soho2023
ELEVENTH ANNUAL MEETING

INCIDENCE AND FEATURES OF SARS-COV-2 BREAKTHROUGH INFECTION IN THE HEMATOLOGICAL CONDITIONS AFTER TIXAGEVIMAB-CILGAVIMAB PROPHYLAXIS

A. DUMINUCO [1], A. NARDO [1], A. OROFINO [1], G. GIUNTA [1], C. CONTICELLO [1], V. DEL FABRO [1], A. FIGUERA [1], A. CHIARENZA [1], G. MILONE [1], S. LEOTTA [1], A. CUPRI [1], M. PARISI [1], E. MAURO [1], C. VETRO [1], F. DI RAIMONDO [1], A. ROMANO [1] and G.A. PALUMBO[1]

1. Hematology Unit with BMT, Policlinico "G.Rodolico-San Marco." Catania, Italy

AZIENDA OSPEDALIERO UNIVERSITARIA POLICLINICO - CATANIA

INTRODUCTION

Despite the development of anti-COVID-19 messenger RNA vaccines, several immunocompromised patients (above all affected by hematological disorders) were unable to produce anti-SARS-CoV-2 spike antibodies in response to vaccination. In this context, preexposure prophylaxis with tixagevimab-cilgavimab (TIX-CIL), approved in 2022 by FSA and EMA, has resulted in an alternative strategy based on the promising results of the phase III PROVENT study (1-2).

AIM

This retrospective observational report aims to collect the clinical data of 202 patients affected by hematological diseases and treated in a single center with prophylactic therapy with TIX-CIL, evaluating the incidence of breakthrough infections and, in infected patients, the duration, the severity (potential reduction of severe forms) and the outcome.

RESULTS

At the end of the observation period, 44 (21.8%) patients experienced breakthrough infection after TIX-CIL prophylaxis, with a median time of occurrence of 76 days (Figure 1). Most of the breakthrough infections (95%) occurred in patients affected by lymphoproliferative disorders. Regarding treatment, ongoing therapy (p<0.001), above all with monoclonal antibodies (MoAb) targeting lymphocytes (p=0.001), was related to a higher frequency. Elderly patients (>70 years) reported a higher incidence (p=0.035). The median duration of infection was 11 (5–50) days, with an asymptomatic course/mild symptom in 30 (68.2%). All data at the last follow-up are reported in Table 1. Comparing the different duration of infection pre- with post-prophylaxis, whole days were significantly fewer after TIX-CIL therapy, with a median of 11 days (in 44 patients) vs. 15 days (in 60 patients) (p<0.001). The duration of positivity in patients who re-experienced the infection after the prophylaxis was significantly lower (p=0.022, Figure 2). The occurrence of breakthrough infection (p<0.05) was associated with 70 years of age and older, with an adjusted odds ratio (AOR) of 2.3, 95% confidence intervals (CI): 1.1 to 4.8, with prior SARS-CoV-2 infection (AOR 2.6, 95% CI: 1.2-5.4), and with treatment with any MoAb (AOR 2.8, 95% CI: 1.3-6). Conversely, the baseline non-lymphoid hematological disease appears as a protective condition compared to the higher risk in the lymphoid disorder (AOR 0.2, 95% CI: <0.1-0.9).

CONCLUSIONS

TIX-CIL is a valuable and safe prophylaxis therapy that can allow passive immunization and warrant long-term protection from severe SARS-CoV-2. Patients treated with MoAb confirmed the persistently higher risk and the difficulty in completing a rapid virus clearance due to impaired B-cell immune system.

	SARS-CoV-2 positive 44 patients (%) [range]	SARS-CoV-2 negative 158 patients (%) [range]	p
Age, years	72 [46-87]	69 [24-87]	0.035
Sex, male/female	26 / 18 (25 / 18.4)	78 / 80 (75 / 81.6)	0.307
Hematology condition			
– B-lymphoproliferative disorders	42 (28.2)	107 (71.8)	<0.001
○ ALL-B	0 (0)	3 (100)	NA
○ NHL	3 (9.4)	29 (90.6)	0.099
○ HL	0 (0)	4 (100)	NA
○ CLL	17 (27)	46 (73)	0.27
○ MM/Amyloidosis	22 (46.8)	25 (53.2)	<0.001
– T-lymphoproliferative disorders	0 (0)	2 (100)	NA
○ NHL	0 (0)	2 (100)	NA
– Myeloid disorders	2 (5.3)	36 (94.7)	0.004
○ AML	0 (0)	6 (100)	NA
○ MPN	2 (6.3)	30 (9.7)	0.019
– Autoimmune disease	0 (0)	4 (2.5)	NA
– Recent BMT	0 (0)	9 (5.7)	NA
Ongoing treatment, Yes/No	43 / 1 (27.9 / 2.1)	111/ 47 (72.1 / 97.9)	<0.001
– MoAb (no anti-CD20)	15 (44.1)	19 (55.9)	0.001
– Anti-CD20 MoAb	4 (33.3)	8 (66.7)	0.298
– BTKi	9 (27.3)	24 (72.7)	0.489
– JAKi	1 (4)	24 (96)	0.019
– IST	2 (18.2)	9 (81.8)	1
– IP	4 (50)	4 (50)	0.07
– Chemotherapy	0 (0)	5 (100)	NA
– Other	8 (30.8)	18 (69.2)	0.307
Prior SARS-CoV-2 vaccine	32 (20.1)	127 (79.9)	0.527
Prior SARS-CoV-2 infection	20 (33.3)	40 (66.7)	0.015
Anti-spike IgG values, AU/mL	23 [0-3663]	414.6 [0.9-40000]	0.033
Time-to-infection from TIX-CIL, days	75.5 [2- 236]	/	/
Duration of infection after TIX-CIL, days	11 [5-50]	/	/
Antiviral treatment for infection, Y/N	17 / 27 (38.6 / 61.4)	/	/

Table 1. Clinical characteristics and treatment overview in 202 hematological patients distinguished on the occurrence or not of breakthrough infection

Figure 1, Event-free survival (EFS) defined as the time elapsed from tixagevimab-cilgavimab (TIX-CIL) prophylaxis to breakthrough infection, evaluated in censored patients at the end of the observation period for the whole cohort

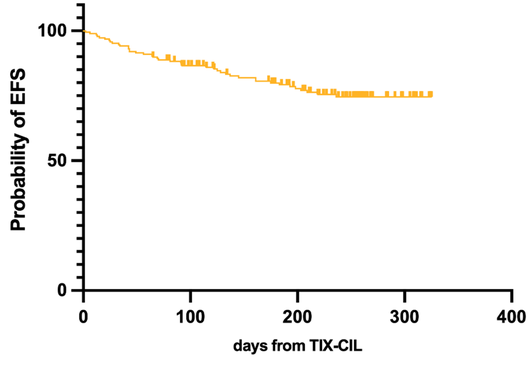
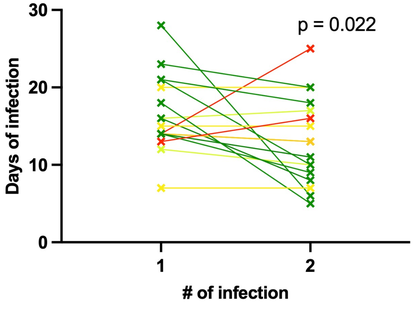


Figure 2. Difference in days of positivity in patients who experienced twice SARS-CoV-2 infection (1 = prior, 2 = after tixagevimab-cilgavimab prophylaxis)



REFERENCES

1. Levin MJ, Ustianowski A, De Wit S, Launay O, Avila M, Templeton A, et al. Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for Prevention of Covid-19. New England Journal of Medicine [Internet]. 2022 Jun 9 [cited 2023 May 12];386(23):2188–200. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2116620
2. Davis JA, Granger K, Roubal K, Smith D, Gaffney KJ, McGann M, et al. Efficacy of tixagevimab-cilgavimab in preventing SARS-CoV-2 for patients with B-cell malignancies. Blood [Internet]. 2023 Jan 12 [cited 2023 May 12];141(2):200–3. Available from: https://ashpublications.org/blood/article/141/2/200/487026/Efficacy-of-tixagevimab-cilgavimab-in-preventing

CONTACT INFORMATION

Dr. Andrea Duminuco
Hematology Unit with BMT, Policlinico "G.Rodolico-San Marco." Catania, Italy
andrea.duminuco@gmail.com