



Evolocumab Rapidly Reverses Impaired Coronary Endothelial Function in People Living with HIV and in Patients with Dyslipidemia

The EVOLVE Study

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Disclosure

- Amgen provided the PCSK9 monoclonal antibody, evolocumab, for this study

Cardiovascular Disease Risk in HIV Positive Individuals (HIV+)

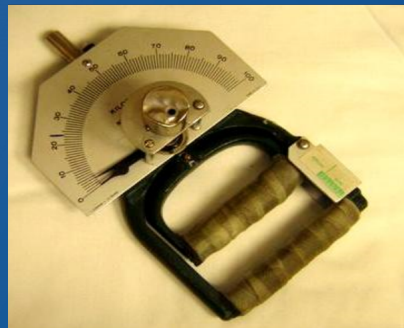
Hypothesis:

1. PCSK9 links inflammation with impaired coronary endothelial cell function



Methods

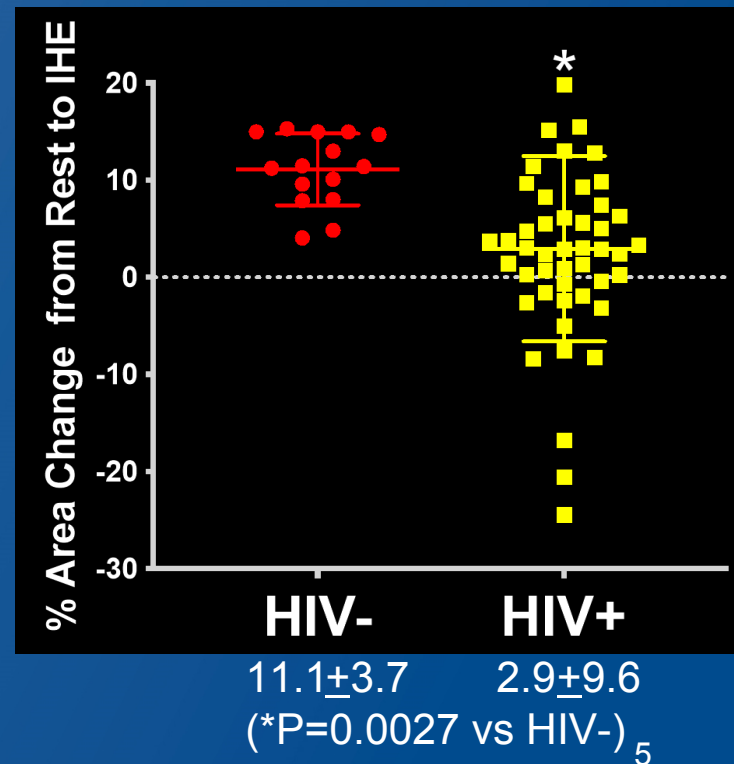
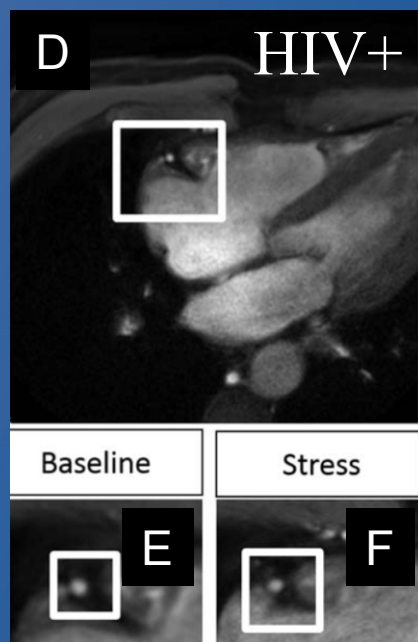
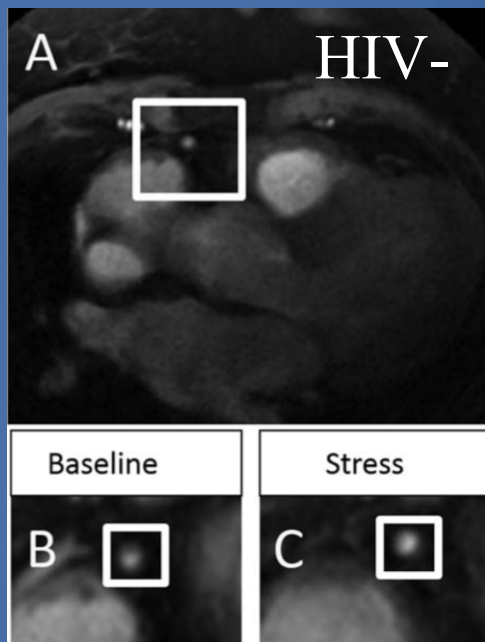
- Subjects: HIV patients and patients with dyslipidemia with no CAD (on prior imaging with CTA)
- Each person underwent MRI with isometric handgrip exercise (IHE) an endothelial dependent stressor to evaluate Coronary Endothelial Function (CEF).
- On the same day they had blood drawn for lipid panels.
- 1x Evolocumab 420mg.
- CEF Endpoints (MRI with IHE):
 - Change in coronary artery cross sectional area (mm^2) from rest to IHE stress
- Statistical analysis:
 - Means \pm SD
 - $p < 0.05$ statistically significant



Continuous isometric handgrip stress at 30% of maximum force

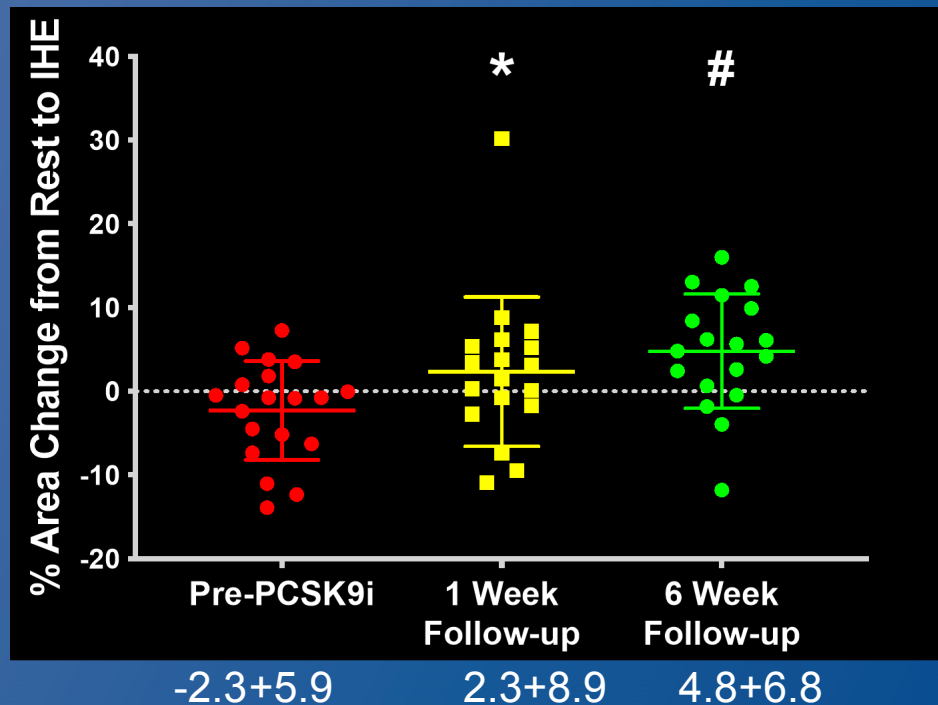
Weiss, RG, et al., *N Engl J Med*, 1990. 323(23):1593-600

Coronary Endothelial Function is Impaired in HIV+



Evolocumab Significantly Improves CEF in People Living with HIV

N= 19

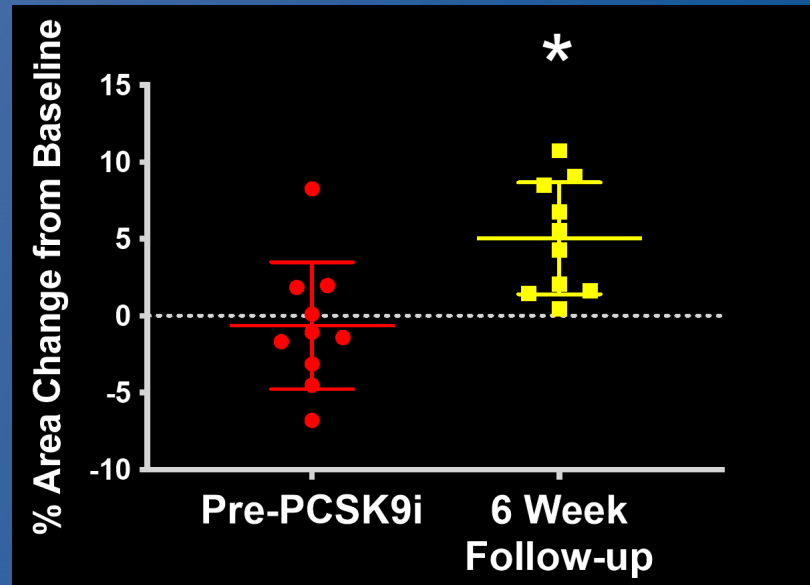


Change in
CEF vs. LDL-C

R=0.1445
P=0.5935

PCSK9i Significantly Improves CEF in Patients with Dyslipidemia

N= 10



Change in LDLc vs CEF
R=0.48
P=0.1874

*p=0.002 vs. Pre-PCSK9i

Conclusion

- In HIV+ people
 - PCSK9 inhibition rapidly (within 1 week) improves abnormal coronary endothelial function (CEF)
 - Independent of LDL-C lowering
 - PCSK9 is a link between HIV-associated inflammation and impaired coronary endothelial function
- In Dyslipidemia
 - PCSK9 inhibition improves CEF at 6 week timepoint
 - Potentially related to LDL-C reduction

Acknowledgements

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- Center for AIDS Research (CFAR) JHU
- AMGEN

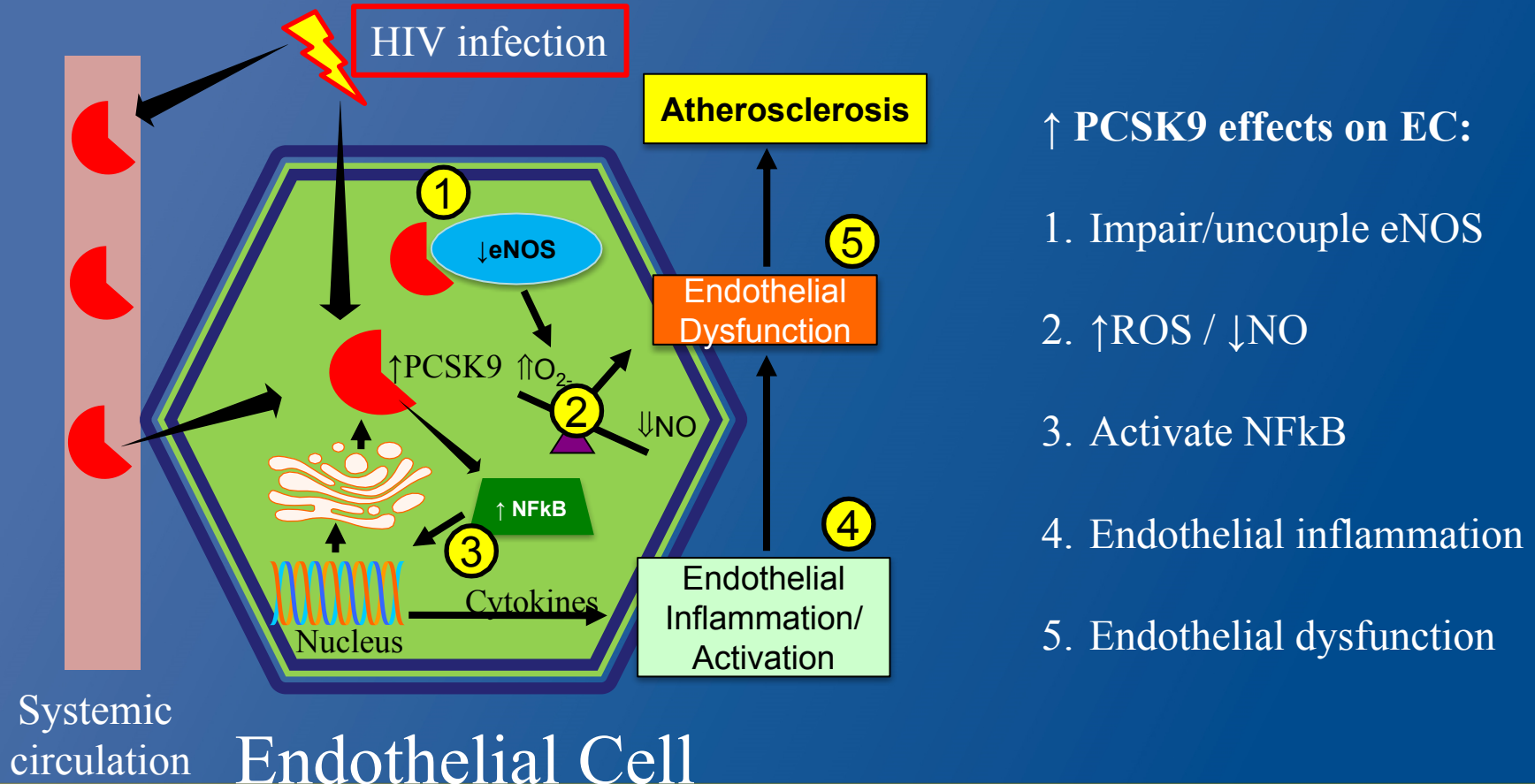
Supplemental Material



Study Population

Characteristics:	Dyslipidemia [n=10]	HIV+ [n=19]	P
Age (years), mean \pm SD	55 \pm 11	52 \pm 8	0.38
Male sex, n (%)	10 (91)	17 (85)	1
African American, n (%)	3 (27)	18 (85)	0.0007
BMI, mean \pm SD	27 \pm 4	26 \pm 4	0.51
PCI, n (%)	0	0	NA
CABG, n (%)	0	0	NA
HTN, n (%)	3 (10)	4 (20)	1
Diabetes, n (%)	2 (18)	0	0.12
Smoker, n (%)	0	3 (15)	0.54
ACE-inhibitor	3 (27)	2 (10)	0.32
Statin, n (%)	5 (45)	4 (20)	0.23
non-statin LDLc lowering, n (%)	9 (81)	0	0.0001
Beta-blocker	2 (18)	1 (5)	0.28
ASA, n (%)	5 (45)	0	0.0027
LDL (mg/dL), mean \pm SD	150 \pm 69	120 \pm 43	0.15
HDL (mg/dL), mean \pm SD	59 \pm 40	49 \pm 11	0.29
Triglycerides (mg/dL), mean \pm SD	165 \pm 79	111 \pm 49	0.02
Non-HDL (mg/dL), mean \pm SD	183 \pm 82	143 \pm 48	0.09
HAART, n (%)	NA	20 (100)	NA
CD4+ cell count (cells/uL) >200 (%)	NA	20 (100)	NA
Viral load <20 copies/mL (%)	NA	20 (100)	NA

PCSK9 May be the Link



- **02/09/2019**

Presenter - from 16:40 to 17:50 - Room: Agora 2 - Poster Area

Sess. Title : Influence of metabolic or infection disease on the heart

Pres. FP : 4313 / from 17:23 to 17:32

Pres. Title : Evolocumab rapidly reverses impaired coronary endothelial function in six weeks in people living with HIV and in patients with dyslipidemia

Fast paced and interactive session with key messages of 8 abstracts.

Each presenter will have 5 minutes (max 5 slides) + 3 minutes Q&A led by the chairpersons who have to enforce the strict timing as well as to initiate and encourage a fruitful discussion.