Poster Number

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Efficacy of First-Line ARV Regimens: An Exploratory "Target Not Detected" Analysis

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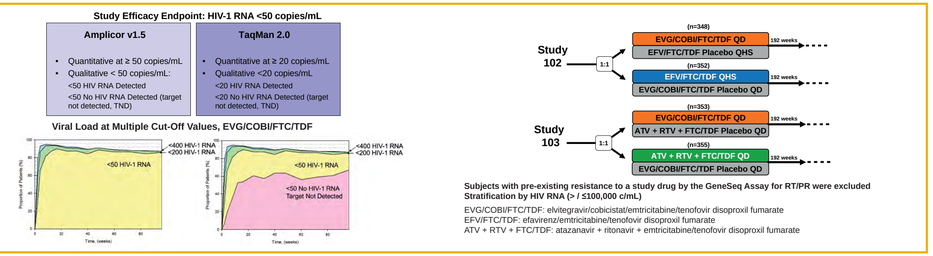
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Background

- Antretroiviral regimens aim to achieve undetectable HIV-1 RNA of <50 copies/mL
- HIV-1 RNA <50 copies/mL but still detectable by the assay has been associated with subsequent viral rebound in some but not all studies[1,2]
- The FDA Snapshot analysis[4] determines efficacy using HIV-1 RNA < 50 copies/mL
- However, clinical trials could be analyzed for HIV-1 RNA lower than 50 copies/mL
  - The Amplicor HIV-1 RNA v1.5 assay provides qualitative results below 50 copies/mL (Figure 1)
    - < 50 copies/mL (i.e., HIV-1 RNA detected but not quantified), or
    - < 50 copies/mL, No HIV-1 RNA Detected (Target Not Detected, TND)
- Two phase 3, randomized, double-blinded, clinical trials of HIV-1-infected, treatment-naive adults through Week 144 were analyzed[3] for the exploratory endpoint of Target Not Detected (Figure 1)
  - Study GS-US-236-0102 (Study 102): Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF) vs. efavirenz/FTC/TDF (EFV/FTC/TDF)
  - Study GS-US-236-0103 (Study 103): EVG/COBI/FTC/TDF vs. atazanavir + ritonavir + FTC/TDF (ATV + RTV + FTC/TDF)

Figure 1. Design of the Phase 3 Studies 102 and 103 in Treatment-Naïve Subjects



Objectives

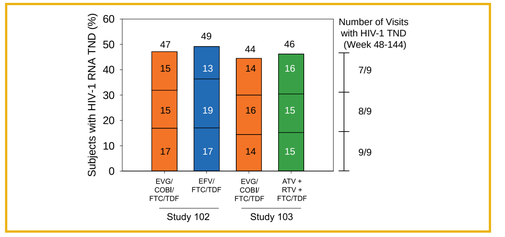
- Determine the rates of HIV-1 RNA of < 50 copies/mL vs. Target Not Detected (TND) in the EVG/COBI/FTC/TDF studies
  - Determine if achieving TND varies by antiretroviral therapy
- Describe the baseline characteristics of subjects with TND at Week 144

Methods

- Plasma HIV-1 RNA levels were assessed at all study visits through Week 144 using the Roche COBAS Amplicor HIV-1 Monitor Test v1.5.
- All subjects in the ITT population from studies 102 and 103 were evaluated (N = 1,408) and missing HIV-1 RNA was considered as ≥ 50 copies/mL (ie, missing = failure)
- HIV-1 RNA levels, including TND, were evaluated by treatment group and baseline characteristics
- P-values were determined by two-sided Fisher's Exact Test and statistical significance was set at p < 0.05

Results (cont'd)

Figure 6. Proportion of Subjects with Consistent Target Not Detected at 7-9 of 9 visits from Week 48 through Week 144



Results

Figure 2. Longitudinal Analysis of HIV-1 RNA

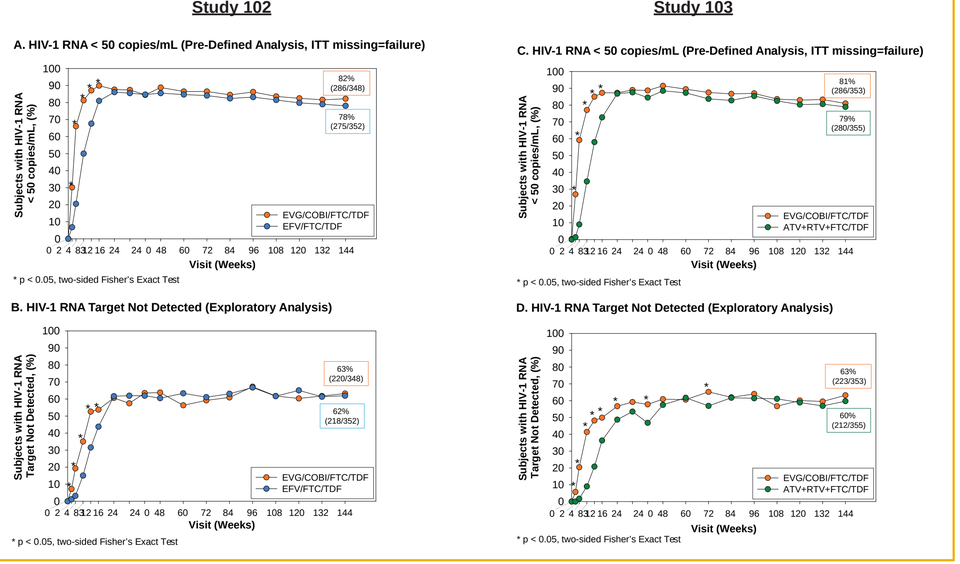


Table 1. Frequency of HIV-1 RNA Target Not Detected by Baseline Viral Load (All Treatment Groups)

Study	Target Not Detected at Week 144		
	Baseline Viral Load	n/N (%)	P-value
102	≤100,000 c/mL	307/466 (65.9%)	0.0129
	>100,000 c/mL	131/234 (56.0%)	
103	≤100,000 c/mL	284/417 (68.1%)	<0.0001
	>100,000 c/mL	151/291 (51.9%)	

Table 2. Frequency of HIV-1 RNA Target Not Detected by Adherence by Pill Count (All Treatment Groups)

Study	Target Not Detected at Week 144		
	Adherence	n/N (%)	P-value
102	≥ 95%	359/517 (69.4%)	<0.0001
	< 95%	79/178 (44.4%)	
103	≥ 95%	329/497 (66.2%)	0.0001
	< 95%	106/209 (50.7%)	

Subjects who did not return a pill bottle were excluded from this analysis

Table 3. Frequency of HIV-1 RNA Target Not Detected at Week 144 by Baseline CD4 (All Treatment Groups)

Study	Target Not Detected at Week 144		
	CD4 Cell Count (cells/μL)	n/N (%)	P-value
102	≥ 200	385/606 (63.5%)	0.2077
	< 200	53/94 (56.4%)	
103	≥ 200	381/615 (62.0%)	0.4939
	< 200	54/93 (58.1%)	

HIV-1 RNA TND at Week 96 was significantly higher in subjects with baseline CD4 cell count of ≥ 200 cells/μL vs. < 200 cells/μL for both studies (p=0.0247 (Study 102) and p=0.0155 (Study 103)).

Figure 3. Frequency of HIV-1 RNA Target Not Detected at Week 144 by Baseline Viral Load (By Treatment Group)

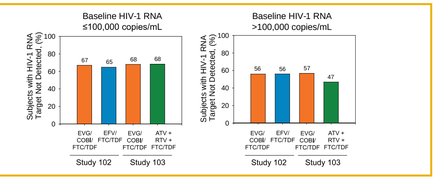


Figure 4. Frequency of HIV-1 RNA Target Not Detected at Week 144 by Adherence (By Treatment Group)

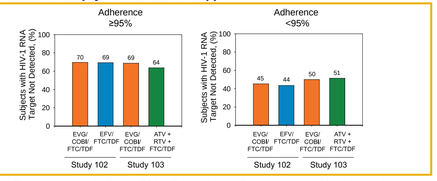
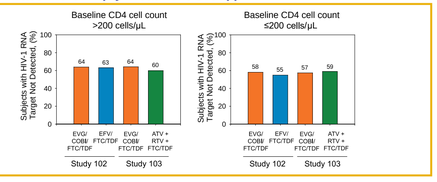


Figure 5. Frequency of HIV-1 RNA Target Not Detected at Week 144 by Baseline CD4 (By Treatment Group)



Conclusions

- Subjects treated with EVG/COBI/FTC/TDF achieved HIV-1 RNA Target Not Detected more rapidly than those treated with EFV/FTC/TDF or ATV+RTV+FTC/TDF
  - By Week 48 through Week 144, the proportion of subjects with HIV-1 RNA Target Not Detected was similar between treatment groups
  - Stable HIV-1 Target Not Detected was achieved from Week 48 through Week 144 (9 visits) in ~15-17% of treated subjects in each treatment group
- Achieving HIV-1 Target Not Detected was associated with lower HIV-1 RNA at baseline and drug adherence ≥ 95%
  - HIV-1 Target Not Detected has been shown in some studies to be associated with a lower risk of virologic failure[1,2]
  - These results support the recent treatment initiation guideline recommendations of early initiation of treatment to reach the lowest HIV-1 RNA levels possible[5]

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