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Human Medicine Division

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006

Dovato

Dolutegravir / Lamivudine

Procedure no.: EMA/PAM/0000309558

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	5 January 2026	17 December 2025
☐	CHMP comments	19 January 2026	19 January 2026
☐	Updated CHMP Rapporteur AR	22 January 2026	N/A
☒	CHMP outcome	29 January 2026	29 January 2026

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List of abbreviations

Abbreviation	Definition
3TC	Lamivudine
AE	Adverse event
AESI	Adverse event of special interest
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine transaminase
ART	Antiretroviral therapy
ARV	Antiretroviral
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body mass index
BSA	Body surface area
c/mL	Copies per milliliter
CD4+/8+	Cluster of differentiation 4/8
CDC	Centers for Disease Control and Prevention
CFR	Code of federal regulations
CI	Confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CKD-EPI	Chronic kidney disease-Epidemiology collaboration
CKiD	Chronic kidney disease in children
COVID-19	Corona virus disease 2019
CRF/eCRF	Case report form/electronic case report form
CRO	Contract research organization
CSR	Clinical study report
CVW	Confirmed virologic withdrawal
DAIDS	Division of AIDS
DTG	Dolutegravir
ECG	Electrocardiogram
eC-SSRS	Electronic Columbia suicide severity rating scale
eGFR	Estimated glomerular filtration rate
ERT	eResearch Technology (now known as Clario)
FDA	Food and Drug Administration, United States of America
FDC	Fixed dose combination
GCP	Good clinical practices
HDL	High density lipoprotein
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human immunodeficiency virus
HIV-1	Human immunodeficiency virus type 1
ICF	Informed consent form
ICH	International Council on Harmonisation
IEC	Independent ethics committee
INSTI	Integrase strand transfer inhibitor
IQR	Interquartile range
IRB	Institutional review board

Abbreviation	Definition
IRIS	Immune reconstitution inflammatory syndrome
ITT-E	Intent-To-Treat Exposed (Population)
IVRS/IWRS	Interactive voice/web response system
IU/L	International units per liter
LDL	Low density lipoprotein
MedDRA	Medical Dictionary for Regulatory Activities
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
OCT2	Organic cation transporter 2
PI	Protease inhibitor
PID	Participant identifier
PK	Pharmacokinetic
PPD	Pharmaceutical Product Development (contract research organization)
PR	Protease
PSRAE	Possible Suicidality-Related Adverse Event
RT	Reverse transcriptase
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SOC	System organ class
uACR	Urinary albumin to creatinine ratio
ULN	Upper limit of normal
uPCR	Urinary protein to creatinine ratio

1. Introduction

On 31 October 2025, the MAH submitted a completed paediatric study for Dovato, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that study "*An open-label, single arm study to evaluate the week 48 efficacy and safety of a two-drug regimen of dolutegravir/lamivudine (DTG/3TC) as a fixed dose combination (FDC), in antiretroviral therapy (ART)-naïve HIV-1-infected adolescents, ≥12 to <18 years of age who weigh at least 25 kg*" (205861) is a stand-alone study.

DTG/3TC is assessed in paediatric participants 2 to <15 years of age in a separate study.

Study 205861 is not part of any Paediatric Investigation Plan.

The MAH has reviewed the results of this study and has concluded that an update to the EU product information is considered necessary. The updated EU product information will be submitted in a variation application by end Q1 2026.

2.2. Information on the pharmaceutical formulation used in the study

Table 1.Study intervention administered

Product name:	Dolutegravir/lamivudine (DTG/3TC), fixed dose combination (FDC)
Dosage form:	Tablet
Unit dose strength/dosage level:	50 mg/300 mg
Route of administration:	Oral
Dosing instructions:	Take 1 tablet daily

2.3. Clinical aspects

2.3.1. Introduction

Dovato (DTG/3TC FDC; 50/300 mg) is approved in the EU for treating adults and adolescents over 12 years old who weigh at least 40 kg.

The purpose of the Study 205861 was to assess the safety, efficacy, and tolerability of the 2-drug regimen DTG/3TC FDC in ART-naïve HIV-1 infected adolescents to supplement the dataset in the adult studies GEMINI-1 and GEMINI-2 studies (204861 and 205543).

The MAH submitted a final report for Study 205861.

2.3.2. Clinical study

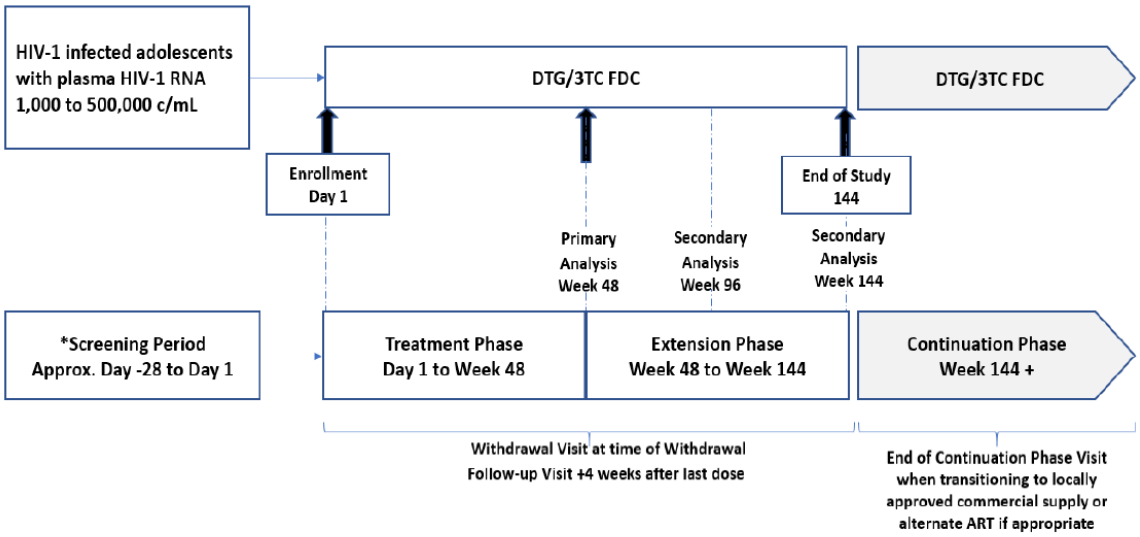
Description

Study 205861 was a Phase 3b, single arm, open-label, multicentre assessment of DTG/3TC FDC in 32 HIV-1 infected, treatment-naive adolescents with plasma HIV-1 RNA between 1000 and ≤500 000 c/mL. All enrolled participants received an open-label DTG/3TC FDC for 48 weeks. Participants who successfully completed 48 weeks of treatment entered the study Extension Phase for an additional 96 weeks.

After Week 144, participants who continued to receive benefit from DTG/3TC FDC and for whom these medications were not locally accessible, were provided access to medication in a Continuation Phase until it was available locally.

Data cut-off date was 10 June 2025, however, the participants' SAE and pregnancy narratives include data captured through 25 June 2025.

Figure 1. Study schematic



* Retesting of an exclusionary lab result (except for exclusionary HIV-1 resistance), is allowed during the screening window (does not require re-screening). In cases of central laboratory assay failure or shipment failure, the screening period may be extended to 35 days to accommodate sample analysis and reporting. Approval of the Medical Monitor is required.

Number of Study Centres and Countries:

This study was conducted at 9 centres that enrolled 1 or more participants in 3 countries (Kenya, South Africa and Thailand).

Study Period:

The study was initiated on 09 April 2019 (first participant screened). The last participant, last visit for Week 144 was on 08 September 2024. The last participant last visit for the Continuation Phase was 22 May 2025.

Methods

Study participants

Key inclusion criteria

1. Male or female HIV-1 infected adolescents ≥12 to <18 years of age and weighing ≥25 kg.
2. Screening plasma HIV-1 RNA between 1,000 and ≤500,000 c/mL.
3. Antiretroviral-naïve (defined as no prior therapy with any antiretroviral agent for the treatment of HIV following a diagnosis of HIV-1 infection).
    - Participants who received antiretroviral therapy for prevention of mother to child transmission of HIV in the first 3 months of life are allowed.
    - Participants who received HIV post-exposure prophylaxis (PEP) or preexposure prophylaxis (PrEP) in the past are allowed as long as the last PEP/PrEP dose was >6 months from HIV diagnosis or there is documented HIV seronegativity at least 2 months after the last prophylactic dose and prior to the date of HIV diagnosis. The study site must have documentation of the seronegative test available and placed into the study source documents.

Key exclusion criteria

1. Females who are breastfeeding or plan to become pregnant or breastfeed during the study.
2. Any evidence of an active CDC Stage 3 and/or Category C or WHO Stage 4 disease. Except cutaneous Kaposi's sarcoma not requiring systemic therapy and historical or current CD4 cell counts less than 200 cells/mm3 or CD4% <15%.
3. Participants with severe hepatic impairment (Class C) as determined by Child-Pugh classification.
4. Unstable liver disease, cirrhosis, known biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
5. Evidence of HBV infection based on the results of testing at Screening for HBV surface antigen (HBsAg), HBV core antibody (anti-HBc), HBV surface antibody (anti-HBs or HBsAb), and HBV DNA.
6. Anticipated need for any HCV therapy during the first 48 weeks of the study and for HCV therapy based on interferon or any drugs that have a potential for adverse drug:drug interactions with study treatment throughout the entire study period.
7. Untreated syphilis infection. Participants who are at least 24 hours post completed treatment are eligible.
8. Participants who in the investigator's judgment, poses a significant suicidality risk.

Treatments

All participants received the FDC tablet of DTG/3TC (50/300 mg) for once daily oral dosing.

Study assessments

Table 2. Objectives and endpoints

Objectives	Endpoints
Primary	
• To assess the antiviral activity of DTG/3TC in antiretroviral naïve HIV-1 infected adolescents.	• The proportion of participants with plasma HIV-1 RNA less than 50 copies per milliliter (c/mL) at Week 48 using the Snapshot algorithm (Intent-to-Treat-Exposed [ITT-E] Population).
Secondary	
• To assess the early antiviral activity of DTG/3TC and to determine the extended long term (≥48 weeks) safety, tolerability, and viral response of DTG/3TC in antiretroviral naïve HIV-1 infected adolescents.	• Proportion of participants with plasma HIV-1 RNA <200 and <50 c/mL at Week 24, Week 96 and Week 144. • Proportion of participants with plasma HIV-1 RNA <200 c/mL at Week 48 • Incidence and severity of AEs and laboratory abnormalities through 144 weeks • Proportion of participants who discontinue treatment due to AEs through 144 weeks. • Safety and tolerability assessments at Weeks 96 and 144. • Viral load monitoring after Week 48 through Week 144.
• To evaluate the effect of DTG/3TC on immunologic response from Baseline to 24 and 48 weeks	• Change from Baseline in cluster of differentiation (CD)4+ and CD8+ cell count and ratio at Week 24 and 48. • Incidence of disease progression (HIV associated conditions, acquired immunodeficiency syndrome [AIDS], and death) through Weeks 24 and 48.
• To assess the safety and tolerability of DTG/3TC in HIV-1 infected adolescents at 24 and 48 weeks	• Incidence and severity of adverse events (AEs) and laboratory abnormalities through 24 and 48 weeks • Proportion of participants who discontinue treatment due to AEs through 24 and 48 weeks
• To assess DTG and 3TC exposure and to evaluate the steady-state pharmacokinetics (PK) of DTG and 3TC in HIV-1 infected adolescents	• Steady-state plasma PK parameters of DTG and 3TC will be assessed using intensive PK collected in a subset of participants.
• To assess development of viral resistance to DTG and 3TC in participants experiencing protocol-defined virologic failure (i.e. meeting confirmed virologic withdrawal [CVW] criteria).	• Incidence of observed genotypic and phenotypic resistance to DTG and 3TC for participants meeting CVW criteria.

Efficacy Assessments

Plasma HIV-1 RNA:

Plasma for quantitative HIV-1 RNA will be collected at screening, baseline, week 4, 8, 12, 16, 24, 36 and 48 during the treatment phase and additionally every 12 weeks in the extension or continuation phase. Methods to be used may include but are not limited to the Abbott RealTime HIV-1 Assay with a lower limit of quantitation of 40 c/mL. In some cases (e.g. where the plasma HIV-1 RNA is below the lower limit of detection for a given assay) additional exploratory methods may be used to further characterize plasma HIV-1 RNA levels.

Lymphocyte Subsets:

Lymphocyte subsets will be collected for assessment by flow cytometry (total lymphocyte counts, percentage, and absolute CD4+ cell counts) at screening, baseline, week 4, 8, 12, 16, 24, 36 and 48 during the treatment phase and additionally every 12 weeks in the extension phase.

Safety Assessments

All AEs will be collected from the start of treatment until the follow-up visit or contact at the time points specified in the protocol.

All SAEs will be collected from the start of treatment until the follow-up visit or contact at the time points specified in the protocol. Any SAEs assessed as related to study participation (e.g., study treatment, protocol-mandated procedures, invasive tests, or change in existing therapy) or related to a sponsor product will be recorded from the time a participant consents to participate in the study. All SAEs will be recorded and reported to the sponsor or designee immediately and under no circumstance should this exceed 24 hours. The investigator will submit any updated SAE data to the sponsor within 24 hours of it being available.

Sample size

It was planned to enrol 30 adolescent participants to provide a descriptive analysis to complement the fully powered non-inferiority evaluation of the DTG/3TC combination performed in adults.

The reported Week 48 response rates for DTG+2NRTIs in adults are 88% to 90% (ITTE, % <50 c/mL by Snapshot algorithm). It is therefore reasonable to conservatively expect a lower response rate of 77% (23/30) or 80% (24/30) in adolescents based on their recognized treatment adherence difficulties.

A single arm study with 30 participants will provide an exact Clopper Pearson 95% CI of 61%-92% for an assumed response rate of 80% (% <50 c/mL by Snapshot algorithm at Week 48). The study will provide an exact Clopper Pearson 95% CI of 58%-90% if the assumed response rate is 77% (% <50 c/mL by Snapshot algorithm at Week 48).

Participants who prematurely discontinue the study will not be replaced. A subset of approximately 12 participants will provide intensive PK samples to ensure data are available from at least 10 evaluable participants.

Randomisation and blinding (masking)

All participants were centrally enrolled using an interactive voice/web response system.

This was a single-arm, open-label study.

Analysis sets

All Screened Participants - This population consisted of participants screened for inclusion in the study.

ITT-E Population - This population consisted of all enrolled participants who received at least 1 dose of study intervention.

ITT-E Sensitivity 1 Population - This population consisted of all participants in the ITT-E Population with the exception of participants at closed site who were withdrawn prior to Week 48 due to site closure.

ITT-E Sensitivity 2 Population - This population consisted of all participants in the ITT-E Population with the exception of participants at the site that was closed before study end.

Safety Population - The Safety Population consisted of all participants who received at least 1 dose of study intervention.

Confirmed Virologic Withdrawal Population - The CVW Population consisted of all participants in the ITT-E Population who met derived CVW criteria specified in the Protocol Section 8.1.1. The CVW algorithm was derived using nominal eCRF visit rather than using the assessment window, taking unscheduled visits into account. A participant could only be classified as CVW for the analyses if the participant had not withdrawn study intervention at the time the HIV RNA sample was taken.

Pharmacokinetic Population - The PK Population consisted of all participants in the Safety Population for whom a PK sample was obtained and analysed.

Statistical Methods

All analyses were descriptive.

All efficacy analyses were performed on the ITT-E Population. The primary endpoint of the proportions of participants meeting the criteria for virologic success (HIV-1 RNA <50 c/mL) as defined by the Snapshot algorithm were reported with exact Clopper Pearson 95% CIs. Change in CD4+/CD8+ count and percent from Baseline to Week 144 were bounded by 95% CIs.

All safety analyses were performed on the Safety Population. Exposure to study intervention, measured by the number of weeks on study intervention, were summarized. The proportion of participants reporting AEs were tabulated. Safety summary statistics were presented for All Available Data, including participants who entered the Continuation Phase and have data available beyond Week 144.

Laboratory data were summarised by visit. In addition, the number and percentage of participants with graded laboratory toxicities (based on DAIDS categories) were summarised.

Safety and efficacy analyses were performed at Week 48, Week 96, and Week 144. In addition to the primary analyses, sensitivity analyses were performed due to the closure of a study site.

Results

Participant flow

Of the 60 participants screened for the study, 28 failed screening. A total of 32 participants were enrolled and treated on the study. Through the End of Study, 20 participants completed the study and 12 participants withdrew. Eleven of the 12 withdrawals had occurred by the Week 96 visit.

One study site was closed (due to GCP noncompliance). In the Sensitivity 1 Population, 2 participants with an absence of Week 48 data as a result of the site closure were excluded. In the Sensitivity 2 Population, all 7 participants from the closed site were excluded.

Extension Phase Disposition: 21 participants in the ITT-E Population completed the study through Week 144, and 6 withdrew from the study. The most common primary reason for withdrawal was closure of study site (3/27, 11%).

Continuation Phase Disposition: 20 participants completed the Continuation Phase of the study, and 1 participant withdrew from the study due to relocating.

Of the 20 participants who completed the Continuation Phase Visit, 7 participants transitioned to a DTG-containing 3 drug local standard of care regimen, and the remaining participants transitioned to a commercially available DTG/3TC regimen.

Table 3. Summary of participant disposition (ITT-E Population) through End of Study

	DTG/3TC FDC N=32 n (%)
Ongoing	0
Completed	20 (63)
Withdrawn[a]	12 (38)
Primary reason[b]/subreason for study withdrawal[c]	
Adverse event[d]	2 (6)
Lack of efficacy[e]	1 (3)
Protocol deviation[f]	1 (3)
Participant reached protocol-defined stopping criteria	0
Study closed / terminated[g]	5 (16)
Lost to follow-up	0
Investigator discretion	0
Withdrew consent	3 (9)
Burden or lack of access to travel	1 (3)
No subreasons	1 (3)
Participant relocated	1 (3)
Outcome of adverse events which led to study withdrawal	
Non-fatal	2 (6)
Fatal	0

a. No withdrawals were related to COVID-19.
b. Participants may have only 1 primary reason for withdrawal.
c. Percentages for subreasons may sum to more or less than 100%. Participants may have more than 1 subreason underneath a single primary reason. Participants are not required to indicate subreasons.
d. 1 participant withdrew because of an AE of glomerular filtration rate decreased (Grade 3) during the Week 24 visit window and 1 participant withdrew from the study during the Week 96 visit window due to AEs of suicidal ideation, which was initially reported at the Week 48 visit, and depression.
e. During the Week 96 visit window, 1 participant withdrew due to Virologic Failure.
f. 1 participant was withdrawn due to pregnancy during the Week 60 study visit window.
g. Refers to the closure of study site. All 7 participants at the site were withdrawn but only 5 due to site closure.

Baseline data

Table 4. Summary of Demographic Characteristics, DTG/3TC, (N=32)

Sex	
N	32
Male	21 (66%)
Female	11 (34%)
Age (Years)	
n	32
Mean	16.0
SD	1.27
Median	17.0
Min.	13
Max.	17
Weight (kg)	
n	32
Mean	55.11
SD	11.884
Median	53.75
Min.	30.0
Max.	96.8
Body Mass Index (BMI) (kg/m^2)	
n	32
Mean	20.245
SD	3.6809
Median	19.959
Min.	14.47
Max.	31.07
Ethnicity	
n	32
Hispanic/Latino	0
Not Hispanic/Latino	2 (100%)
High Level Race	
n	32
American Indian or Alaska native	0
Asian	19 (59%)
Black or African American	13 (41%)
Native Hawaiian or Other Pacific Islander	0
White	0
Mixed race	0
Baseline Plasma HIV-1 RNA (log10 copies/mL)	
n	32
Mean	4.484
SD	0.7893
Median	4.590
Q1	4.070
Q3	5.100
Min.	2.61
Max.	5.64

Baseline CD4+ (10^6/L)	
n	31
Mean	431.2
SD	261.65
Median	373.0
Q1	277.0
Q3	509.0
Min.	20
Max.	1122

Numbers analysed

Table 5. Summary of study populations

Population	**No Treatment**	**DTG/3TC FDC**	**Total**
All Participants Screened	28	32	60
Enrolled	-	32	32
Safety	-	32	32
ITT-E	-	32	32
ITT-E Sensitivity 1	-	30	30
ITT-E Sensitivity 2	-	25	25
CVW	-	1	1
PK	-	32	32
Sparse and Trough PK	-	32	32
Intensive PK	-	12	12

Efficacy results

Table 6. Summary of analysis for proportion of participants with plasma HIV-1 RNA <50 c/mL up to Week 144 – composite Snapshot analysis (ITT-E, ITT-E Sensitivity 1, ITT-E Sensitivity 2 Populations)

Treatment	**Number of responders/ Total assessed (%)**	**Proportion (95% CI)**
DTG/3TC FDC at Week 24 (N=32, ITT-E)	27/32 (84)	(67, 95)
DTG/3TC FDC at Week 48[a] (N=30, ITT-E Sensitivity 1 Population)	26/30 (87)	(69, 96)
DTG/3TC FDC at Week 96 (N=25, ITT-E Sensitivity 2 Population)	22/25 (88)	(69, 97)
DTG/3TC FDC at Week 144 (N=25, ITT-E Sensitivity 2 Population)	21/25 (84)	(64, 95)

Note: Table based on central and/or local laboratory data.
Note: CIs are calculated using Exact Clopper-Pearson Method.
a. Denotes primary endpoint.

The sensitivity analyses were performed to remove participant data associated with imputed failures resulting from site closure.

Table 7. Summary of analysis for proportion of participants with plasma HIV-1 RNA <200 c/mL up to Week 144 – composite Snapshot analysis (ITT-E, ITT-E Sensitivity 1, ITT-E Sensitivity 2 Populations)

Treatment	**Number Responded/ Total Assessed (%)**	**Proportion (95% CI)**
DTG/3TC FDC at Week 24 (N=32, ITT-E)	29/32 (91)	(75, 98)
DTG/3TC FDC at Week 48 (N=30, ITT-E Sensitivity 1 Population)	27/30 (90)	(73, 98)
DTG/3TC FDC at Week 96 (N=25, ITT-E Sensitivity 2 Population)	22/25 (88)	(69, 97)
DTG/3TC FDC at Week 144 (N=25, ITT-E Sensitivity 2 Population)	21/25 (84)	(64, 95)

Note: Table based on central and/or local laboratory data.
Note: CIs are calculated using Exact Clopper-Pearson Method.

Table 8. Summary of change from Baseline in plasma HIV-1 RNA (log10 c/mL) by visit (ITT-E Population)

Actual relative time	**n**	**DTG/3TC FDC (N=32) Median (IQR)**
Baseline	32	4.592 (4.071, 5.099)
Week 4	32	−2.803 (−3.295, −2.189)
Week 8	32	−2.878 (−3.269, −2.189)
Week 12	32	−2.922 (−3.413, −2.189)
Week 16	30	−2.946 (−3.379, −2.587)
Week 24	29	−2.993 (−3.346, −2.587)
Week 36	29	−2.993 (−3.379, −2.587)
Week 48	28	−2.988 (−3.425, −2.408)
Week 60	27	−2.993 (-3.471, −2.606)
Week 72	23	−2.862 (-3.471, −2.541)
Week 84	23	−3.013 (-3.545, −2.606)
Week 96	23	−2.993 (-3.545, −2.587)
Week 108	21	-3.013 (-3.545, -2.781)
Week 120	21	-3.013 (-3.545, -2.781)
Week 132	21	-2.993 (-3.545, -2.781)
Week 144	21	-3.013 (-3.545, -2.781)

Note: Table summarizes central and/or local laboratory data.
Note: Baseline value is defined as the last non-missing pre-treatment value observed. Baseline results present the result recorded at Baseline, whereas post-Baseline results present change from Baseline.

Table 9. Summary of change from Baseline in CD4+ cell count (10^6/L) by visit (ITT-E Population)

Actual relative time	DTG/3TC FDC ITT-E Population (N=32)		
	n	Median (IQR)	Mean (SD)
Baseline	32	371.500 (270.00-507.50)	418.281 (267.5122)
Week 4	28	95.500 (29.00-197.50)	119.929 (129.4129)
Week 24	29	167.000 (103.00-319.00)	206.073 (188.3612)
Week 48	28	223.500 (85.50-380.50)	234.286 (216.5018)
Week 72	23	295.000 (217.00-526.00)	320.217 (250.2470)
Week 96	23	285.000 (140.00-529.00)	299.739 (217.6060)
Week 120	21	274.000 (121.00-373.00)	261.238 (218.3112)
Week 144	21	214.000 (115.00-318.00)	233.524 (187.0066)

Note: Table summarizes central and/or local laboratory data.
Note: Baseline value is defined as the last non-missing pre-treatment value observed. Baseline results present the result recorded at Baseline, whereas post-Baseline results present Change from Baseline.

In the ITT-E Population, moderate decreases from Baseline in CD8+ cell counts were observed, with median change from Baseline at Week 24 of −15.0 10^6/L, at Week 48 of −78.5 10^6/L, at Week 96 of −60.0 10^6/L, and at Week 144 of -207.0 10^6/L.

In the ITT-E Population, the CD4+/CD8+ cell count ratio generally increased at each visit, with median change from Baseline at Week 24 of 0.215, at Week 48 of 0.345, at Week 96 of 0.420, and at Week 144 of 0.430.

Extent of exposure and adherence

Table 10. Summary of Extent of Exposure

	DTG/3TC (N=32)
Time on Treatment (Days)[1]	
n	32
Mean	1053.5
SD	521.62
Median	1159.5
Q1	595.5
Q3	1500.5
Min.	125
Max.	1927
Total Number of Tablets Dispensed	
n	32
Mean	1164.3
SD	563.33
Median	1260.0
Q1	669.5
Q3	1620.0
Min.	150
Max.	2130

[1] The time on study drug does not exclude dose interruptions.

Safety results

Unless stated otherwise, the Safety Population including all participants who received at least 1 dose of study intervention was used for safety analyses. Safety data is presented through Week 144 and the end of the Continuation Phase.

Table 11. Overall summary of adverse events (Safety Population, DTG/3TC FDC)

Event	**Week 24 N=32 n (%)**	**Week 48 N=32 n (%)**	**Week 96 N=32 n (%)**	**Week 144 N=32 n (%)**	**All Available Data N=32 n (%)**
Any AE	23 (72)	28 (88)	29 (91)	29 (91)	29 (91)
Drug-related AEs	1 (3)	1 (3)	1 (3)	1 (3)	1 (3)
Grade 2 to 5 AEs	14 (44)	17 (53)	21 (66)	24 (75)	24 (75)
Drug-related Grade 2 to 5 AEs	1 (3)	1 (3)	1 (3)	1 (3)	1 (3)
AEs leading to study/treatment withdrawal	1 (3)	2 (6)	2 (6)	2 (6)	2 (6)
Any SAE	1 (3)	2 (6)	3 (9)	6 (19)	6 (19)
Drug-related SAEs	0	0	0	0	0
Drug-related Fatal AEs	0	0	0	0	0

Table 12. Most common adverse events (reported in >=2 participants) by preferred term (Safety Population)

Preferred term	**DTG/3TC FDC**				
	Week 24 N=32 n (%)	**Week 48 N=32 n (%)**	**Week 96 N=32 n (%)**	**Week 144 N=32 n (%)**	**All Available Data N=32 n (%)**
Any AE	23 (72)	28 (88)	29 (91)	29 (91)	29 (91)
COVID-19	1 (3)	1 (3)	4 (13)	10 (31)	10 (31)
Nasopharyngitis	4 (13)	6 (19)	7 (22)	7 (22)	8 (25)
Upper respiratory tract infection	3 (9)	3 (9)	5 (16)	6 (19)	6 (19)
Pharyngitis	1 (3)	2 (6)	2 (6)	3 (9)	5 (16)
Cough	1 (3)	1 (3)	3 (9)	3 (9)	4 (13)
Headache	2 (6)	2 (6)	3 (9)	3 (9)	4 (13)
Folliculitis	1 (3)	3 (9)	3 (9)	3 (9)	3 (9)
Influenza like illness	0	0	2 (6)	3 (9)	3 (9)
Secondary syphilis	0	0	2 (6)	3 (9)	3 (9)
Tonsillitis	1 (3)	1 (3)	3 (9)	3 (9)	3 (9)
Acne	0	0	1 (3)	2 (6)	2 (6)
Allergic cough	2 (6)	2 (6)	2 (6)	2 (6)	2 (6)
Anal abscess	2 (6)	2 (6)	2 (6)	2 (6)	2 (6)
Anogenital warts	1 (3)	1 (3)	2 (6)	2 (6)	2 (6)
Aphthous ulcer	1 (3)	1 (3)	1 (3)	2 (6)	2 (6)
Back pain	0	1 (3)	1 (3)	1 (3)	2 (6)
Decreased appetite	2 (6)	2 (6)	2 (6)	2 (6)	2 (6)
Depression	0	1 (3)	1 (3)	2 (6)	2 (6)
Dermatitis allergic	1 (3)	1 (3)	2 (6)	2 (6)	2 (6)

Preferred term	DTG/3TC FDC				
	Week 24 N=32 n (%)	Week 48 N=32 n (%)	Week 96 N=32 n (%)	Week 144 N=32 n (%)	All Available Data N=32 n (%)
Diarrhoea	0	0	2 (6)	2 (6)	2 (6)
Food poisoning	1 (3)	1 (3)	2 (6)	2 (6)	2 (6)
Genital herpes	2 (6)	2 (6)	2 (6)	2 (6)	2 (6)
Glomerular filtration rate decreased	1 (3)	1 (3)	1 (3)	2 (6)	2 (6)
Herpes zoster	1 (3)	1 (3)	2 (6)	2 (6)	2 (6)
Hypersensitivity	1 (3)	1 (3)	1 (3)	1 (3)	2 (6)
Immunisation reaction	0	1 (3)	2 (6)	2 (6)	2 (6)
Impetigo	0	0	0	1 (3)	2 (6)
Myalgia	1 (3)	1 (3)	2 (6)	2 (6)	2 (6)
Rhinitis allergic	2 (6)	2 (6)	2 (6)	2 (6)	2 (6)
Suicidal ideation	0	1 (3)	1 (3)	2 (6)	2 (6)
Urethritis	0	0	0	2 (6)	2 (6)
Urinary tract infection	0	1 (3)	2 (6)	2 (6)	2 (6)
Vulvovaginal candidiasis	0	2 (6)	2 (6)	2 (6)	2 (6)

Note: Table summarizes post-Baseline AEs. A post-Baseline AE is defined as any AE onset after the treatment start date. AE with missing onset date is considered as a post-Baseline AE. AEs were grouped by preferred term using MedDRA 28.0.

Table 13. Summary of treatment emergent adverse events by system organ class (Safety Population)

System organ class	DTG/3TC FDC				
	Week 24 N=32 n (%)	Week 48 N=32 n (%)	Week 96 N=32 n (%)	Week 144 N=32 n (%)	All Available Data N=32 n (%)
Any AE	23 (72)	28 (88)	29 (91)	29 (91)	29 (91)
Infections and infestations	18 (56)	23 (72)	25 (78)	26 (81)	26 (81)
Gastrointestinal disorders	5 (16)	5 (16)	7 (22)	10 (31)	10 (31)
Respiratory, thoracic and mediastinal disorders	4 (13)	4 (13)	6 (19)	6 (19)	7 (22)
Skin and subcutaneous tissue disorders	3 (9)	3 (9)	5 (16)	6 (19)	7 (22)
General disorders and administration site conditions	0	0	4 (13)	5 (16)	5 (16)
Injury, poisoning and procedural complications	1 (3)	4 (13)	5 (16)	5 (16)	5 (16)
Investigations	2 (6)	2 (6)	3 (9)	5 (16)	5 (16)
Psychiatric disorders	1 (3)	3 (9)	3 (9)	5 (16)	5 (16)
Immune system disorders	2 (6)	2 (6)	2 (6)	3 (9)	4 (13)
Musculoskeletal and connective tissue disorders	1 (3)	3 (9)	3 (9)	3 (9)	4 (13)
Nervous system disorders	2 (6)	2 (6)	3 (9)	3 (9)	4 (13)
Blood and lymphatic system disorders	2 (6)	3 (9)	3 (9)	3 (9)	3 (9)
Eye disorders	2 (6)	2 (6)	3 (9)	3 (9)	3 (9)
Metabolism and nutrition disorders	2 (6)	2 (6)	3 (9)	3 (9)	3 (9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (3)	2 (6)	2 (6)	2 (6)	2 (6)
Reproductive system and breast disorders	2 (6)	2 (6)	2 (6)	2 (6)	2 (6)

Note: Table summarizes post-Baseline AEs. A post-Baseline AE is defined as any AE onset after the treatment start date. AE with missing onset date is considered as a post-Baseline AE. AEs were grouped by SOC and preferred term using MedDRA 28.0.

Adverse events by grade

The majority of AEs reported had a maximum intensity of Grade 1 or Grade 2. Through Week 144, 5 maximum toxicity Grade 3 AEs (major depression, blood creatine phosphokinase increased, glomerular filtration rate decreased (for eGFR information see section below), liver function test abnormal and food allergy were reported. No participant had a Grade 4 (potentially life-threatening) or Grade 5 (fatal) event.

The Grade 3 AE of major depression is also an SAE. It is not considered related to study intervention and there were other factors which may have contributed to the AE such as psychosocial stressors and concurrent medication. The AE was ongoing through the End of Study.

The Grade 3 AE of blood creatine phosphokinase increased resolved in 22 days without changes to the study treatment and was not deemed drug-related.

The Grade 3 AE of liver function test abnormal was not considered serious, did not lead to withdrawal, and was not considered related to study intervention.

The Grade 3 AE of food allergy was non-serious not considered study intervention-related and resolved on continued treatment.

Adverse events related to study intervention

Grade 3 glomerular filtration rate decreased (which started after Week 16) was the only study intervention-related AE reported and lead to study intervention being discontinued. Follow-up data indicated improvement after discontinuation.

Adverse events leading to withdrawal

Through Week 48, 2 participants experienced an AE leading to withdrawal/permanent discontinuation of study intervention. 1 participant had glomerular filtration rate decreased (described above) and the other participant had suicidal ideation and depression. Through Week 144, and through the end of the Continuation Phase, no additional AEs leading to withdrawal were reported.

Deaths

No deaths were reported in the study.

Serious adverse events (SAEs)

Table 14. Summary of all serious adverse events by preferred term (Safety Population)

Preferred term	**DTG/3TC FDC**				
	Week 24 N=32 n (%)	**Week 48 N=32 n (%)**	**Week 96 N=32 n (%)**	**Week 144 N=32 n (%)**	**All Available Data N=32 n (%)**
Any serious adverse event	1 (3)	2 (6)	3 (9)	6 (19)	6 (19)
Anal abscess	1 (3)	1 (3)	1 (3)	1 (3)	1 (3)
Major depression	0	0	0	1 (3)	1 (3)
Orchitis	0	0	1 (3)	1 (3)	1 (3)
Postoperative wound complication	0	0	1 (3)	1 (3)	1 (3)
Ulcerative keratitis	0	0	0	1 (3)	1 (3)
Vulvovaginal warts	0	1 (3)	1 (3)	1 (3)	1 (3)

Adverse events of special interest

Drug hypersensitivity and rash:

Through the Continuation Phase, a total of 7 (22%) participants experienced AEs in the Skin and subcutaneous tissue disorders SOC (acne Grade 1, dermatitis allergic Grade 1 [n=2], dermatitis contact Grade 1, and rash pruritic Grade 2). Five of seven AEs were reported through Week 96. The 2/7 additional AEs were a second AE of acne (Grade 1) which occurred through Week 144 and an AE of acanthosis nigricans (Grade 1) which occurred during the Continuation Phase.

Psychiatric disorders including suicidality:

Through the Continuation Phase, 5 (16%) participants reported 8 AEs in the Psychiatric disorders SOC including bipolar disorder (Grade 2; reported through Week 96), conversion disorder (Grade 1; reported through Week 24), depression (n=2, both toxicity Grade 2; one reported through Week 48 and one reported through Week 144), depression suicidal (Grade 2; reported through Week 48), suicidal ideation (n=2, both toxicity Grade 2; one reported through Week 48 and one reported through Week 144), and major depression (Grade 3; reported through Week 144).

None of the AEs were considered to be study intervention-related. 1 AE, major depression, was considered serious and was considered ongoing through the End of Study. Study intervention was discontinued in 1 participant due to Grade 2 AEs of suicidal ideation and depression; both of these events were considered ongoing through the End of Study.

Gastrointestinal disorders:

Through the End of Study, AEs in the Gastrointestinal disorders SOC were reported in 10 (31%) participants, all events were Grade 1 or Grade 2.

Musculoskeletal Disorders:

Through the End of Study, AEs in the Musculoskeletal and connective tissue disorders SOC were reported in 4 (13%) participants and included arthralgia (Grade 1), myalgia (Grade 1, reported in 2 participants), and back pain (Grade 1 reported in 1 participant and Grade 2 reported in another participant).

Pregnancies

Throughout the study, 1 participant became pregnant and was withdrawn from the study.

Viral genotyping and phenotyping results

Protocol-defined confirmed virologic withdrawal (CVW) through Week 144 was low with 1 participant meeting CVW criteria at Week 72. No resistance was identified to NRTI, NNRTI or PI. The assay failed in the integrase region.

2.3.3. Discussion on clinical aspects

Dovato (DTG/3TC FDC; 50/300 mg) is approved in the EU for treating HIV-1 in adults and adolescents over 12 years old who weigh at least 40 kg. Efficacy and safety in the adolescent population have been established through extrapolation from adults, via exposure-matching. The purpose of the single arm, open-label, phase 3b Study 205861 was to provide additional descriptive safety, efficacy, and tolerability data in ART-naïve HIV-1 infected adolescents up to Week 144.

Participants ≥12 to <18 years of age and weighing ≥25 kg with screening plasma HIV-1 RNA between 1,000 and ≤500,000 c/mL were included. All participants received the FDC tablet of DTG/3TC (50/300 mg) for once daily oral dosing up to 144 weeks. Thereafter the participants were offered to enter a continuation phase until the medication were locally available.

Overall, 32 participants were enrolled and treated on the study. All participants were either Asian (Southeast Asian Heritage, [59%]) or Black (41%). The median (min, max) age was 17 (13, 17) years.

At Week 48 (Primary Endpoint) 87% (26/30) (95% Confidence Interval [CI]: 69, 96) of participants had a plasma HIV-1 RNA <50 copies/mL (ITT-E Sensitivity 1 Population by Snapshot Analysis), and at Week 144 84% (21/25) (95% CI: 64, 95) of participants had a plasma HIV-1 RNA <50 copies/mL (ITT-E Sensitivity 2 Population by Snapshot Analysis).

The sensitivity populations consisted of all participants who received 1 dose with the exception of participants from the site which was closed due to GCP issues raise prior to the Week 48 analysis.

The median CD4+ cell count change from Baseline at Week 48 was 223.5 10^6/L. These increases were stable over time, with median change from Baseline at Week 144 of 214.0 10^6/L.

The effect of DTG/3TC in the adolescent population are in line with the effect observed in the pooled adult studies GEMINI-1 and -2. In the adult studies at week 48, 91% (655/716) of the participants achieved HIV-1 RNA < 50 copies/mL and the mean change from Baseline in CD4+ cells was 220 cells/mL.

Regarding the safety of DTG/3TC, most adolescent participants who experienced AEs reported an AE in the first 24 weeks of study intervention, 23/32 (72%). Through week 144 the most commonly reported AEs were infections, 26/32 (81%). None of these AEs were considered drug-related.

Other common AEs in the adolescent population such as headache (13%, n= 4/32) and diarrhoea (6%, n=2/32) are listed as very common adverse reactions in the SmPC. The only other AE observed in the adolescent population which is listed as common in the SmPC was depression, reported in 2 of 32 (6%) adolescent participants. Most of the other reported AEs were observed in 2-3 participants, thus, it is difficult to draw any conclusions regarding these AEs.

There was one AE considered related to study intervention which was a Grade 3 glomerular filtration rate decreased reported through Week 24 and led to discontinuation of study intervention. There were no renal AEs reported for this participant.

There were 6 SAE reported through End of Study (anal abscess, major depression, orchitis, postoperative wound complication, ulcerative keratitis, vulvovaginal warts), none considered related to study intervention. Through the End of Study, no deaths were reported.

In summary, the effect of DTG/3TC in the adolescent population was similar to the effect demonstrated in adult studies. The study did not identify any new safety concerns or new safety signals relative to the established safety profile for DTG/3TC FDC. The limitations of the study include the descriptive nature, small study population (32 participants) and lack of control arm.

No urgent changes to the Product Information are warranted. However, current statements in the SmPC regarding the absence of clinical data in the paediatric population should be revised at the next opportunity. The MAH proposes that updated EU product information will be submitted in a variation application by end Q1 2026.

3. Rapporteur’s overall conclusion and recommendation

☒ **Fulfilled:**

No further action required, however further data are expected in the context of a grouped variation procedure prior to any conclusion on the product information. The MAH has committed to submit this variation application by end Q1 2026.