TREATMENT OF HCV-HIV CO-INFECTION

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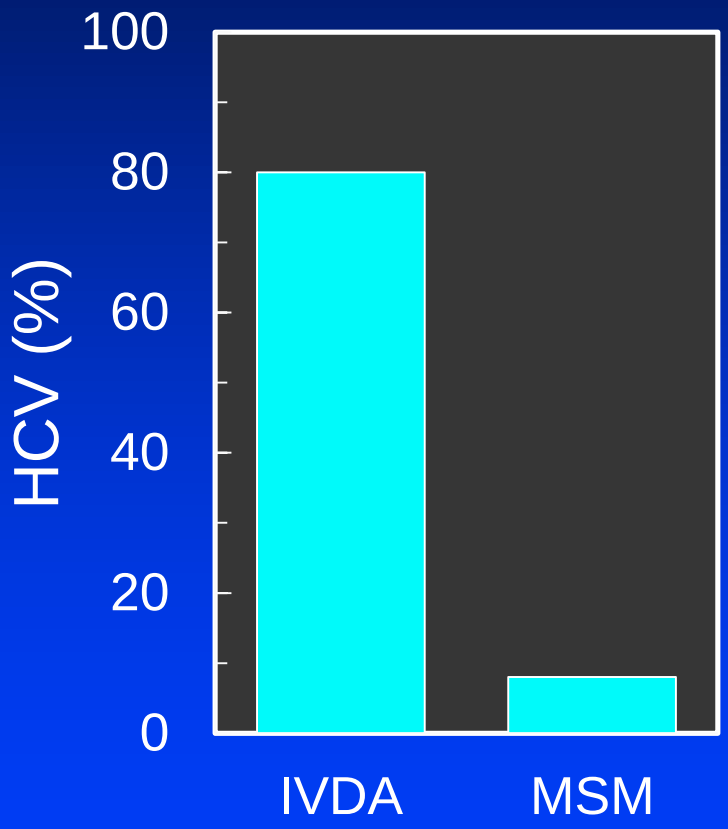
PATIENTS WITH HIV
HCV AND CAUSES OF DEATH

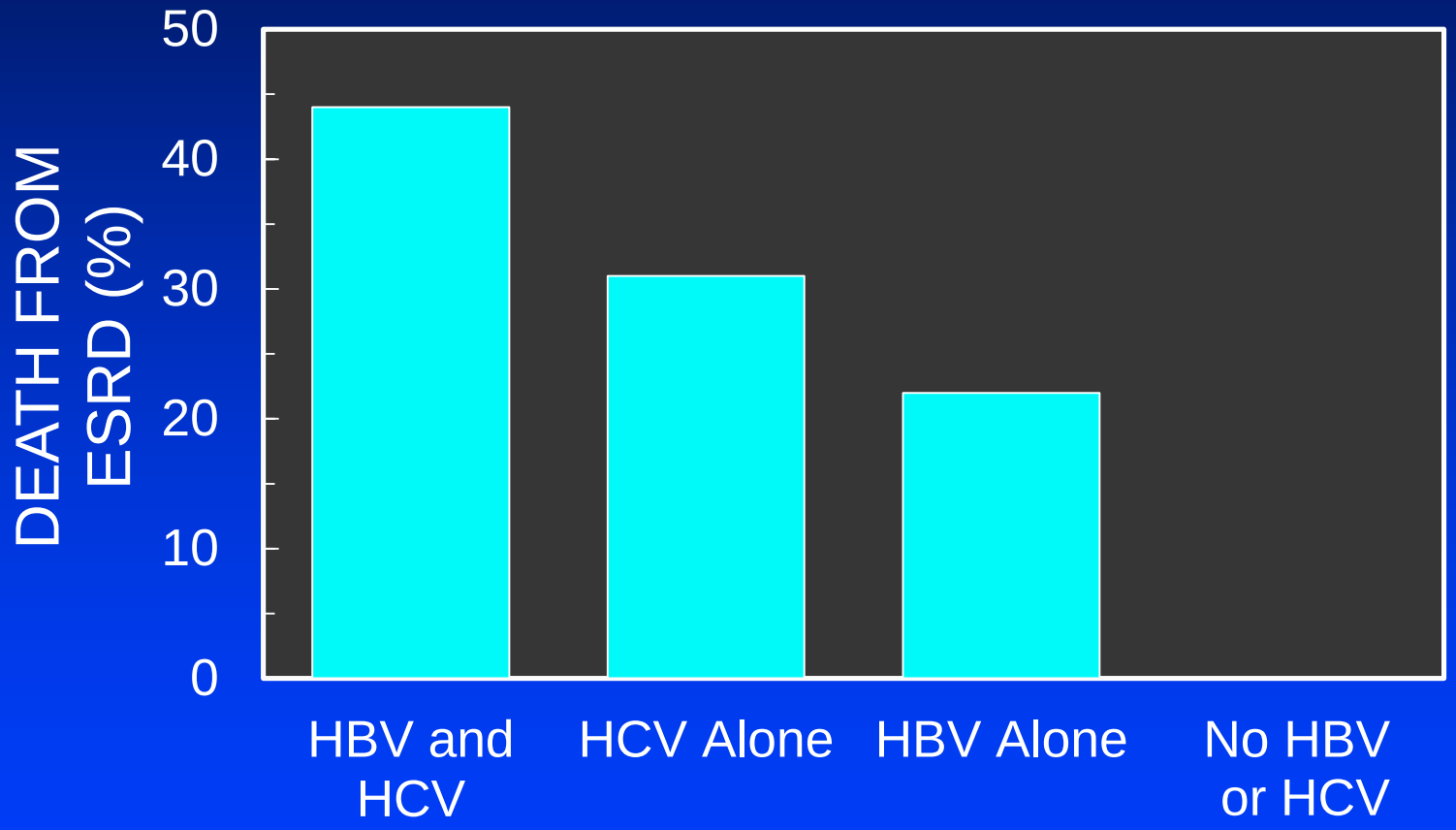


75% of patients with HIV have HCV

	% of Deaths
Non-AIDS Malignancy	19%
Liver failure and HCC	18%
AIDS	16%
Non-AIDS infections	9%
Substance abuse	7%
MI	6%
Suicide	6%

M Sulkowski et al. Ann Int Med 2003;
R Weber et al. HIV Med. 2013; 14:195-207.

PATIENTS WITH HIV
DEATH FROM ESRD



Salmon-Ceron et al.
J Hepatol 2005; 42:799-805.

TREATMENT OF HCV-HIV CO-INFECTION CHOICES: NOW AND IN FUTURE

NS3/4A	NS5A	NS5B	Ribavirin
Paritaprevir/rtv	Ombitasvir	Dasabuvir	GT 1A non-CX only
	Ledipasvir	Sofosbuvir	No
	Daclatasvir	Sofosbuvir	No
Grazoprevir	Elbasvir		No

TREATMENT OF HCV-HIV CO-INFECTION
ARV AGENTS STUDIED

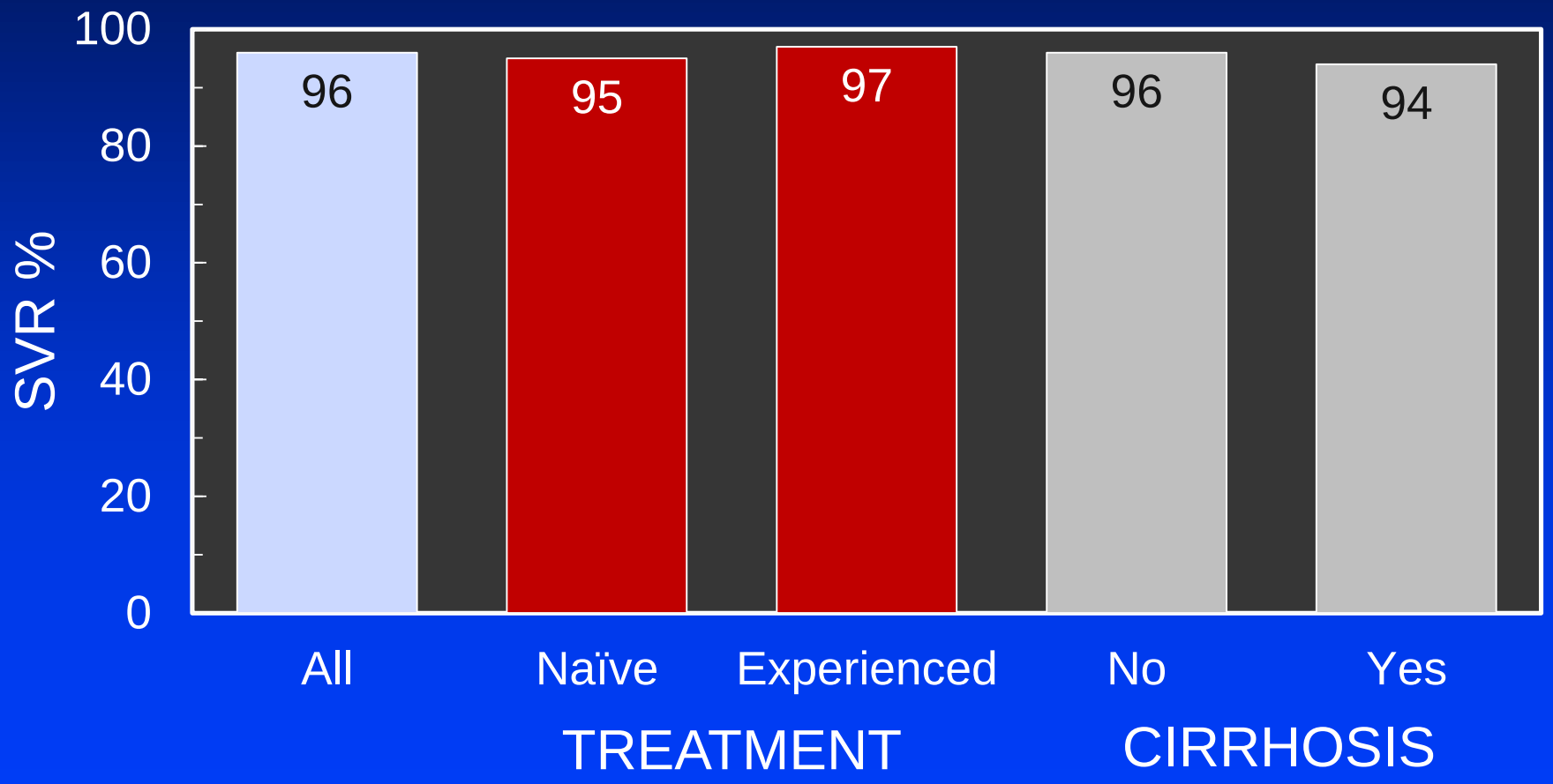
	DAC-SOF	LDV-SOF	3D	GRZ-ELB
Atazanavir/r	X		X	
Darunavir/r	X			
Lopinavir/r	X			
Efavirenz	X	X		
Nevirapine	X			
Rilpivirine	X	X	X	X
Dolutegravir	X			X
Raltegravir	X	X	X	X
Enfuvirtide	X			
Maraviroc	X			
Zidovudine	X			
Lamivudine	X		X	X
Abacavir	X		X	X
Tenofovir	X	X	X	X
Emtricitabine	X	X	X	X

LEDIPASVIR-SOFOSBUVIR
ION-4: HCV-HIV CO-INFECTION

- Phase 3 open-label multicenter study (N=335)
- Genotype 1 only
- LDV/SOF for 12 weeks
- No ribavirin
- End-point SVR12
- HIV RNA< 50,000
- CD4 >100 cells
- Platelet count >50,000
- Hemoglobin >10 gm/dl
- HIV regimens

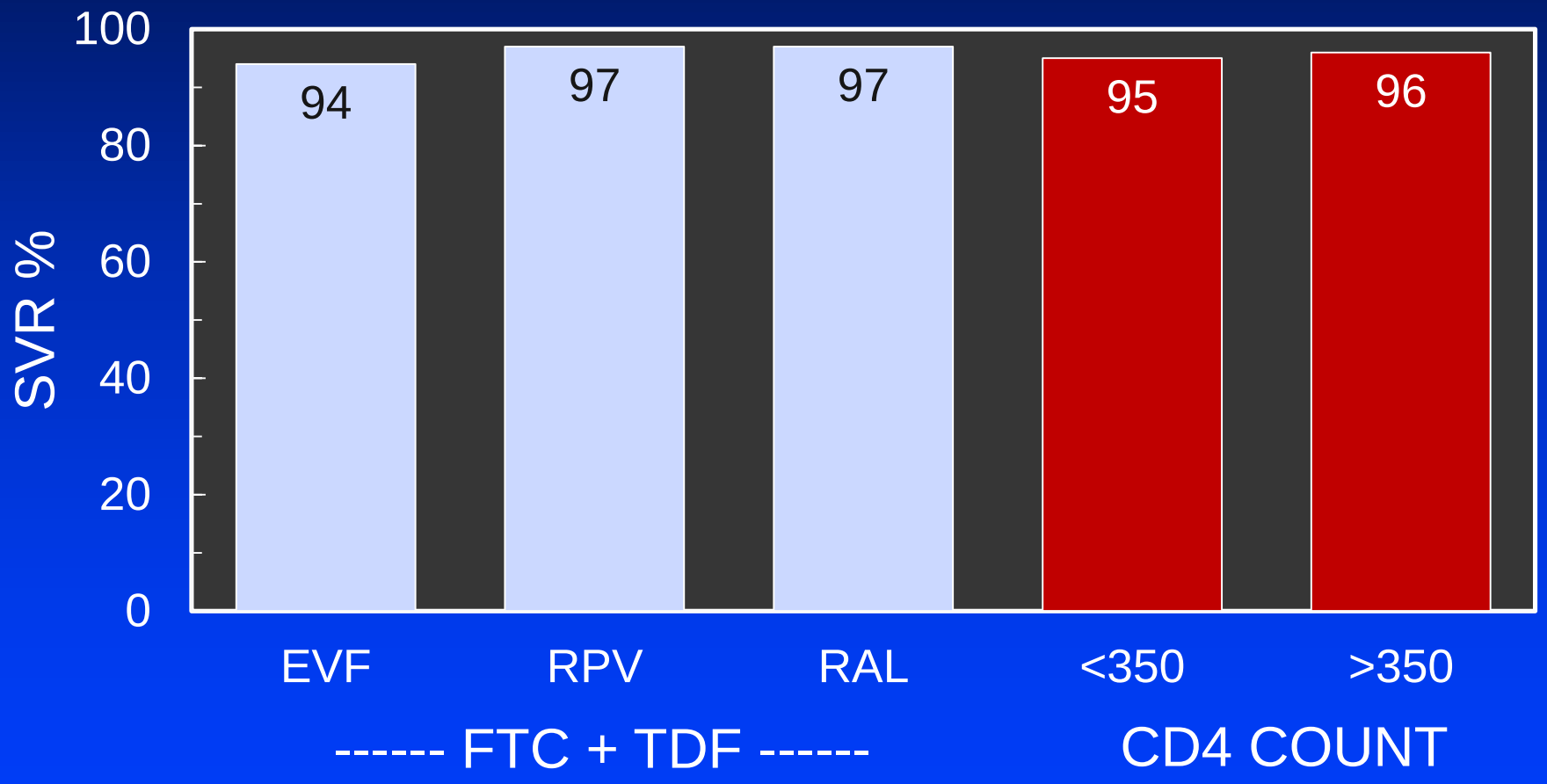
Efavirenz + FTC + TDF	48%
Raltegravir + FTC + TDF	44%
Rilpivirine + FTC + TDF	9%

ION-4: LDV-SOF
HCV-HIV CO-INFECTION



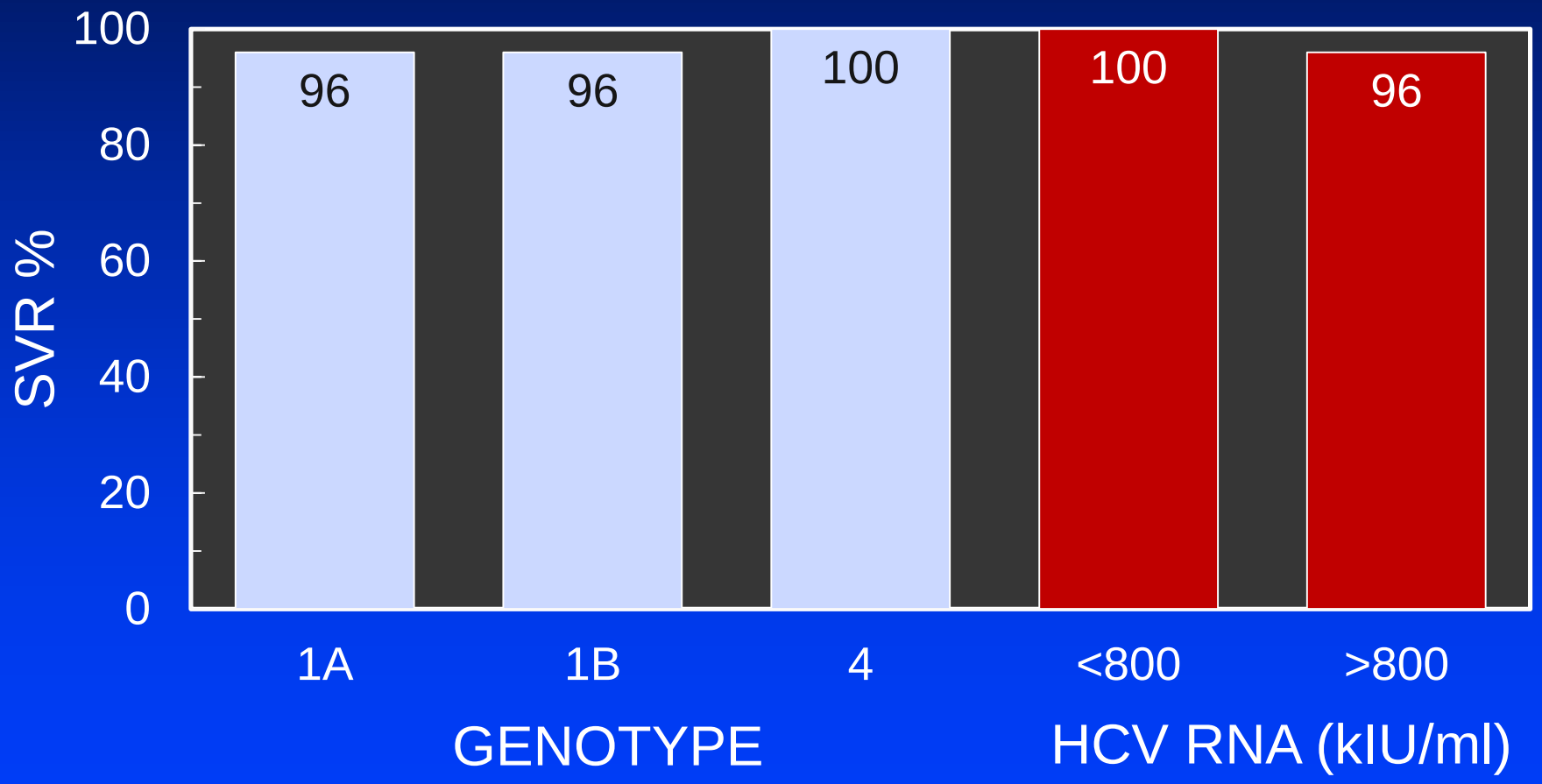
Naggie et al,
CROI 2015, Oral #LB-152

LDV-SOF FOR HCV-HIV CO-INFECTION
BASELINE HIV REGIMEN AND CD4



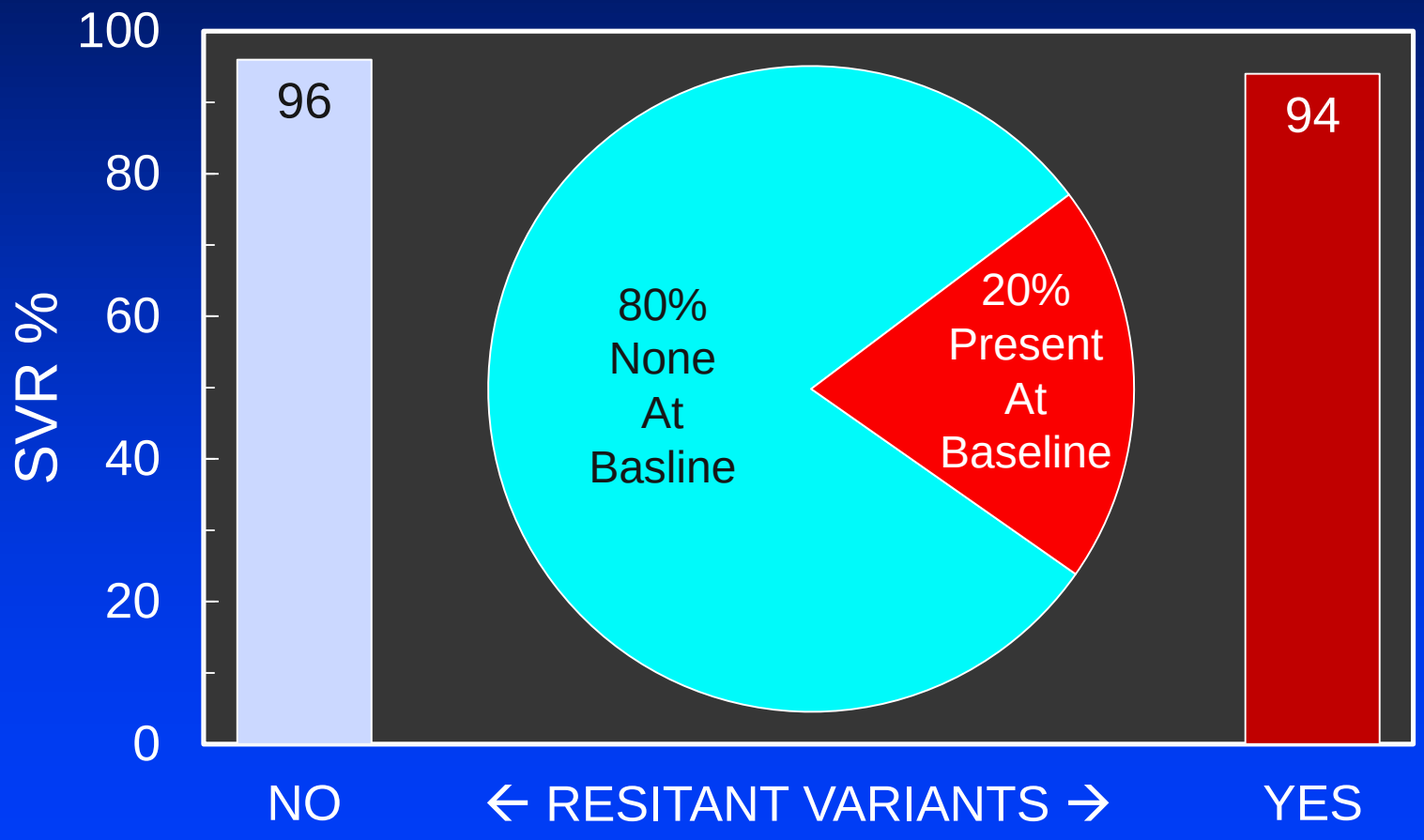
Naggie et al,
CROI 2015, Oral #LB-152

LDV-SOF FOR HCV-HIV CO-INFECTION
GENOTYPE AND HCV RNA LEVEL



Naggie et al,
CROI 2015, Oral #LB-152

LDV-SOF FOR HCV-HIV CO-INFECTION
BASELINE NS5A MUTATIONS



Naggie et al,
CROI 2015, Oral #LB-152

LDV-SOF FOR HCV-HIV CO-INFECTION ADVERSE EVENTS

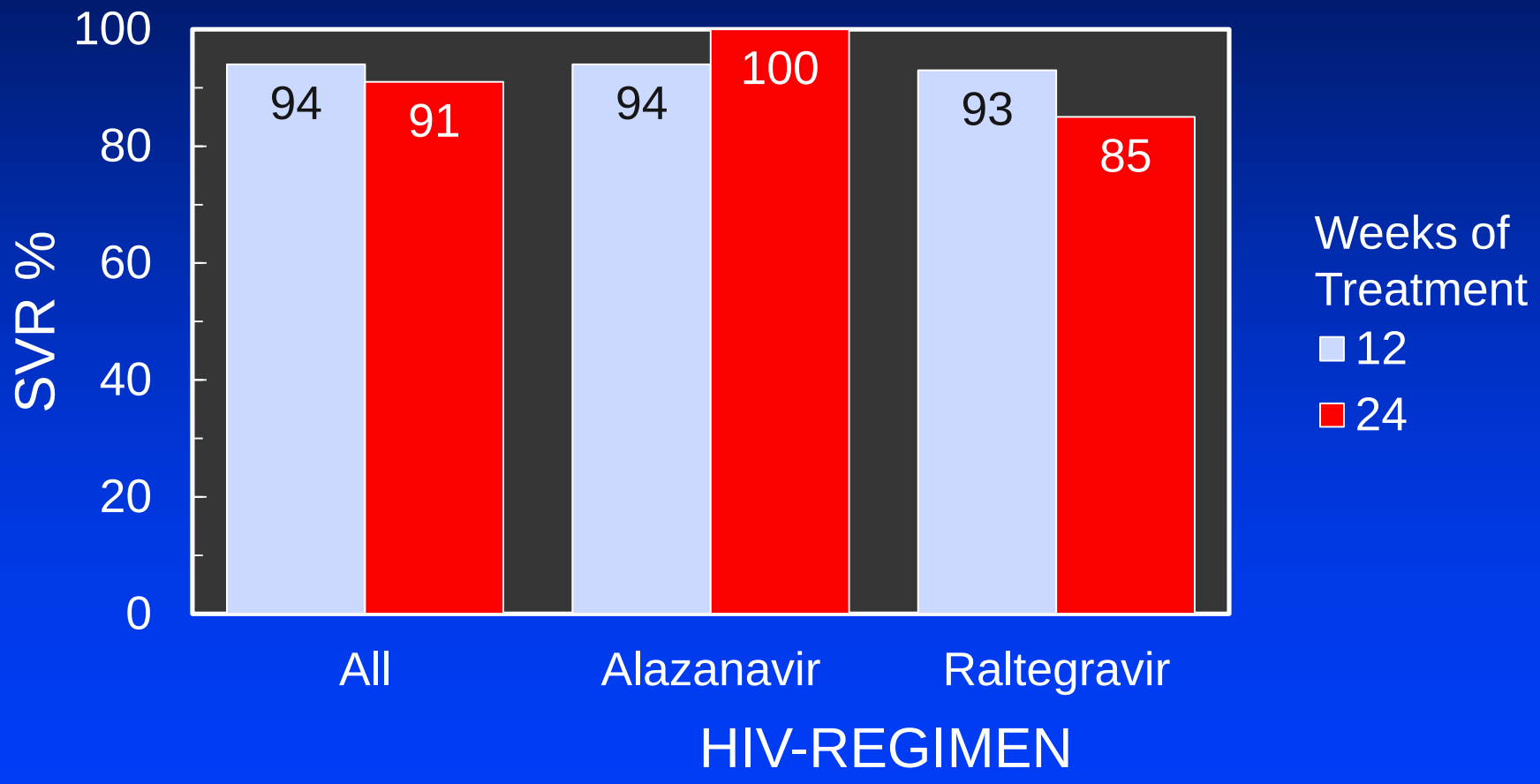
N	335
Adverse Events: Headache Fatigue Diarrhea Nausea Arthralgia URI	77% 25% 21% 11% 10% 7% 5%
DC due to AE	0%
Serious AE	2%
Death	<1% (1)
Grade 3-4 Lab abnormalities	11%

Naggie et al,
CROI 2015, Oral #LB-152

PTV-OBV-DBV (3D)
HCV-HIV CO-INFECTION

- Phase 2/3 open-label multicenter study (N=63)
- Genotype 1 only
- All patients treated
- 3D for 12 or 24 weeks
- Ribavirin (WB) utilized in both treatment arms
- End-point SVR12
- HIV RNA< 40
- CD4 >200 cells
- Atazanavir or raltegravir ART regimens

3D
HCV-HIV CO-INFECTION



JJ Eron et al.
HIV Drug Therapy 2014

3D FOR HCV-HIV CO-INFECTION
ADVERSE EVENTS

	Atazanavir		Raltagravir	
Weeks of Treatment	12	24	12	24
Any AE	81%	83%	100%	90%
Fatigue	44%	50%	73%	30%
Insomnia	19%	25%	13%	20%
Nausea	13%	33%	20%	10%
Headache	13%	17%	27%	10%
URI	13%	25%	13%	10%
T BILI (3-10mg)	50%	50%	13%	0%
ALT>5xULN	0%	0%	0%	0%

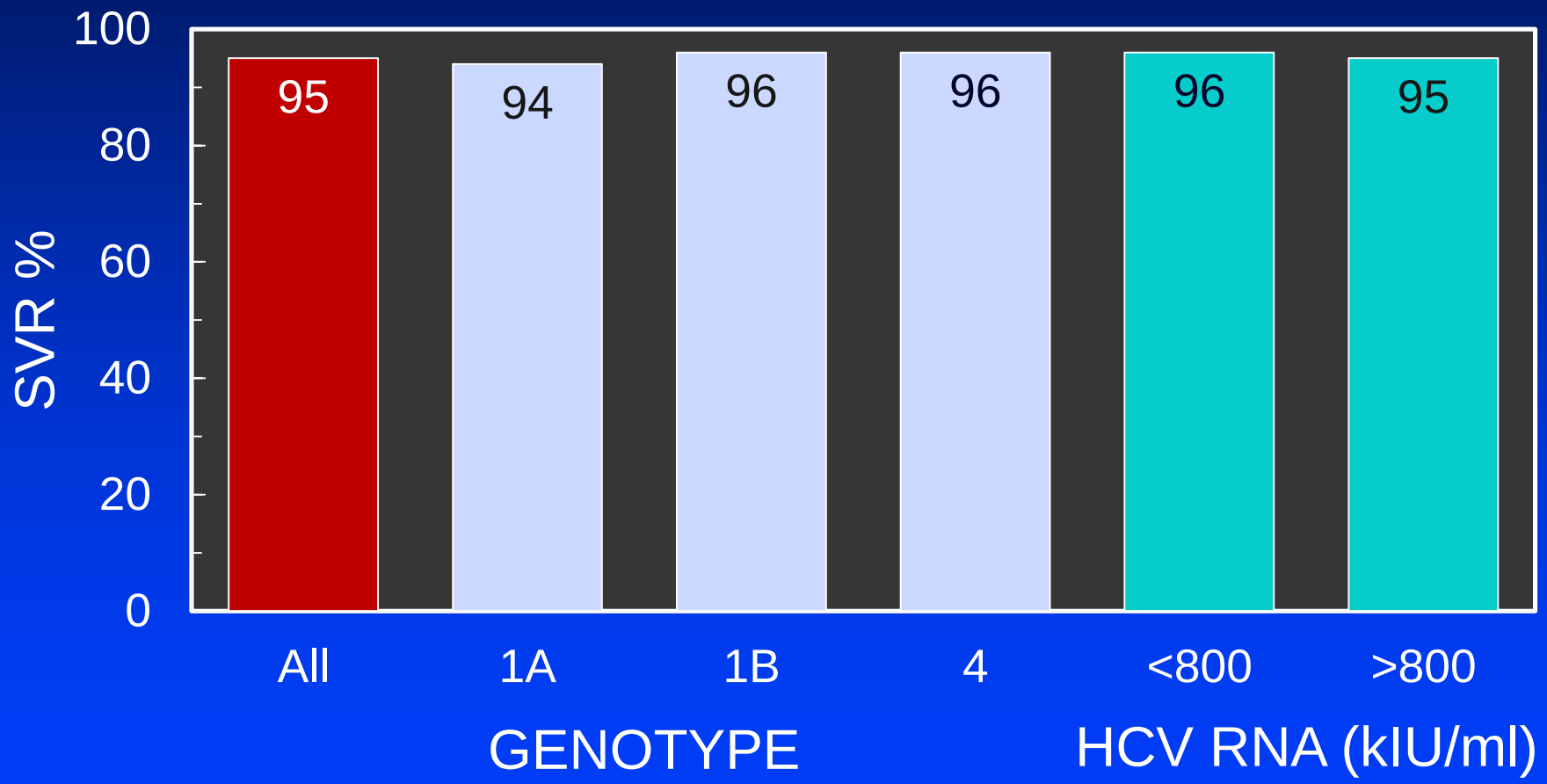
JJ Eron et al.
HIV Drug Therapy 2014

GRAZOPREVIR-ELBASVIR HCV-HIV CO-INFECTION

- Phase 2/3 open-label, single arm (N=218)
- Genotype 1, 4, 6
- All patients treated 12 weeks
- No Ribavirin
- End-point SVR12
- HIV RNA< 50,000 copies/ml
- CD4 >500 cells
- ART

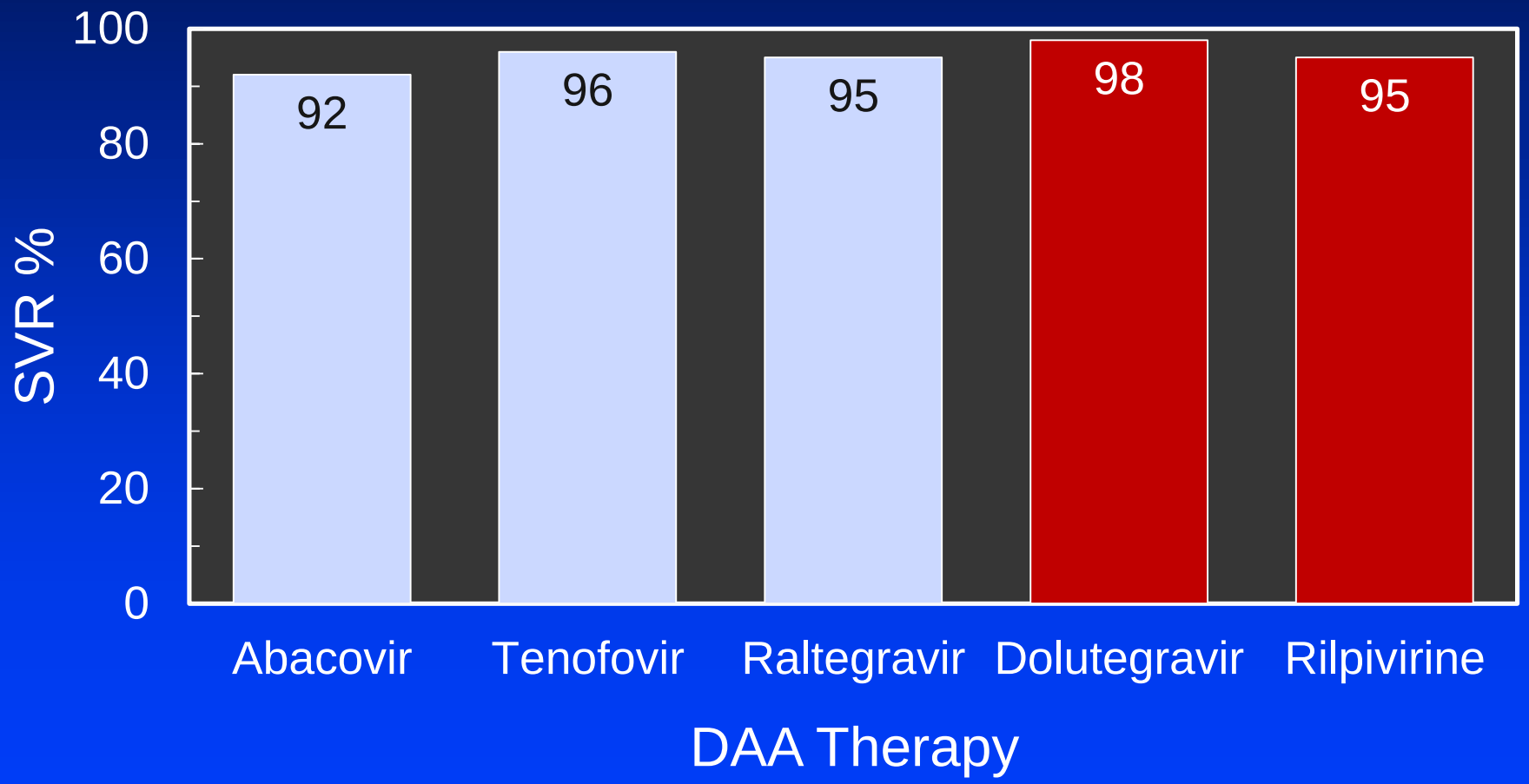
	ART Naïve	On ART
CD4 count (cells/ml)	>500	>200
HIV RNA (copies/ml)	>200	UD

LDV-SOF FOR HCV-HIV CO-INFECTION
GENOTYPE AND HCV RNA LEVEL



JK Rockstroh et al,
EASL 1025

LDV-SOF FOR HCV-HIV CO-INFECTION HIV REGIMEN



JK Rockstroh et al,
EASL 1025

GRZ – ELB FOR HCV-HIV CO-INFECTION ADVERSE EVENTS

N	218
Adverse Events: Fatigue Headache Nausea	77% 13% 12% 9%
DC due to AE	0%
Serious AE	3%
Death	0%
TBILI >2.5-5x baseline	4%
Creatinine >2.5x baseline	0%

JK Rockstroh et al,
EASL 1025

GRZ-ELB FO HCV-HIV CO-INFECTION RELAPSE AND RESISTANCE

- Relapse 6
  - 5 receiving ART treatment
  - 1 reinfection
  - 5 had RAV at baseline
- No change in CD4 count
- HIV became transiently detectable in 2 patients

JK Rockstroh et al,
EASL 1025

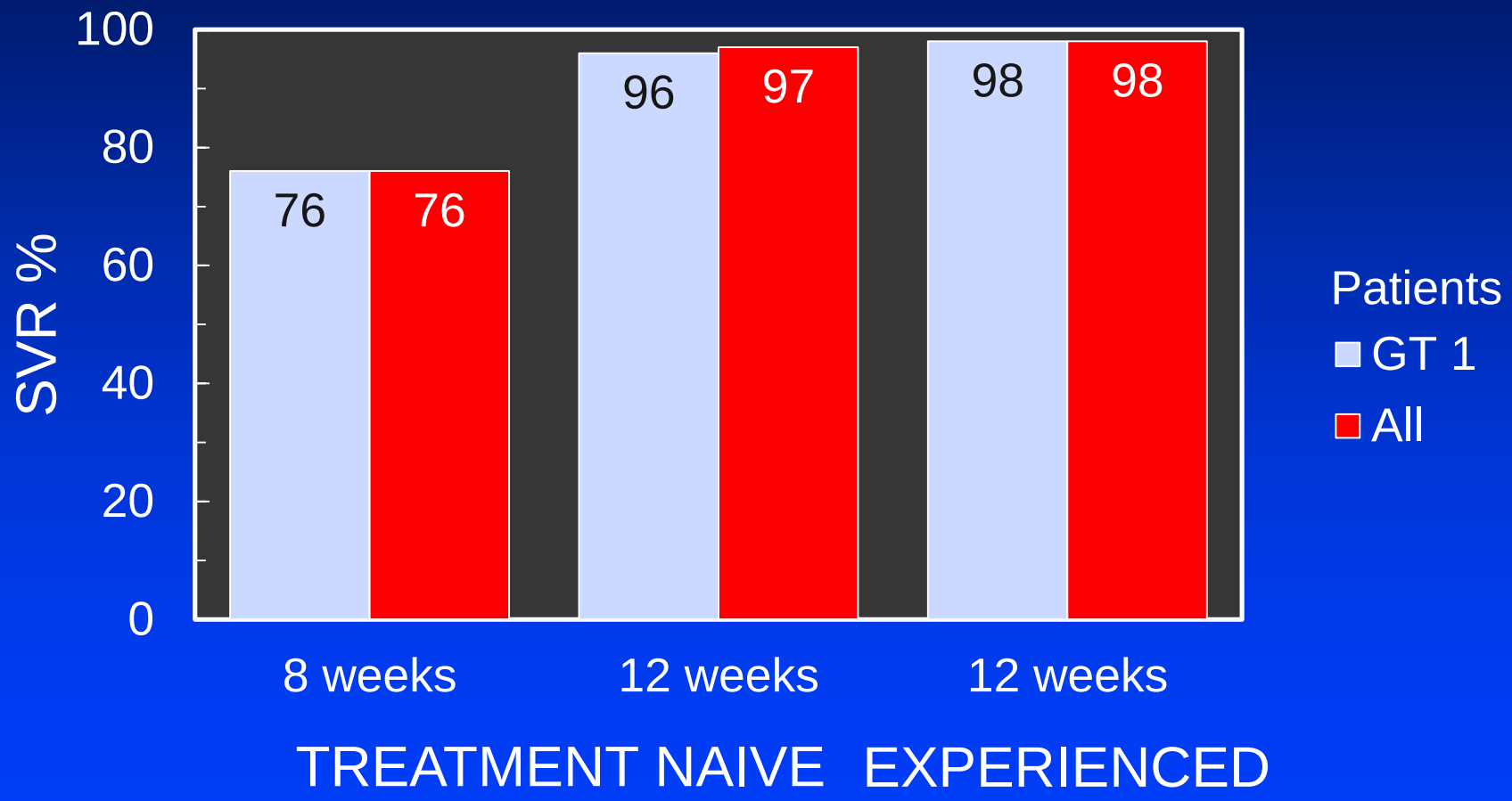
DACLATASVIR - SOFOSBUVIR HCV-HIV CO-INFECTION

- RCT of 8 versus 12 weeks for treatment naïve
- Single arm of 12 weeks for treatment experienced
- Total N=203
- All Genotypes
- End-point SVR12
- Creatinine clearance >50 ml/min
- HIV regimen not specified
- With or without ART

	No ART	On ART
CD4 count (cells/ml)	>350 (cells/ml)	>100
HIV RNA (copies/ml)		<50 (copies/ml)

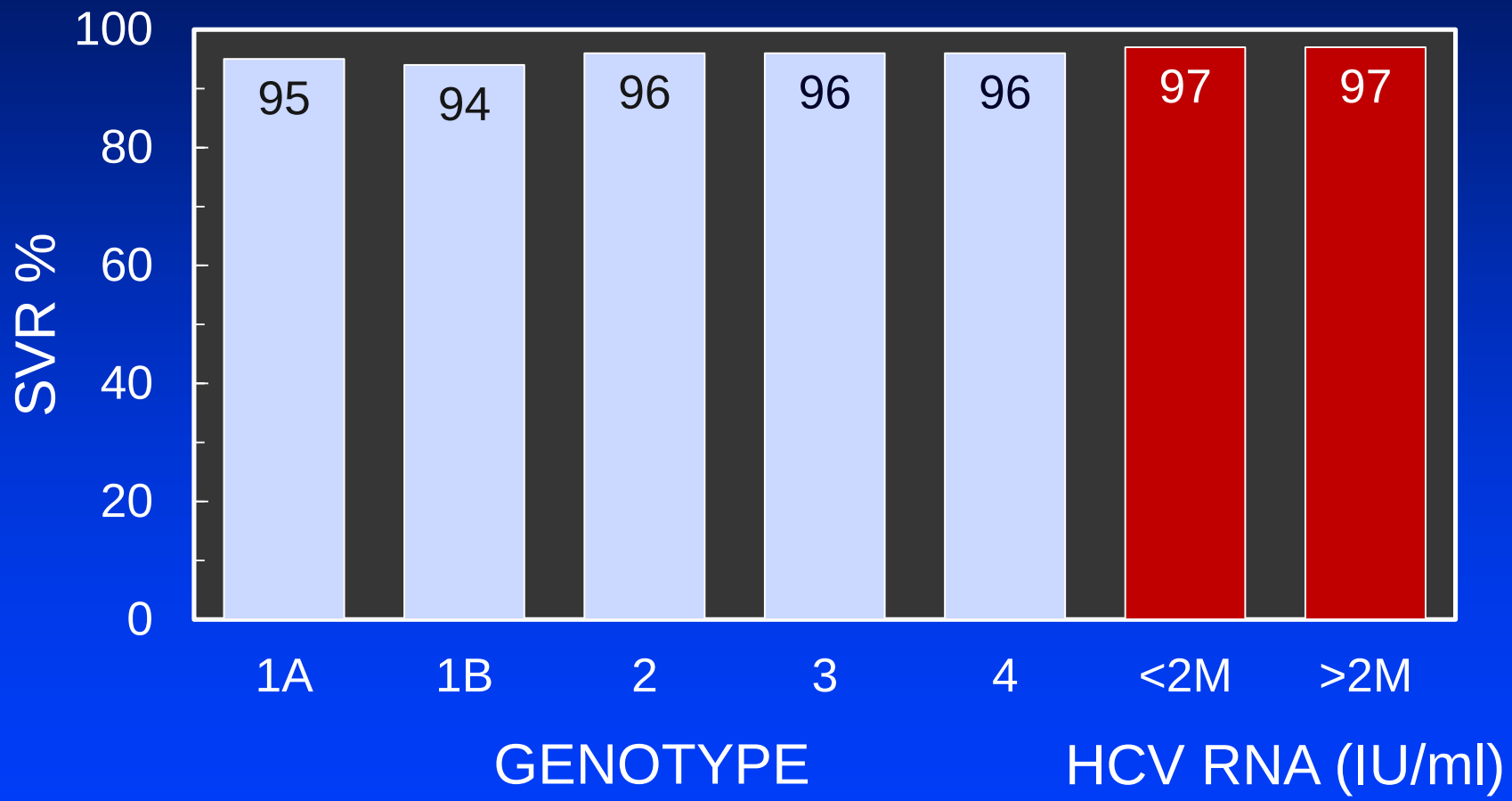
DL Wyles et al
EASL 2014

DAC-SOF
HCV-HIV CO-INFECTION



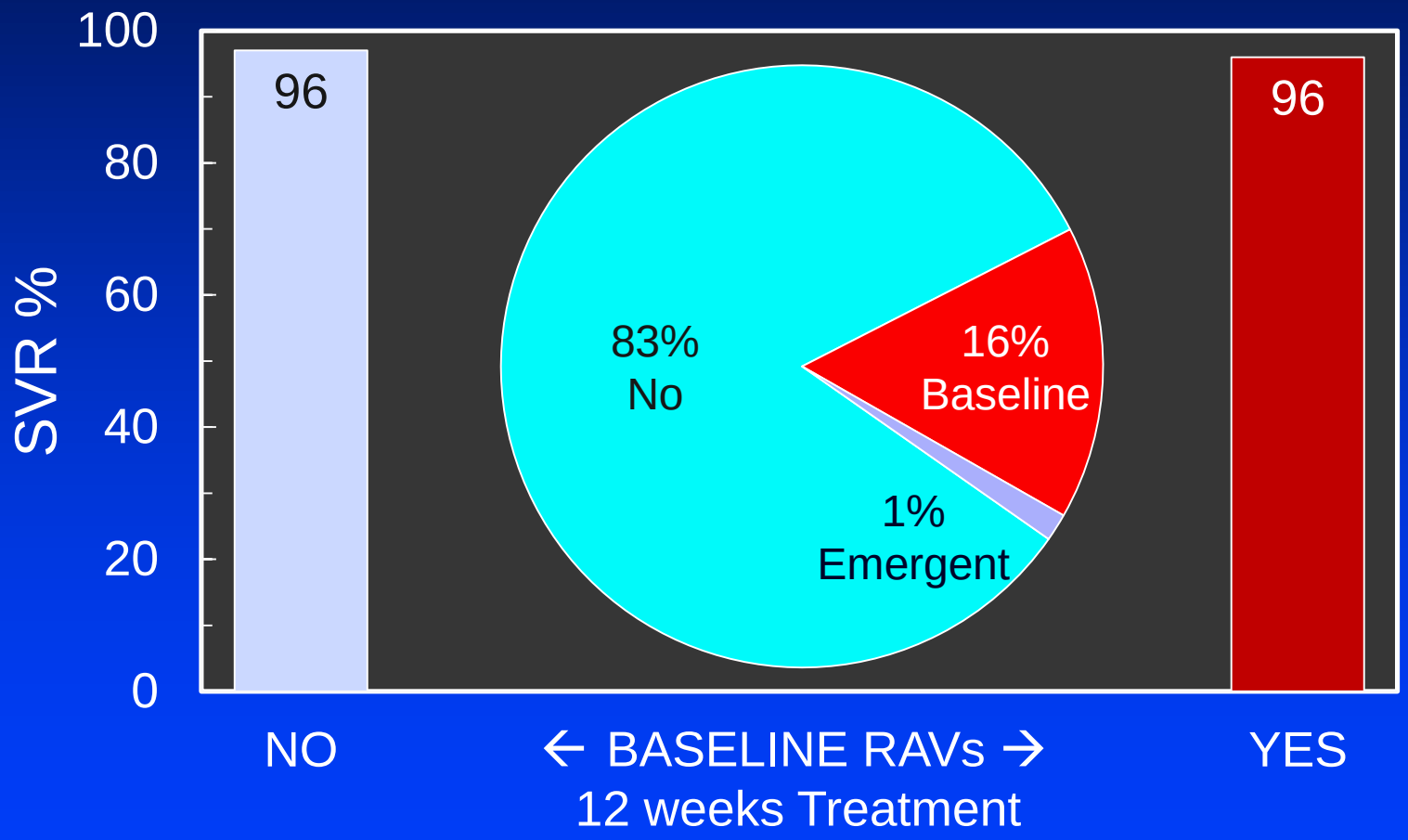
DL Wyles et al
EASL 2014

DCA-SOF FOR HCV-HIV CO-INFECTION
12 WEEKS TREATMENT



DL Wyles et al
EASL 2014

DCT-SOF FOR HCV-HIV CO-INFECTION NS5A MUTATIONS



DL Wyles et al
EASL 2014

DCT – SOF FOR HCV-HIV CO-INFECTION ADVERSE EVENTS

	Naïve	Experienced
N	101	52
Adverse Events: Fatigue Nausea Headache Diarrhea	73% 19% 14% 12% 11%	71% 19% 15% 15% 6%
DC due to AE	0%	0%
Serious AE	1%	6%
Death	0%	0%
TBILI >2.5-5x baseline	5%	4%
AST >5x ULN	0%	0%

DL Wyles et al
EASL 2014

TREATMENT OF HCV-HIV CO-INFECTION SUMMARY

- Patients with HCV-HIV co-infection have:
  - High rate of liver related death
  - More rapid progression to cirrhosis
  - Higher incidence of ERSD
- Patients with HCV-HIV co-infection have very high rates of SVR with all the oral DAA regimens
- These appear very similar to the SVR rates achieved in patients with HCV mono-infection
- Patients with HCV co-infection should be treated with the same regimens as patients with HCV mono-infection