SPIRIT: Switching to Rilpivirine/Emtricitabine/Tenofovir DF Single-Tablet Regimen from Boosted Protease Inhibitor Demonstrated High Adherence and High Rates of Virologic Suppression

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8th International Conference on HIV Treatment and Prevention Adherence
Abstract #151

Background

- Regimen simplification
  - improves quality of life[1-3]
  - increases long-term adherence[1-3]
  - reduces virologic failure (VF)[1-3]
  - reduces long-term toxicities[1-3]
- RPV/FTC/TDF is a well-tolerated, once daily single-tablet regimen (STR) treatment option[4,5]
- This is the first study to evaluate the safety and efficacy of switching from ritonavir-boosted protease inhibitor (PI+RTV) -based HAART to a simplified regimen of the STR RPV/FTC/TDF in virologically suppressed patients

1. Claxton, Clin Ther. 2001;23(8): 1296-1310
2. Stone, J Acquir Immune Defic Syndr. 2004;36(3)
3. DHHS Guidelines. February 12, 2013
4. COMPLERA®. US Prescribing Information 01/2013. Gilead Sciences, Inc.
5. EVIPLERA®. Summary of Prescribing Characteristics 01/2013. Gilead Sciences, Inc.

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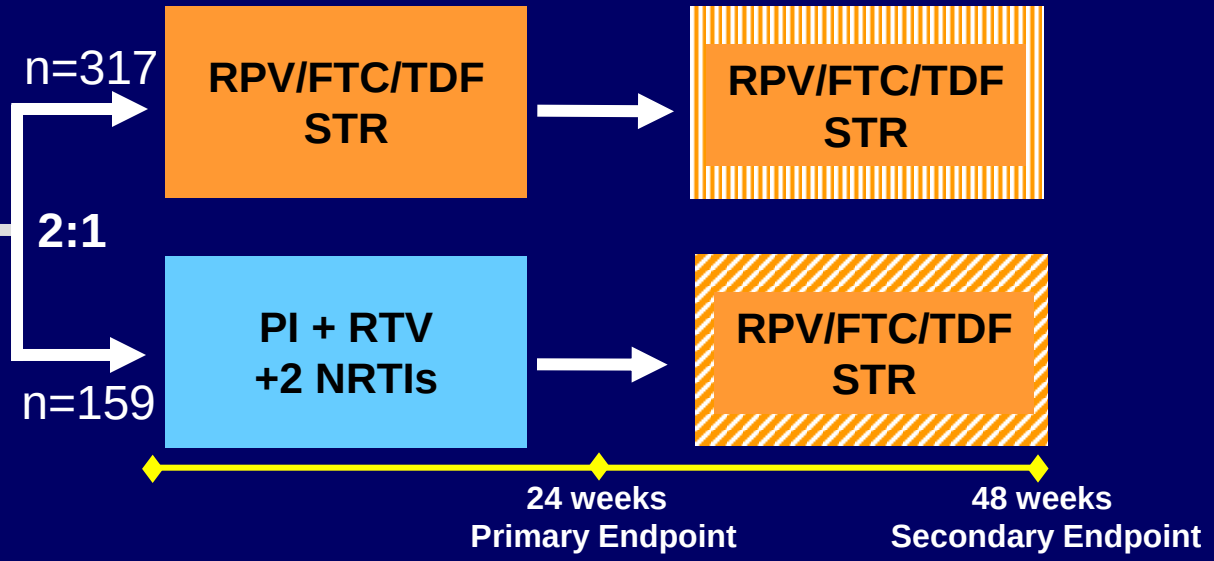
Study Design

Switching boosted PI to Rilpivirine In-combination with Truvada as an STR
Multicenter, international, randomized, open-label, Phase 3b, 48-week study

- **Stable PI+RTV+2 NRTI ≥ 6 months with HIV-1 RNA <50 c/mL**
- **On 1st or 2nd regimen**
- **No prior NNRTI use**
- **No known resistance to study agents**

N=476



Primary Endpoint:

Non-inferiority (12% margin) of RPV/FTC/TDF to PI+RTV+2 NRTIs by FDA snapshot analysis HIV-1 RNA <50 copies/mL at 24 weeks

Secondary Endpoints:

Proportion of subjects on RPV/FTC/TDF who have HIV-1 RNA <50 copies/mL at Week 48
Change in fasting lipid parameters and CD4+ cell count at 24 and 48 weeks
Safety and tolerability to RPV/FTC/TDCF at 24 and 48 weeks
Proportion of subjects who have HIV-1 RNA <50 copies/mL (missing = excluded) through Week 48

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Baseline Characteristics

	RPV/FTC/TDF n = 317	PI+RTV+ 2NRTIs n = 159
Median age, years (Q1, Q3)	42 (35, 48)	43 (36, 49)
Male	86%	91%
White race	76%	78%
Black race	19%	14%
Latino ethnicity	16%	20%
Median time since first ART, years (Q1, Q3)	2.9 (1.9, 4.4)	2.6 (1.7, 4.8)
Mean CD4 cell count, cells/mm^3 (SD)	576 (237)	600 (259)

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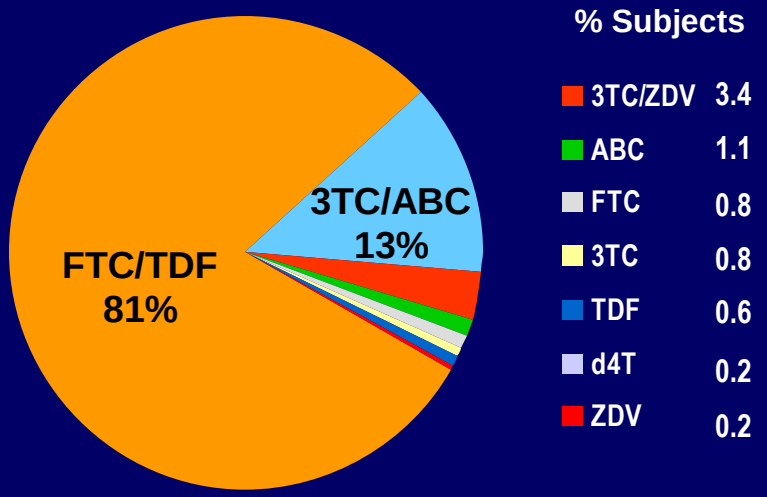
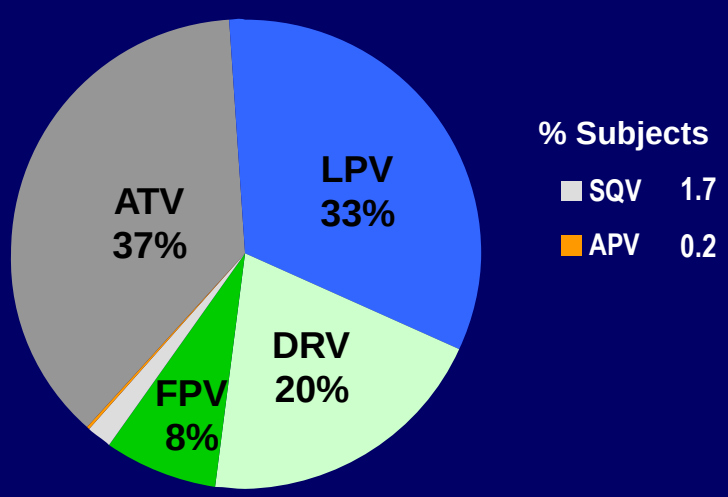
Antiretroviral Therapy at Screening

NRTI



RTV-boosted PI†



3TC: lamivudine; d4T: stavudine; ABC: abacavir; APV: amprenavir; ATV: atazanavir; DRV: darunavir; FPV: fosamprenavir; FTC: emtricitabine; LPV: lopinavir; RTV: ritonarvir; SQV: saquinavir; TDF: tenofovir disoproxil fumarate; ZDV: zidovudine

† Includes all treated participants. 2 subjects enrolled on EFV/FTC/TDF instead of a boosted PI (protocol violation)

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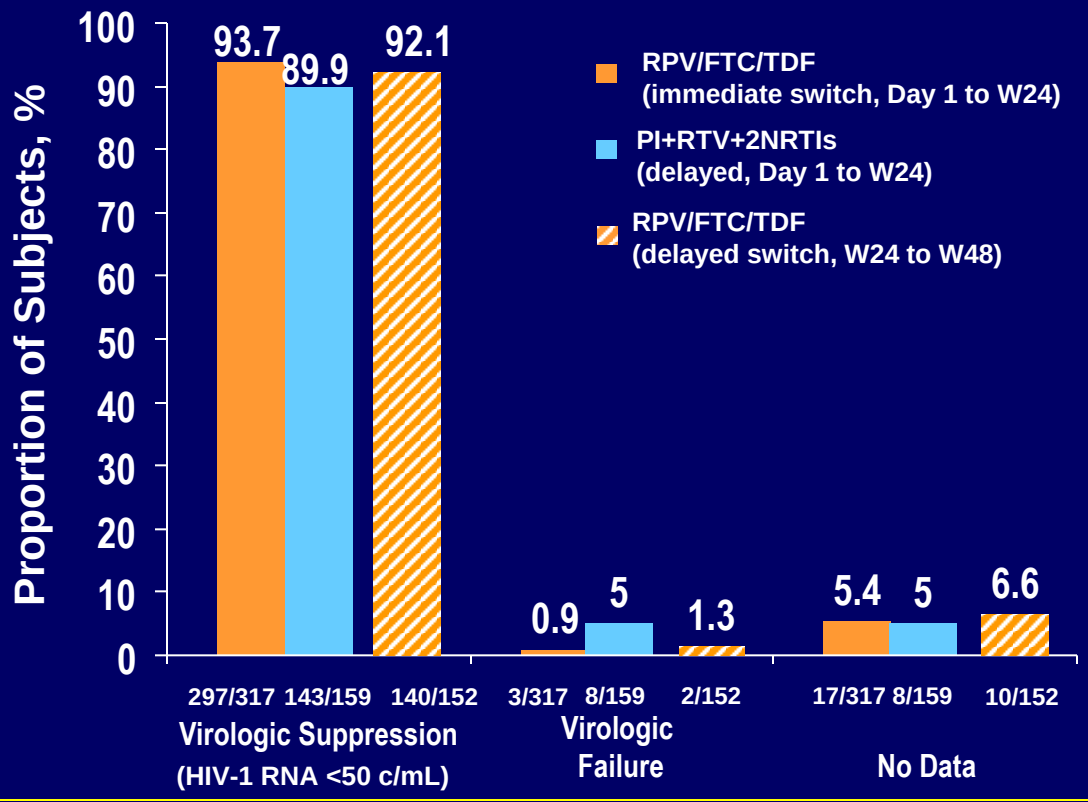
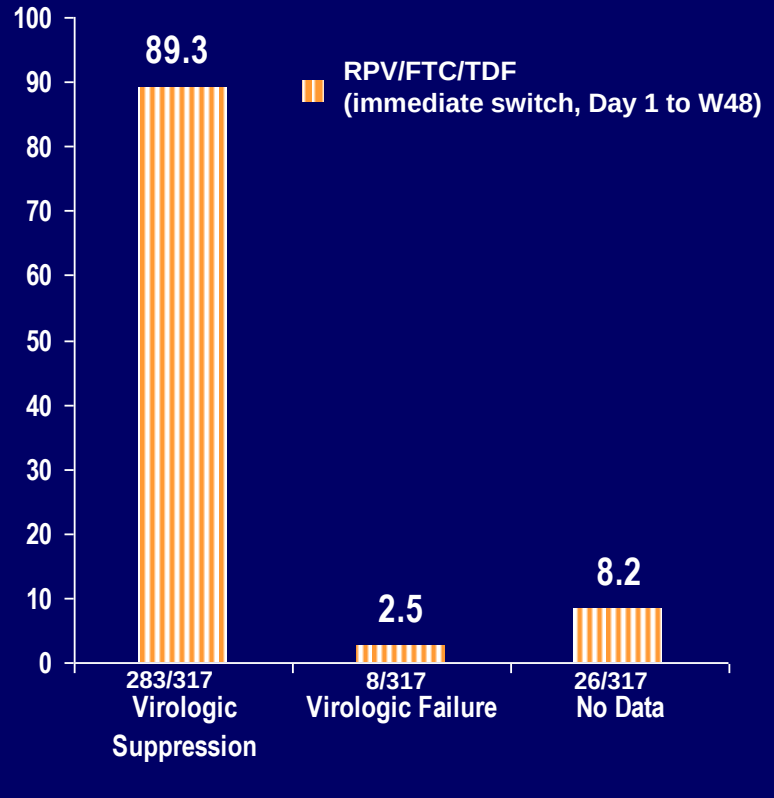
Virologic Outcomes at Weeks 24 and 48
FDA Snapshot Analysis – ITT Population

Switching to RPV/FTC/TDF was non-inferior to remaining on PI+RTV+2NRTIs for 24 weeks (difference 3.8; 95% CI, -1.6 – 9.1). Similar rates of virologic suppression were also seen with 48 weeks of treatment with RPV/FTC/TDF

FDA Snapshot at 24 Weeks



FDA Snapshot at 48 Weeks



CD4+ mean change (cells/mm^3): Week 24, RPV/FTC/TDF immediate switch +20, PI+RTV+2NRTIs +32 (p=0.28), RPV/FTC/TDF delayed switch -7. Week 48, RPV/FTC/TDF immediate switch +10

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Study Drug Adherence

	RPV/FTC/TDF Immediate Switch (Day 1 – Week 48) n=317	RPV/FTC/TDF Delayed Switch (Week 24 – Week 48) n=152
Mean rate of study drug adherence	99%	99%
Proportion with adherence ≥95%	89.9% (285/317)	92.8% (141/152)

- Adherence was not measured for the PI+RTV+2NRTI arm because drug was not supplied through the study
- Adherence was measured by pill count of returned study medication bottles for the RPV/FTC/TDF arms
- Adherence to the STR RPV/FTC/TDF was high in both arms

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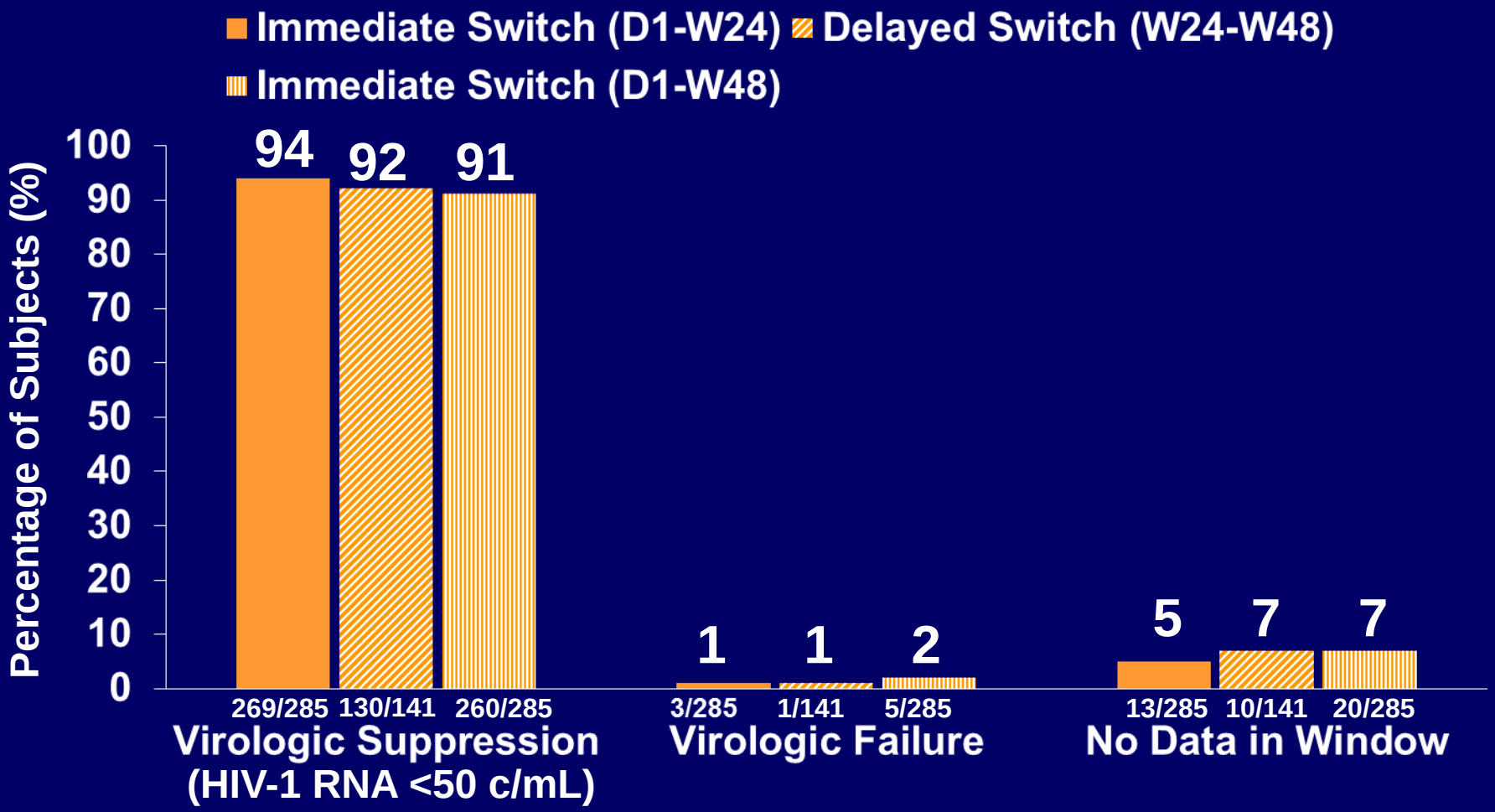
Virologic Outcomes and Change in CD4+ Count for Subjects with ≥95% Adherence*

FDA Snapshot Analysis – ITT Population

*Post hoc analysis



Mean change from baseline in CD4+ count for subjects with ≥95% adherence (cells/mm^3): At Week 24, immediate switch +19, delayed switch -13. At Week 48, immediate switch +9

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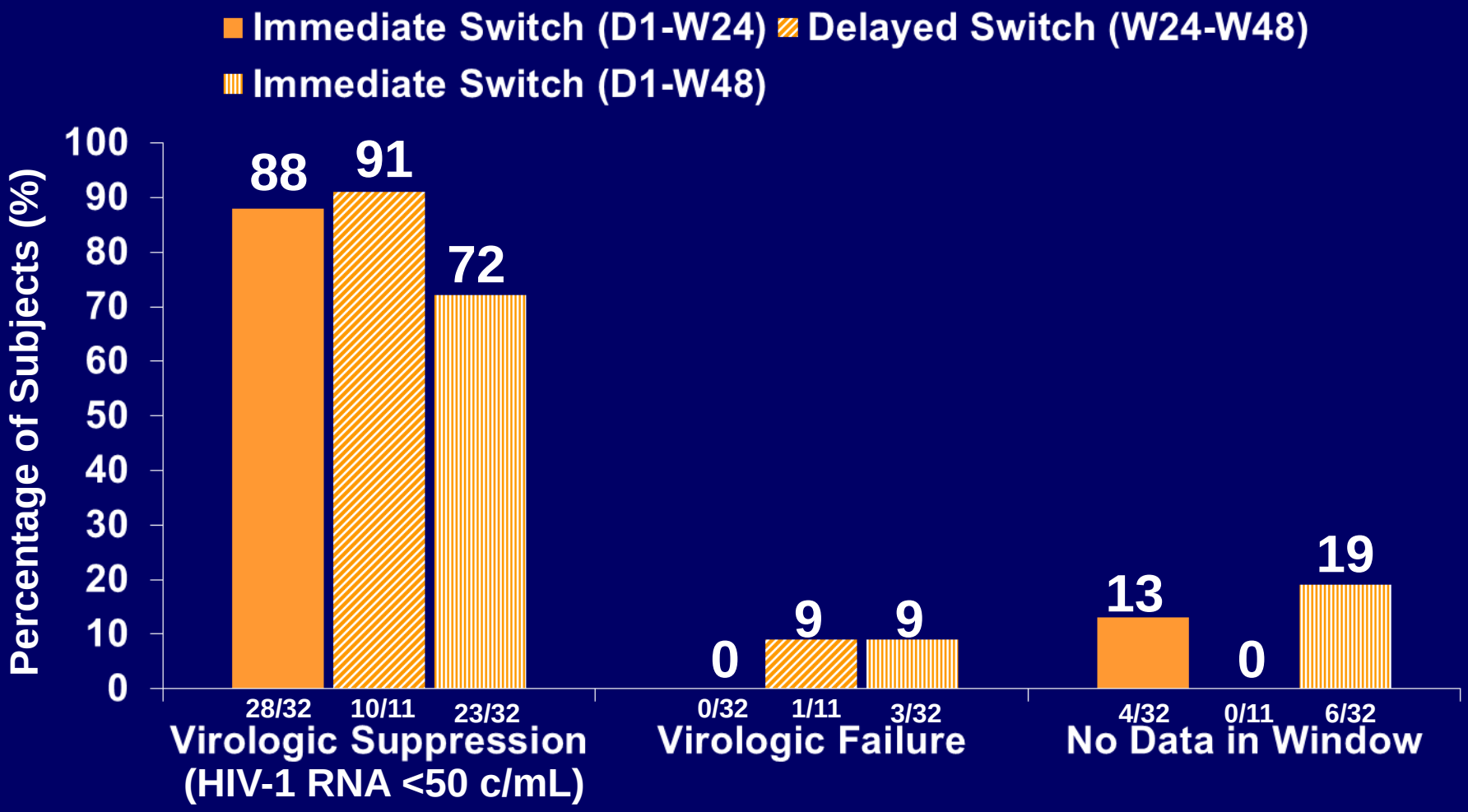
Virologic Outcomes and Change in CD4+ Count for Subjects with <95% Adherence*
FDA Snapshot Analysis – ITT Population

*Post hoc analysis



Mean change from baseline in CD4+ count for subjects with <95% adherence (cells/mm^3): At Week 24, immediate switch +27, delayed switch +80. At Week 48, immediate switch +22

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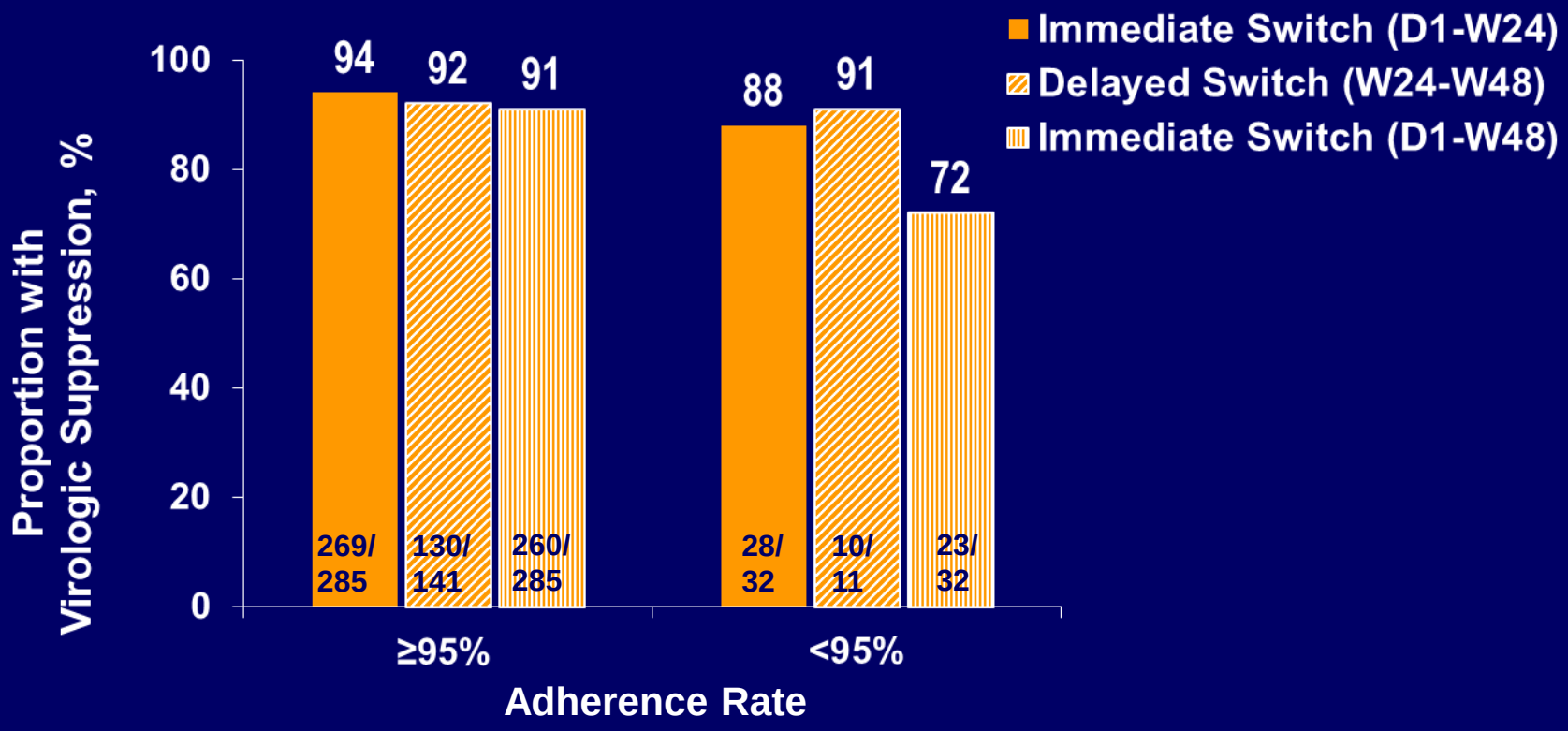
Virologic Suppression at Week 48 Stratified by Adherence Rate - FDA Snapshot Analysis



Mean Change in CD4+ Count (cells/mm^3)

≥95% Adherence: At Week 24, immediate switch +19, delayed switch -13. At Week 48, immediate switch +9

<95% Adherence: At Week 24, immediate switch +27, delayed switch +80. At Week 48, immediate switch +22

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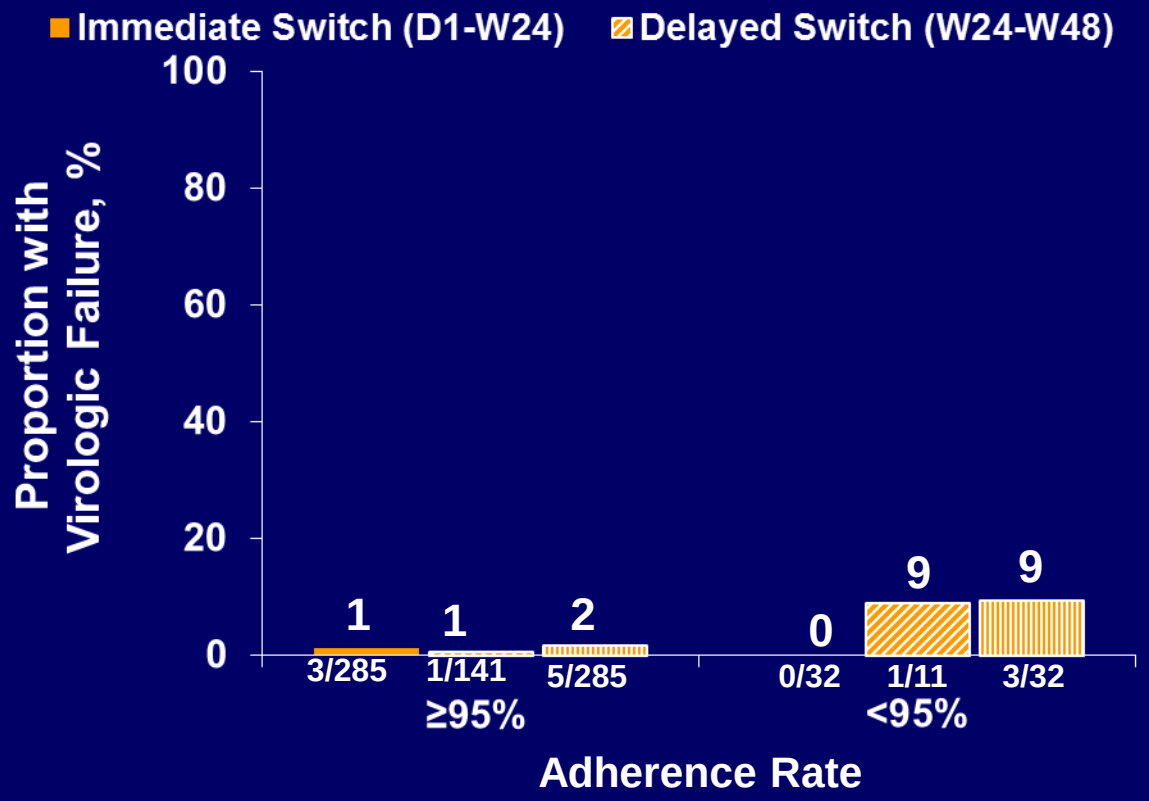
Virologic Failure at Week 48 Stratified by Adherence Rate – FDA Snapshot Analysis



Virologic Failure: HIV-1 RNA > 50 copies/mL, or discontinued study drug due to lack of efficacy or discontinued study due to other reasons and last available HIV-1 RNA >50 copies/mL

Better adherence is associated with lower rates of virologic failure

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Grade 3 or 4 Adverse Events

Grade 3 Adverse Events Related to Study Drug, n (%)	Immediate Switch (D1-W48)	Delayed Switch (W24-W48)
≥95% Adherence	3 (1.1%)	4 (2.8%)
<95% Adherence	0	0

- Overall, the incidence of Grade 3 or 4 adverse events related to study drug was low in subjects treated with RPV/FTC/TDF
- There were no Grade 4 adverse events related to study drug in either adherence strata

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Conclusions

- **Overall, switching to RPV/FTC/TDF was non-inferior to remaining on PI+RTV+2NRTIs for the primary endpoint of virologic suppression**
- **There were high rates of adherence for subjects treated with RPV/FTC/TDF**
- **Better adherence to RPV/FTC/TDF treatment was associated with better efficacy outcomes in terms of higher rates of virologic suppression and lower rates of virologic failure**
- **Adverse events were low for subjects treated with RPV/FTC/TDF, regardless of adherence rate**

Acknowledgements

We greatly appreciate the involvement of all study subjects, Investigators and their staff, and the SPIRIT Study Team

AUSTRIA
Greil, Richard
Haas, Bernhard
Rieger, Armin
Schalk, Horst
Vetter, Norbert

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