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. Two-Year Interim Analysis Results

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Key Takeaways

- **The effectiveness and sustainability of the 2-drug regimen dolutegravir/lamivudine fixed-dose combination (DTG/3TC) were described using data collected from routine clinical care in France**
- **These real-world data demonstrated high virological success after 2 years of follow-up, without significant weight change. The main reason for DTG/3TC discontinuation for both groups was patient request to switch to long-acting injectable cabotegravir + rilpivirine**

Introduction

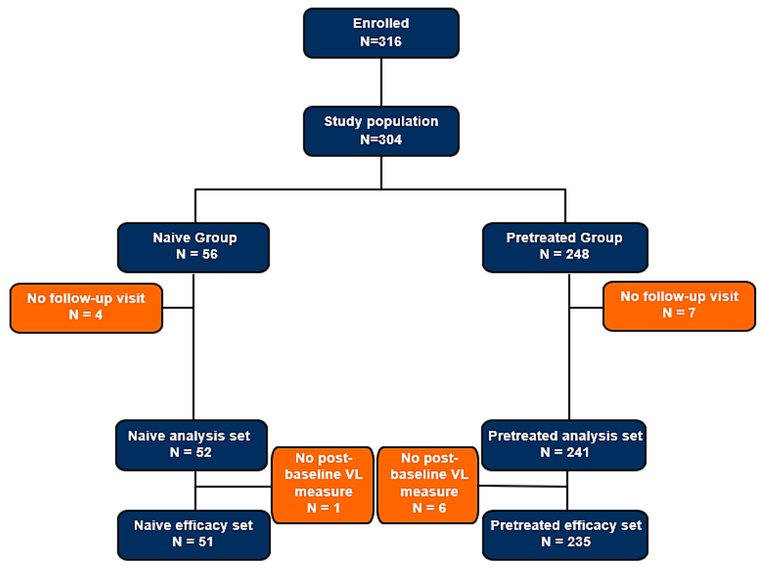
- 2-drug regimens have been developed to address problems of drug-drug interactions, resistance, and tolerance issues of existing ARVs
- Dolutegravir/Lamivudine (DTG/3TC) is a complete therapeutic regimen with just 2 active substances
- This study was conducted to supplement data gathered from clinical trials[1-3] with real-world evidence to evaluate the antiretroviral efficacy and safety of DTG/3TC in attaining or maintaining virological suppression in treatment-naive people living with HIV (TN-PLWH) and in pre-treated PLWH (PT-PLWH) in routine clinical care in France

Methods

- CARAVEL is a French, prospective, non-interventional, single-arm, multi-center cohort study with a planned 3-year follow-up
- Patients 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 patients 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 patients who maintain a viral load <50 c/mL from 6 months up to 3 years
  - PT-PLWH: Number and percentage of patients who maintain a viral load <50 c/mL after switch to DTG/3TC from 6 months up to 3 years
- Patients with no post-baseline VL measure were excluded from efficacy set
- Here, we present the 2-year interim analysis results

Figure 1. Study Flow Chart

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



Results

Patients

- 49 centers included 304 patients:
  - 56 TN-PLWH (mean age at baseline, 37 years; 84% men)
  - 248 PT-PLWH (mean age at baseline, 51 years; 75% men)

Effectiveness

- For the primary endpoint, 49 TN-PLWH and 234 PT-PLWH were evaluable
- 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 month [1.0; 2.1] (Figure 2). All TN-PLWH (N=51) using DTG/3TC attained a virological suppression during the 2-year follow-up (maximum time to virological suppression: 12.4 months), and there were no TN-PLWH with virological failure (VF) during the 2-year follow-up
- 2 years after switch to DTG/3TC, 222 (94.8%) PT-PLWH maintained a VL<50 c/mL (Figure 3)
- During the follow-up, 12 PT-PLWH did not maintain a VL<50 c/mL:
  - 6 were due to intermittent viraemia (*PLWH with VL <50 c/mL at most measurements, without 2 consecutive VL measurements ≥50 c/mL and without blip >200 c/mL*)
  - 6 were due to VF, with a median time to VF of 9.6 months [7.2; 15.1]. Among these 6 patients with VF, a genotypic resistance test was available for 2 patients, of whom 1 developed 3TC resistance (M184V/I) due to non-adherence (declarative non-adherence; VL=387 c/mL); 4 of the 6 patients with VF discontinued DTG/3TC
- In patients who were evaluable, CD4+ cell count was ≥500 cells/mm^3 at 2 years for 81.8% (N=18) of TN-PLWH vs 48.1% (N=26) at baseline and 81.0% (N=85) for PT-PLWH vs 79.1% (N=185) at baseline

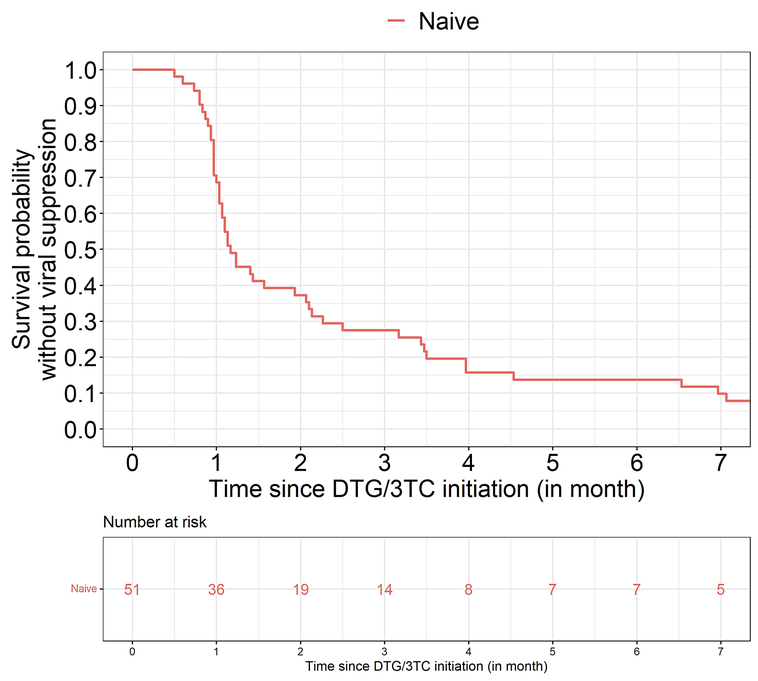
Study treatment discontinuations and safety

- Overall, DTG/3TC was discontinued in 56 PLWH:
  - 7 TN-PLWH: 5 due to patient choice (71.4%) and 2 for safety reasons (28.6%)
  - 49 PT-PLWH: 31 due to patient choice (64.6%), 13 for safety reasons (27.1%), 4 for VF (8.3%), and 1 for data missing
- Safety cases leading to DTG/3TC discontinuation are presented in Table 1
- 19 PLWH who discontinued DTG/3TC were switched to long-acting injectable cabotegravir + rilpivirine (CAB/RPV-LA) and 6 to oral-form cabotegravir + rilpivirine (CAB/RPV-OF); all these switches were upon patient request

Body weight

- Median change in body weight over the first 2 years was 0.5 kg in TN-PLWH (IQR -2.0 to +2.0; N=33) and 0.0 kg in PT-PLWH (IQR -3.0 to +2.0; N=170). Table 2 presents changes in body weight

Figure 2. Kaplan-Meier of the Time to Virological 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

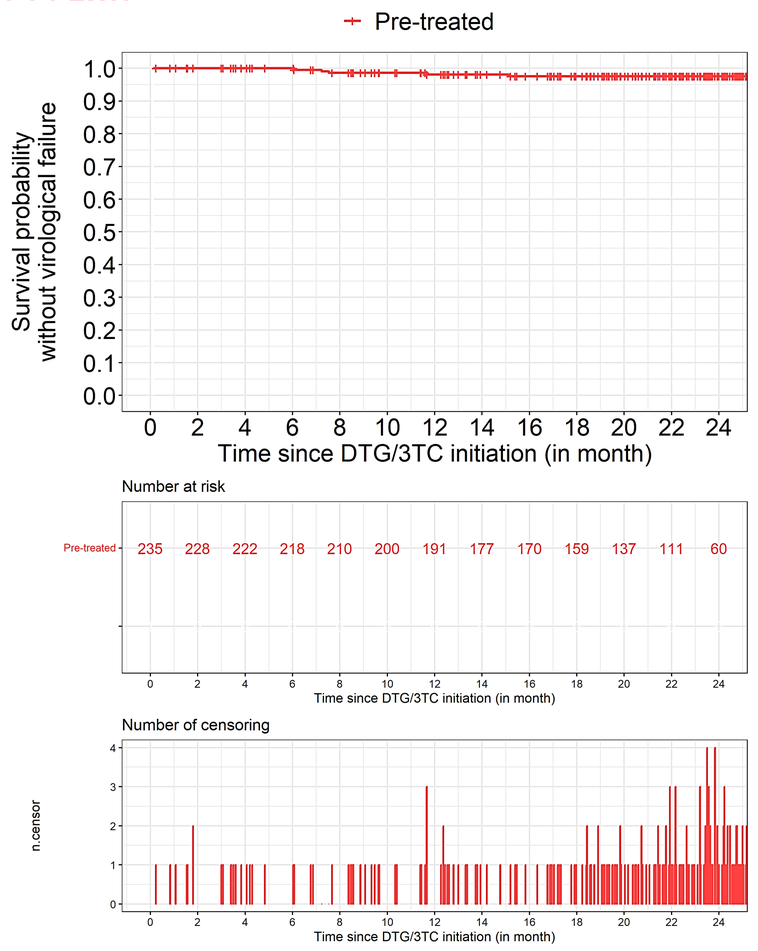


Table 1. Safety Cases Leading to DTG/3TC Discontinuation for TN-PLWH and PT-PLWH

Adverse events (AEs)*	TN-PLWH (N=56)	PT-PLWH (N=248)
Musculoskeletal and connective tissue disorders	0	7 (2.8%)
General disorders and administration site conditions	0	5 (2.0%)
Nervous system disorders	1 (1.8%)	5 (2.0%)
Investigations	1 (1.8%)	4 (1.6%)
Psychiatric disorders	0	4 (1.6%)
Gastrointestinal disorders	1 (1.8%)	3 (1.2%)
Hepatobiliary disorders	0	3 (1.2%)
Infections and infestations	0	3 (1.2%)
Injury, poisoning, and procedural complications	0	3 (1.2%)
Metabolism and nutrition disorders	1 (1.8%)	3 (1.2%)
Vascular disorders	0	2 (0.8%)
Ear and labyrinth disorders	0	1 (0.4%)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	0	1 (0.4%)
Skin and subcutaneous tissue disorders	0	1 (0.4%)
Social circumstances	0	1 (0.4%)

*MedDRA classification.

Table 2. Change in Body Weight

		TN-PLWH (N=33)	PT-PLWH (N=170)
Change in body weight between last weight (more than 18 months) and baseline weight (in kg)	Missing value	9	23
	N	24	147
	Mean (±SD)	-0.1 (±4.0)	0.0 (±5.7)
	Median [Q1-Q3]	0.5 [-2.0; 2.0]	0.0 [-3.0; 2.0]
	Range	-10.0 / 6.0	-17.0 / 26.0

Conclusions

- Based on 2-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 6 in PT-PLWH during the 2-year follow-up
- DTG/3TC was discontinued in 56 PLWH; most discontinuations were due to patient choice to switch to CAB/RPV-LA
- In patients who were evaluable during the 2-year follow-up, DTG/3TC had no significant impact on body weight
- **These real-world data demonstrated high virological success after 2 years on DTG/3TC in both TN-PLWH and PT-PLWH populations, without significant weight change. The main reason for DTG/3TC discontinuation was due to patient request to switch to CAB/RPV-LA**

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References: 1. Figueroa et al. IAS 2017; Paris, France. Poster MOPEB0287. **2.** Joly et al. EACS 2017; Milan, Italy. Poster PE9/11. **3.** An Efficacy, Safety, and Tolerability Study Comparing Dolutegravir Plus Lamivudine With Dolutegravir Plus Tenofovir/Emtricitabine in Treatment naïve HIV Infected Subjects (Gemini 1). Retrieved November 24, 2017.

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