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IMMUNOGENICITY OF TIXAGEVIMAB/CILGAVIMAB FOR COVID-19 IN IMMUNOCOMPROMISED CHILDREN AND ADOLESCENTS

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Background:

- COVID-19 vaccination prevents severe manifestations, hospitalization, and mortality in healthy patients.
- Immunocompromised populations have a higher risk of complications, but poorer responses to vaccination.
- Long-acting monoclonal antibodies Tixagevimab/Cilgavimab effectively prevented COVID-19 and improved clinical outcomes when administered early after infection.
- They were approved for emergency use in ≥40 kg. and ≥12 years old immunocompromised patients.
- While younger immunocompromised children/adolescents may be benefit from passive immunization, the study among younger children is lacking.
- This is a pilot study to assess the immunogenicity and safety of Tixagevimab/Cilgavimab in immunocompromised 20-<40 kg. children/adolescents using half of the adult dose.

Methods:

- A single-center, prospective, open-labelled, randomized clinical trial.
- Participants: immunocompromised children/adolescents aged 6–18-years
- Intervention: Single dose, intramuscular:
  - Tixagevimab 150-mg and -Cilgavimab 150-mg for body weight 20-<40 kg.
  - Tixagevimab 300-mg and -Cilgavimab 300-mg for body weight ≥40 kg.
- Endpoints:
  - Anti-SARS-CoV-2 receptor binding domain IgG (anti-RBD IgG) and pseudovirus neutralizing antibody (NAb) at 4, 12, and 24 weeks after administration of each group.
  - Adverse events: observed 30 min after administration and telephone calls up to 7 days after administration.
- Statistical Analysis:
  - Comparing antibodies between groups of 20-<40 kg and ≥40 kg.
  - Comparing antibodies at 4 weeks after administration with antibodies from reference data in 5-11-year-old healthy Thai children at 2 weeks after a third dose of 10-µg-BNT162b2[1].

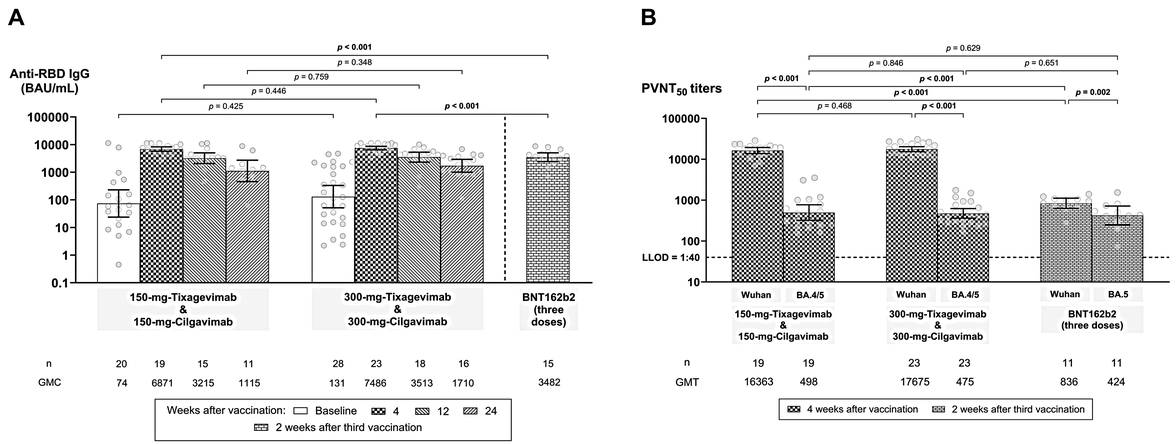

Figure 1: Anti-SARS-CoV-2 receptor binding domain IgG (anti-RBD IgG) **(A)** and pseudovirus neutralizing antibody (NAb) titers against the Wuhan and Omicron BA.4/5 strains **(B)** at baseline and 4 weeks after vaccination with 150-mg-Tixagevimab/ 150-mg-Cilgavimab (for participants weighing 20-<40 kg) and 300-mg-Tixagevimab/300-mg-Cilgavimab (for participants weighing ≥40 kg). Immunogenicity data at 4 weeks was compared with reference data from 5-11-year-old healthy children 2 weeks after receiving a third dose of 10-µg-BNT162b2 [1].

Conclusions:

- Half-dose Tixagevimab/Cilgavimab (150/150 mg) in 20-<40 kg immunocompromised children/adolescents induces equivalent and significantly higher antibody levels than in those ≥40 kg, and also higher than the peak levels induced 3rd dose BNT162b2 in healthy children/adolescent 5-11 years old.
- This study support immunogenicity and safety of passive long-acting monoclonal antibody immunization in younger immunocompromised children/adolescents.
- Further study of next generation long-acting monoclonal antibodies in younger children and adolescents is warranted.

Reference:
[1]. Wittawatmongkol O, Bunjoungmanee P, Kosalaraksa P, Laoprasopwattana K, Boonsathorn S, Chantasrisawad N, et al. Immunogenicity and reactogenicity of fractional, heterologous primary COVID-19 vaccination schedules with BNT162b2 boosters in 5–11-year-old Thai children: A multicenter, prospective, double-blind, randomized control trial. Vaccine. 2023;41(40):5834-40.

Results:

- A total of of 59 participants were enrolled, 49.2% were female, with a median (IQR) age of 12 (9, 15) years. Fourteen participants (24%) had malignancies. (Table 1)

Table 1: Demographic characteristics of participants by the Tixagevimab/Cilgavimab dosing.

Characteristics	Total	Tixagevimab + Cilgavimab 150 + 150 mg (BW 20-<40 kg)	Tixagevimab + Cilgavimab 300 + 300 mg (BW ≥ 40 kg)	*p*-value
Number of participants; n (%)	59 (100.00)	26 (44.07)	33 (55.93)	
Age (years); Median (IQR)	12.00 (9.00, 15.00)	9.00 (7.00-11.00)	14.00 (12.00-16.00)	<0.001
Female gender; n (%)	29 (49.15)	8 (30.77)	21 (63.64)	0.012
Body Mass Index (BMI: kg/m²); Median (IQR)	20.11 (17.62, 22.59)	16.97 (15.45, 19.62)	22.02 (19.79, 24.72)	<0.001
Underweight	22 (37.29)	18 (69.23)	4 (12.12)	<0.001
Normal	29 (49.15)	8 (30.77)	21 (63.64)	
Overweight	8 (13.56)	0 (0.00)	8 (24.24)	
Malignant status; n (%)	15 (25.42)	8 (30.77)	7 (21.21)	0.403
Immune system	12 (80.00)	7 (87.50)	5 (71.42)	0.713
Musculoskeletal system	2 (13.33)	1 (12.50)	1 (14.29)	
Nervous (sensory)	1 (6.67)	0 (0.00)	1 (14.29)	
Health condition; n (%)				
Any health condition	117 (100.00)	40 (34.19)	77 (65.81)	0.535
Immune system	41 (35.04)	18 (45.00)	23 (29.87)	
Cardiovascular system	16 (13.68)	6 (15.00)	10 (12.98)	
Renal	13 (11.11)	3 (7.50)	10 (12.98)	
Metabolism system	11 (9.40)	2 (5.00)	9 (11.69)	
Digestive system	9 (7.69)	1 (2.50)	8 (10.39)	
Nervous (sensory)	6 (5.13)	3 (7.50)	3 (3.90)	
Respiratory system	4 (3.42)	2 (5.00)	2 (2.60)	
Integumentary system	3 (2.56)	2 (5.00)	1 (1.30)	
Endocrine system	2 (1.71)	0 (0.00)	2 (2.60)	
Musculoskeletal system	2 (1.71)	0 (0.00)	2 (2.60)	
Reproductive system	2 (1.71)	0 (0.00)	2 (2.60)	
Nervous system	1 (0.86)	0 (0.00)	1 (1.30)	
Others	7 (5.98)	3 (7.50)	4 (5.19)	

Table 2: Anti-SARS-CoV-2 receptor binding domain IgG (anti-RBD IgG) and pseudovirus neutralizing antibody (NAb) titers response after Tixagevimab/Cilgavimab administration.

Tixagevimab - Cilgavimab	All	150 + 150 mg (BW 20-<40 kg)	300 + 300 mg (BW ≥ 40 kg)	*p*-value
Level of anti-RBD IgG (BAU/mL)				
Number of participants; n (%)	48 (100.00)	20 (41.67)	28 (58.33)	
GMC before administration (95% CI)	102.99 (51.24, 207.02)	73.92 (23.78, 229.82)	130.51 (51.33, 331.82)	0.425
Number of seropositive at baseline; n (%)	41 (85.42)	17 (85.00)	24 (85.71)	0.999
Number of participants; n (%)	42 (100.00)	19 (45.24)	23 (54.76)	
GMC at 4 weeks after administration (95% CI)	7201.36 (6442.49, 8049.63)	6871.26 (5723.84, 8248.70)	7485.98 (6456.98, 8678.97)	0.446
Number of seropositive at 4 weeks after administration; n (%)	42 (100.00)	19 (100.00)	23 (100.00)	N/A
Number of participants; n (%)	33 (100.00)	15 (45.45)	18 (54.55)	
GMC at 12 weeks after administration (95% CI)	3374.22 (2536.03, 4489.45)	3215.28 (2064.53, 5007.45)	3512.66 (2323.95, 5309.39)	0.759
Number of seropositive at 12 weeks after administration; n (%)	33 (100.00)	15 (100.00)	18 (100.00)	N/A
Number of participants; n (%)	27 (100.00)	11 (40.74)	16 (59.26)	
GMC at 24 weeks after administration (95% CI)	1436.27 (915.13, 2254.17)	1114.77 (458.98, 2707.55)	1709.60 (1001.36, 2918.76)	0.348
Number of seropositive at 24 weeks after administration; n (%)	27 (100.00)	11 (100.00)	16 (100.00)	N/A
GMR between 4 weeks after and before administration (95% CI)	82.00 (39.59, 169.86)	92.59 (29.31, 292.45)	74.17 (26.91, 204.42)	0.764
Pseudovirus Neutralization Titer (PVNT50)				
Number of participants; n (%)	42 (100.00)	19 (45.24)	23 (54.76)	
GMT against Wuhan strain at 4 weeks after administration (95% CI)	17069.17 (15363.66, 18964.01)	16363.16 (13765.90, 19450.45)	17675.32 (15367.92, 20329.16)	0.468
$PVNT_{50}$ ≥ 1:40 against Wuhan strain at 4 weeks after administration; n (%)	42 (100.00)	19 (100.00)	23 (100.00)	N/A
GMT against Omicron BA.4/5 strain at 4 weeks after administration (95% CI)	485.04 (383.05, 614.20)	497.54 (320.98, 771.22)	474.96 (362.31, 622.64)	0.846
$PVNT_{50}$ ≥ 1:40 against Omicron BA.4/5 Strain at 4 weeks after administration; n (%)	42 (100.00)	19 (100.00)	23 (100.00)	N/A
GMR against Wuhan strain between 4 weeks after administration and before administration (95% CI)	163.88 (99.82, 269.05)	171.45 (77.33, 380.13)	157.89 (79.90, 311.99)	0.870
GMR against Omicron BA.4/5 strain between 4 weeks after administration and before administration (95% CI)	4.73 (3.36, 6.67)	4.21 (2.42, 7.35)	5.20 (3.27, 8.28)	0.543

Abbreviation: - GMC: geometric mean concentration, BAU: binding antibody unit, GMR: geometric mean ratio, GMT: geometric mean title, CI: confidence interval, mg: milligram, and N/A: not applicable
- Titer values reported as below the lower limit of detection (LLOD = 1:40) were replaced with 20