

Paul Benn,¹ Romina Quercia,¹ Krischan Hudson,² Yuanyuan Wang,³ Vasiliki Chounta,¹ Christine Talarico,² Susan Ford,² Amy Cutrell,² David A. Margolis,² Rodica Van Solingen-Ristea,⁴ Simon Vanveggel,⁴ Veerle Van Eygen,⁴ Joseph W. Polli,² Annemiek de Ruiter,¹ Kimberly Smith,² William R. Spreen²

¹ViiV Healthcare, Brentford, UK; ²ViiV Healthcare, Research Triangle Park, NC, USA; ³GlaxoSmithKline, Collegeville, PA, USA; ⁴Janssen Research & Development, Beerse, Belgium

Introduction

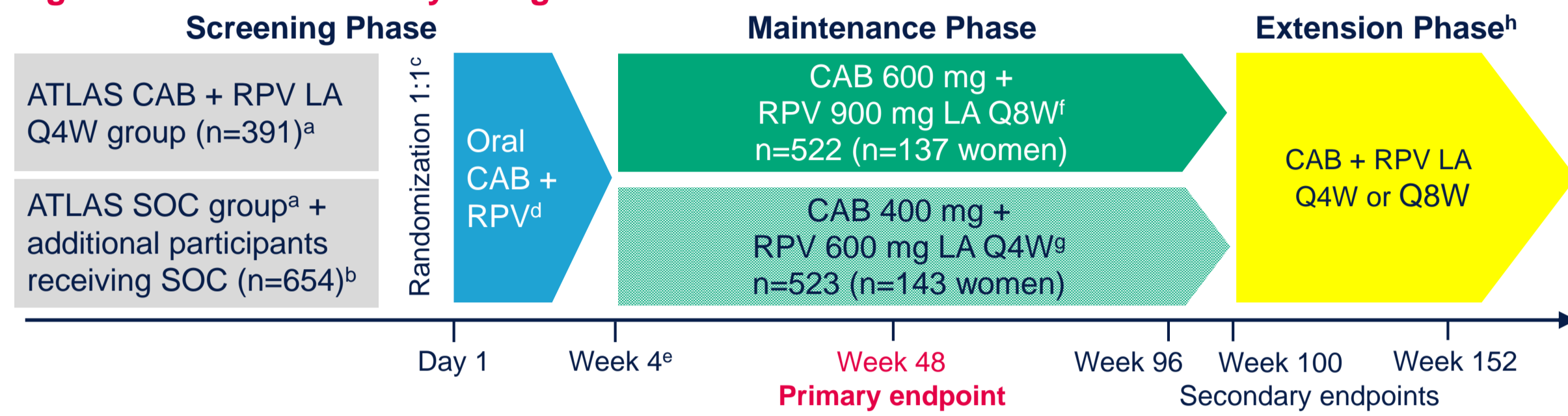
- LA injectable CAB + RPV provides a highly effective ART regimen with the potential to improve treatment convenience, adherence, and quality of life for people living with HIV-1¹
- CAB + RPV LA Q4W demonstrated noninferiority vs daily oral ART in the phase III ATLAS and FLAIR studies^{2,3}
- CAB + RPV LA dosing Q8W demonstrated noninferiority vs Q4W dosing in the ATLAS-2M study for maintenance of virologic suppression⁴
- Although >50% of people living with HIV are women, they are often under-represented in HIV ART clinical trials^{5,6}
- This analysis examines the efficacy, safety, and treatment satisfaction outcomes for the women participating in the ATLAS-2M study vs men at Week 48

Methods

Study Design

- Subgroup analyses were performed on the primary and secondary endpoints (Figure 1) of the ATLAS-2M study by sex at birth
- Differences between Q8W and Q4W groups for women and men in snapshot analyses were based on Cochran-Mantel-Haenszel stratified analysis and adjusted for prior exposure to CAB + RPV

Figure 1. ATLAS-2M Study Design



*Participants from ATLAS must have been taking CAB + RPV LA Q4W or a current ART regimen through at least Week 52 with HIV-1 RNA <50 c/mL at screening. *Participants receiving SOC not from ATLAS must have been taking an uninterrupted ART regimen ≥6 mo prescreening with ≥2 HIV-1 RNA measurements <50 c/mL in the 12 mo prescreening (one between 12 and 6 mo and one ≤6 mo of screening). Exclusion criteria: history of virologic failure or evidence of viral resistance. *Randomization stratified by prior CAB + RPV exposure. *Except those from ATLAS on LA therapy. *Tolerability in participants on oral lead-in ART assessed at Week 4. *After oral lead-in period, participants in the Q8W group received intramuscular injections at Weeks 4 and 8, then Q8W thereafter. *In participants in the Q4W group with oral lead-in, first LA dose was CAB 600 mg + RPV 900 mg. *Optional extension phase to continue randomized CAB + RPV LA Q4W or Q8W at Week 100.

Results

Baseline Characteristics

- Baseline characteristics were similar between women and men in Q8W and Q4W groups (Table 1)

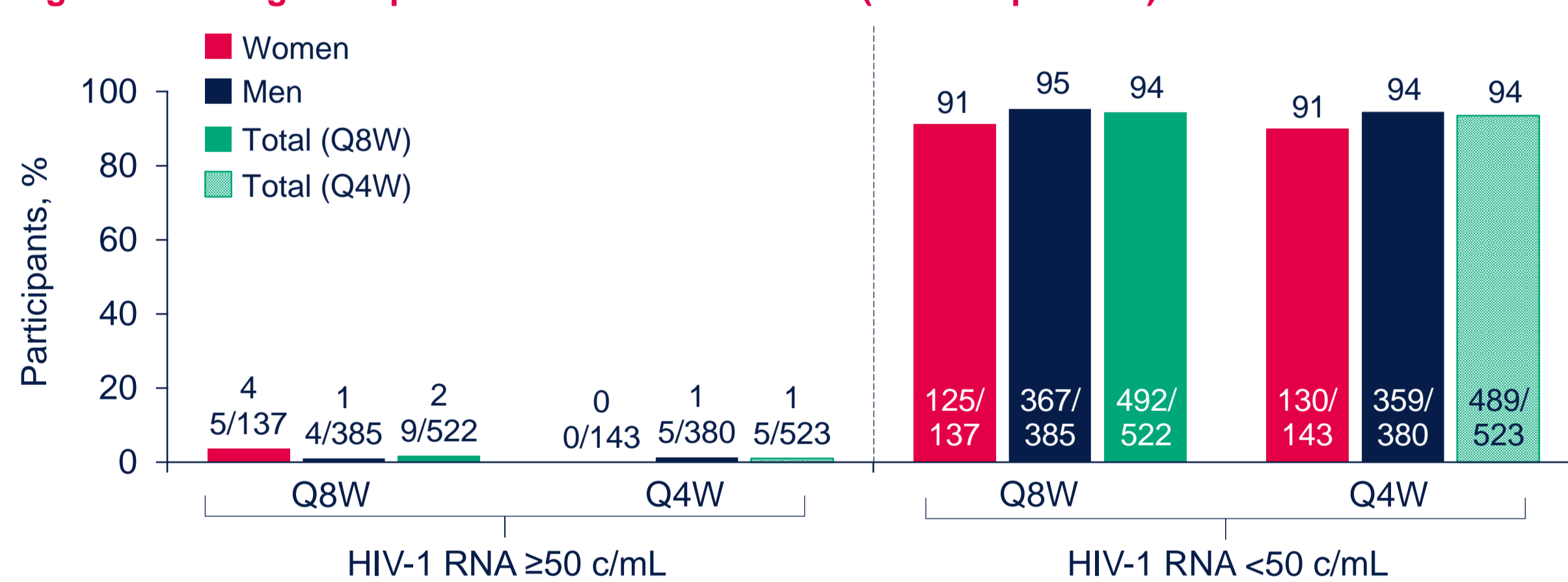
Table 1. Baseline Characteristics (ITT-E Population)

Characteristic	Q8W (N=522)		Q4W (N=523)	
	Women	Men	Women	Men
Sex at birth, n (%)	137 (26)	385 (74)	143 (27)	380 (73)
Mean age, y	46	42	44	42
Black/African American, n (%)	52 (38)	49 (13)	54 (38)	36 (9)
BMI, median (IQR), kg/m ²	27 (23-32)	25 (23-28)	27 (23-32)	26 (23-28)
≥30 kg/m ² , n (%)	52 (38)	61 (16)	42 (29)	56 (15)
Prior CAB + RPV exposure, n (%)	64 (47)	131 (34)	68 (48)	128 (34)

Snapshot Outcomes at Week 48

- Proportions of women and men with HIV-1 RNA ≥50 c/mL were similar between groups (adjusted differences [95% CI], 3.5% [0.4 to 6.6] for women and -0.3% [-1.8 to 1.3] for men; Figure 2)
- HIV-1 RNA <50 c/mL was maintained in the majority of women and men in each group (adjusted differences [95% CI], 0.4% [-6.2 to 7.1] for women and 0.8% [-2.3 to 4.0] for men)

Figure 2. Virologic Snapshot Outcomes at Week 48 (ITT-E Population)



Other Virologic Outcomes

- The proportion of women and men with HIV-1 RNA <2 c/mL was similar at baseline and at Week 48 across both groups. At baseline, 81% (109/135) Q8W and 83% (116/139) Q4W of women and 74% (281/379) Q8W and 73% (276/377) Q4W of men had HIV-1 RNA <2 c/mL, respectively. At Week 48, 81% of women (Q8W, 96/119; Q4W, 105/129) and 76% of men (Q8W, 277/364; Q4W, 267/352) in both arms had HIV-1 RNA <2 c/mL

Confirmed Virologic Failure

- 8 (1.5%) and 2 (<1%) participants in the Q8W and Q4W groups had CVF, with 5/8 (Q8W) and 0/2 (Q4W) occurring in women (Table 2)
- On baseline PBMC DNA samples, 3/5 and 1/5 women with CVF had only RPV and both RPV and INSTI RAMs, respectively
- 4/5 women with CVF were subsequently suppressed on oral ART and 1/5 had continued low-level viral replication due to poor adherence on a boosted PI regimen

Table 2. Women Receiving CAB + RPV LA Q8W with CVF^a at Week 48

Country (HIV-1 subtype)	SVF, wk	VL at SVF/CVF, c/mL	Baseline RAM ⁷ (PBMC/HIV-1 DNA; Day 1)		SVF timepoint RAM ⁷ (HIV-1 RNA)		Drug sensitivity at SVF, FC ^b		
			RT	IN	RT	IN	RPV	CAB	DTG
South Africa (Complex)	8	267/2355	V108V/I Y181Y/C H221H/Y	None	K103N	None	2.4	1.1	0.9
South Africa (C)	16	938/2374	Y188Y/F/H/L	G140G/R	Y188L	Q148Q/R N155N/H	6.8	2.6	1.3
Russia (A1)	16	141,132/19,099	None	None	K101E	Q148R	4.7	9.1	1.6
Canada (A1)	24	16,205/874	Y188L P225H	None	Y188L P225H	NA ^c	15.0	NA ^c	NA ^c
Russia (A)	24	211,639/38,015	E138E/A	None	K101E E138A	N155H	2.6	7.0	2.2

FC, fold-change; RAM, resistance-associated mutation; RT, reverse transcriptase; SVF, suspected virologic failure. *CVF=2 consecutive plasma HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL. *Monogram biologic/clinical cutoffs: RPV=2.0, CAB=2.5, DTG=4.0. *Integrase analysis failed.

Pharmacokinetics

- CAB and RPV plasma median concentrations in women were generally >1× and 4× PA-IC₉₀ values through Week 48 and within the same range as concentrations in men⁸
- Plasma CAB and RPV concentrations for the 5 women with CVF were generally below the population median but within the range of exposures that showed efficacy in most participants

Safety and Tolerability

- Overall AE types were similar between treatment groups and sexes (Table 3)
- Rates of any AE and drug-related AEs were numerically lower in women vs men

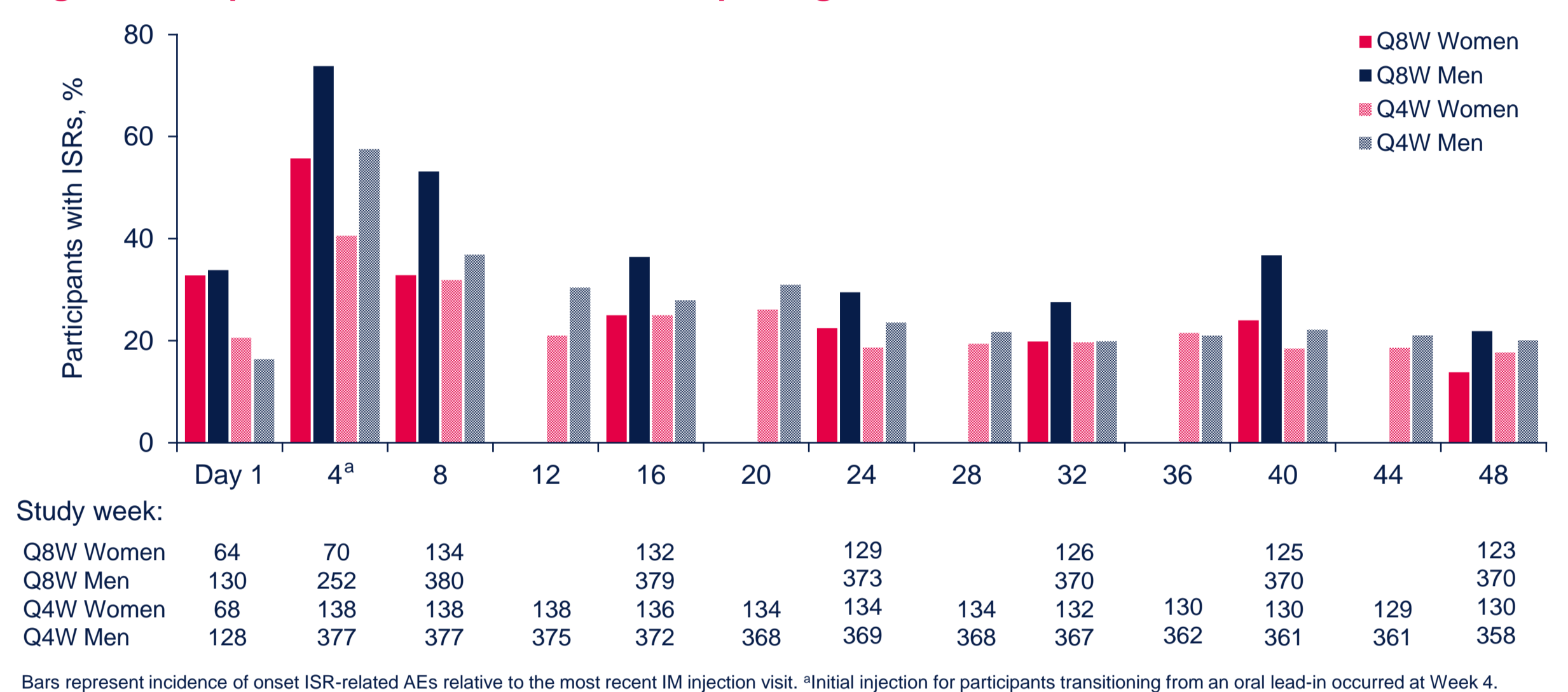
Table 3. Summary of AEs, Including ISRs

Event	Q8W (N=522)		Q4W (N=523)	
	Women (n=137)	Men (n=385)	Women (n=143)	Men (n=380)
Any AE	116 (85)	357 (93)	125 (87)	357 (94)
Drug-related AE ^a	88 (64)	312 (81)	97 (68)	302 (79)
SAE	6 (4)	21 (5) ^b	6 (4)	13 (3)
Drug related ^c	2 (1)	1 (<1)	1 (<1)	0
AE leading to withdrawal ^d	5 (4)	7 (2)	5 (3)	8 (2)
ISR event/Injection ^{e,f}	477/2124 (23)	2030/6346 (32)	809/4191 (19)	2343/11,520 (20)
Grade ≥3 ^{f,g}	9 (<1)	34 (1)	9 (<1)	39 (<1)
ISR leading to withdrawal ^h	3 (<1)	8 (<1)	2 (<1)	12 (<1)

^aHigh proportion of drug-related AEs associated with ISRs. ^bOne fatal SAE not considered drug related. ^cDrug-related SAEs were injection-site abscess, presyncope, acute pancreatitis, and hypersensitivity. ^dNon-ISR AEs leading to withdrawal occurred in 1 participant each, except for fatigue (1 in Q8W and 2 in Q4W), abnormal dreams and hyperhidrosis (2 in Q4W), and acute hepatitis B, headache, presyncope, and pyrexia (1 each in Q8W and Q4W). ^eMost commonly reported ISRs were pain, induration, and nodule formation. ^fPercentages calculated from total injections. ^gNo grade 4/5 ISRs were reported. ^hPercentages calculated from total ISR events.

- ISRs per injection tended to be lower in women vs men, and the proportion of participants with ISRs generally decreased over time through Week 48 in both sexes (Figure 3)
- 98% of ISRs were grade 1/2 with a median duration of 3 days in both treatment groups
- Adherence rates to injection visits within the allowable ±7-day window were 98% overall, 99% in women, and 98% in men

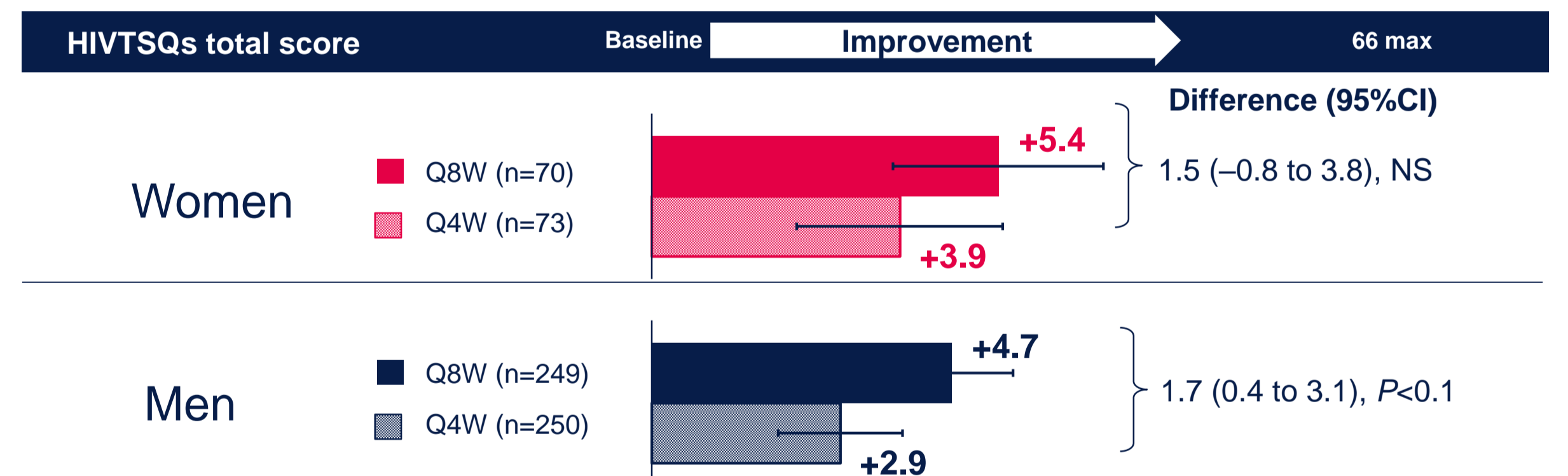
Figure 3. Proportion of Women and Men Reporting ISRs Over Time



Patient-Reported Outcomes

- Women and men with no prior CAB + RPV LA exposure reported improvement from baseline in treatment satisfaction at Week 48 (Figure 4)
- Treatment satisfaction for women and men with prior CAB + RPV exposure was high at baseline and remained high through Week 48

Figure 4. Mean Change From Baseline in HIVTSQs Total Score^a at Week 48 in Women and Men Without Prior CAB + RPV LA Exposure



^aAdjusted for baseline score, age, and race. Error bars show 95% CI.

- Participants with no prior CAB + RPV LA exposure reported increases from baseline in treatment acceptance (mean changes from baseline at Week 48, 6.0 vs 9.4 [women] and 7.1 vs 4.6 [men]) in Q8W vs Q4W, respectively
- Men and women with prior CAB + RPV exposures maintained high treatment acceptance scores over time through Week 48
- The majority of women in Q8W group with prior CAB + RPV exposure preferred Q8W dosing (56/64 [88%]) vs Q4W (5/64 [8%]) and oral (1/64 [2%]) dosing
- Increased convenience/ease to integrate into daily life was cited as a key benefit for Q8W in 73% (41/56)

Conclusions

- CAB + RPV LA Q8W and Q4W demonstrated high and similar rates of efficacy in women and men⁴
- Rates of CVF were low and similar for women and men; 4/5 CVFs in women (Q8W) had archived preexisting resistance
- Multivariable analysis across ATLAS, FLAIR, and ATLAS-2M phase III studies (n=1039) suggests that reasons for CVF are multifactorial and that ≥2 baseline factors (baseline RPV RAMs, subtypes A1/A6, and BMI ≥30 kg/m²) were associated with an increased risk of CVF
- Female sex at birth and Q4W or Q8W dosing had no significant association with CVF in this analysis⁹
- Q8W and Q4W dosing were generally well tolerated among women, with treatment discontinuations due to ISRs being low among both women and men
- Treatment satisfaction was high with Q8W and Q4W LA dosing for both sexes, with women expressing preference for Q8W compared with Q4W and daily oral dosing¹⁰
- These results support the therapeutic potential of CAB + RPV LA Q8W in women

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