Efficacy and Safety of Doravirine in Treatment-Naive Adults ≥50 Years Old With HIV-1

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BACKGROUND: Nearly 50% of people living with HIV in the US are ≥50 years old; however, this age group is often under-represented in clinical trials.

OBJECTIVE: To compare the Week 96 efficacy and safety results in treatment-naïve adults ≥50 years old with those <50 years old using data from the doravirine (DOR) Phase 2 and Phase 3 clinical trials.

STUDY DESIGN: Post-hoc analysis of 3 multicenter, double-blind, randomized, active-controlled trials:

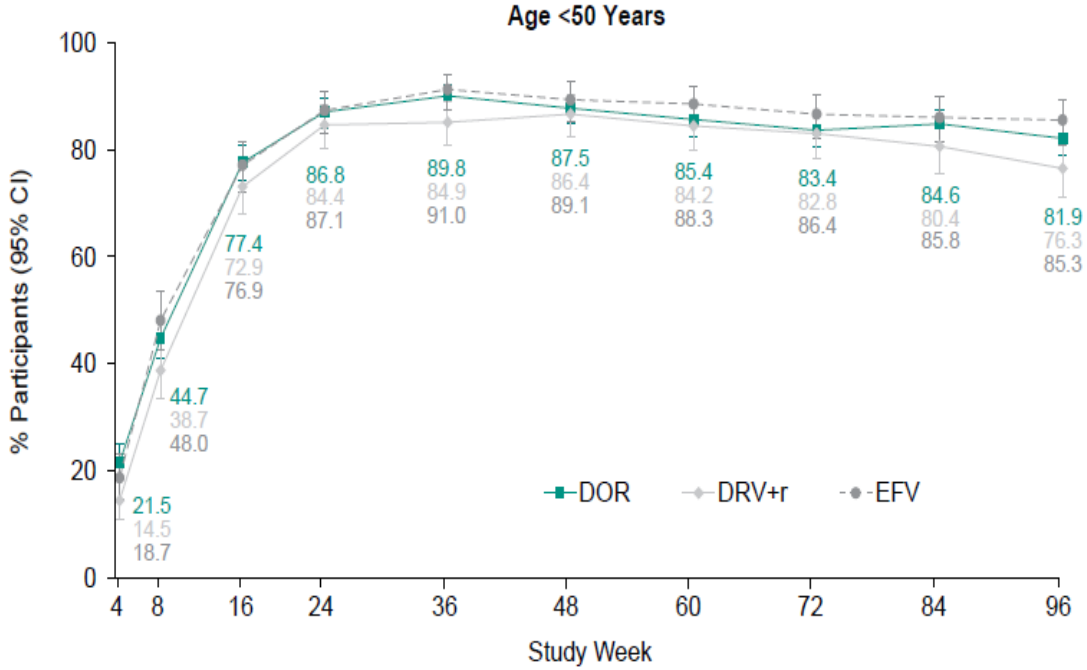
- MK-1439A Protocol 007 (Phase 2b): DOR (25-100 mg) vs EFV (600 mg), each given with FTC/TDF
- DRIVE-FORWARD (Phase 3): DOR (100 mg) vs DRV+r (800/100 mg), each given with FTC/TDF or ABC/3TC
- DRIVE-AHEAD (Phase 3): Fixed-combination DOR/3TC/TDF vs EFV/FTC/TDF

PARTICIPANTS: Antiretroviral-naïve adults with HIV-1 RNA ≥1000 copies/mL and no genotypic resistance to any study drugs.

- Of 1,710 participants, 187 (11%) were 50 to 70 years of age (median 54 years) at study entry.

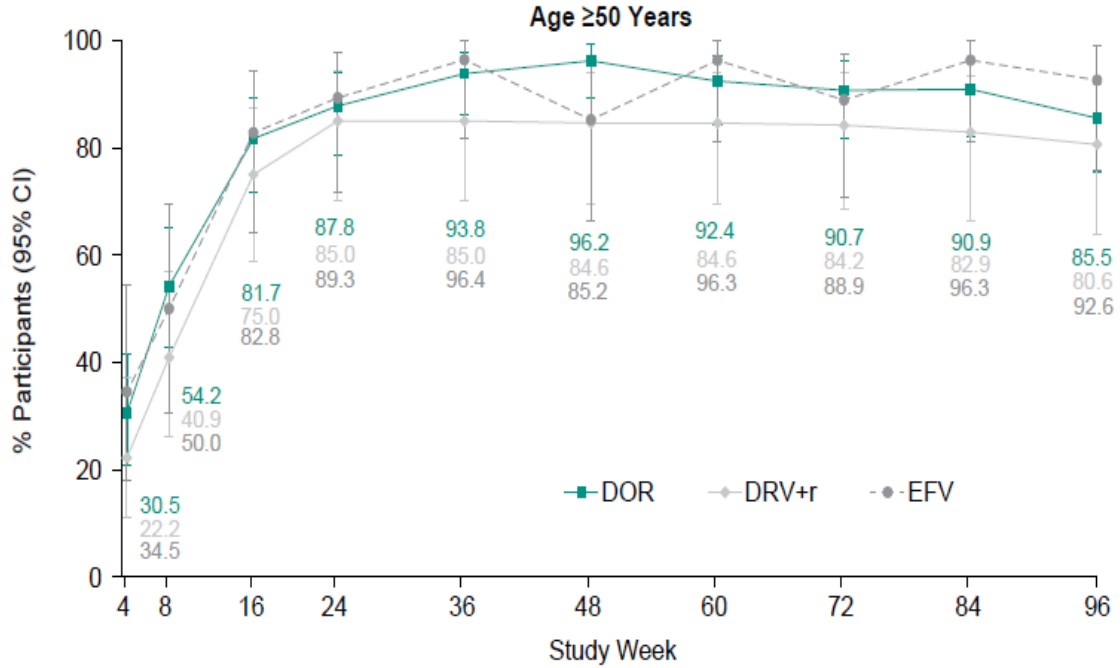
Efficacy Outcomes (Observed Failure Approach)

- At Week 96, the proportion of participants with HIV-1 RNA <50 copies/mL tended to be higher for older participants compared with younger participants in all treatment groups (DOR, 85.5% vs 81.9%; DRV+r, 80.6% vs 76.3%; EFV, 92.6% vs 85.3%)



Number of participants <50 years of age

DOR	655	656	650	651	644	631	622	610	609	603
DRV+r	332	331	329	326	324	317	310	303	296	287
EFV	327	319	316	310	310	304	300	294	288	285



Number of participants ≥50 years of age

DOR	82	83	82	82	80	79	79	75	77	76
DRV+r	45	44	40	40	40	39	39	38	35	36
EFV	29	28	29	28	28	27	27	27	27	27

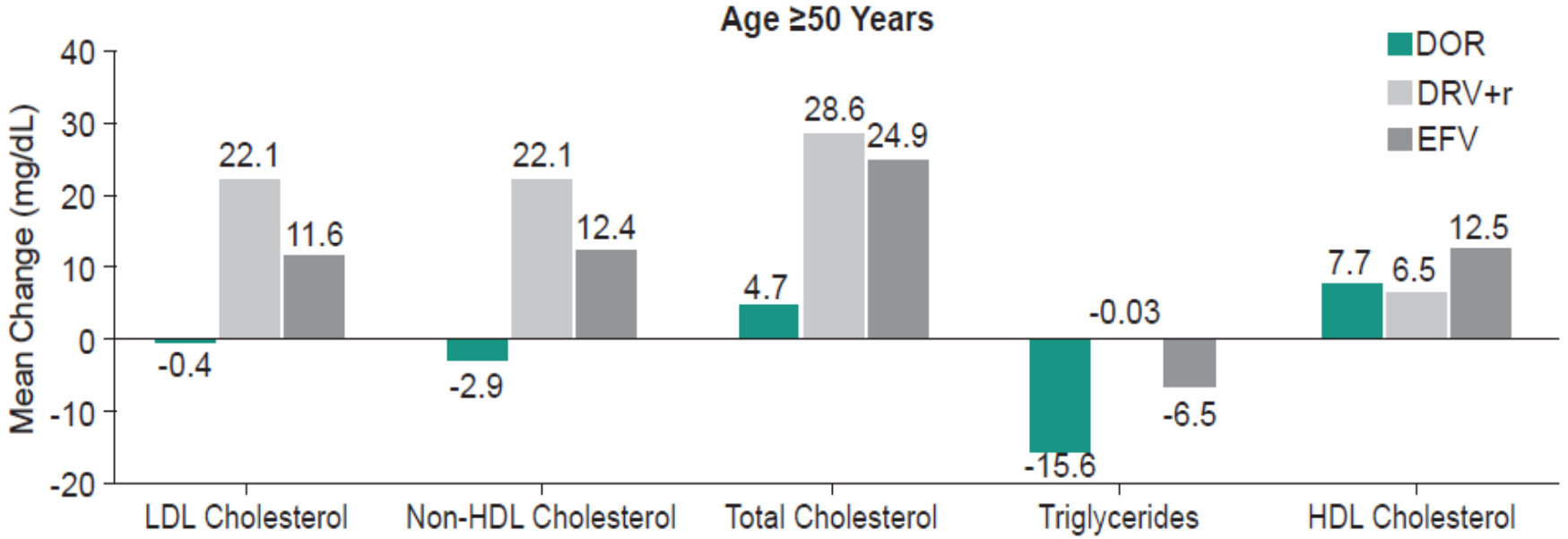
- At Week 96, the mean change in CD4+ T-cell count was similar for older and younger participants in the DOR group (234.6 vs 230.4 cells/mm^3) and the DRV+r group (194.7 vs 208.2 cells/mm^3) but was lower for older participants in the EFV group (165.0 vs 228.5 cells/mm^3)

Safety Outcomes

	Age <50 Years			Age ≥50 Years		
	DOR	DRV+r	EFV	DOR	DRV+r	EFV
% of participants with:	N=754	N=337	N=432	N=101	N=46	N=40
Any AE	86.3	84.3	94.2	90.1	71.7	90.0
Drug-related[a] AE	32.1	32.3	64.6	34.7	30.4	50.0
Serious AE	5.7	6.8	7.9	15.8	21.7	22.5
Serious drug-related AE	0.3	0.3	1.4	0.0	0.0	2.5
Discontinued[b] due to any AE	2.4	3.0	7.6	4.0	6.5	12.5
Discontinued due to drug-related AE	1.9	1.8	6.9	1.0	4.3	10.0
Discontinued due to serious AE	0.4	0.6	1.2	2.0	2.2	0.0

- Serious AEs were more common in the older cohort but were classified as drug-related in only one older participant (in the EFV group).
- Discontinuations due to drug-related AEs were similar across age cohorts in the DOR group but were slightly higher for older participants on DRV or EFV.

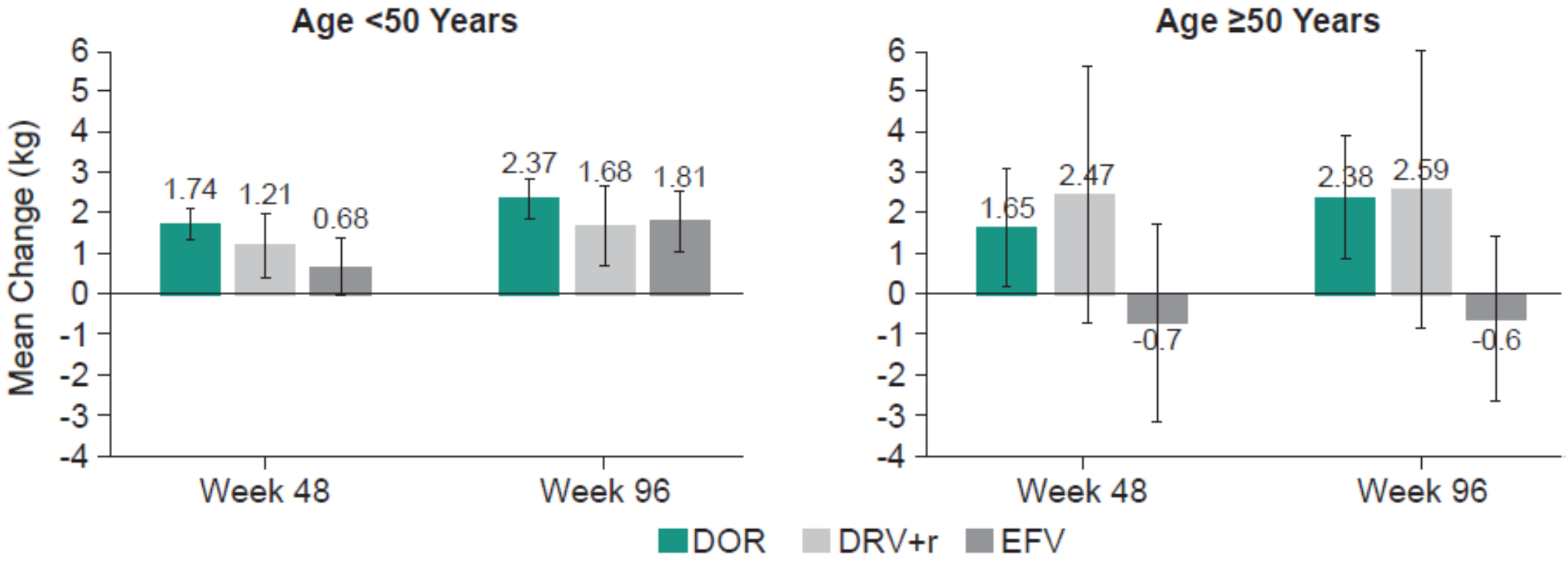
- Mean changes in fasting lipid values from baseline to Week 96 were minimal in older adults who received a DOR regimen.



- Mean change in total cholesterol/HDL ratio: -0.35 for DOR, +0.03 for DRV+r, -0.52 for EFV

Weight Change from Baseline, Mean (95% CI)

- Mean weight gain at Week 48 and Week 96 was similar for older and younger adults in the DOR group.



- Median values for weight gain also were similar for older and younger adults receiving DOR: 1.0 kg (IQR, -1.3 to 3.8) vs 1.0 kg (IQR, -1.2 to 4.0) at Week 48 and 1.5 kg (-1.6 to 4.0) vs 1.5 kg (-1.0 to 5.0) at Week 96.

Conclusions

- Virologic response rates in adults ≥50 years of age were comparable across regimens and similar to response rates in adults <50 years of age.
- Mean increase in CD4 T-cell count in older adults receiving DOR was similar to younger adults and higher than in the comparator groups.
- Incidence of drug-related AEs and discontinuations due to drug-related AEs in older adults in the DOR group were similar to those in younger adults and lower than those in the EFV group.
- Changes in fasting lipids and changes in weight through 96 weeks of treatment were similar for older and younger adults receiving DOR-based regimens.
- DOR appears to be a useful treatment option for adults ≥50 years old, demonstrating a similar efficacy and safety profile compared with younger adults, a neutral lipid profile, and minimal effect on weight.