CROI 2023 Conference on Retroviruses and Opportunistic Infections

SARS-CoV-2 infections among 275 patients with tixagevimab/cilgavimab prophylaxis

#354

Valentine Marie Ferré[1], Laura Kramer[2], Christophe Rioux[3], Tiphaine Goulenok[4], Nathan Peiffer-Smadja[3], Mathilde Salpin[5], Quentin Le Hingrat[1], Eric Daugas[6], Michael Thy[3], Richard Dorent[7], Sebastien Ottaviani[8], Yazdan Yazdanpanah[3], Diane Descamps[1], Jade Ghosn[3], Véronique Joly[3]

1. Université Paris Cité, INSERM, IAME, UMR 1137, Service de Virologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris; 2. Pharmacie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris; 3. Université Paris Cité, INSERM, IAME, UMR 1137, Service de Maladies Infectieuses et Tropicales, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris; 4. Service de Médecine Interne, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris; 5. Service de Pneumologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018. 6. Université Paris Cité, INSERM U1149, Service de Néphrologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris. 7. Service de Cardiologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris; 8. , Service de Rhumathologie, AP-HP, Hôpital Bichat-Claude Bernard, F-75018, Paris

BACKGROUND

- Immunocompromised patients have an increased risk of severe form of COVID-19 pneumonia and are more likely to have impaired vaccine response
- Monoclonal antibodies against SARS-CoV-2 have been approved by French Health Authorities as pre-exposure prophylaxis (PREP) of COVID-19 for patients at risk of severe disease with impaired immune response in December 2021
- At the end of 2021, concomitantly with the beginning of Omicron variant circulation, PREP with the dual long-acting monoclonal antibodies tixagevimab/cilgavimab (Evushled®) became available in France to protect patients non-responding or not eligible to SARS-CoV-2 vaccination at risk of severe COVID-19

OBJECTIVE

This study objective was to describe the incidence and the outcomes of COVID-19 among immunocompromised patients receiving tixagevimab/cilgavimab as PREP during the Omicron wave in France

METHODS

- This was a retrospective observational monocentric cohort study of immunocompromised patients receiving tixagevimab/cilgavimab in pre-exposure prophylaxis
- Patients having received tixagevimab/cilgavimab as PREP at Bichat Claude Bernard University Hospital, Paris, since December 17th 2021, were included independently from vaccination status or previous SARS- CoV-2 infection
- Last date of follow-up was November 1st, 2022.
- Demographic and clinical data were retrospectively collected from clinical files. Vaccinal status was obtained from data collected by national Health Insurance.
- Prophylaxis recommendations evolved in France in 2022 due to Omicron sublineages circulation :
  - Firstly 150mg/150mg of tixagevimab/cilgavimab were recommended
  - In April, a readministation of 150/150 mg was recommended for patients having received a 150/150 mg at initiation and new prophylaxis initiation were recommended at 300/300 mg
  - At the end of June, the recommendation was issued to administer 300/300 in patients having received only 1 dose of 150/150mg more than 3 months before should receive 300/300mg as soon as possible
- Incident SARS-CoV-2 infections were detected based on positive RT-PCR results and/or anti-nucleocapsid antibodies seroconversion.
- The patients were classified as follows :
  - absence of infection (negative RT-PCR or absence of seroconversion)
  - asymptomatic or mild disease diagnosed > 5 days after the first administration of tixagevimab/cilgavimab (independently from further specific treatment)
  - severe disease (requiring hospitalization for oxygen therapy).

Prophylactic tixagevimab/cilgavimab prevented SARS-CoV-2 infections in 208 out of 275 severely immunosuppressed patients (76%) in context of Omicron variant circulation. Only 6 (2%) severe breakthrough infections despite pre-exposure prophylaxis were observed without any death.

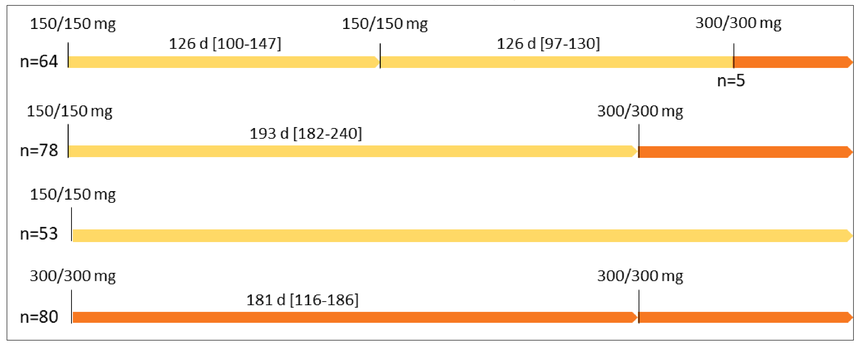
RESULTS

- Between December 17th, 2021 and November 1st, 2022, 275 patients received a tixagevimab/cilgavimab pre-exposure prophylaxis as described in Figure 1. Patients' characteristics are depicted in Table 1.
- No severe adverse event of tixagevimab/cilgavimab was observed.

Table 1: Characteristics of the 275 patients with tixagevimab / cilgavimab prophylaxis

	All patients (*n* = 275)
Age – *years (mean+/- SD)*	61 (+/- 15)
Age ≥ 60 years-old - *(n,%)*	154 (56)
Sex – *female (n,%)*	139 (51)
Cause of immunosuppression	
Heart transplant	6
Lung Transplant	78
Kidney Transplant	69
Immunosuppressive therapy for auto-immune disease or vasculitis	109
Other	13
Patients receiving Rituximab - *(n,%)*	141 (51%)
SARS-CoV-2 infection prior to prophylaxis - (n,%)	81 (29%)
Vaccination status before prophylaxis (n=274)	
RNA vaccines only - *(n, %)*	263 (81)
Vaccine doses received before prophylaxis	41 (45)
>2 doses	223 (81)
2 doses with previous SARS-CoV-2 infection	15 (5)
≤ 2 doses without prior infection	36 (13)

Figure 1: Tixagevimab/Cilgavimab administration schemes for the 275 patients (median delay and IQR between administrations are indicated in days)



- **Incident SARS-CoV-2 infection was diagnosed in 67 patients (24%)**. Among them, 59% (n=40) were solid organ transplant recipients, 36% (n=24) had an autoimmune disease and overall 52% (n=35) had received rituximab (Table 2).
- Occurrence of COVID19 and its severity were not influenced by vaccinal status or administration of rituximab.
- **Only 6 patients had severe COVID-19 despite pre-exposure prophylaxis**, 5 were solid organ transplant recipients. No death due to COVID-19 was reporte

Table 2: Severity of COVID according to vaccinal status and immunosuppression

	No SARS-CoV-2 infection (*n* = 208)	Asymptomatic or mild COVID-19 (*n* = 61)	Severe COVID (*n = 6)*
Vaccination status before prophylaxis (n=274)			
≤ 2 doses	39 (18%)	9 (15%)	2 (33%)
> 2 doses	169 (81%)	51 (85 %)	4 (66%)
Depth of immunosuppression			
Treatment with Rituximab	102 (49%)	32 (52%)	3 (50%)
Solid organ transplant recipient	113 (54%)	35 (57%)	5 (83%)
Tixagevimab/Cilgavimab doses received before infection			
1 administration - 150mg/150 mg	-	44 (72%)	3 (50%)
2 administations - 150mg/150 mg and 150mg/150mg	-	6 (10%)	2 (30%)
1 administration 300mg/300 mg	-	9 (15%)	1 (20%)
2 administations -150mg/150mg and 300mg/300mg	-	2 (3%)	-

- For the 56 patients whose infection date was available, the median delay between the last infusion of tixagevimab/cilgavimab and SARS-CoV-2 infection was 62 days (IQR=[30-97]).
- Most patients (70%) who developed a SARS-CoV-2 infection despite prophylaxis had only received a singe dose of 150mg/150mg tixagevimab/cilgavimab
- During the study period, 57% of incident infections occurred between December 17th, 2021 and May 31st, 2022, when BA.1 and BA.2 were the major Omicron sublineages in France, and 43% between June 1st, 2022 and November 2022 1st, a period during which BA.4 and BA.5 were predominant in France.

CONCLUSIONS

- In this retrospective study, 76% of patients receiving PREP with tixagevimab/cilgavimab had no incident SARS CoV-2 infection. The rate of infection was higher than the value recently reported by Nguyen et al[1]. This could be explained by the high proportion of asymptomatic patients diagnosed through systematic screening in our cohort.
- Although Omicron variants have been associated with less severe disease than Delta variant, mortality among immunocompromised patients has been reported to be high without adequate pre-exposure prophylaxis and early specific treatment[2]
- The rate of severe disease in this study was low (9%), as reported by Nguyen[1], suggesting a beneficial effect of prophylactic tixagevimab/cilgavimab. This is to be mitigated by the fact that specific antiviral curative therapies were available in the same period
- Since BA.5 and other recent Omicron sublineages are highly circulating, tixagevimab/cilgavimab prophylaxis is no more recommended in France

ADDITIONAL KEY INFORMATION

Funded by ANRS | MIE EMERGEN consortium

Author Contact Information : valentinemarie.ferre@aphp.fr

REFERENCES

1. Ngyuen et al, Clin Microbiol Infect., 2022
2. Chavanot et al, Kidney Int., 2022