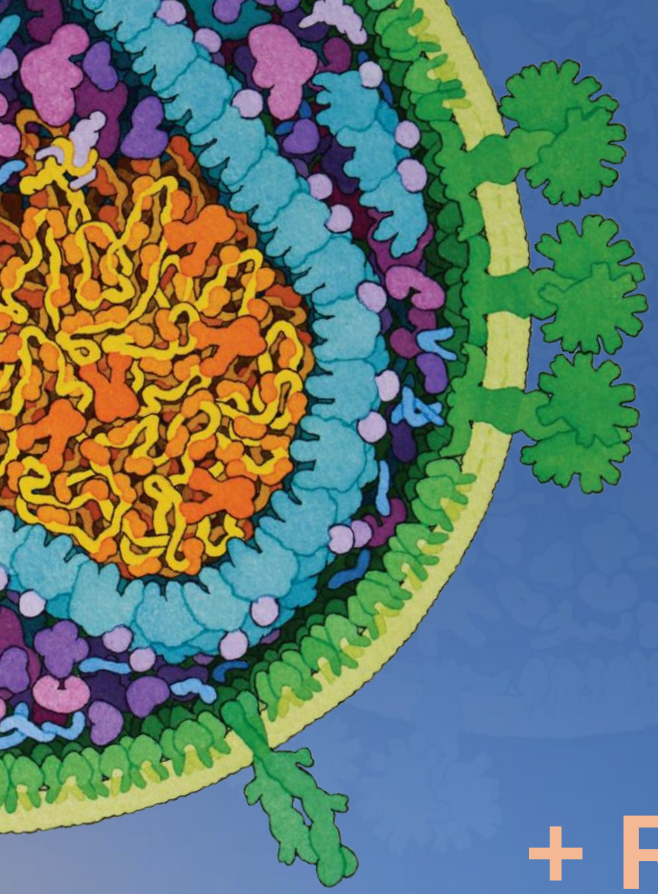

SCIENCE SPOTLIGHT™

RENAL/BONE OUTCOMES AFTER LONG-ACTING CABOTEGRAVIR + RILPIVIRINE IN ATLAS + ATLAS-2M

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Disclosure: *Employee of ViiV Healthcare and stockholder of GlaxoSmithKline

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Renal and Bone Outcomes: Background

- Cabotegravir (CAB), an INSTI, and rilpivirine (RPV), an NNRTI, have been approved in the US, Canada, and Europe as the first complete long-acting (LA) injectable regimen indicated for the maintenance of virologic suppression in PLWH[1–3]
- Tenofovir disoproxil fumarate (TDF) has been associated with renal and bone toxicities. Improvements in renal and bone markers have been reported after cessation of TDF regimens in PLWH[4]
- We present data from Week 48 of the ATLAS (NCT02951052) and ATLAS-2M (NCT03299049) studies examining changes in renal markers and bone turnover markers for participants switching from TDF and non-TDF regimens to CAB + RPV LA or continuing their prior antiretroviral regimen (SoC)

INSTI, integrase strand transfer inhibitor; PLWH, people living with HIV-1; NNRTI, non-nucleoside reverse transcriptase inhibitor; SoC, standard of care.

1. ViiV Healthcare. Cabotegravir extended-release injectable suspension; rilpivirine extended-release injectable suspension (Cabenuva) Prescribing Information. US, January 2021.
2. ViiV Healthcare. Vocabria Summary of Product Characteristics. EU, January 2020.
3. ViiV Healthcare. Vocabria (cabotegravir tablets) and Cabenuva (cabotegravir and rilpivirine extended release injectable suspensions) Product Monograph. Canada, March 2020.
4. Casado JL. AIDS Rev. 2016;18(2):59–68.

Renal and Bone Outcomes: Methods

- Data from ATLAS and ATLAS-2M were stratified by TDF use at baseline
  - Data from ATLAS-2M participants who transitioned to ATLAS-2M from CAB + RPV in ATLAS were excluded. This ensured all participants included in this analysis had only 48 weeks of CAB + RPV follow-up
  - Eligible participants had an estimated creatinine clearance ≥50 mL/min/1.73 m^2
- Outcomes assessed at Week 48 included:
  - Changes in renal markers
    - Dipstick proteinuria
    - Urine protein-to-creatinine ratio (UPCR)
    - Urine albumin-to-creatinine ratio (UACR)
  - Changes in bone turnover markers (available only for ATLAS participants)
    - Bone formation: bone-specific alkaline phosphatase, osteocalcin, and procollagen 1 N-terminal propeptide
    - Bone resorption: type 1 collagen C telopeptides
  - Overall safety
    - Incidence and severity of AEs
    - Renal- and bone-related AEs

AE, adverse event; CAB, cabotegravir; LA, long-acting; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate.

Renal and Bone Outcomes: Baseline Characteristics (1/2)

Baseline parameter, n (%)	TDF at baseline			No TDF at baseline		
	CAB + RPV LA Q8W, n=151	CAB + RPV LA Q4W, n=333	SoC n=181	CAB + RPV LA Q8W, n=176	CAB + RPV LA Q4W, n=302	SoC n=127
Female (sex at birth)	39 (26)	106 (32)	67 (37)	34 (19)	68 (23)	37 (29)
Age, mean (range, years)	43 (21–71)	42 (19–68)	44 (18–72)	43 (20–83)	42 (21–74)	43 (25–82)
Race						
Black/African American	31 (21)	75 (23)	63 (35)	26 (15)	32 (11)	14 (11)
White	102 (68)	217 (65)	104 (57)	136 (77)	253 (84)	103 (81)
Other	18 (12)	41 (12)	14 (8)	14 (8)	17 (6)	10 (8)
Third agent class						
INI	31 (21)	76 (23)	44 (24)	105 (60)	167 (55)	55 (43)
NNRTI	101 (67)	224 (67)	117 (65)	50 (28)	87 (29)	38 (30)
PI	19 (13)	33 (10)	20 (11)	21 (12)	48 (16)	34 (27)

CAB, cabotegravir; INI, integrase inhibitor; LA, long-acting; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SoC, standard of care; TDF, tenofovir disoproxil fumarate.

Renal and Bone Outcomes: Baseline Characteristics (2/2)

Baseline parameter, n (%)	TDF at baseline			No TDF at baseline		
	CAB + RPV LA Q8W, n=151	CAB + RPV LA Q4W, n=333	SoC n=181	CAB + RPV LA Q8W, n=176	CAB + RPV LA Q4W, n=302	SoC n=127
Musculoskeletal and connective tissue disorder	26 (17)	61 (18)	33 (18)	30 (17)	49 (16)	18 (14)
Renal and urinary disorder	8 (5)	12 (4)	5 (3)	8 (5)	23 (8)	10 (8)
eGFR, mL/min/1.73 m^2						
60–<90	50 (33)	81 (24)	40 (22)	65 (37)	95 (31)	28 (22)
≥90	100 (66)	249 (75)	140 (77)	109 (62)	203 (67)	94 (74)
UACR, mean (SD) (normal range, <3 mg/mmol)	1.4 (2.4)	1.4 (2.7)	2.4 (9.8)	1.2 (2.9)	0.8 (1.3)	1.5 (4.9)
UPCR, mean (SD) (normal range, <15 mg/mmol)	12.6 (9.7)	11.9 (9.4)	14.6 (18.0)	8.3 (6.1)	8.3 (5.7)	8.7 (6.9)
No dipstick proteinuria at baseline	129 (85)	294 (88)	148 (82)	164 (93)	285 (94)	120 (94)

CAB, cabotegravir; eGFR, estimated glomerular filtration rate; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SD, standard deviation; SoC, standard of care; TDF, tenofovir disoproxil fumarate; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

Renal and Bone Outcomes: Safety Overview

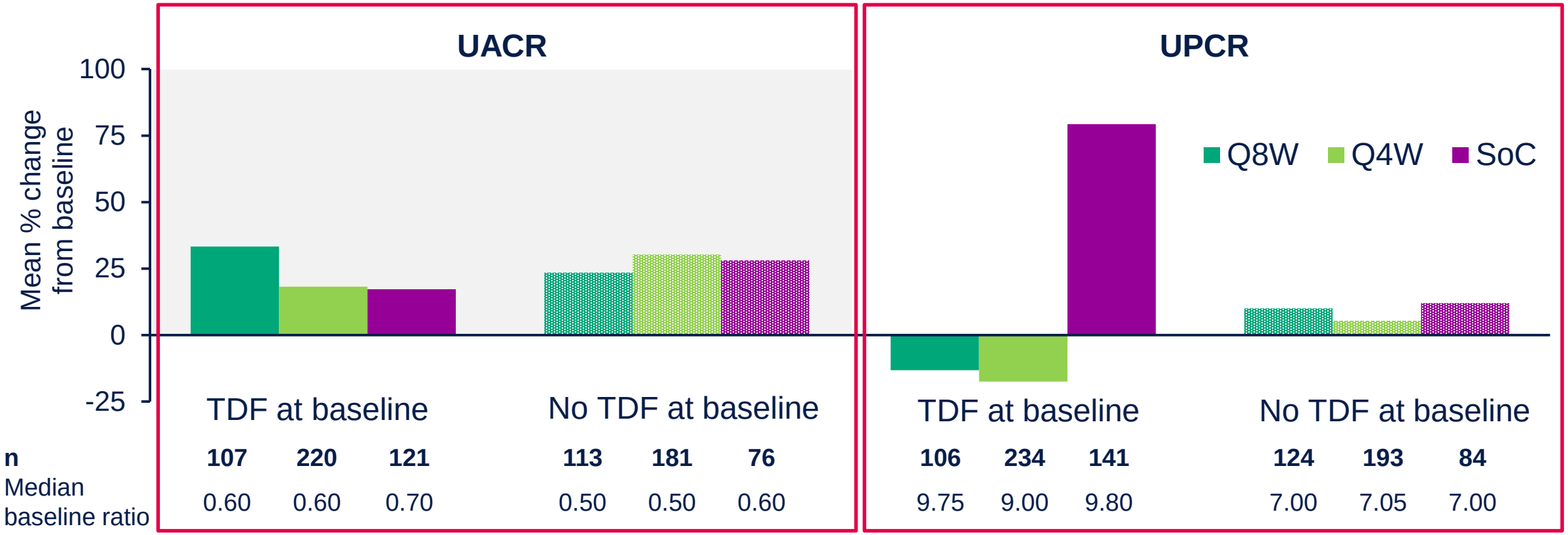
Baseline parameter, n (%)	TDF at baseline			No TDF at baseline		
	CAB + RPV LA Q8W, n=151	CAB + RPV LA Q4W, n=333	SoC n=181	CAB + RPV LA Q8W, n=176	CAB + RPV LA Q4W, n=302	SoC n=127
Drug-related AEs	130 (86)	280 (84)	4 (2)	142 (81)	247 (82)	4 (3)
Leading to withdrawal	1 (<1)	9 (3)	1 (<1)	5 (3)	9 (3)	0
Serious AEs	6 (4)	12 (4)	9 (5)	9 (5)	10 (3)	3 (2)
Any musculoskeletal and connective tissue AE	23 (15)	82 (25)	27 (15)	37 (21)	58 (19)	16 (13)
Osteopenia	1 (<1)	1 (<1)	1 (<1)	0	0	0
Any renal and urinary AE	3 (2)	17 (5)	1 (<1)	3 (2)	7 (2)	5 (4)
Proteinuria	0	0	0	0	1 (<1)	1 (<1)
Renal impairment	0	1 (<1)	1 (<1)	0	0	0

- At Week 48, safety outcomes were similar for participants switching from TDF and non-TDF regimens

AE, adverse event; CAB, cabotegravir; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SoC, standard of care; TDF, tenofovir disoproxil fumarate.

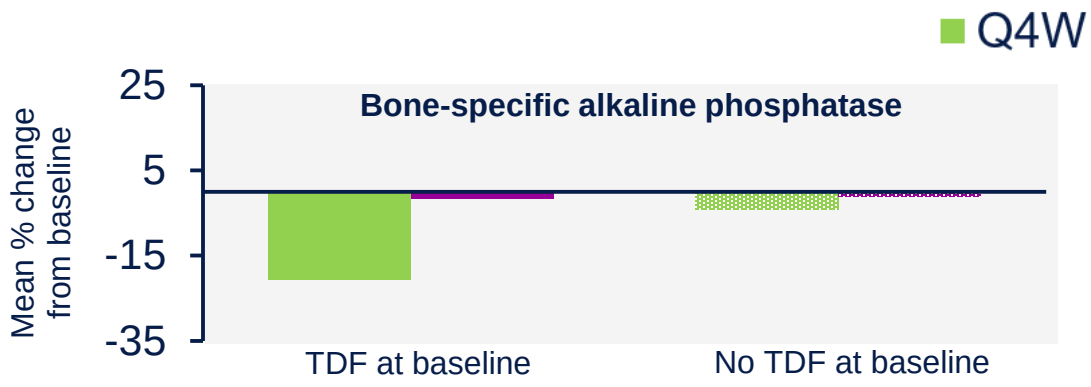
Renal and Bone Outcomes: Renal Markers

- Participants switching from TDF to CAB + RPV LA had reductions in UPCR vs. participants continuing TDF regimens
- Most participants demonstrated no change in maximum post-baseline dipstick proteinuria at Week 48 (TDF at baseline: Q8W, 77%; Q4W, 83%; SoC, 80%; No TDF at baseline: Q8W, 81%; Q4W, 88%; SoC, 80%)*

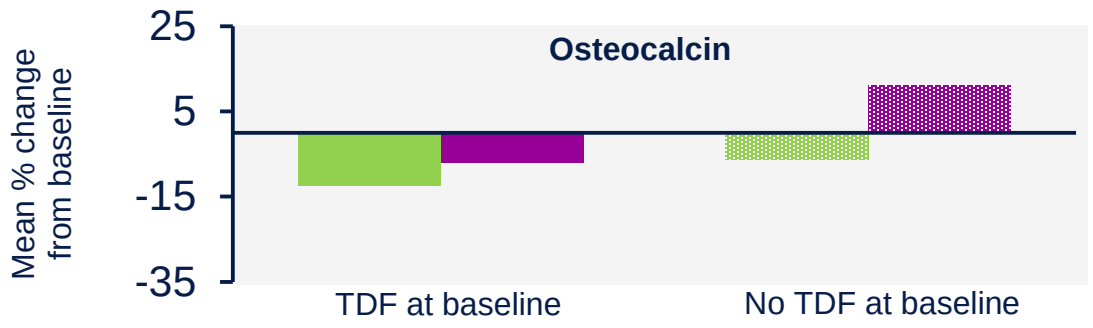


UACR normal range, <3 mg/mmol; UPCR normal range, <15 mg/mmol. *TDF at baseline: Q8W, n=114/149; Q4W, n=270/324; SoC, n=140/174; No TDF at baseline: Q8W, n=140/173; Q4W, n=261/298; SoC, n=101/126.
CAB, cabotegravir; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SoC, standard of care; TDF, tenofovir disoproxil fumarate; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

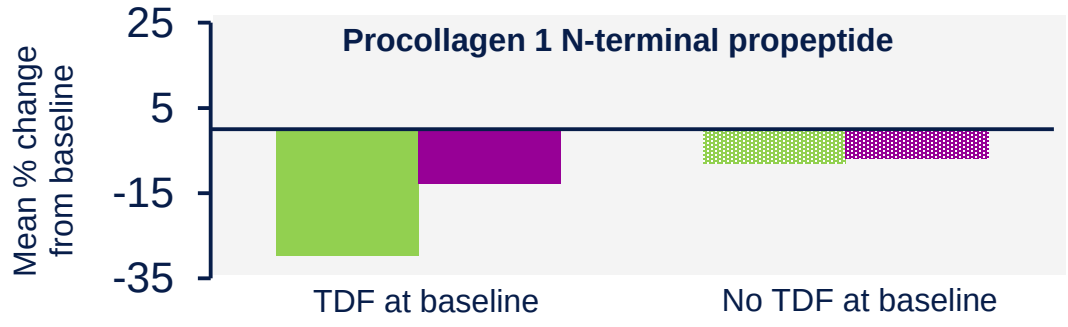
Renal and Bone Outcomes: Bone Turnover Markers (ATLAS Only)



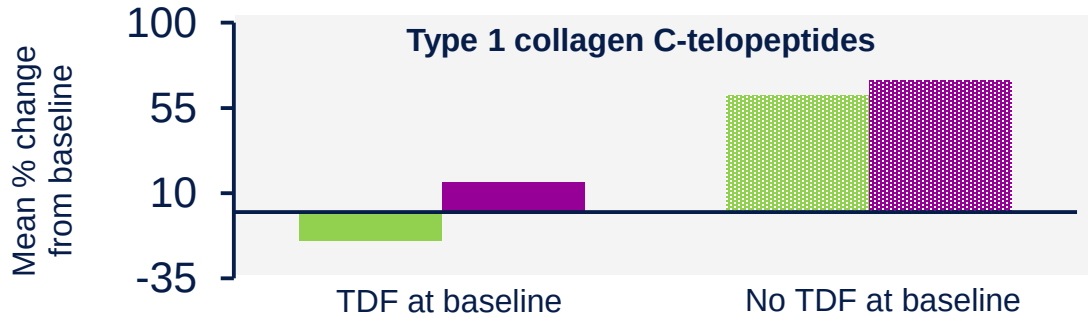
n	**178**	**170**	**99**	**118**
Median baseline value (µg/L)	14.55	15.80	12.70	12.40



n	**179**	**172**	**99**	**120**
Median baseline value (µg/L)	22.10	22.00	20.00	20.00



n	**177**	**172**	**102**	**119**
Median baseline value (µg/L)	56.0	55.0	51.0	51.0



n	**175**	**163**	**101**	**114**
Median baseline value (µg/L)	0.512	0.497	0.364	0.376

- Participants switching from TDF to CAB + RPV LA had improved bone formation markers vs. participants continuing TDF regimens

CAB, cabotegravir; LA, long-acting; Q4W, every 4 weeks; RPV, rilpivirine; SoC, standard of care; TDF, tenofovir disoproxil fumarate; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

Renal and Bone Outcomes: Conclusion

- The majority of participants in the ATLAS and ATLAS-2M studies had normal renal function, UACR, and UPCR at baseline
- Overall, CAB + RPV LA was well tolerated by participants switching from TDF and non-TDF regimens, with few drug-related AEs leading to withdrawal or renal- and bone-related AEs through 48 weeks
- Participants switching from TDF to CAB + RPV LA demonstrated improvements in renal markers and bone turnover markers vs. participants continuing TDF regimens
- These results suggest that CAB + RPV LA is not associated with significant renal or bone toxicities and that PLWH switching from TDF regimens may have improvements in renal markers and bone turnover markers

AE, adverse event; CAB, cabotegravir; LA, long-acting; PLWH, people living with HIV-1; RPV, rilpivirine; TDF, tenofovir disoproxil fumarate; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

Acknowledgments

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