Efficacy and Safety of Co-formulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide in Virologically Suppressed Asian Adults with Renal Impairment

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Introduction

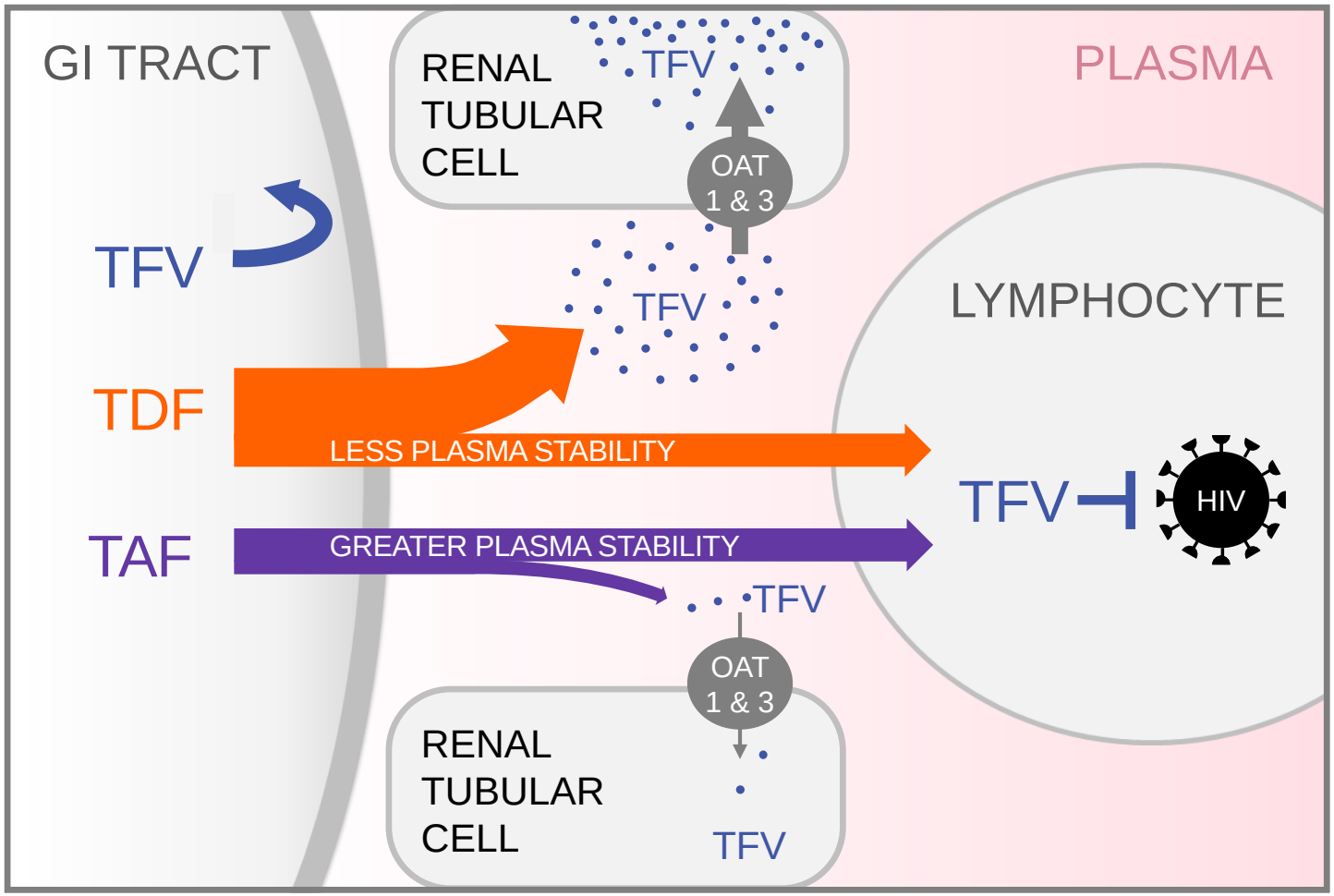
- Tenofovir alafenamide (TAF) is a novel prodrug of tenofovir (TFV) that results in >90% lower plasma TFV levels compared to tenofovir disoproxil fumarate (TDF). As a result, TAF has an improved renal and bone safety profile relative to TDF and is efficacious as demonstrated in multiple patient populations
- The efficacy and safety of co-formulated elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, and TAF 10mg (E/C/F/TAF) through Week 144 in HIV-suppressed adults with stable renal impairment ($eGFR_{CG}$ of 30 to 69 mL/min) have been reported[1]
- Previously, we described Week 96 efficacy and safety of E/C/F/TAF in HIV-infected Asian adults with stable renal impairment*
- We now describe efficacy and safety of E/C/F/TAF in HIV-suppressed Asian adults with stable renal impairment through Week 144

$eGFR_{CG}$=Estimated glomerular filtration rate by Cockcroft-Gault

*Chin BS et al. Korea Society for AIDS, 2017. Poster # P-28

Prodrug Pharmacology

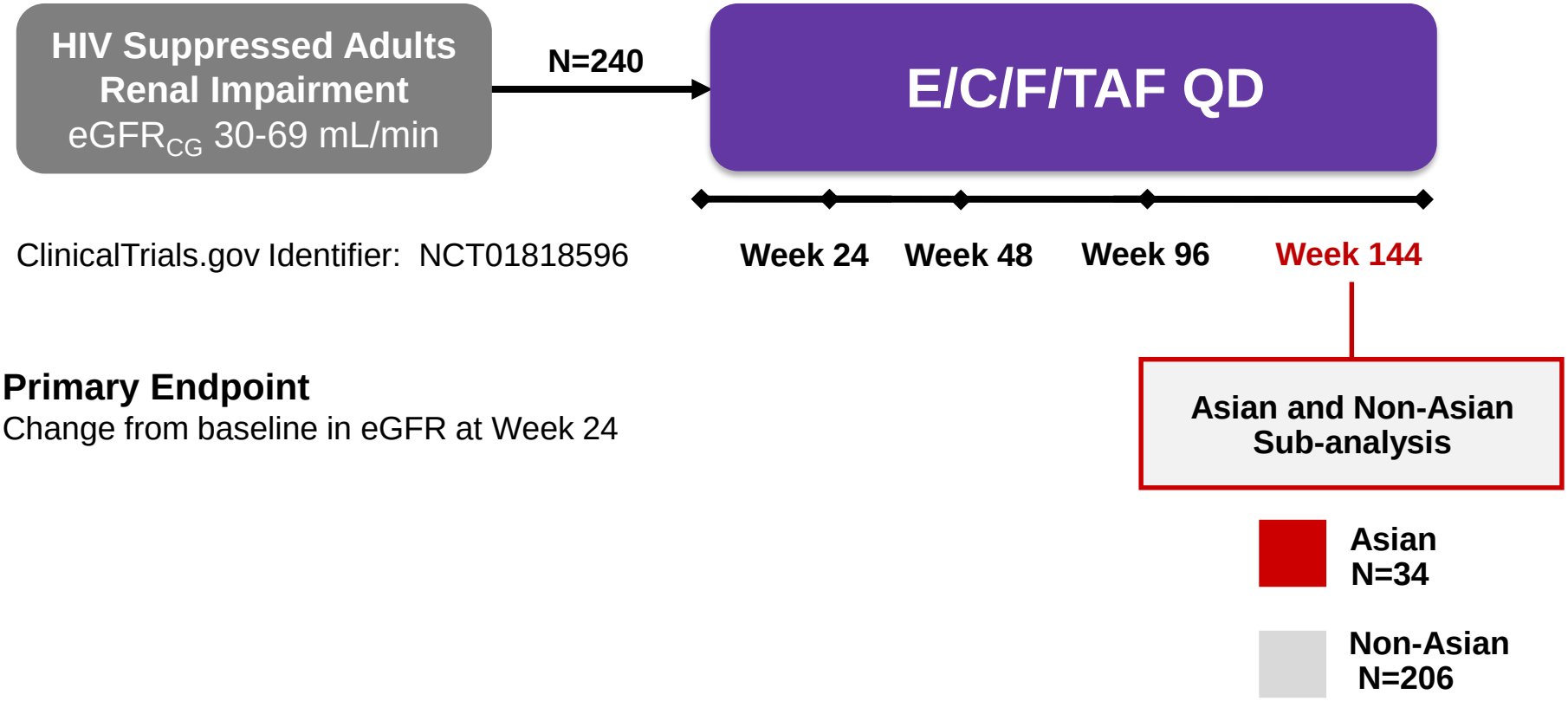
Tenofovir Disoproxil Fumarate and Tenofovir Alafenamide



TAF results in >90% lower TFV plasma levels[2,3,4]

OAT, organic anion transporter; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TFV, tenofovir

Study Design



ClinicalTrials.gov Identifier: NCT01818596

Primary Endpoint
Change from baseline in eGFR at Week 24

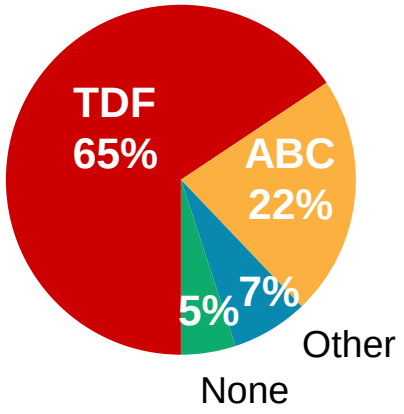
QD=once daily, eGFR$_{CG}$=Estimated glomerular filtration rate by Cockcroft-Gault

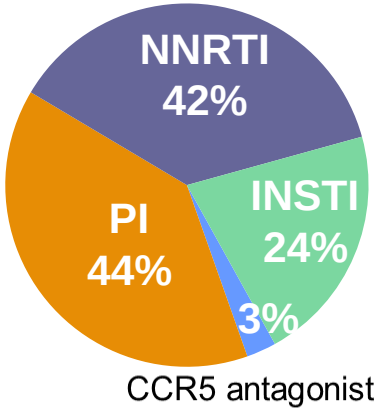
Baseline Characteristics

240 participants switched to E/C/F/TAF: 14% (N=34) self-identified as Asian

Baseline Characteristics	Asian N=34	Non-Asian N=206
Median age, years	55	59
Female	**26%**	19%
Geography: Ex-US	**94%**	20%
Median Body Mass Index, kg/m^2	**20.5**	**24.8**
Median CD4 count, cells/µL	**498**	**652**
Median eGFR$_{CG}$, mL/min	**44**	**58**
Proportion with eGFR$_{CG}$ <60 mL/min	**91%**	**62%**
Median UACR, mg/g	267	145
Median spine BMD, g/cm^2	0.94	1.08
Median hip BMD, g/cm^2	0.84	0.92
Diabetes mellitus	18%	13%
Hypertension	35%	40%

Pre-switch Regimens (N=240)

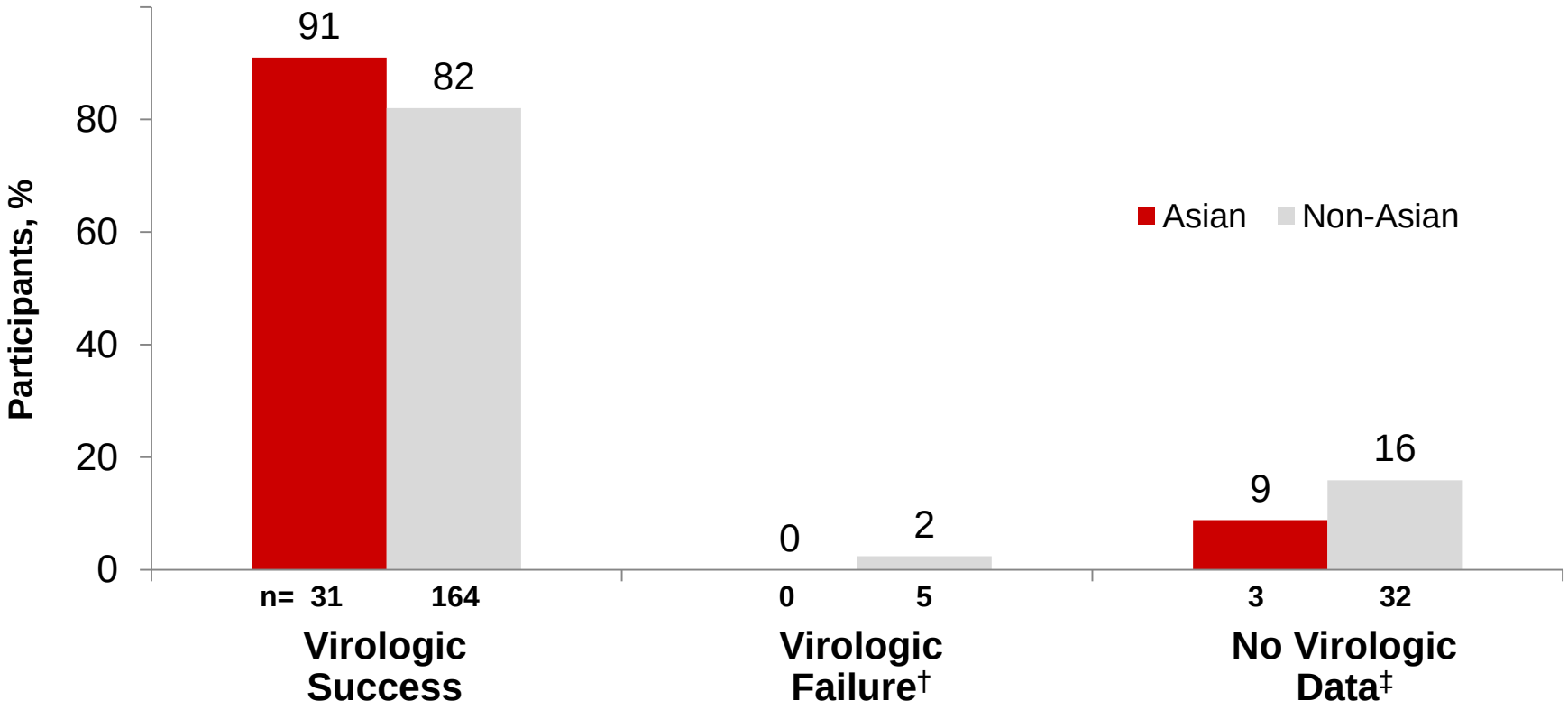




UACR=Urine Albumin to Creatinine Ratio

Total >100% as some regimens included >1 third agent

Virologic Outcomes (HIV-1 RNA <50 copies/mL) at Week 144

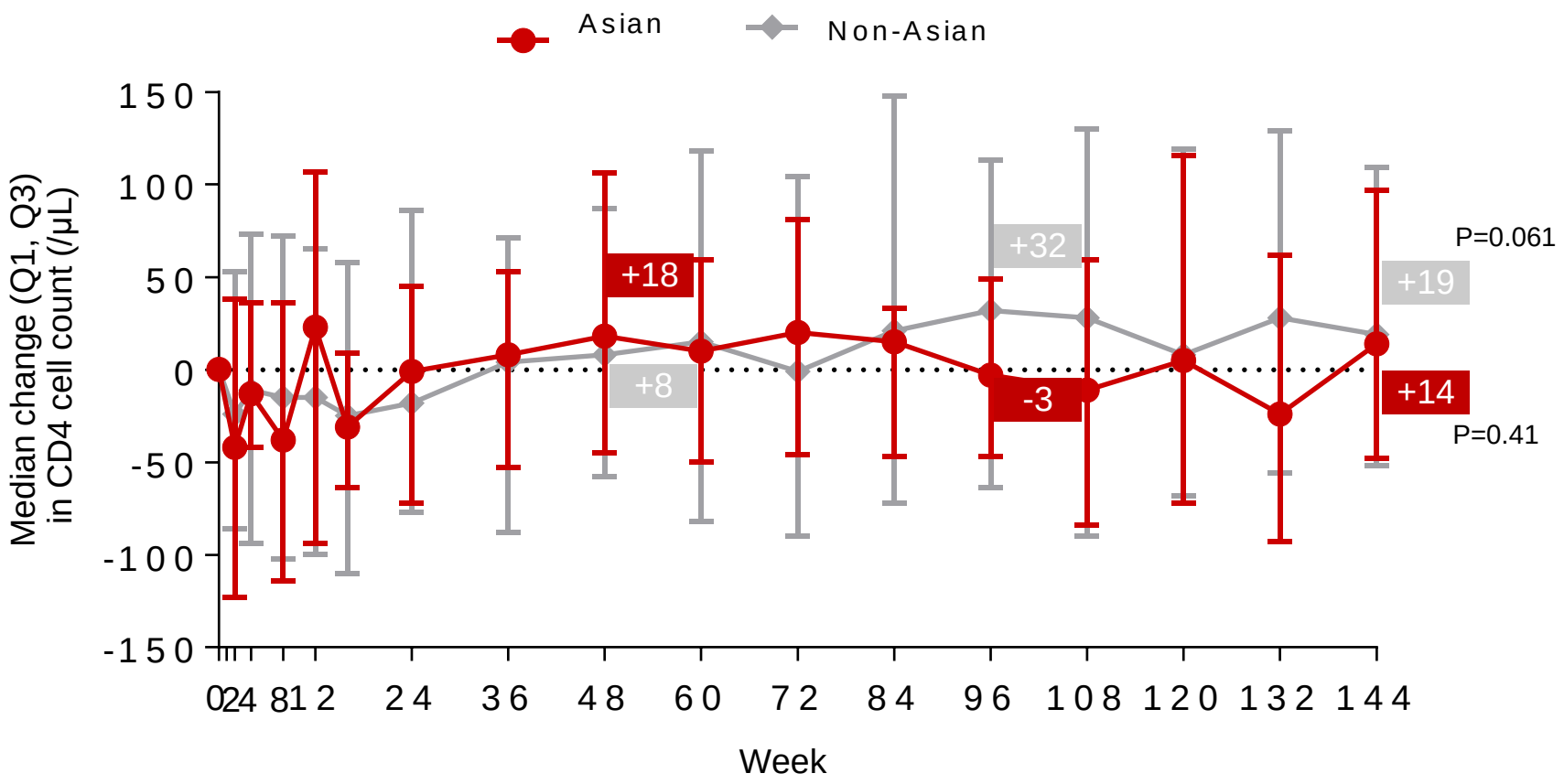


† Virologic failure with emergent resistance: 1 non-Asian (A62A/V, K65R, M184V in reverse transcriptase; E138K, S147G, Q148R in integrase).

‡ **Discontinuation due to adverse events/death (0 Asian**; **11 non-Asian**) or other reasons e.g. lost to follow-up, protocol violation (1 Asian; 18 non-Asian) or missing data in the Week 144 window (2 Asian; 3 non-Asian).

E/C/F/TAF maintained high rates of virologic suppression at Week 144

Changes in CD4 Count from Baseline to Week 144



Median baseline CD4 cell counts: 498 cells/μL for Asian and 649 cells/μL for Non-Asian

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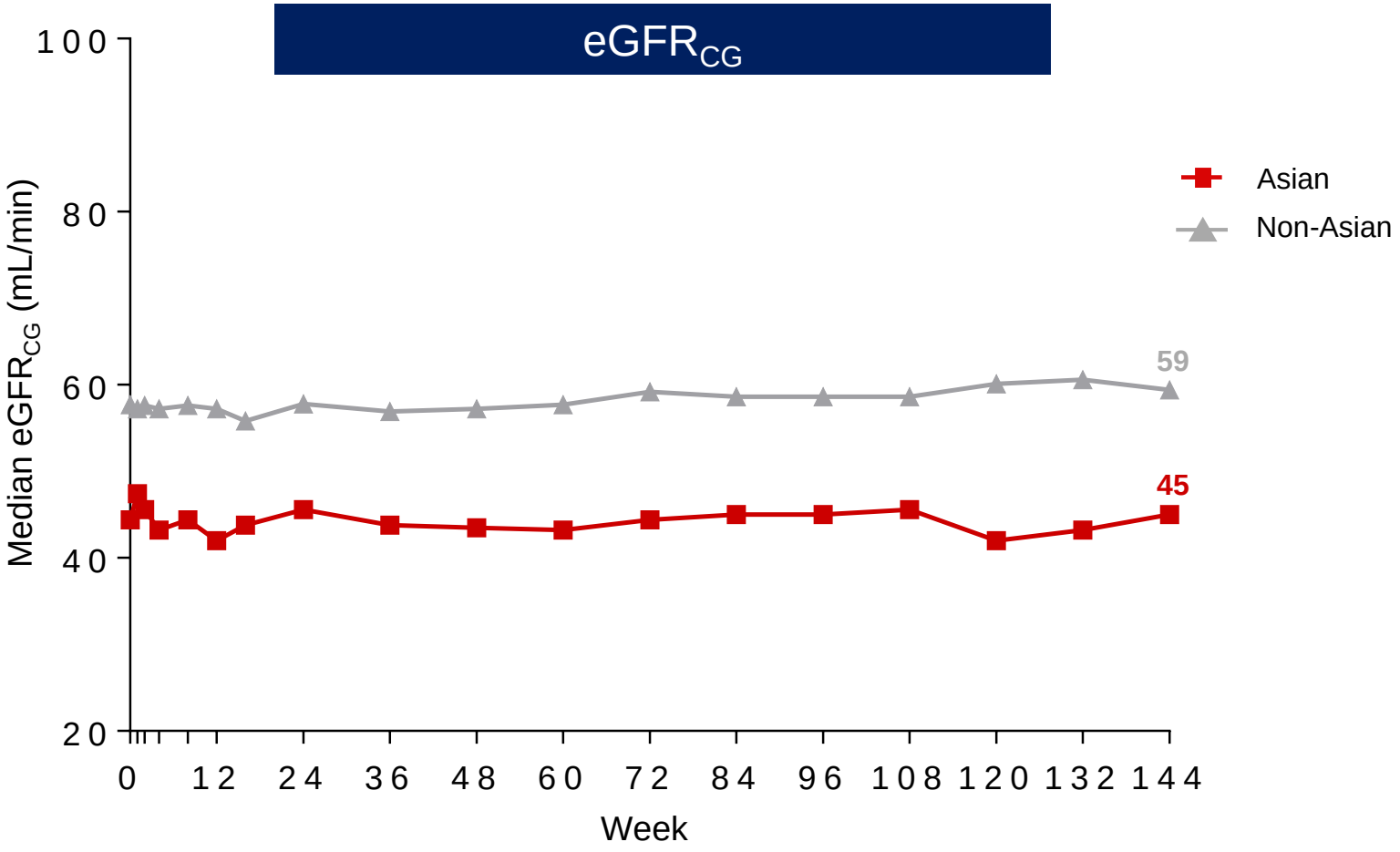
Adverse Events through Week 144

	Asian N=34	Non-Asian N=206
Adverse events in ≥ 15% of participants in either group, % (N)		
Bronchitis	9% (3)	17% (35)
Upper respiratory tract infection	3% (1)	17% (35)
Arthralgia	3% (1)	16% (32)
Diarrhea	0	16% (32)
Summary of Adverse Events		
Any Grade 3 or 4 AEs, % (N)	26% (9)	20% (42)
Discontinuations due to AEs, % (N)	0	6% (12)
Discontinuations due to renal AEs, N	0	5†

† Details on 5 discontinuations due to declining eGFR were previously reported by Post F, et al. Poster #680, CROI February 2016.

- No proximal renal tubulopathy or Fanconi Syndrome in either group
- No discontinuations due to renal AEs among Asian participants

Estimated GFR by Cockcroft-Gault from BL to Week 144



Estimated GFR$_{CG}$ in Asian and non-Asian participants remained stable over 144 weeks after switching to E/C/F/TAF

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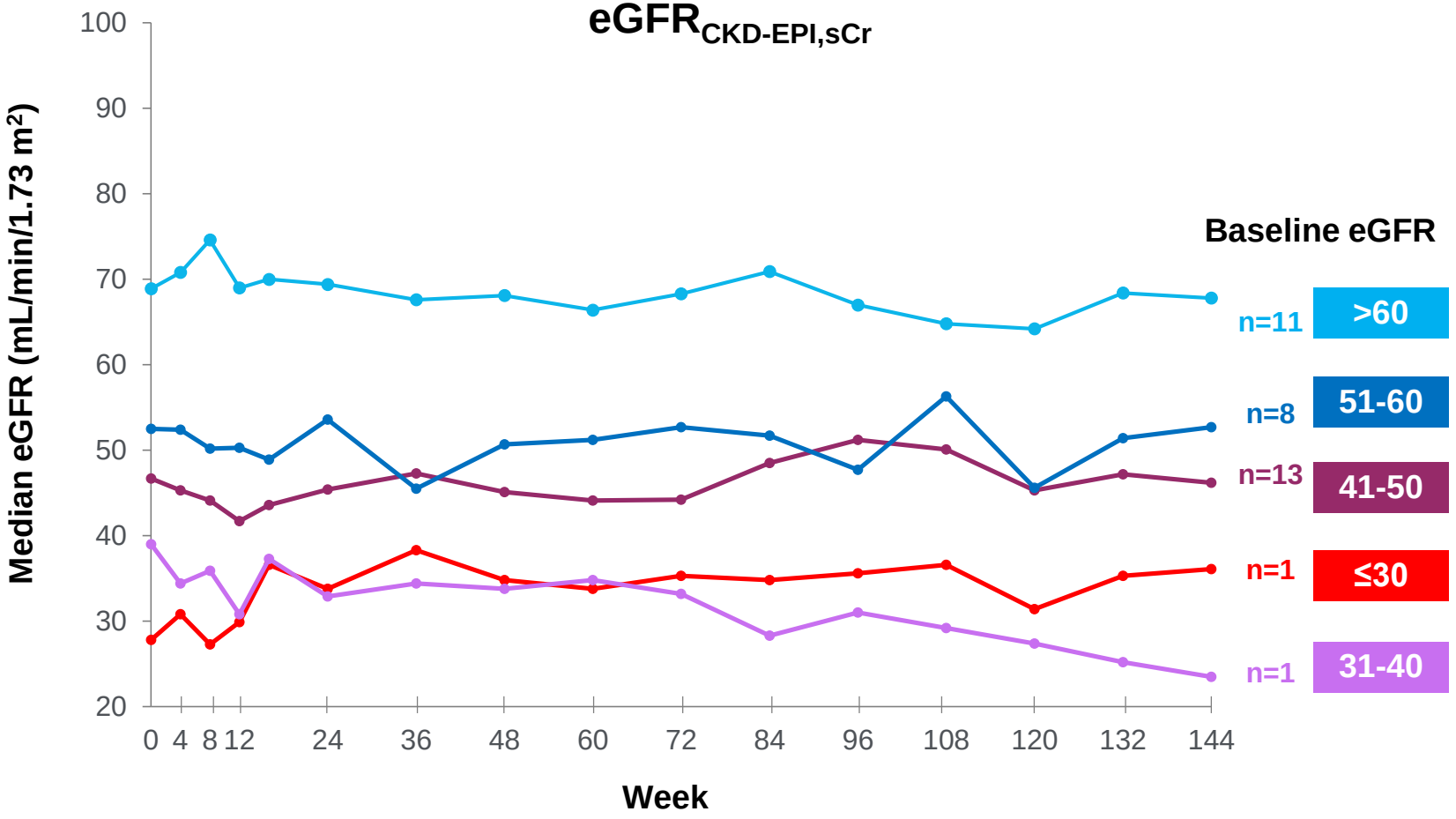
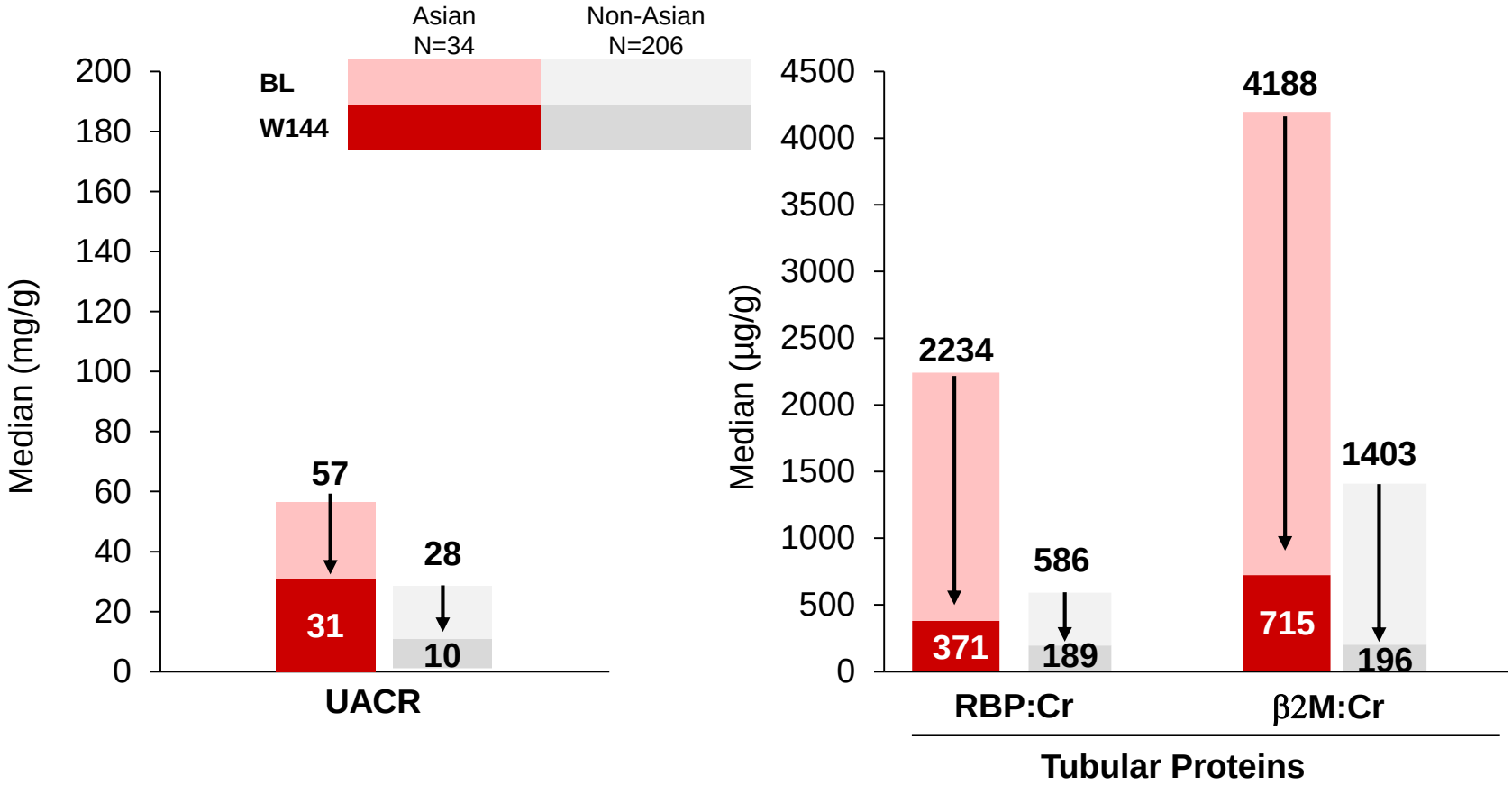
Changes in $eGFR_{CKD\text{-}EPI}$ by Baseline eGFR Strata Among Asian Subjects



Asian subjects eGFR generally remained stable over 144 weeks regardless of their BL baseline eGFR

$eGFR_{CKD\text{-}EPI}$: estimated glomerular filtration rate by Chronic Kidney Disease Epidemiology Collaboration equation

Quantitative Proteinuria at Baseline and Week 144



- After switching to E/C/F/TAF, Asian and non-Asian participants had decreases in all measures of proteinuria with no proximal renal tubulopathy or Fanconi syndrome
- Two Asian participants with a history of TDF-associated Fanconi's syndrome switched to E/C/F/TAF. Their renal function have remained stable without recurrence of tubulopathy for over two years

UACR=Urine Albumin to Creatinine Ratio; β-2M:Cr=β-2-microglobulin to Creatinine Ratio; RBP:Cr=Retinol Binding Protein to Creatinine Ratio

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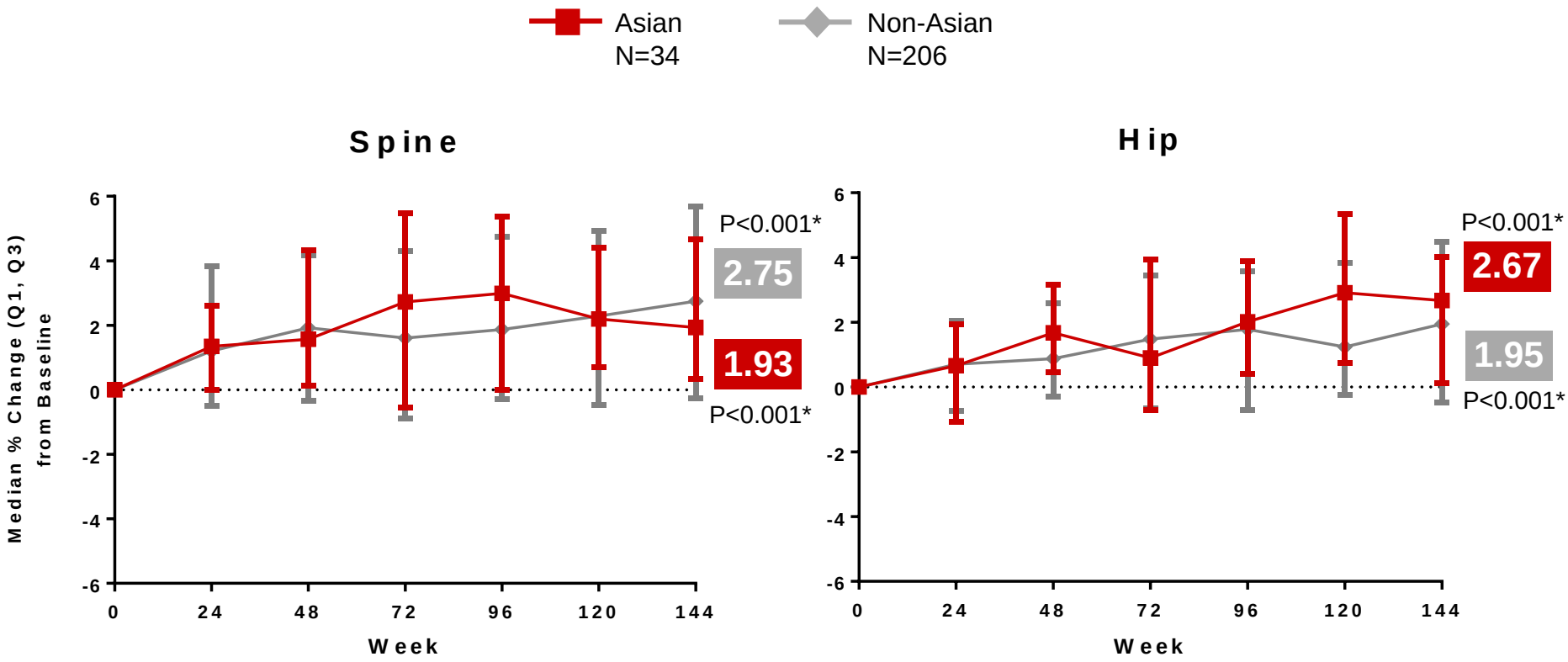
Median % Change in Spine and Hip BMD



Switching to E/C/F/TAF resulted in increases in spine and hip BMD in both Asian and non-Asian participants

* P-values show statistical significance of Week 144 changes from baseline

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Conclusions

- **Asian adults (N=34) with renal impairment who switched to E/C/F/TAF**
  - **Maintained HIV suppression (91%) at Week 144**
  - **No emergent resistance**
  - **No discontinuations due to adverse events (inclusive of renal AEs)**
  - **No recurrence of tubulopathy in 2 adults with prior TDF-associated tubulopathy**
- Both Asian and non-Asian adults with stable renal impairment
  - Maintained stable renal function with decreases in all measures of proteinuria and no emergence of proximal renal tubulopathy or Fanconi syndrome
  - Notable improvements in spine and hip BMD over three years
- These longer-term data support the use of E/C/F/TAF in HIV-suppressed Asian adults with renal impairment

References

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