

XX Corso avanzato

Patogenesi, diagnosi e terapia dell'infezione-malattia da HBV, HCV, HIV

Pavia, 15-16 giugno 2017

**Terapia anti - HIV: linee guida
nazionali ed internazionali**

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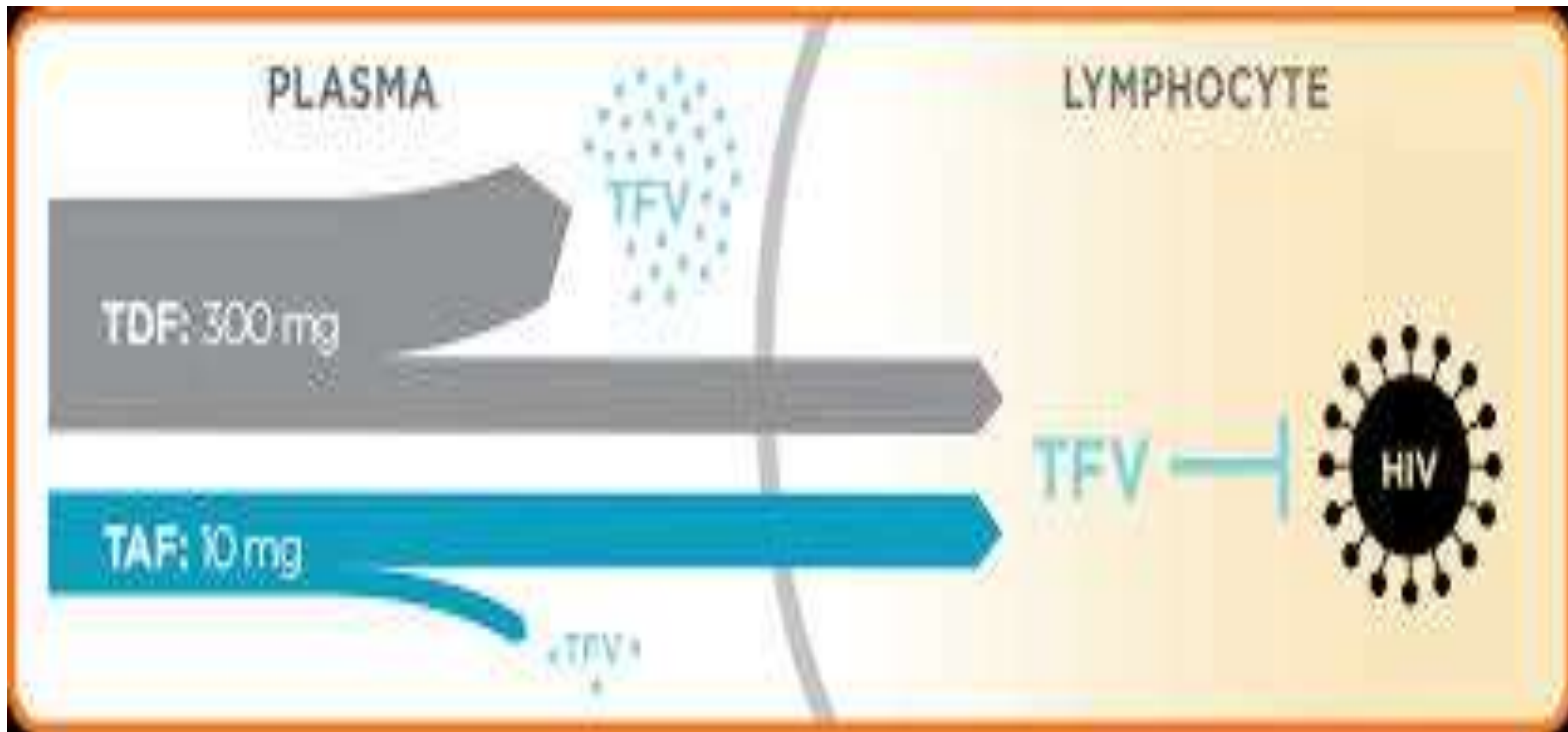
Le novità nelle linee-guida 2016/2017

- Introduzione di **nuovi farmaci**
TAF Tenofovir alafenamide
COBI Cobicistat
- Dibattito su **tossicità** legate a farmaci «raccomandati» in prima linea
cardiovascolari ABC vs TDF
DRV/r vs ATZ/r
psichiatriche DTG
- **Senescenza** dei pazienti HIV+
- Maggiore enfasi su **Semplificazione/Ottimizzazione**
- Preconizzazione di PrEP



TAF

- Is TAF better for bones and kidney?

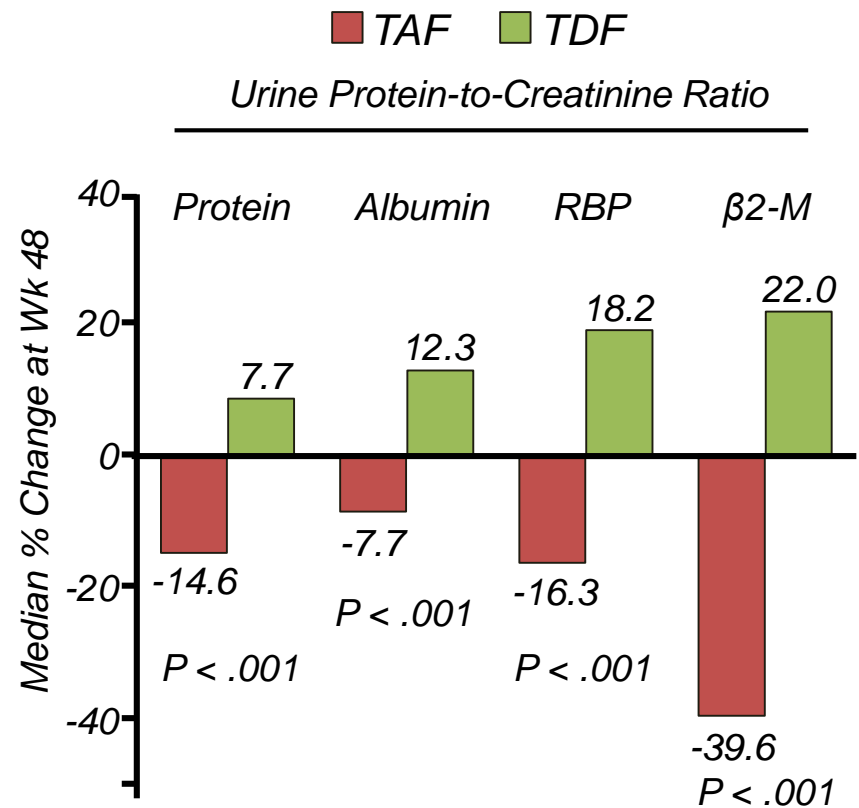
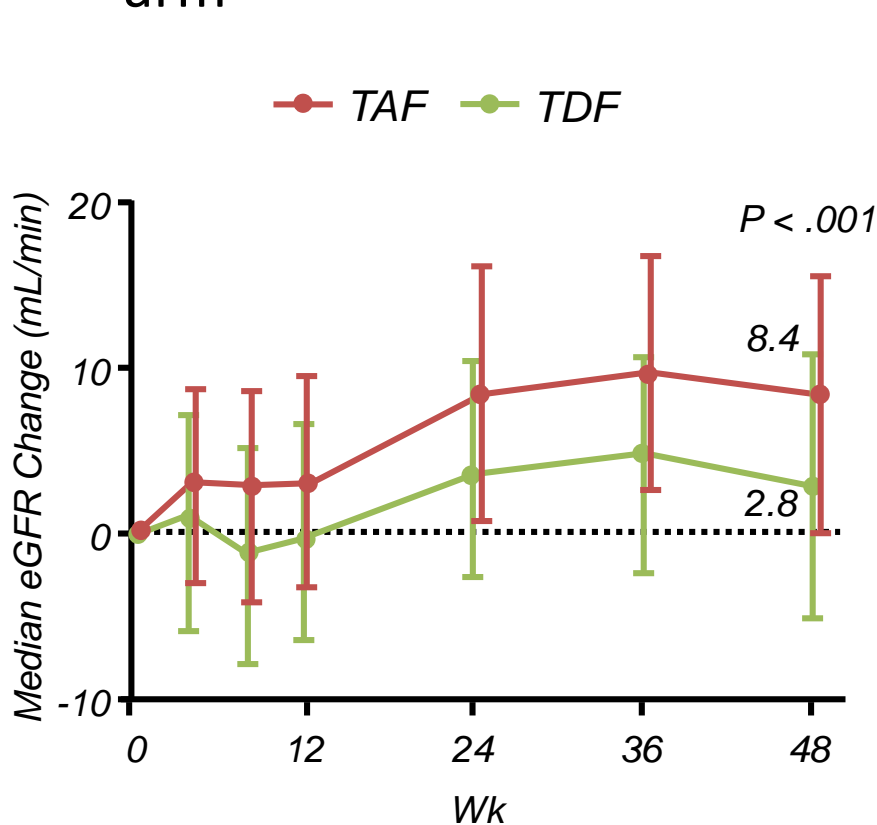


TFV 91% lower

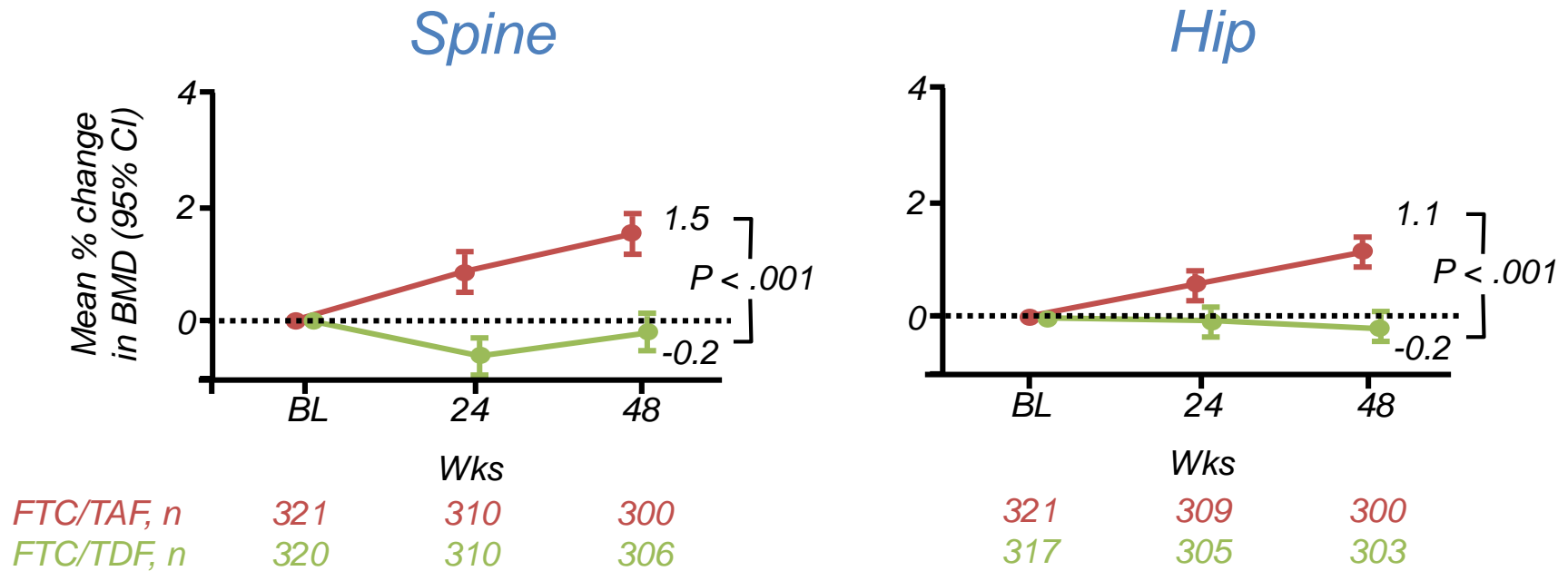
TFV 5,3 fold higher

GS-1089: renal outcomes with switch from TDF- to TAF-containing ART

- No proximal renal tubulopathy or Fanconi syndrome in either arm



GS-1089: BMD changes with switch from TDF- to TAF-containing ART



≥ 3% BMD Increase at Wk 48, %	FTC/TAF	FTC/TDF	P Value
Spine	30	14	< .001
Hip	17	9	.003

TAF Associated With More Favorable Renal and Bone Marker Changes vs TDF

- In both initial therapy and switch studies, **TAF-based ART** associated with the following (vs TDF-based ART) at Wk 48:
 - Higher eGFR_{CG}
 - Less proteinuria (urinary protein, albumin, RBP, and β_2 -M to urine Cr ratio)
- No proximal renal tubulopathy or Fanconi syndrome has been observed with TAF-based treatment
- In initial therapy studies: **smaller declines in spine and hip BMD with TAF-based ART** vs TDF-based ART at Wk 48 ($P < .001$)
- In switch studies: **TAF-based treatment improved spine and hip BMD** vs remaining on TDF-based treatment at Wk 48
- TAF lipid neutral, **lacks lipid lowering effects** observed with TDF

Sax PE, et al. *Lancet*. 2015;385:2606-2615. Mills A, et al. *Lancet Infect Dis*. 2016;16:43-52. Gallant JE, et al. *Lancet HIV*. 2016;3:e158-e165. Wohl D, et al. *J Acquir Immune Defic Syndr*. 2016;72:58-64.

- ✓ TAF raggiunge una **concentrazione plasmatica di TFV 90% inferiore** a TDF e questo giustifica la **minore tossicità renale e ossea**
- ✓ TAF raggiunge una **concentrazione intracellulare di TFV-DP** nelle cellule linfoidi (e negli epatociti) **5 volte superiore** a TDF e questo giustifica l'**elevata attività anti-virale**
- ✓ Quale la **concentrazione nelle cellule renali**? Se altrettanto elevata può motivare una **ulteriore efficacia nella HIV-AN**
- ✓ TAF è **trasportato da P-gp**: la posologia di **10 mg** è raccomandata se co-somministrato con inibitori di P-gp (rtv, cob), la posologia di **25 mg** se co-somministrato con induttori di P-gp o indifferenti (EFV, RPV, DTG)
- ✓ **Non sono necessari aggiustamenti di dose** con valori di **cell ≥ 30 mL/mn** come in presenza di **danno epatico lieve o moderato**

Boosting PIs: Cobicistat(Tybost) vs Ritonavir (Norvir)






Characteristic	Finding
Potency	<ul style="list-style-type: none">▪ Similar potency associated with ATV/RTV and ATV/COBI when combined with FTC/TDF^[1]
Drug interactions	<ul style="list-style-type: none">▪ Both inhibit CYP3A and P-gp^[2]▪ Caution recommended regarding DDIs when switching from RTV to COBI^[3]<ul style="list-style-type: none">▪ RTV an inducer of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or UGT1A1; COBI is not
Resistance potential	<ul style="list-style-type: none">▪ RTV has antiviral activity; COBI does not^[2]

1. Gallant JE, et al. *J Acquir Immune Defic Syndr.* 2015;69:338-340.

2. Marzolini C, et al. *J Antimicrob Chemother.* 2016;71:1755-1758.

3. COBI [package insert]. 2016.

New drugs with TAF and/or with COBI

Brand name TDF contained drug		Brand name TAF contained drug
Truvada TDF/FTC		Descovy TAF/FTC
Eviplera TDF/FTC+RPV		Odefsey TAF/FTC+RPV
Stribild TDF/FTC+EVG/c		Genvoya TAF/FTC+EVG/c
Prezista/Norvir DRV/rtv		Rezolsta DRV/cobi
Reyataz/Norvir ATZ/rtv		Evotaz ATZ/cobi