CARAVEL: Evaluation of Real-World Effectiveness and Sustainability of the 2-Drug Regimen Dolutegravir/Lamivudine Fixed-Dose Combination in Treatment-Naive and Pre-Treated Adults Who Are Virologically Suppressed, in Routine Clinical Care, in France. Three-Year Analysis Results

eP049

P. Philibert,[1] C. Charpentier,[2] N. Naguleswaran,[3] C. Philippe,[3] L. Roustand,[4] C. Vouillot,[5] L. Hocqueloux[6]

[1]Hôpital Européen, Marseille, France; [2]Hôpital Bichat-Claude Bernard, Paris, France; [3]QUALEES, Paris, France; [4]GSK, Rueil-Malmaison, France; [5]ViiV Healthcare, Rueil-Malmaison, France; [6]CHU, Orléans, France

Key Takeaways

- **These real-world data, from routine clinical care in France, demonstrated high virological success after 3 years on DTG/3TC in both TN-PLWH and PT-PLWH populations, without significant weight change.**
- **The low number of serious adverse event related to DTG/3TC supports the overall favorable safety profile. The main reason for DTG/3TC discontinuation was due to patient request to switch to CAB/RPV-LA.**

Purpose

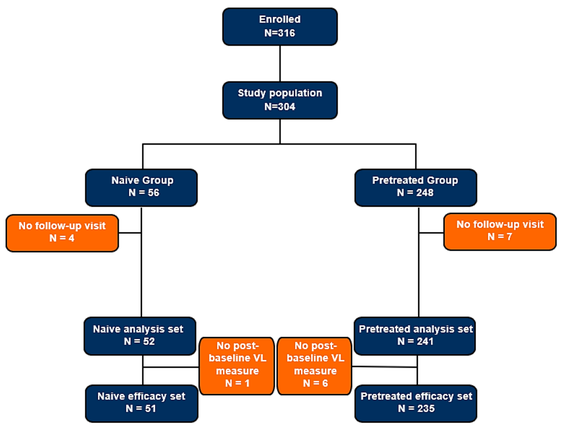
- To describe virological outcome of DTG/3TC for the initial suppression of HIV replication in treatment-naïve people living with HIV (TN-PLWH), as well as maintaining viral suppression in pre-treated PLWH who are virologically suppressed (PT-PLWH).
- To describe safety in clinical practice.

Methods

- CARAVEL is a French, prospective, non-interventional, single-arm, multi-center cohort study with a planned 3-year follow-up
- PLWH were stratified into 2 groups: TN-PLWH or PT-PLWH (Figure 1)
- To be included, adult PLWH should have started DTG/3TC for the first time in accordance with the summary of product characteristics
- Primary endpoint:
  - TN-PLWH: Number and percentage of subjects who attain initial suppression (i.e., a viral load [VL] <50 c/mL after 6 months of initiation of DTG/3TC), and number and percentage of subjects who maintain a viral load <50 c/mL from 6 months up to 3 years
  - PT-PLWH: Number and percentage of subjects who maintain a viral load <50 c/mL after switch to DTG/3TC from 6 months up to 3 years
- PLWH with no post-baseline VL measure were excluded from efficacy set
- Here, we present the 3-year analysis results

Figure 1. Study Flow Chart

French, prospective, non-interventional, single-arm, multi-center cohort study



Results

Participants

- 49 centers included 304 PLWH:
  - 56 TN-PLWH (median age at baseline, 33 years (IQR: 27-45); 84% men)
  - 248 PT-PLWH (median age at baseline, 52 years (IQR: 41-60); 75% men)

Participant flow

- 30 TN-PLWH were followed during the 3-year follow-up and 26 left the study prematurely, with a mean follow-up time of 14.2 (±9.7) months and a median of 12.4 months (IQR: 7.7-21.1)
- 154 PT-PLWH were followed during the 3-year follow-up and 94 left the study prematurely, with a mean follow-up time of 14.9 (±9.4) months and a median of 13.4 months (IQR: 7.7-20.8).

Effectiveness

- For the primary endpoint, 49 (87%) TN-PLWH and 234 (94%) PT-PLWH are evaluable on the effectiveness criteria.
- Initial virological suppression (VL <50 c/mL) was attained for 44 (89.8%) TN-PLWH after 6 months of initiating DTG/3TC, with a median time to virological suppression of 1.1 months (IQR: 1.0-2.1) (Figure 2). All TN-PLWH (N=51) using DTG/3TC attained a virological suppression during the 3-year follow-up (maximum time to virological suppression: 12.4 months), and there were no TN-PLWH with virological failure (VF) during the 3-year follow-up.
- The median pre-treatment VL of PT-PLWH was 70490 cp/mL (IQR: 15880-292810). After switch to DTG/3TC, 220 (94%) PT-PLWH maintained viral suppression <50 cp/mL (Figure 3), including 7 who experienced a blip (PLWH with VL < 50 cp/mL at most measurement, without two consecutives measurements with VL ≥ 50 cp/mL, and without VL > 200 cp/mL).
- During the follow-up, 14 PT-PLWH did not maintain a VL<50 c/mL:
  - 5 were due to intermittent viraemia (PLWH with VL < 50 cp/mL at most measurement, without two consecutives measurements with VL ≥ 50 cp/mL, and with blip > 200 cp/mL)
  - 9 were due to VF (PLWH with at least two consecutive measurements with VL ≥ 50 cp/mL or change in treatment strategy), with a median time to VF of 15.1 months (IQR: 7.5-27.0). Among these 9 subjects with VF, a genotypic resistance test was available for 3 subjects, of whom 1 developed 3TC resistance [M184V] in a context of non-adherence (declarative non-adherence; VL=387 cp/mL); 5 out of the 9 subjects with VF discontinued DTG/3TC.
- In PLWH who were evaluable, CD4+ cell count was ≥500 cells/mm^3 at 3 years for 90.0% (N=18) of TN-PLWH vs 48.1% (N=26) at baseline and 78.2% (N=86) for PT-PLWH vs 79.1% (N=185) at baseline.

Study treatment discontinuations

- Overall, DTG/3TC was discontinued for 63 (21.2%) PLWH:
  - 8 TN-PLWH, with a median time to treatment discontinuation of 19.1 months (IQR: 14.8-22.5): 6 due to participant choice (75.0%) and 2 for safety reasons (25.0%)
  - 55 PT-PLWH, with a median time to treatment discontinuation of 15.7 months (IQR: 8.1-21.8): 34 due to participant choice (63.0%), 15 for safety reasons (27.8%), 5 for VF (9.3%), and 1 for data missing

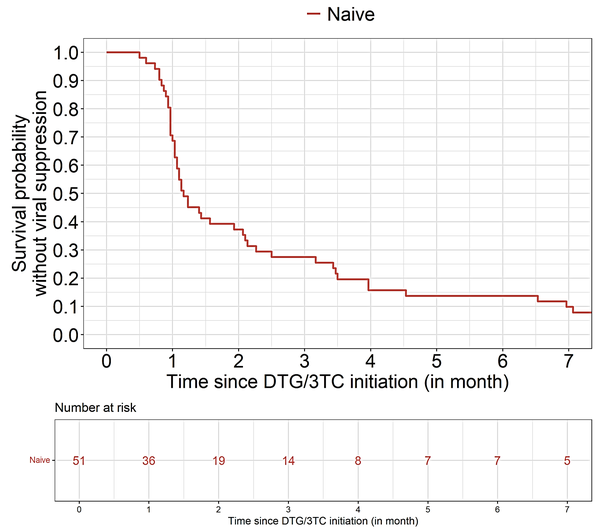
Safety

- 11 (4.4%) PT-PLWH and 1 (1.8%) TN-PLWH experienced at least one serious adverse drug reaction related to DTG/3TC.
- 50 (20.2%) PT-PLWH and 12 (21.4%) TN-PLWH experienced at least one non-serious adverse drug reaction related to DTG/3TC.
- Safety cases leading to DTG/3TC discontinuation are presented in Table 1
- 21 PLWH who discontinued DTG/3TC were switched to long-acting injectable cabotegravir + rilpivirine (CAB/RPV-LA) and 8 to oral-form cabotegravir + rilpivirine; all these switches were upon participant request

Body weight

- The average change in body weight over 3-years of follow-up was 2.0 (±5.5) (p=0.08) kg in TN-PLWH and 0.0 (±6.5) (p=0.98) kg in PT-PLWH. Table 2 presents changes in body weight

Figure 2. Kaplan-Meier of the time to viral suppression for TN-PLWH



No censored TN-PLWH, and virological suppression was attained for all TN-PLWH (N=51) using DTG/3TC (maximum time to virological suppression: 12.4 months).

Figure 3. Kaplan-Meier of Virological Failure for PT-PLWH

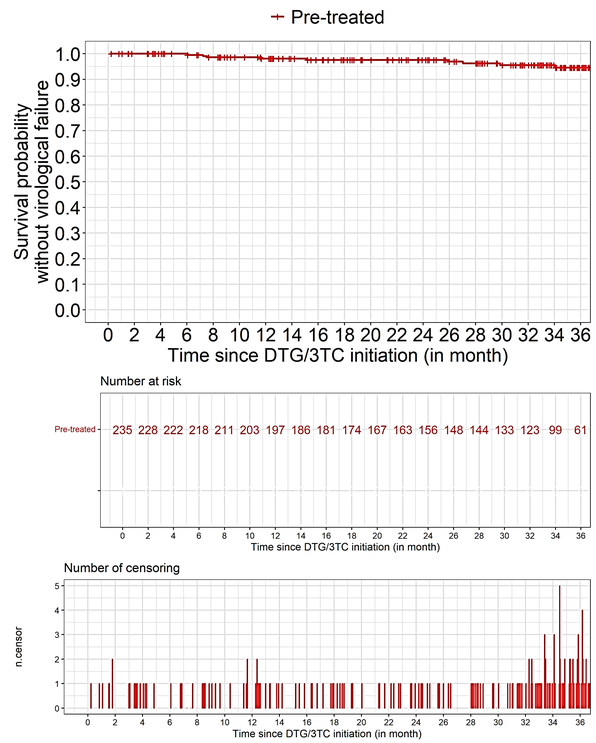


Table 1. Safety Cases Leading to DTG/3TC Discontinuation for TN-PLWH and PT-PLWH

Adverse Events (AEs)*	TN-PLWH (N=56)	PT-PLWH (N=248)
Musculoskeletal and connective tissue disorders	0	8 (3.2%)
General disorders and administration site conditions	0	6 (2.4%)
Nervous system disorders	1 (1.8%)	6 (2.4%)
Investigations	1 (1.8%)	6 (2.4%)
Psychiatric disorders	0	4 (1.6%)
Gastrointestinal disorders	1 (1.8%)	3 (1.2%)
Hepatobiliary disorders	0	2 (0.8%)
Infections and infestations	1 (1.8%)	3 (1.2%)
Injury, poisoning and procedural complications	0	3 (1.2%)
Metabolism and nutrition disorders	2 (3.6%)	3 (1.2%)
Vascular disorders	0	2 (0.8%)
Ear and labyrinth disorders	0	1 (0.4%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	2 (0.8%)
Skin and subcutaneous tissue disorders	0	2 (0.8%)
Social circumstances	0	1 (0.4%)
Respiratory, thoracic and mediastinal disorders	1 (1.8%)	0
Blood and lymphatic system disorders	1 (1.8%)	0
Renal and urinary disorders	0	1 (0.4%)
Surgical and medical procedures	0	1 (0.4%)

*MedDRA classification

Table 2. Change in body weight

		TN-PLWH (N=30)	PT-PLWH (N=152)
Change in body weight between last weight (more than 30 months) and baseline weight (in kg)	Missing value	4	11
	N	26	141
	Mean (±SD)	2.0 (±5.5) (p=0.0823)*	0.0 (±6.5) (p=0.9795)*
	Median (IQR)	1.5 (0.0-5.0)	0.0 (-3.0-3.0)
	Range	-8.0 / 18.0	-22.0 / 26.0

* Paired T-test

Conclusions

- Based on 3-year follow-up analysis results, DTG/3TC demonstrated virological efficacy in both TN-PLWH and PT-PLWH in routine clinical care
- There were no VFs in TN-PLWH and only 9 in PT-PLWH during the 3-year follow-up; of the 3 PT-PLWH for whom genotypic resistance test was available, only 1 had a drug resistance-associated mutation (M184V)
- DTG/3TC was discontinued in 63 PLWH; most discontinuations were due to participant choice to switch to CAB/RPV-LA
- Treatment-related serious adverse events were reported only in 12 PLWH during the 3-year follow-up.
- In PLWH who were evaluable during the 3-year follow-up, DTG/3TC had no significant impact on body weight
- **These real-world data demonstrated high virological success after 3 years on DTG/3TC in both TN-PLWH and PT-PLWH populations, without significant weight change. The low number of serious adverse event related to DTG/3TC supports the overall favorable safety profile. The main reason for DTG/3TC discontinuation was due to participant request to switch to CAB/RPV-LA.**

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Presenting author: Patrick Philibert; p.philibert@hopital-europeen.fr

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