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HIV-positive Ukrainian refugees in the Czech Republic: a retrospective, observational study

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Conflicts of interest

R.M., D.J., D.B., Z.B., J.C., A.C., P.D., S.C., S.G.d.S., J.K., M.K., S.S., R.S., M.Z., O.S., and D.S. report no conflict of interest related to this study.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request: ricardo.massmann@kr.unb.sk.

Abstract

Objective: Over 480 000 Ukrainian refugees have arrived in the Czech Republic since the Russian invasion of Ukraine in 2022, including over 500 people with HIV. This study describes the demographics, characteristics, and management of Ukrainian refugees with HIV in the Czech Republic.

Design: Retrospective, observational, non-interventional study.

Methods: Ukrainian nationals registering at HIV centers in the Czech Republic with war refugee status were included. Data were collected from medical records between 1 March and 31 July 2022. The study was registered with the Czech State Institute for Drug Control, ID number 2301200000.

Results: 482 patients were included in the study. Most patients were female (69.5%; *n* = 335/482) with well-controlled HIV. The median [interquartile range] CD4+ cell count was 597 [397] cells/mm^3 of blood, and 79.3% (*n* = 361/455) of patients had HIV RNA <40 copies/ml. Coinfections of hepatitis C virus, hepatitis B virus, and/or tuberculosis were reported for 17.4% (*n* = 78/449), 9% (*n* = 40/446) and 1.3% (*n* = 6/446) of patients, respectively. In Ukraine, 85.7% (*n* = 384/448) of patients had been receiving an integrase strand transfer inhibitor-based regimen and most (69.7%; *n* = 310/445) did not switch therapy upon arrival in the Czech Republic.

Conclusion: Migration from Ukraine is changing the characteristics of HIV epidemiology in the Czech Republic. Ukrainian refugees with HIV have been provided with a high standard of medical care in the Czech Republic. Improved coordination between medical services within the Czech Republic and between countries in the European Union is necessary to optimize patient care.

Keywords: HIV; Czech Republic; Ukraine; refugees; antiretroviral therapy; observational studies as topic

Introduction

Russia invaded Ukraine on 24 February 2022, initiating a major conflict in Europe and causing a humanitarian crisis. Over 7 million people have been displaced from Ukraine, predominantly women and children [1,2]. The Council of the European Union has adopted a Temporary Protection Directive, offering protection and rights to Ukrainian refugees, including rights to medical assistance [3,4]. Nearly 5 million individuals have registered for temporary protection schemes across Europe [1].

In 2021, there were an estimated 240 000 adults and children living with HIV in Ukraine [5]. The prevalence of HIV was estimated to be 355 per 100 000 people in Ukraine, one of the highest in Europe [5–7]. In three regions in eastern Ukraine (Odessa, Dnipro, and Mykolayiv), the HIV prevalence was more than 700 per 100 000 people [7]. In total, 390 sites in Ukraine provided HIV-related healthcare, and an estimated 75% of people living with HIV were aware of their status, of whom 83% were receiving antiretroviral therapy (ART) [5,8].

However, Ukraine's healthcare infrastructure has been severely damaged in the war with Russia, and access to specialist healthcare services has become increasingly challenging [9]. Nearly 500 attacks on healthcare facilities in Ukraine have been reported [10]. In some areas, medical staff have been evacuated and HIV clinics have closed, including the AIDS Healthcare Foundation's HIV clinics in Kharkiv and Mariupol [11]. Although HIV centers in Kyiv have mostly been able to operate without significant interruption [12], those in other areas have experienced problems accessing ART and HIV tests.

The Czech Republic has taken in over 480 000 Ukrainian refugees since the start of the conflict with Russia [1]. This has resulted in a 5% increase in the population of the Czech Republic [13]. Under the ‘Lex Ukraine’ law package introduced in March 2022 and amended in June 2022, Ukrainian refugees were granted access to free healthcare in the Czech Republic for 150 days (no time limitation for

children and the elderly) [14]. After this period of time, they qualify for general health insurance with the same healthcare rights as Czech citizens.

The prevalence of HIV in the Czech Republic was traditionally low. From the start of national data collection for the HIV epidemic in 1985 to the latest available data on 30 December 2022, a cumulative total of 4366 people have been diagnosed with HIV in the Czech Republic [15]. Nearly half (47%; *n* = 2038) of these patients were treated in Prague [15]. Over the past 5 years, an average of 210 new patients have been diagnosed with HIV each year in the Czech Republic. However, according to the National Reference Laboratory for HIV/AIDS, from March to December 2022 inclusive, 578 HIV-positive refugees from Ukraine (198 men, 380 women) were registered at HIV clinics across the Czech Republic [15], which has substantially increased the prevalence of HIV in the Czech Republic.

Ukrainian refugees living with HIV have arrived in the Czech Republic and other European countries with little to no medication and often in need of immediate access to treatments. This has increased the economic burden on local Czech healthcare systems and increased staff workload. There is a need to understand the impact of the arrival of Ukrainian refugees living with HIV on the Czech healthcare system to inform policy and ensure ongoing access to treatment for new arrivals.

This study aimed to describe the demographics and characteristics of Ukrainian refugees living with HIV who arrived in the Czech Republic in the first months of the Russian invasion of Ukraine in 2022, and to describe the management of those who may no longer have access to their previous ART.

Methods

Study design and population

This study was a retrospective, observational, non-interventional analysis of Ukrainian refugees registering at Czech HIV clinics. All eight HIV centers in the Czech Republic participated in this multicenter study. Ukrainian nationals with war refugee status who were aware of their HIV diagnosis or had received a new diagnosis of HIV since arriving in the Czech Republic were included. Ukrainian nationals with Czech Republic resident status were excluded.

Data collection

Data were collected between 1 March and 31 July 2022. HIV center staff retrospectively collected data from patient medical records, and in some instances, questionnaires were also sent to Ukraine to supplement these records.

At each initial HIV center consultation, blood samples were drawn to confirm the HIV diagnosis, measure HIV RNA levels, and assess CD4+ cell counts. HIV drug resistance tests were only performed for patients with a high viral load. Serology for viral hepatitis B and hepatitis C was also carried out. All patients were asked about respiratory symptoms, and chest x-rays were performed to identify any patients with possible active tuberculosis (TB), if TB was suspected. Pregnancy tests were provided on demand. Data on baseline characteristics and treatments were also collected.

Treatment switches were defined as a change of both nucleoside reverse transcriptase inhibitors (NRTIs) in the regimen, or a change of the integrase strand transfer inhibitor (INSTI), boosted protease inhibitor, or non-nucleoside reverse transcriptase inhibitor. A change from a dual to a single NRTI or a reduction in the number of active molecules was not considered a treatment switch. The reasons for switching treatments were not recorded but included drug-related adverse events, drug toxicity, drug availability, simplification of a current regimen, and virologic failure.

Study outcomes

This study aimed to describe the demographics, patient characteristics, immunological characteristics, and coinfections of Ukrainian refugees living with HIV, and to describe the management of those who may no longer have access to their previous ART. Given that this was an observational study, no formal hypotheses were tested. Descriptive statistics were reported.

Ethical conduct

The study protocol was approved by the relevant independent ethics committee for each participating center in the Czech Republic. The study was performed in accordance with ethical principles that comply with the Declaration of Helsinki and are consistent with the International Council for Harmonisation guidelines. This study was registered with the Czech State Institute for Drug Control (Státní ústav pro kontrolu léčiv), with the ID number 2301200000.

Results

Baseline demographics, patient characteristics, and immunological status

Overall, 482 patients were included in the study. Baseline demographics, patient characteristics and immunological status are presented in Table 1. The median age of patients was 42 years (range 9–70). On arrival in the Czech Republic, 4.4% (*n* = 21/482) of patients were born after 2003 and so were aged 18 years or younger. Most patients were female (69.5%; n = 335/482). In total, 95.4% (*n* = 436/457) of patients self-reported that they were heterosexual. Of the male patients, 14.3% (*n* = 21/147) self-identified as men who have sex with men. A small number of patients self-reported active intravenous drug use (IVDU) (1.7%; *n* = 8/466), and 5.8% (*n* = 27/466) of patients self-reported past IVDU or had IVDU recorded in their medical history. HIV was acquired via vertical transmission in 4.3% (*n* = 20/465) of patients.

The median (interquartile range) CD4+ count among patients was 597 (397) cells/mm^3 of blood. Most patients (79.3%; *n* = 361/455) were virally suppressed (defined as HIV RNA of <40 copies/ml) (Table 1).

Coinfections

In total, 17.4% (*n* = 78/449) of patients tested positive for hepatitis C virus (HCV), and 10.0% (*n* = 45/449) of patients had previously received treatment for an HCV infection in the Ukraine. Additionally, 9.0% (n = 40/446) of patients had serological evidence of a previous hepatitis B virus

(HBV) infection and 16.1% (*n* = 72/446) of patients had serological evidence of seroconversion. In total, 1.3% (*n* = 6/446) of patients had active pulmonary and/or extrapulmonary TB. Moreover, 39 patients with a history of pulmonary and/or extrapulmonary TB were identified from patient medical records received from the Ukrainian Ministry of Health. No history or documentation of the treatment of TB in Ukraine was available for these patients.

Treatments

Most patients had received an INSTI-based therapy in Ukraine (Table 2), with 83.9% (*n* = 376/448) having received a dolutegravir (DTG)-based regimen. Primarily, patients received DTG/lamivudine (3TC)/tenofovir disoproxil fumarate (TDF) (70.3%; *n* = 315/448) in a single-tablet regimen. Only one patient received bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF).

Most patients (69.7%; *n* = 310/445) did not switch therapy when they first received ART in the Czech Republic. Of these, 86.8% (*n* = 269/310) were receiving a DTG-based regimen, 7.7% (*n* = 24/310) were receiving an efavirenz-based regimen, 2.9% (*n* = 9/310) were receiving a lopinavir/ritonavir-based regimen, and 1.9% (*n* = 6/310) were receiving a raltegravir-based regimen (Fig. 1). Among patients without HBV infection who were receiving a three-drug DTG-based regimen containing TDF in Ukraine, 19.3% (*n* = 45/233) were instead given a two-drug regimen without tenofovir (DTG/3TC) in the Czech Republic, which was considered a treatment simplification rather than a treatment switch.

Overall, 30.3% (*n* = 135/445) of patients switched therapy in the Czech Republic. Although the majority of patients who were receiving DTG-based regimens in Ukraine continued to receive their existing treatment, most (62.5%; *n* = 65/104) of those who switched from a DTG-based regimen received BIC/FTC/TAF in the Czech Republic (Fig. 2). This regimen was not available in Ukraine in 2022 (Supplemental Table 1, http://links.lww.com/QAD/C913).

Almost all patients receiving zidovudine-, lopinavir/ritonavir- and efavirenz-based regimens who were switched in the Czech Republic, received BIC-, DTG-, rilpivirine- or raltegravir-based regimens instead (Fig. 2). Overall, in the Czech Republic, most patients (90.5%; *n* = 430/475) received an INSTI-based therapy (Table 2).

Pregnancy

Of the female patients, 5.1% (*n* = 17/335) were pregnant. Two of these patients were first diagnosed with HIV in the Czech Republic and so had not previously been receiving ART in Ukraine. In the Czech Republic, seven of these women switched treatment.

Discussion

This study provides comprehensive recent data on the management of Ukrainian refugees living with HIV who fled to the Czech Republic as a result of the war with Russia. This is an unprecedented situation in Europe, and these data have implications for healthcare management both in the Czech Republic and in other countries that have accepted large numbers of Ukrainian refugees. Overall, most refugees registering at Czech HIV clinics were female, had been receiving ART in Ukraine, and were

completely virally suppressed. Although most patients were able to continue to receive the same treatment in the Czech Republic, those who switched treatment did so mainly owing to differences in drug availability rather than clinical need.

The demographics of patients in this study likely reflect the demographics of those most able to travel from Ukraine, primarily women and children. Most Ukrainian men aged 18–60 years old were prevented from leaving Ukraine and are more likely than women and children to have remained in Ukraine to fight against the Russian invasion. Exceptions to travel prohibition and military obligations for men include: fathers of families with three or more children, fathers of families caring for a disabled or adopted child, single fathers, and men with poor health (including those with moderate to severe AIDS [WHO clinical stages 3 and 4]) [16]. Patients who were older and those with lower CD4+ cell counts, higher HIV RNA levels, or active coinfections may have been more likely to remain in Ukraine owing to poor health. Additionally, given that low numbers of patients reported active IVDU in this study, these individuals may also have been less likely to leave Ukraine.

The patients who registered at HIV centers in the Czech Republic were largely those who were diagnosed with HIV in Ukraine and were receiving treatment. These patients were generally well treated and had good medication adherence. These data are in accordance with estimates from the Czech National Reference Laboratory for HIV/AIDS that approximately 90% of Ukrainian refugees living with HIV are aware of their status [15]. However, given the huge number of refugees who have arrived in the Czech Republic, it is possible that a significant number have entered the country with undiagnosed HIV. Additionally, as of December 2022, the prevalence of HIV in the Ukrainian refugee population is estimated to be 118 per 100 000 people (578 HIV-positive patients registered from a total of 489 148 refugees) [1,15]. This is lower than expected given the high prevalence of HIV in Ukraine [5,6], although this may be partially explained by the fact that most refugees are women and children. It is also possible that Ukrainian refugees with a known HIV-positive status may be unwilling to access the Czech HIV clinics owing to concerns of stigma and rejection by the community or their host family, as well as an unfounded fear that they may lose their refugee status, benefits, or job opportunities.

Most patients had been receiving DTG-based regimens in Ukraine. Upon arrival in the Czech Republic, some of these patients were switched to a BIC-based regimen. In Ukraine, an estimated 80% of patients receive a single-tablet regimen (DTG/3TC/TDF) once daily. Although there is no national health insurance system in Ukraine, the Ukrainian Ministry of Health and non-governmental organizations provide ART free of charge to patients.

Despite the reason for a treatment switch not being recorded, most regimen changes were due to drug availability rather than being clinically indicated. For example, some patients without HBV infection were moved from a three-drug to a simplified two-drug, regimen in the Czech Republic. Many patients receiving older drug regimens, such as those containing efavirenz or lopinavir/ritonavir, have had their treatments switched to newer generation therapies such as BIC- or DTG-based regimens. It is the hope of the Ukrainian government that all refugees will return to Ukraine, and the Ministry of Health will likely need to review the provision of BIC-based regimens because these are unavailable in Ukraine.

Czech HIV centers have registered 17 female refugees living with HIV who are pregnant. These women are managed according to the European AIDS Clinical Society guidelines, although specifics vary by hospital [17]. For example, in the Faculty Hospital Bulovka in Prague, which has the largest number of patients with HIV in the Czech Republic, linkage to care with a gynecologist or obstetrician usually occurs no later than week 30 of pregnancy.

A significant number of patients had a recorded coinfection. In Ukraine, TB coinfection has been identified in over 12% of patients with newly diagnosed HIV, and multidrug-resistant TB is a major problem [19]. The possibility of increased multidrug-resistant TB transmission as a result of migration from Ukraine is a significant public health threat in the Czech Republic. At the study cut-off date (31 July 2022), six active TB cases had been identified in our study cohort and no cases of multidrug-resistant TB were detected.

The majority of Ukrainian refugees come from the Eastern regions of Ukraine, an area with a high prevalence of HIV and IVDU [20]. This also correlates with a high incidence of HCV infection, which can be seen in our results. Liver cirrhosis and hepatocellular carcinoma as a result of chronic hepatitis are both devastating for the patient and extremely costly for the health service to diagnose and treat [21]. Treatment for HCV infection is provided free of charge in both Ukraine and the Czech Republic. Although incurable, HBV infection can be controlled by tenofovir, an NRTI used as primary treatment of HIV [22]. Most patients in this study received a tenofovir-containing regimen.

Language barriers have been challenging for patients and staff at HIV centers in the Czech Republic [19,23]. Most Ukrainian refugees with HIV speak only Russian or Ukrainian, with very limited knowledge of English or Czech. The use of translators, sometimes provided by charities and non-governmental organizations, results in a less discreet consultation and it is possible to lose information during the exchange. Physicians and nurses have been reliant on online translation services for many patient interactions. Language barriers have also made it impossible to conduct telephone consultations.

Staff and resources at HIV centers in the Czech Republic have been severely stretched by the influx of new patients. Physicians managing these patients must seek individual solutions for each patient, but owing to the difficulties in communication, it can be challenging to explain the indications for specialist consultation. When healthcare appointments are made, patients are sometimes rejected out of fear or a lack of knowledge about HIV by the non-HIV specialist medical community. This increases the burden of stigma on the patients and may result in missed diagnoses of other morbidities. Most patients do not undergo routine healthcare procedures/examinations (e.g. gynecology, urology, dermatology, surgery, diabetology, endocrinology, cardiology) owing to the burden on the capacity of the healthcare system. Additionally, owing to overburdened services and communication difficulties, mental health provision is often unavailable. Psychiatric consultations have not been possible for most refugees despite many presenting with anxiety disorders and post-traumatic stress.

The war and the resulting influx of refugees have resulted in a significant organizational and economic burden on host countries. Ukrainian President Volodymyr Zelenskyy awarded Prague the honorary title of ‘Savior City’ on 28 October 2022 in recognition of the humanitarian assistance the Czech

people have provided Ukrainian refugees [24]. It is unknown how long the conflict in Ukraine may last, and even once peace is established the severe damage that Ukrainian healthcare infrastructure has sustained will take time to repair. A substantial number of refugees living with HIV in the Czech Republic and other European countries are unlikely to return to Ukraine for the foreseeable future. Governments and healthcare institutions must provide adequate healthcare provision for all refugees, including those with HIV, for an indefinite amount of time. The consequence of inadequate care will likely be an increase in the prevalence of HIV in the Czech population.

This study had some limitations. Some refugees had very limited documentation on their medical history, resulting in information gaps. Language barriers and ad hoc collection of information may also have resulted in missing data. Owing to fear of discrimination and stigmatization, some personal or medical information may have been withheld by patients. Treatment interruptions were not recorded, and it was not possible to confirm virologic failure until HIV RNA testing was performed in the Czech Republic. Population movement made follow-up difficult, both within the Czech Republic and internationally, and there is limited coordination between HIV centers in the Czech Republic and Europe, leading to loss of follow-up for patients who leave the country. Some patients may be intending to move to another country and therefore not register at an HIV clinic upon arrival in the Czech Republic, especially if they arrived with sufficient medication. Additionally, Ukrainians who were already living in the Czech Republic and being treated at a clinic before the war may have registered as refugees and been listed twice in the clinic databases. Finally, the study cut-off date of 31 July 2022 was determined before the extent of migration in the subsequent months was known. However, given that arrivals peaked in March 2022, most patients registering at the clinics since the outbreak of the war have been included in this study.

In conclusion, the Czech Republic is facing an unprecedented situation with the influx of a large number of Ukrainian refugees. Owing to the rapid reaction of governmental and public health organizations, healthcare professionals, and the general public, refugees living with HIV have been provided with a high standard of medical care in the Czech Republic. ART is being prescribed in line with the latest European AIDS Clinical Society guidelines. Improved coordination between medical services both within the Czech Republic and between countries in the European Union is necessary to optimize patient care. Accessible online patient databases may help with inter- and intra-country coordination; however data protection challenges remain.

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Fig. 1. ARTs received in Ukraine by refugees who did not switch treatment in the Czech Republic (*n* = 310). 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BIC, bictegravir; c, cobicistat; DTG, dolutegravir; EFV; efavirenz; FTC, emtricitabine; LPV, lopinavir; r, ritonavir; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine.

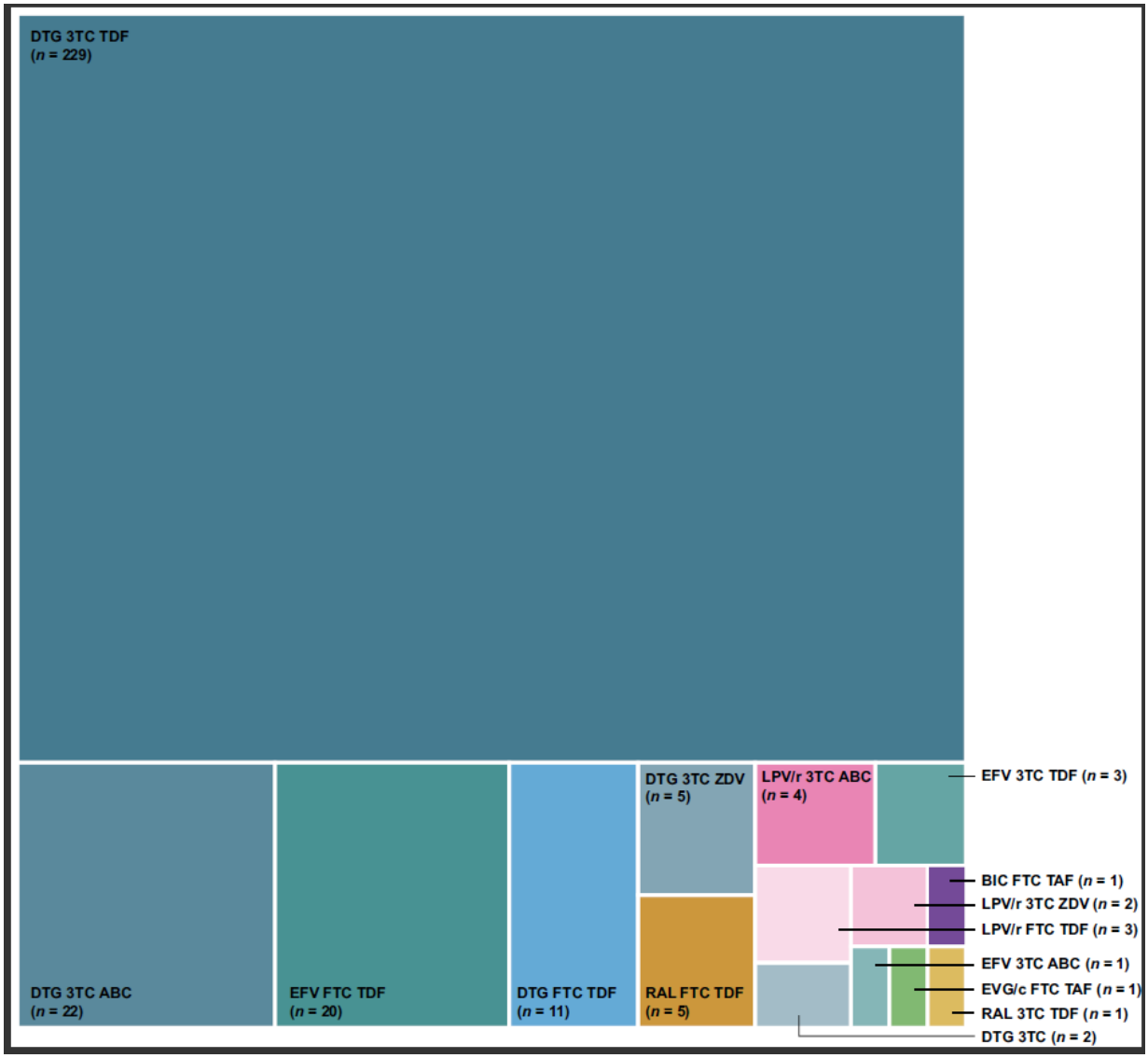

Fig. 2. ARTs received in Ukraine compared with the Czech Republic among refugees who switched therapies (*n* = 135). 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; ATV, atazanavir; BIC, bictegravir; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; LPV, lopinavir; r, ritonavir; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; ZDV, zidovudine.

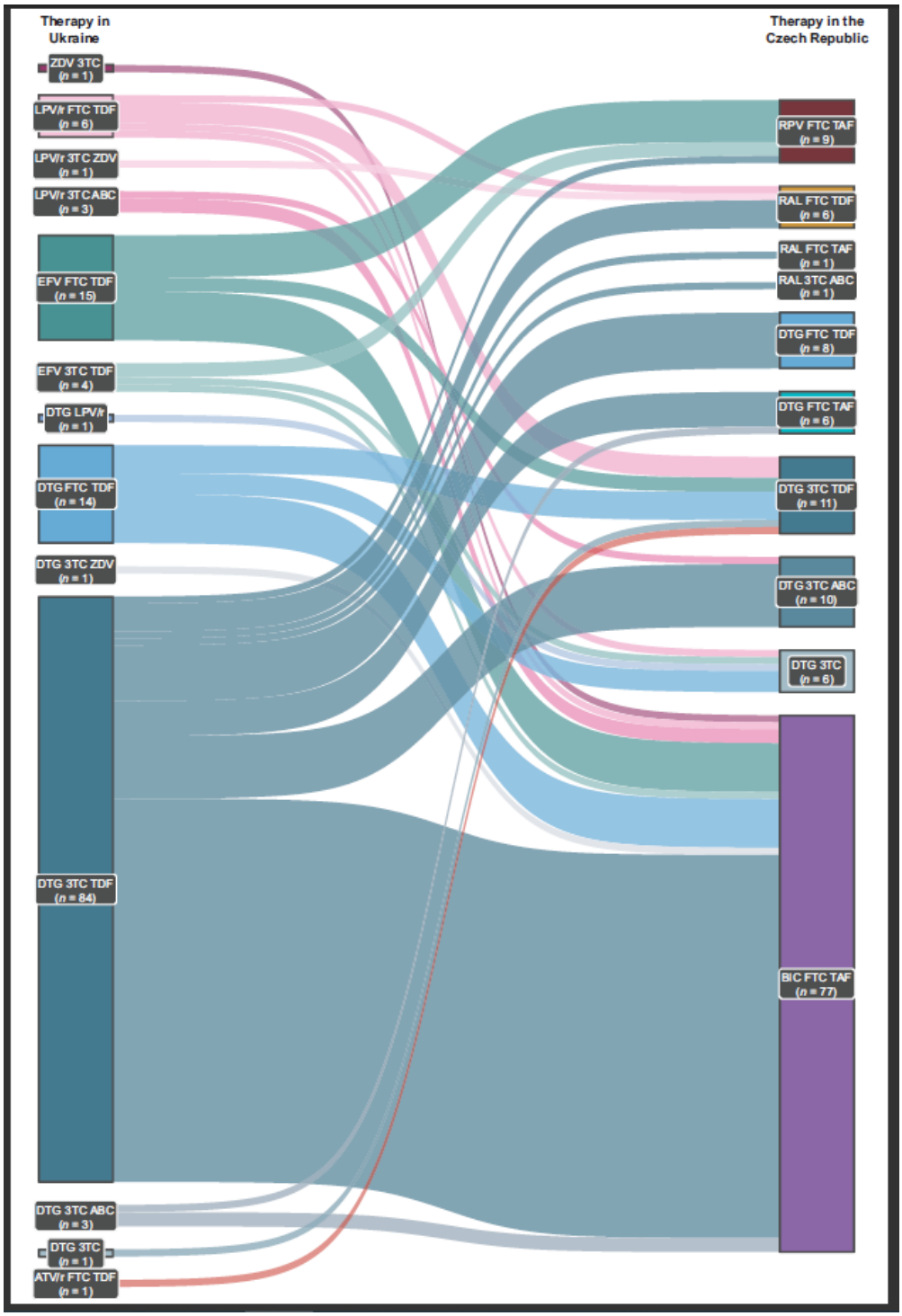

Table 1. Baseline demographics, patient characteristics and immunological status.

Demographic/characteristic	Value	*n*[a]
Median age, years (range)	42 (9–70)	482
Sex, *n* (%)		
Male	147 (30.5)	482
Female	335 (69.5)	482
Median weight, kg	67	397
MSM, *n* (%)	21 (14.3)	147
IVDU, *n* (%)		
Active IVDU	8 (1.7)	466
Past IVDU	27 (5.8)	466
Infected via vertical transmission, *n* (%)	20 (4.3)	465
Pregnant, *n* (%)	17 (5.1)	335
Median CD4+ count, cells/mm^3 (IQR)	597 (397)	452
HIV RNA <40 copies/ml, *n* (%)	361 (79.3)	455
Median time between HIV diagnosis and ART initiation, years (IQR)	0 (1)	446

ART, antiretroviral therapy; IQR, interquartile range; IVDU, intravenous drug use; MSM, men who have sex with men.
[a]Number of patients with data recorded for each variable.

Table 2. ARTs received in Ukraine and the Czech Republic.

	Percentage of patients (*n*/*N*)[a]	
ART	**Ukraine**	**Czech Republic**
INSTI-based therapy	85.7 (384/448)	90.5 (430/475)
DTG-based regimen	83.9 (376/448)	66.9 (318/475)
RAL-based regimen	1.3 (6/448)	4.2 (20/475)
BIC-based regimen	0.2 (1/448)	18.1 (86/475)
EVG-based regimen	0.2 (1/448)	1.3 (6/475)

ART, antiretroviral therapy; BIC, bictegravir; DTG, dolutegravir; EVG, elvitegravir; INSTI, integrase strand transfer inhibitor; RAL, raltegravir.
[a]The number of patients with data recorded for each treatment was used as the denominator.