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Antiretroviral therapeutic drug monitoring in a patient with small bowel resection and new HIV diagnosis

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ABSTRACT

Antiretroviral (ARV) absorption in persons living with human immunodeficiency virus (PLWH, HIV) with short bowel syndrome is limited. We describe a case of a 28-year-old male with newly diagnosed HIV and plasmablastic lymphoma with proximal jejunostomy necessitating parenteral nutrition. ARV therapy with dolutegravir 50 mg twice daily and once daily tenofovir/emtricitabine was initiated with documented malabsorption and delayed virologic suppression (VS). Dolutegravir dose titration with therapeutic drug monitoring (TDM) resulted in VS at month 12. ARV TDM with dose titration is an option for PLWH with malabsorptive states to maintain VS.

Introduction

Limited data exist to support the use of antiretroviral (ARV) therapy (ART) in persons living with human immunodeficiency virus (PLWH, HIV) and malabsorptive states. Some data are available in patients with gastric bypass and demonstrate virologic suppression (VS) [1]. Short bowel syndrome alters absorptive capacity and data with non-ARVs (anticoagulation e.g., warfarin) demonstrate therapeutic effects [2]. We report the successful use of dolutegravir (DTG) with therapeutic drug monitoring (TDM) to achieve VS in a patient with lymphoma, small bowel (SB) resection and parenteral nutrition.

Case report

A 28-year-old male presented to the hospital with a new HIV diagnosis [viral load (VL 1060,000 copies/mL CD4 count 48 (8 %)] and stage IV plasmablastic lymphoma. Chemotherapy [etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin (EPOCH)] and an oral (PO) ARV regimen [daily dolutegravir (DTG) 50 mg with emtricitabine (FTC) 200 mg/tenofovir alafenamide (TAF) 25 mg] were initiated on hospital day 8. Six days later, a SB perforation resulted in an emergent operative proximal jejunostomy and omentectomy with approximately 15 cm of SB removed necessitating total parenteral nutrition. On hospital day 18, a full liquid diet with crushed ARVs including DTG 50 mg twice daily (BID) and standard dose FTC/TAF was initiated [3,4].

Insufficient data regarding ART efficacy in SB resection prompted TDM to guide DTG dosing (Fig. 1). Initial DTG TDM resulted in subtherapeutic concentrations (usual mean values of 1100 ng/mL in HIV-infected persons) [5] necessitating a dose increase (100 mg PO BID). Abacavir (ABC) was added secondary to low DTG concentrations, persistent HIV viremia, concern for decreased absorption after patient reported visualizing whole tablets in the ostomy output and intra-abdominal polymicrobial abscesses requiring ultrasound guided drainage with broad spectrum antimicrobials over the next three months. DTG trough concentrations increased but remained low, necessitating an increase to 150 mg PO BID, which resulted in a therapeutic value and continued to increase as he remained on this regimen.

Despite therapeutic DTG trough concentrations, the viral load (VL) response plateaued between 100–200 copies/mL at which point maraviroc (MVC) 300 mg PO BID was added (goal trough >50 ng/mL).[6] Five months after adding MVC to the ART regimen, subtherapeutic trough concentrations resulted (>10 ng/mL on two separate occasions) with a peak concentration of only 17.6 ng/mL. With presumed poor bioavailability but resultant VS (39.9 copies/mL), MVC was discontinued six months after initiation. Ten months after the HIV diagnosis, a bone marrow transplant was successfully completed. DTG dosing was progressively reduced in response to increased trough concentrations indicating improved ARV absorption. Fifteen months after diagnosis, a SB jejunostomy takedown with side-to-side anastomosis occurred, with therapeutic DTG trough concentrations and continued

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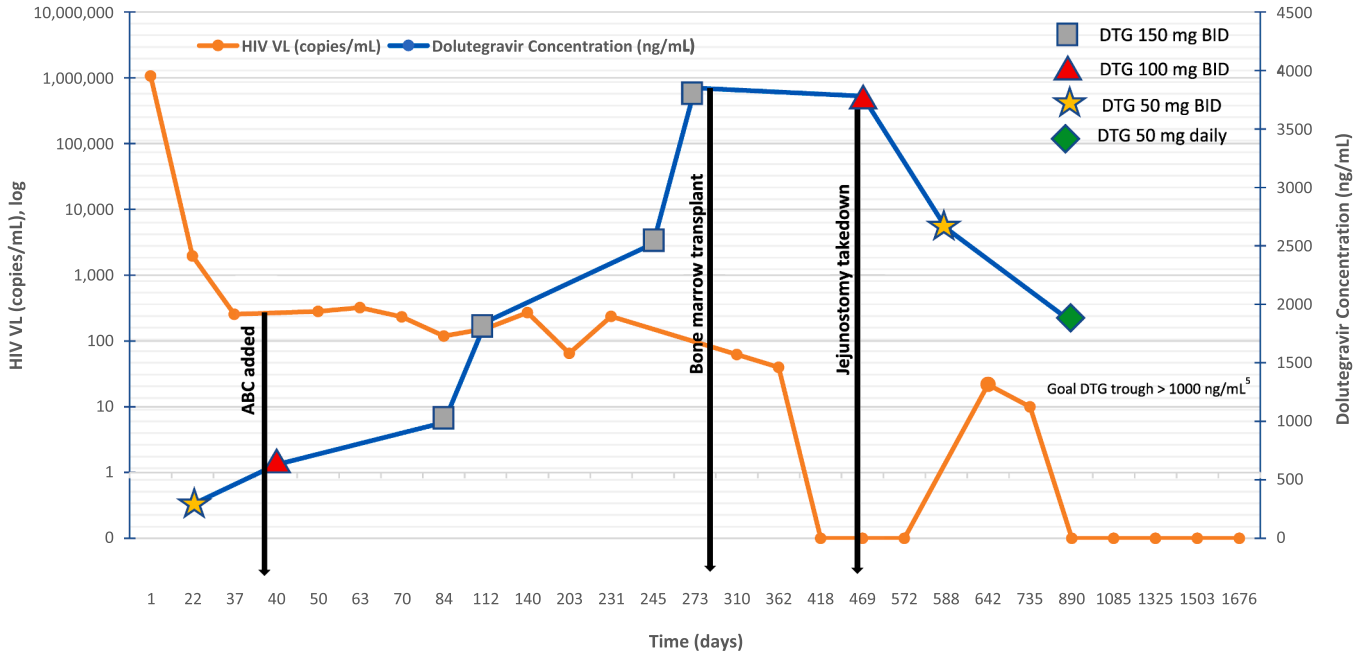

Fig. 1. Management of HIV Medication Therapy and Corresponding Virologic Response.

VS. Four months post jejunostomy reversal, the patient transitioned to once daily fixed dose DTG 50 mg/ABC 600 mg/lamivudine 300 mg with VS for 3 years and a CD4 count of 741 cells/mm^3.

Discussion

This report adds to the limited data on ART initiation in SB resection. Most oral medications are absorbed in the proximal SB, although the specific intestinal sites are incompletely described [7]. ARV absorption in gastric bypass reports are helpful but limited by the type of surgery, many of which do not affect the SB absorptive capacity, and a predominance describing patients maintained on ART with baseline VS [1,8,9]. The role of TDM in nucleoside reverse transcriptase inhibitors (NRTIs), which are intracellularly activated pro-drugs, is not regarded as useful [10]. This report adds to the present but sparse literature to support using TDM for other ARV classes [integrase strand transfer inhibitors (INSTIs) and chemokine receptor blockers] as a tool for assessing adequate gastrointestinal absorption [10].

Parenteral cabotegravir/rilpivirine (CAB/RPV) or ibalizumab may be an option for similarly presenting patients but was unavailable at the time of presentation [11]. Recent data demonstrate CAB/RPV VS in persons with malabsorption or inability to adhere to an oral regimen with baseline viremia using a direct to injection option [12]. In a compassionate use evaluation (N = 35), (non-NRTI/INSTI resistance history excluded), including 28 persons with baseline viremia, 57 % achieved VS [13]. The recently approved long-acting subcutaneous injection, lenacapavir, could be considered in conjunction with CAB/RPV for PLWH with malabsorption, but oral loading appears necessary for initial concentrations and early VS [14]. FDA approval is limited to use in treatment experienced PLWH on failing ARV regimens. Ongoing research exists in treatment-naïve patients in combination with either bictegravir or TAF for long term VS [15].

This case uniquely describes ART initiation in a patient with an HIV VL above one million copies/mL necessitating immediate ARV treatment with SB resection and malabsorption. VS was maintained using high dose DTG, FTC/TAF with ABC utilizing TDM guidance for dose titration/optimization and describes an option to providers with similarly presenting cases.

Ethical approval

Not applicable.

CRediT authorship contribution statement

Leigh Cervino Ahern: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Daniel Nixon:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Patricia Pecora Fulco:** Conceptualization, Writing – original draft, Writing – review & editing, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Consent

Written informed consent was obtained from the patient for publication of this case report and.

accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

All the authors participated in the process of data collection as well as writing and approving the manuscript.

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