Pharmacokinetic of raltegravir (800 mg) once-daily in switching strategies in HIV-1-infected patients with suppressed viremia

- **RALONE Study:** prospective, multicenter, observational cohort
- **PK Substudy Primary objective:** evaluation of RAL plasma Concentration 24 hours (C24h) after the last intake 800mg QD actual formulation (OCT)
- **Inclusion criteria:** HIV-1 infected ≥ 18 years, suppressed viremia (pVL) ≤ 50 copies/mL and stable antiretroviral treatment ≥ 6 months, naïve patients for integrase inhibitors or receiving RAL 400 mg BID without previous history of RAL virological failure
- **Endpoints:** PK and immuno-virological data at W48

Patient's Baseline characteristics (n = 71)

Age (years)*	46 (40 ; 53)
Male*	47 (66 %)
CD4 (cells/mm^3)*	588 (462 ; 783)
ARV duration (years)*	14 (7 ; 16)
Previous lines of treatment*	5 (3 ; 9)
Patients with RAL 400mg BID before 800mg QD (n, %)	17 (24 %)
Backbone associated with RAL 800mg QD (n, %) **•TDF/FTC (300/200mg QD)** •ABC/3TC (600/300mg QD) •ETR (400mg QD) •NVP XR (400mg QD) •ATV/r (300/100mg QD) and ATV (400mg QD)	 **42 (60 %)** 13 (18 %) 7 (10 %) 3 (4 %) 3 (4 %) & 3 (4 %)

**Median (IQR25-75 %)*

Previous treatment and reasons for switching to RAL QD (n = 71)

Previous treatment	
•NRTIs	4 (6 %)
•NRTIs + PIs/r	**45 (63 %)**
•NRTIs + NNRTI	18 (25 %)
•PIs/r + NNRTI	4 (6 %)
Reasons for switching	
•Intolerance	**47 (66 %)**
•Drug-drug interaction	6 (8 %)
•Simplification	4 (6 %)
•Others	14 (20 %)

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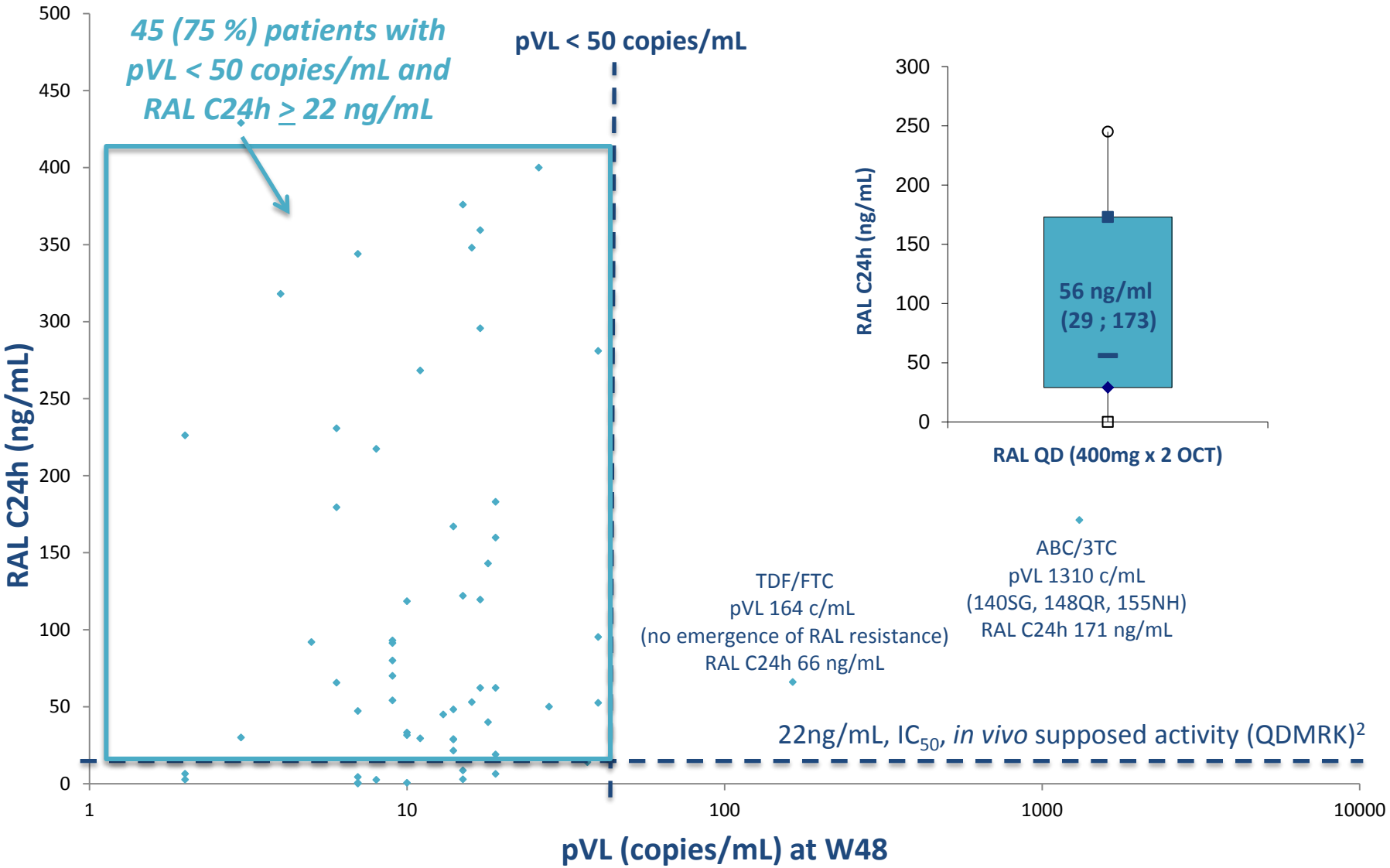
Results: Plasma Viral Load (pVL) at W48 and RAL C24h from W12 to W24 (n = 60)



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Discussion - Conclusion

- Switching to RAL 800mg QD (OCT as 400mg x 2) containing regimen
  - demonstrates 78% of adequate RAL C24h

Study	*This study*	*Rizk et al.[2] QDMRK*		*Rizk et al.[3]*
RAL Daily Dose	**800mg QD** as 400mg x 2 **OCT (n=61)**	**800mg QD** as 400mg x 2 **OCT (n=245)**	**400mg BID** as 400mg x 1 **OCT (n=304)**	**1200mg QD** as 600mg x 2 **reformulated** tablet (n=24)
Population	HIV-1 infected patient			Healthy subjects
GM* RAL Cmin (ng/mL)	50 ng/mL	40 ng/mL	183 ng/mL	39 ng/mL
CV% RAL C24h (ng/mL)	~ 122%	~ 140%	~ 126%	~ 72%
RAL C24h $\leq$ 14 ng/mL (IC_{95} *in vitro*, WT HIV-1)	11 (18 %)	104 (43 %)	42 (14 %)	N.A
RAL C24h $\leq$ 22 ng/mL (EC_{50} *in vivo*, supposed efficacy threshold)	13 (22 %)	N.A	N.A	2 (9 %)

  - maintains virological suppression (pVL < 50 copies/mL) and immunological efficacy at W24 and W48 in all patients except three (96 %)
  - emergence of RAL resistance in two patients (Q148R/K, N155H, G140S) with virological failure
  - is well tolerated

**Geometric Mean*

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