost per episode of hospital-onset CDI [8]	$43,677
Cost per episode recurrent CDI [8]	$88,828
CDI recurrence rates [8,9]	0% and 20%
Omadacycline wholesale costs	$2070

CAP, community-acquired pneumonia; CDI, *Clostridioides difficile* infection; Davis Risk Score, DRS. Costs are given in US dollars

Model Output and Analyses

- Total and incremental attribute costs associated for each treatment scenario in base-case analysis:
  - Guideline-concordant CABP treatments scenario: Cost of CDI (overall, first CDI episode, and recurrent CDI episode) for the predicted 14,000 CABP patients with CDI.
  - OMC scenario: Cost of 5 days of inpatient treatment for the 100,000 CABP patients with DRS ≥ 6.
- One-way sensitivity analyses were performed to determine the excess CDI rates in the guideline-concordant CABP treatment group that still resulted in costing saving with OMC (**OMC dominance threshold**).
  - Recurrence rates set at 0% and 20%

RESULTS

- Results of the base-care scenario analyses are shown in **Table 2**.
  - The use of OMC in place of guideline-concordant CABP treatment for patients with DRS ≥ 6 resulted in cost savings of up to $404 million per year with 0% CDI recurrence rate and $531 million per year with 20% CDI recurrence rate.

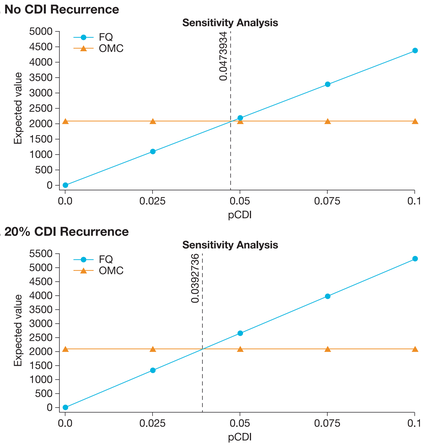
Table 2. Estimated CDI-associated costs with use of guideline-concordant CABP treatment versus omadacycline.

Factor	Cost ($ million)	
	0% Recurrence rate	20% Recurrence rate
Standard-of-care scenario for CABP patients with DRS ≥ 6	611	738
First-episode CDI	611	489
Recurrent CDI	0	249
Cost of 5-day hospital treatment with OMC	207	207
Cost saving from omadacycline scenario	404	531

CABP, community-acquired bacterial pneumonia; CDI, *Clostridioides difficile* infection; DRS, Davis risk score; OMC, omadacycline. Costs are given in US dollars

- Results of the one-way sensitivity analyses to determine the absolute difference CDI rates between groups that still resulted in costing saving with OMC (**OMC dominance threshold**) is shown in **Figure 3.**

Figure 3. One-way sensitivity analyses



RESULTS

Limitations

- The findings are not unique to OMC and could be applied to any antibiotic that confers a lower risk of CDI relative to current CABP treatments.
- We focused on excess rather than total costs because many costs (e.g., hospitalization for initial treatment period, nursing time) would be the same regardless of the choice of antimicrobial agent.
- We did not factor in a series of outcomes and costs such as hospital readmissions and patient satisfaction/quality of life/productivity, due to lack of comparator data on these endpoints between omadacycline and guideline concordant CABP treatments.
- We did not incorporate mortality into the model.
- The conceptual models assumed that OMC did not lead to any cases of CDI. Thus, the one-way sensitivity analyses reflect the absolute difference in CDI rates between groups (i.e., excess CDI rate in guideline-concordant CABP treatment group) that still resulted in costing saving with OMC.

CONCLUSIONS

- Our findings suggest prioritizing use of omadacycline over guideline-concordant CABP treatments in hospitalized CABP patients with a DRS ≥ 6 has the potential to substantially reduce attributable CDI costs.
- Findings suggest that OMC will result in cost savings if use of guideline-concordant CABP treatment results in 4-5 excess cases of CDI per 100 CABP treated relative to OMC.
- Further study is needed to validate model findings, but these results can serve as the basis of antibiotic stewardship initiatives for healthcare institutions aspiring to reduce hospital CDI rates and associated costs.

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Medical information: medinfo@paratekpharma.com