IMPACT OF ONE OR MORE COMORBIDITIES AND THE MICROBIOME METABOLIC THERAPY (MMT™) KB109 ON SYMPTOM RESOLUTION IN NON-HOSPITALISED PATIENTS WITH MILD TO MODERATE COVID-19

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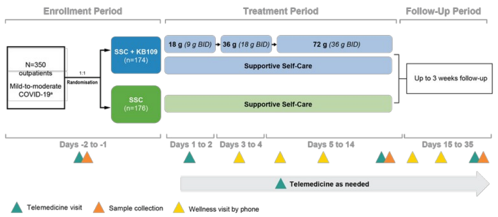
I. INTRODUCTION AND OBJECTIVE

- Most COVID-19 cases in the United States are managed via outpatient care, yet the natural history of COVID-19 in the outpatient setting is not well understood[1-3]
- Many studies of COVID-19 have focused on symptom duration and clinical outcomes in adults hospitalised with severe COVID-19
  - Monoclonal antibodies are indicated for treating mild to moderate COVID-19 in adults and children over 12 years of age who are at high risk for progressing to severe COVID-19 and/or hospitalisation[4]
- Little prospective data are available in the largest segment of patients—those with low risk for progressing to severe COVID-19 and/or hospitalisation[5]
  - Retrospective reports[6,7] suggest it can take 3 to 4 weeks for symptom resolution and the return to usual health in so-called "mild" COVID-19 patients but a subset go on to have long-lasting symptoms of 10 weeks or greater
- KB109 is a novel synthetic glycan developed to support immune system homeostasis through modulation of the gut microbiome
- The objective of this study was to evaluate KB109 safety and its effects on select health measures when combined with supportive self-care (SSC) vs SSC alone in an outpatient setting (Figure 1)

II. METHODS

FIGURE 1. K031 STUDY DESIGN



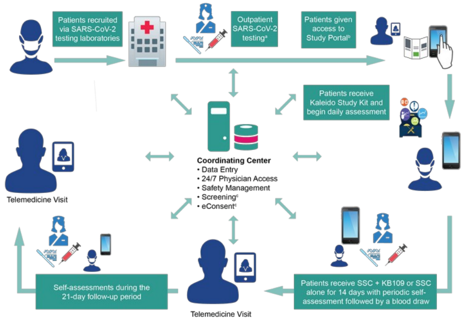
aSymptomatic patients must not have reported significant improvement in cardinal symptoms in 48 hours immediately before randomisation. If patients were presymptomatic, symptoms must have developed within 7 d of a positive test, and patients must have been randomly assigned to treatment within 5 d of the presenting symptoms.

TABLE 1. COVID-19–RELATED SYMPTOMS

8 cardinal symptoms known to be associated with COVID-19	5 additional symptoms associated with COVID-19
– Fever	– GI disturbance/symptoms (other than diarrhoea)
– Chills/repeated shaking with chills	– Diarrhoea
– Cough	– Fatigue
– Shortness of breath	– Nasal congestion
– Headache	– Chest tightness
– Muscle pain	
– Anosmia/ageusia	
– Sore throat	

Patients were instructed to rate their symptoms on a scale of 0-3 where:
0 = Absent (no symptoms evident)
1 = Mild (symptoms present but easily tolerated)
2 = Moderately severe (definite awareness of symptoms; bothersome but tolerable)
3 = Very severe (hard to tolerate; considerable interference with daily activity)

FIGURE 2. FRAMEWORK OF THE VIRTUAL STUDY

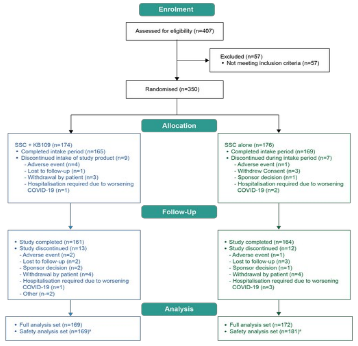


aBlood draws as feasible and only for those patients consenting before COVID-19 testing. bPatients had the option of consenting following testing and discharge; these patients had a telemedicine visit to confirm inclusion/exclusion criteria. cFor those patients consenting following discharge.

- Eligible adult patients were randomised 1:1 to SSC alone or SSC + KB109 (Figure 1)
- Randomisation was stratified by site, age subgroup, and comorbidity status
- Signs/symptoms of COVID-19 and other end points were evaluated over a 35-d study period
- Patients self-assessed COVID-19–related symptoms (Table 1)
- Overall, symptoms were considered to be resolved by d 35 if composite symptom score became 0 (absent) or 1 (mild) without further worsening
- Safety was monitored through adverse event reporting
- Full analysis set (FAS) included all randomised patients with both baseline and ≥1 postbaseline assessments during the intake period. Patients included in analyses of time to resolution of symptoms had composite symptom scores >1 at baseline. Resolution was defined as composite score ≤1
- Safety analysis set (SAS) included all randomised patients. Patients who actually consumed any amount of KB109 were included in the SSC + KB109 group; otherwise, patients were included in the SSC-alone group
- Subgroup analyses of time to resolution of COVID-19–related symptoms were conducted for the following subgroups based on the FAS: age group (≥18 to <45 years, ≥45 to <65 years, ≥65 years) and comorbidity status (yes/no)

III. RESULTS

FIGURE 3. PATIENT DISPOSITION



aSafety analysis set was based on the actual treatment patients received. Five patients were randomised to receive SSC + KB109 but did not take any KB109. Therefore, these 5 patients were analysed in the safety analysis set for the SSC alone group.

TABLE 2. BASELINE DEMOGRAPHICS (SAS)

Demographic	SSC + KB109 (n=169)a	SSC Alone (n=181)a
Age (years), median (range)	37.0 (18-72)	35.0 (18-76)
Age group (years), No. (%)		
≥18 to <45	113 (66.9)	121 (66.9)
≥45 to <65	48 (28.4)	51 (28.2)
≥65	8 (4.7)	9 (5.0)
Sex, No. (%)		
Male	68 (40.2)	75 (41.4)
Female	101 (59.8)	106 (58.6)
Race, No. (%)		
Asian	2 (1.2)	2 (1.1)
Black or African American	15 (8.9)	11 (6.1)
White	151 (89.3)	167 (92.3)
Other	1 (0.6)	1 (0.6)
Ethnicity, No. (%)		
Hispanic or Latino	109 (64.5)	112 (61.9)
Not Hispanic or Latino	59 (34.9)	68 (37.6)
Not reported	1 (0.6)	0
Unknown	0	1 (0.6)
BMI subgroup, No. (%)		
<30 kg/m^2	111 (65.7)	108 (59.7)
≥30 kg/m^2	57 (33.7)	67 (37.0)

aData set did not include patients who were American Indian, Alaskan Native, Native Hawaiian, or other Pacific Islander.

TABLE 3. SELF-REPORTED COMORBIDITIES (SAS)

Category	SSC + KB109 (n=169) n (%)	SSC Alone (n=181) n (%)
Patients with ≥1 comorbidity	69 (40.8)	66 (36.5)
Patients with ≥2 comorbidities	17 (10.1)	31 (17.1)
Hypertension	29 (17.2)	34 (18.8)
Chronic lung disease (asthma, emphysema, COPD)	13 (7.7)	17 (9.4)
Diabetes mellitus	8 (4.7)	11 (6.1)
Obesity	8 (4.7)	5 (2.8)
Cardiovascular disease	3 (1.8)	5 (2.8)
Neurologic disorder/prior stroke	3 (1.8)	3 (1.7)
Cancer	2 (1.2)	1 (0.6)
Hypothyroidism	2 (1.2)	3 (1.7)
Environmental allergies	2 (1.2)	0
Gastro-oesophageal reflux	2 (1.2)	0
Hashimoto's disease	2 (1.2)	0
Insomnia	2 (1.2)	0
Depression	1 (0.6)	2 (1.1)
Chronic liver disease	0	2 (1.1)
Hypercholesterolaemia	0	2 (1.1)
Overweight	0	2 (1.1)
Other chronic disease	36 (21.3)	36 (19.9)

TABLE 4. TEAEs REPORTED IN ≥5 PATIENTS (SAS)

System Organ Class Preferred Term	SSC + KB109 (n=169)a n (%)	SSC Alone (n=181)a n (%)
Patients with any TEAE	61 (36.1)	48 (26.5)
Patients with TEAEs by severity		
Mild	29 (17.2)	17 (9.4)
Moderate	28 (16.6)	26 (14.4)
Severe	4 (2.4)	5 (2.8)
GI disorders		
Diarrhoea	18 (10.7)	6 (3.3)
Nausea	6 (3.6)	1 (0.6)
Abdominal pain	5 (3.0)	1 (0.6)
Respiratory, thoracic, and mediastinal disorders		
Dyspnoea	8 (4.7)	10 (5.5)
Oropharyngeal pain	4 (2.4)	7 (3.9)
Cough	2 (1.2)	8 (4.4)
Nervous system disorders		
Headache	3 (1.8)	5 (2.8)

aSafety analysis set was based on the actual treatment patients received. Five patients were randomised to receive SSC + KB109 but did not take any KB109. Therefore, these 5 patients were analysed in the safety analysis set for the SSC alone group.

TABLE 5: COVID-19–RELATED HOSPITALISATION, EMERGENCY DEPARTMENT, OR URGENT CARE VISITS (SAS)

Population	SSC + KB109 (n=169)	SSC Alone (n=181)	Overall (N=350)	SSC + KB109 vs SSC Alone, % Change
Overall study population	7 (4.1%)	15 (8.3%)	22 (6.3%)	-50.0%
Comorbidity patient subgroup	4 (5.8%)	10 (15.2%)	14 (10.4%)	-61.7%

EFFECT OF COMORBIDITY ON TIME TO RESOLUTION OF COVID-19 SYMPTOMS

- Time to resolution of overall 13 symptoms was shorter for patients with no comorbidities than for patients with ≥1 comorbidity (21 d vs 30 d, respectively; HR=1.163 [95% CI, 0.723-1.872])[8]
  - The difference in time to resolution was similar for the 8 cardinal symptoms (15 d vs 21 d, respectively; HR=1.283 [95% CI, 0.809-2.035])

FIGURE 4. MEDIAN TIME TO RESOLUTION OF SYMPTOMS WAS REDUCED WITH KB109 IN PATIENTS WITH ≥1 COMORBIDITY (FAS)

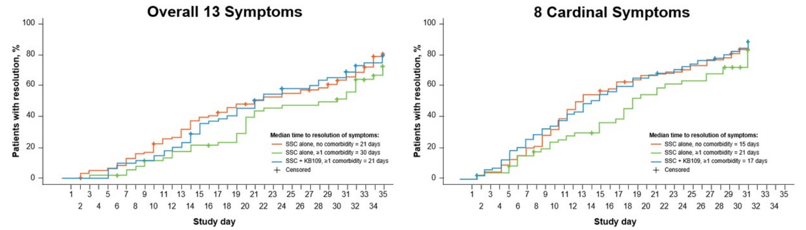


FIGURE 5. MEDIAN TIME TO RESOLUTION OF SYMPTOMS WAS REDUCED WITH KB109 IN PATIENTS AGED ≥45 YEARS OR WITH ≥1 COMORBIDITY (FAS)

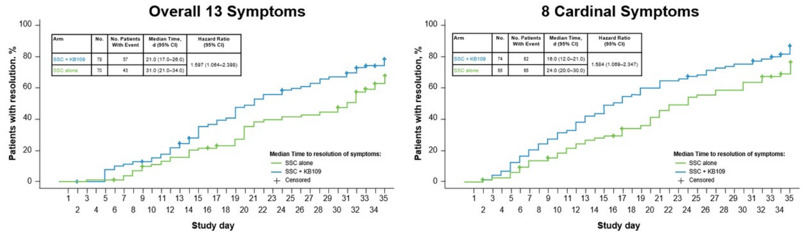


TABLE 6. MEDIAN TIME TO RESOLUTION OF SYMPTOMS WITH KB109 BY AGE AND COMORBIDITY STATUS (FAS)

Intake Period and Follow-up Period

Subgroup	SSC + KB109 (N=169) No.	SSC + KB109 (N=169) No. (%) Patients With Event	SSC + KB109 (N=169) Median Time, d (95% CI)	SSC Alone (N=172) No.	SSC Alone (N=172) No. (%) Patients With Event	SSC Alone (N=172) Median Time, d (95% CI)	SSC + KB109 vs SSC Alone Hazard Ratio (95% CI)
Overall 13 Symptoms							
Age ≥45 years or comorbidity							
Yes	79	57 (71.4)	21.0 (17.0–26.0)	70	43 (60.9)	31.0 (21.0–34.0)	1.597 (1.064–2.398)
No	67	56 (84.0)	17.0 (13.0–24.0)	77	63 (81.9)	18.0 (14.0–24.0)	1.068 (0.741–1.540)
8 Cardinal Symptoms							
Age ≥45 years or comorbidity							
Yes	74	62 (84.0)	16.0 (12.0–21.0)	66	46 (69.3)	24.0 (20.0–30.0)	1.584 (1.069–2.347)
No	56	45 (79.8)	14.0 (11.0–21.0)	68	59 (86.1)	13.5 (12.0–17.0)	0.846 (0.570–1.255)

IV. SUMMARY

- KB109 was well tolerated, with most TEAEs being mild to moderate in severity
- In the SSC + KB109 arm, 69/169 (40.8%) of patients self-reported ≥1 comorbidity (66/181 [36.5%] for SSC alone)
  - The most common comorbidities were hypertension (SSC + KB109: 17.2%; SSC alone: 18.8%) and chronic lung disease (SSC + KB109: 7.7%; SSC alone: 9.4%)
- In the SSC + KB109 arm, medically attended visits (ie, hospitalisation, emergency department visits, or urgent care visits) were reduced by 50% in the overall population and by 61.7% in patients with ≥1 comorbidity
- Decreased time to resolution of COVID-19–related symptoms in patients aged ≥45 years or with ≥1 comorbidity was observed in the SSC + KB109 arm
  - Median time to resolution of overall 13 COVID-19 symptoms with patients reporting ≥1 comorbidity was 21 d with SSC + KB109 vs 30 d with SSC-alone (HR=1.4217 [95% CI, 0.8982-2.2501]); similar results were observed for resolution of 8 cardinal symptoms (17 d vs 21 d)
  - Median time to resolution of overall 13 COVID-19 symptoms with patients aged ≥45 years or with ≥1 comorbidity was 21 d with SSC + KB109 vs 31 d with SSC-alone (HR=1.597 [95% CI, 1.064-2.398]); similar results were observed for resolution of 8 cardinal symptoms (16 d vs 24 d)

V. CONCLUSIONS

- Results from this clinical study suggest KB109 is well tolerated in non-hospitalised patients with mild to moderate COVID-19
- Administration of SSC + KB109 was associated with reduced times to resolution of COVID-19 symptoms and decreased rates of medically attended visits in non-hospitalised patients with mild to moderate COVID-19
- Median time to resolution was reduced the greatest with the administration of SSC + KB109 vs SSC alone in patients aged ≥45 years or ≥1 comorbidity with mild to moderate disease

VI. REFERENCES

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VII. DISCLOSURES AND ACKNOWLEDGEMENTS

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