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Key Takeaways

- An exploratory analysis compared low-level viremia and lymphocyte outcomes in virologically suppressed people with HIV (PWH) receiving either long-acting cabotegravir + rilpivirine (CAB + RPV LA) intramuscular injections every 2 months (Q2M IM), CAB + RPV LA injections every 1 month (Q1M IM), or daily oral abacavir/dolutegravir/lamivudine (ABC/DTG/3TC)
- Low and comparable numbers of “blips” of temporarily increased viral load were experienced by participants receiving Q2M IM, Q1M IM, and ABC/DTG/3TC across study visits in ATLAS-2M and FLAIR; blips were not associated with virologic failure and did not affect overall proportions maintaining virologic suppression
- Long-acting Q2M IM and Q1M IM HIV-1 RNA blip, low-level viremia (HIV-1 RNA <40 c/mL and target not detected [TND], and/or HIV-1 RNA <2 c/mL), and CD4+/CD8+ ratio outcomes were similar to those with daily oral ABC/DTG/3TC through at least 96 weeks

Introduction

- CAB + RPV LA is the only long-acting therapy approved for maintenance of viral suppression in PWH who are already virologically suppressed^{1,2}
- Non-inferiority of CAB + RPV LA administered Q2M IM to Q1M IM through Week 152 was demonstrated in the phase 3b ATLAS-2M study,³ and non-inferiority of CAB + RPV LA administered Q1M IM to daily oral ABC/DTG/3TC through Week 96 was demonstrated in the phase 3 FLAIR study⁴
- Week 48 study data showed that the proportion of participants with HIV-1 RNA blips (single HIV-1 RNA values between 50 to <200 c/mL with adjacent values <50 c/mL), TND, and HIV-1 RNA <2 c/mL were similar in the CAB + RPV LA (Q2M IM and Q1M IM) and daily oral ABC/DTG/3TC groups⁵
- Blips were not associated with developing confirmed virologic failure (CVF), defined as 2 consecutive HIV-1 RNA ≥200 c/mL
- Here we report HIV-1 RNA blip, TND, HIV-1 RNA <2 c/mL, and CD4+/CD8+ ratio data and the impact of HIV-1 RNA blips on CVF through Week 96 in the FLAIR study and Week 152 in the ATLAS-2M study

Methods

- ATLAS-2M and FLAIR are phase 3b and 3, respectively, randomized (1:1), open-label studies assessing efficacy and safety of CAB + RPV LA (Q2M IM or Q1M IM); the primary endpoint of each was the proportion of participants with HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot, ITT-E)
- Eligible participants were aged ≥18 years with HIV-1 and were either virologically suppressed (HIV-1 RNA <50 c/mL) at randomization with no history of virologic failure (ATLAS-2M), or treatment naive (FLAIR)
- Participants were given IM injections of CAB LA 600 mg + RPV LA 900 mg Q2M (ATLAS-2M Q2M IM group) or CAB LA 400 mg + RPV LA 600 mg Q1M (ATLAS-2M and FLAIR Q1M IM groups) as maintenance doses or remained on current antiretroviral regimen (FLAIR ABC/DTG/3TC group)
- CAB + RPV LA-naïve participants received a 4-week oral lead-in of daily CAB 30 mg + RPV 25 mg
- This exploratory study quantitatively and qualitatively analyzed plasma HIV-1 RNA samples from participants from baseline through Week 96 in the FLAIR study and from baseline through Week 152 in the ATLAS-2M study
- Quantitative blips and qualitative TD/TND outcomes were assessed using Abbott RealTime HIV-1 assay (Abbott Molecular Inc, Des Plaines, IL), low-copy HIV-1 RNA (<2 c/mL) was assessed using bioMONTR Labs HIV-1 SuperLow Assay (Research Triangle Park, NC), and lymphocyte subsets were assessed using flow cytometry (Q2 Solutions, Durham, NC)

Results

- The proportion of participants with at least 1 HIV-1 blip was similar between the CAB + RPV LA Q2M IM and Q1M IM groups at Week 152 in ATLAS-2M and between the Q1M IM CAB + RPV LA and ABC/DTG/3TC groups at Week 96 in FLAIR
- In the ATLAS-2M Q2M IM and Q1M IM groups, 11/522 (2%) and 2/523 (<1%) participants met CVF criteria through Week 152, respectively
- Most CVFs in ATLAS-2M occurred by Week 48 (10/13 [77%]); 12/13 participants resuppressed on alternative treatment regimens (1 participant was non-adherent to a protease inhibitor-based regimen)
- In FLAIR, 4/283 (1%) participants in the Q1M IM group and 4/283 (1%) in the ABC/DTG/3TC group met CVF criteria through Week 96
- In the FLAIR Q1M IM group, 1 participant had oral CAB/RPV dosing interrupted due to a false-positive pregnancy test; upon re-initiation of oral therapy, a suspected virologic failure was confirmed

Table 1. Participants With Blips and/or CVF at Week 152 (ATLAS-2M; ITT-E) or Week 96 (FLAIR; ITT-E)

Parameter, n/N (%)	ATLAS-2M (Week 152)		FLAIR (Week 96)	
	Q2M IM	Q1M IM	Q1M IM	ABC/DTG/3TC
Participants with blips ^a	42/522 (8)	48/523 (9)	45/283 (16)	48/283 (17)
CVF ^b in participants with blips	1/42 (2) ^c	0/48	0/45	1/48 (2)

CVF, confirmed virologic failure; IM, intramuscular; Q1M, monthly dosing. ^aDefined as HIV-1 RNA values between 50 to <200 c/mL and adjacent HIV-1 RNA values <50 c/mL. ^bDefined as 2 consecutive HIV-1 RNA ≥200 c/mL. ^cParticipant met CVF criteria at Week 24.

- At Week 152 in ATLAS-2M and Week 96 in FLAIR, the proportions of participants with HIV-1 RNA <50 c/mL were generally similar between treatment groups, regardless of whether participants had blips
- Few participants with HIV-1 RNA blips had viral loads ≥50 c/mL

Figure 1. Snapshot Outcomes by Presence of Blips in ATLAS-2M at Week 152 (ITT-E)

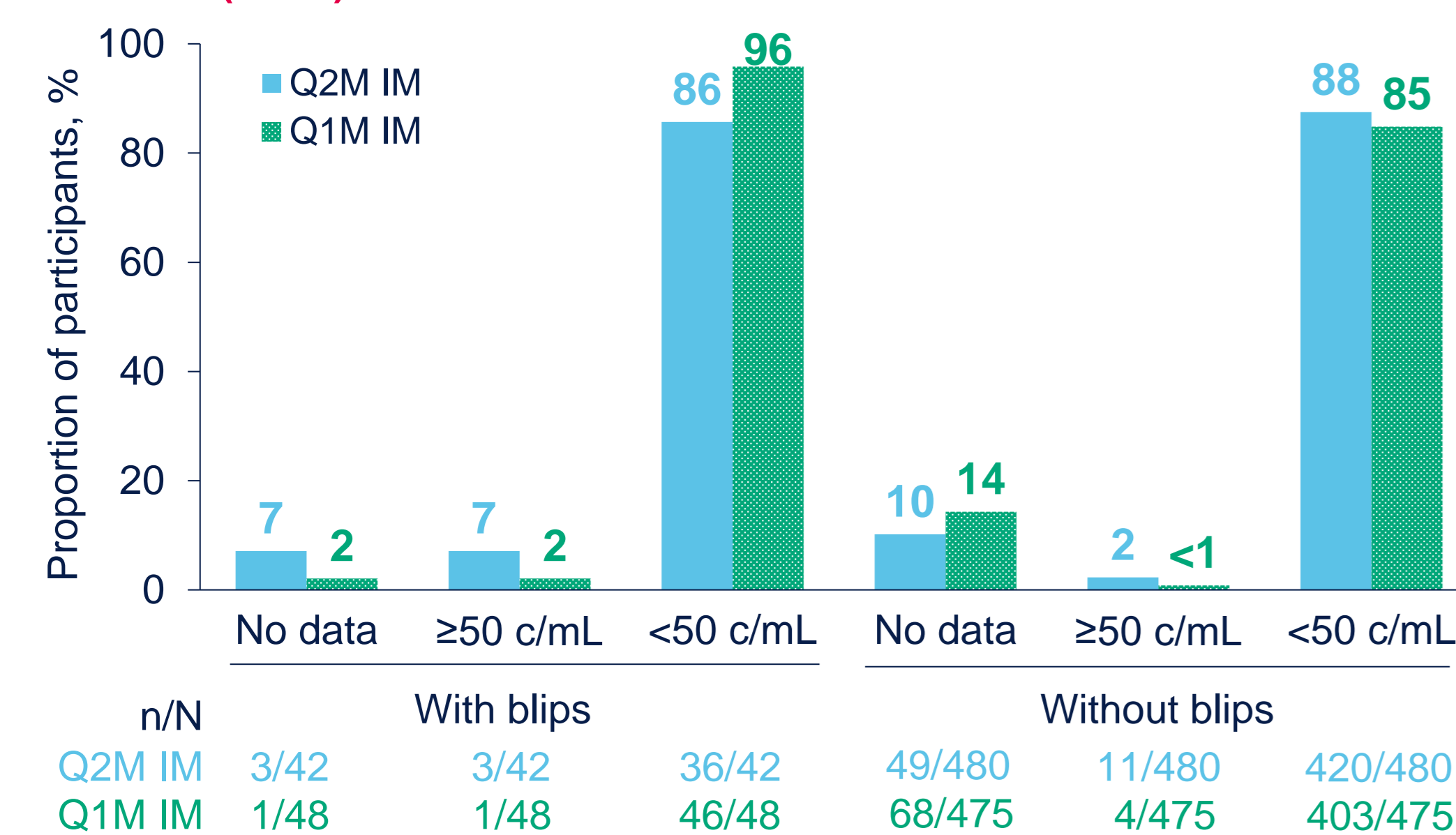
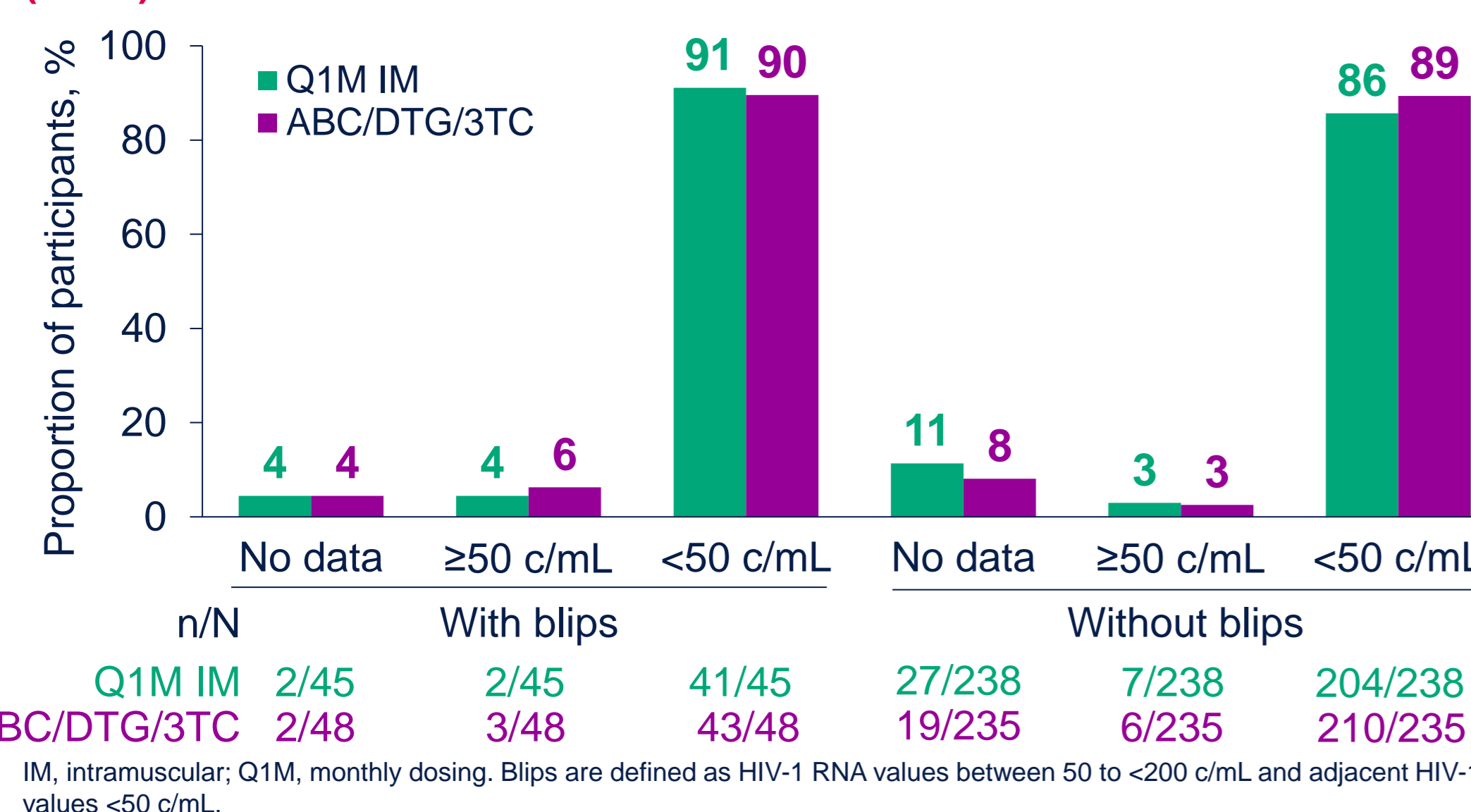


Figure 2. Snapshot Outcomes by Presence of Blips in FLAIR at Week 96 (ITT-E)



- Proportions of participants with blips were consistently <4% of participants with available data across all studies and treatment groups at any time point

Low-Level Viremia Outcomes

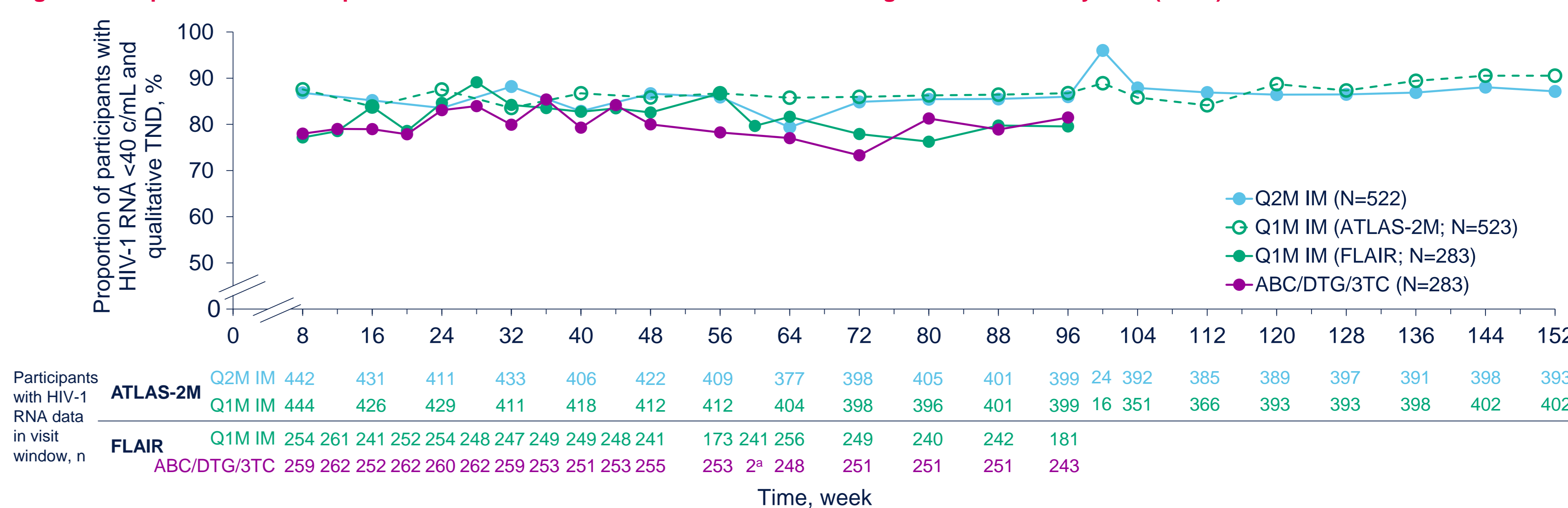
- In each scheduled visit window, >70% of participants had HIV-1 RNA <40 c/mL and qualitative TND outcomes across all studies and treatment groups
- The proportion of participants with HIV-1 RNA <2 c/mL was comparable between groups through Week 152 in ATLAS-2M and between groups through Week 96 in FLAIR

Figure 3. Proportion of Participants With Blips by Visit (ITT-E)



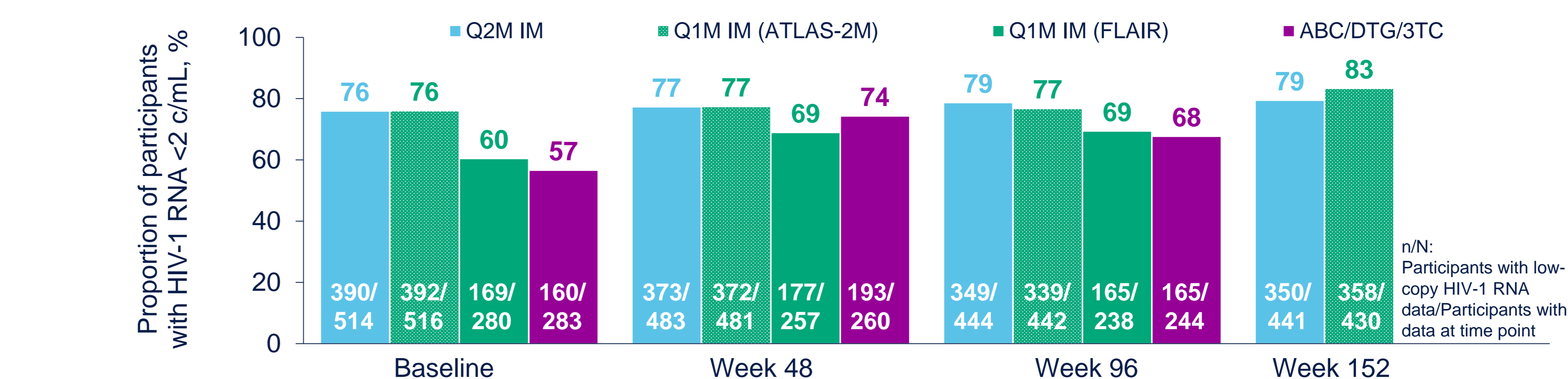
IM, intramuscular; Q1M, monthly dosing. Blips are defined as HIV-1 RNA values between 50 to <200 c/mL and adjacent HIV-1 RNA values <50 c/mL. Week 8 is the first maintenance week; Weeks 0-4 are the induction period. *Week 60 was not a scheduled HIV-1 RNA assessment visit for participants in the ABC/DTG/3TC group; 0/3 ABC/DTG/3TC participants with HIV-1 RNA data had a blip at Week 60 (not plotted above).

Figure 4. Proportions of Participants With HIV-1 RNA <40 c/mL and Qualitative Target Not Detected by Visit (ITT-E)



IM, intramuscular; TND, target not detected; Q1M, monthly dosing. Blips are defined as HIV-1 RNA values between 50 to <200 c/mL and adjacent HIV-1 RNA values <50 c/mL. Week 8 is the first maintenance week; Weeks 0-4 are the induction period. *Week 60 was not a scheduled HIV-1 RNA assessment visit for participants in the ABC/DTG/3TC group; 1/2 (50%) ABC/DTG/3TC participants with HIV-1 RNA data at Week 60 had HIV-1 RNA <40 c/mL and qualitative TND (not plotted above).

Figure 5. Proportions of Participants With Low-Copy (<2 c/mL) Plasma HIV-1 RNA (ITT-E)



- CD4+/CD8+ ratios were similar at individual study visits between treatment groups and in those with vs without blips
- Mean (SD) ratios in the Q2M IM and Q1M IM groups in ATLAS-2M increased from baseline to Week 152 (with blips: 0.93 [0.48] to 1.09 [0.58] and 1.21 [0.63] to 1.38 [0.81], respectively; without blips, 1.07 [0.51] to 1.14 [0.53] and 1.11 [0.61] to 1.23 [0.70], respectively)
- Mean (SD) ratios in the Q1M IM and ABC/DTG/3TC groups in FLAIR increased from baseline to Week 96 (with blips: 0.78 [0.45] to 1.08 [0.57] and 0.75 [0.43] to 0.97 [0.56], respectively; without blips, 0.83 [0.41] to 1.12 [0.50] and 0.84 [0.41] to 1.08 [0.47], respectively)

Conclusions

- The proportion of participants with HIV-1 RNA blips, TND, HIV-1 RNA <2 c/mL, and mean CD4+/CD8+ ratio (with and without blips) was similar between the Q2M IM and Q1M IM CAB + RPV LA groups through Week 152 in ATLAS-2M and between the Q1M IM CAB + RPV LA and oral ABC/DTG/3TC groups through Week 96 in FLAIR
- The number of CVFs in ATLAS-2M and FLAIR is low and the presence of HIV-1 RNA blips was not associated with CVF development through Week 152 and Week 96, respectively
- Of the 17 total CVFs on CAB + RPV LA, only 1 had a transient blip; these data and the overall rate of blips being similar support that blips alone do not identify those at risk of CVF
- These data support the robustness of CAB + RPV LA for the maintenance of virologic suppression in PWH