NORTHWEST AIDS EDUCATION AND TRAINING CENTER

CROI 2015: What's New in Hepatitis?

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No financial conflicts of interest

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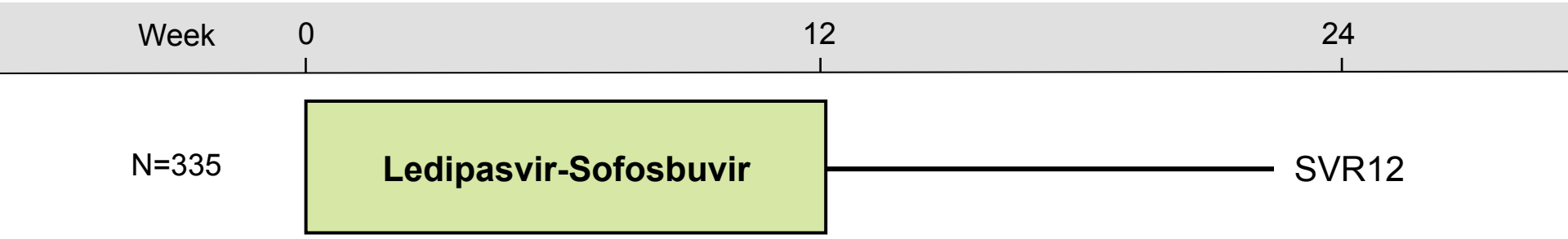
ION-4
Ledipasvir-Sofosbuvir for 12 weeks in HCV-HIV Co-infected Patients

Naggie et. al. CROI 2015. Abstract 152LB.

ION-4: Study Design



- Phase 3 open-label single-arm trial
- US, Canada and New Zealand
- Inclusion criteria:
  - Treatment-naïve or experienced
  - 20% had compensated cirrhosis
  - HIV RNA <50 copies/mL, CD4 cell count> 100 cells/mm^3
- ART regimens were TDF/FTC + one of the following:
  - Efavirenz
  - Raltegravir
  - Rilpivirine

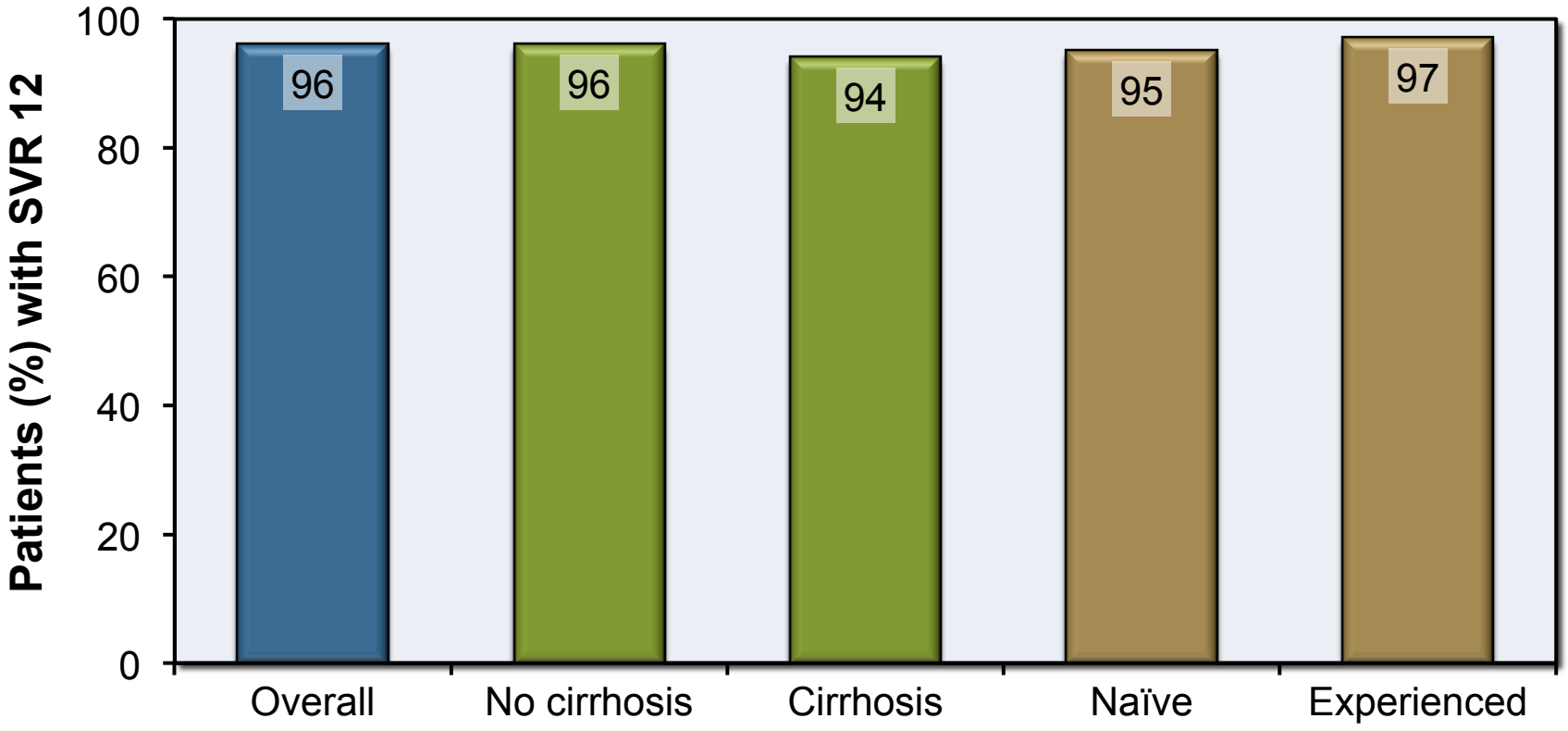
Naggie et. al. CROI 2015. Abstract 152LB.

ION-4: Study Participants

	LDV/SOF (n=335)
Age, mean (range)	52 (26-72)
Male, n (%)	276 (82%)
Black, n (%)	115 (34%)
Hispanic or Latino, n (%)	56 (17%)
IL-28B CT or TT, n (%)	254 (76%)
Genotype 1, n (%)	327 (98%)
Treatment-experienced, n (%)	185 (55%)
Cirrhosis, n (%)	67 (20%)
CD4 cell count, cells/mm, median (range)	628 (106-2069)
ART regimen TDF/FTC + Efavirenz TDF/FTC + Raltegravir TDF/FTC + Rilpivirine	 160 (48%) 146 (44%) 29 (9%)

Naggie et. al. CROI 2015. Abstract 152LB.

ION-4: Results
Overall and by Cirrhosis & Treatment experience



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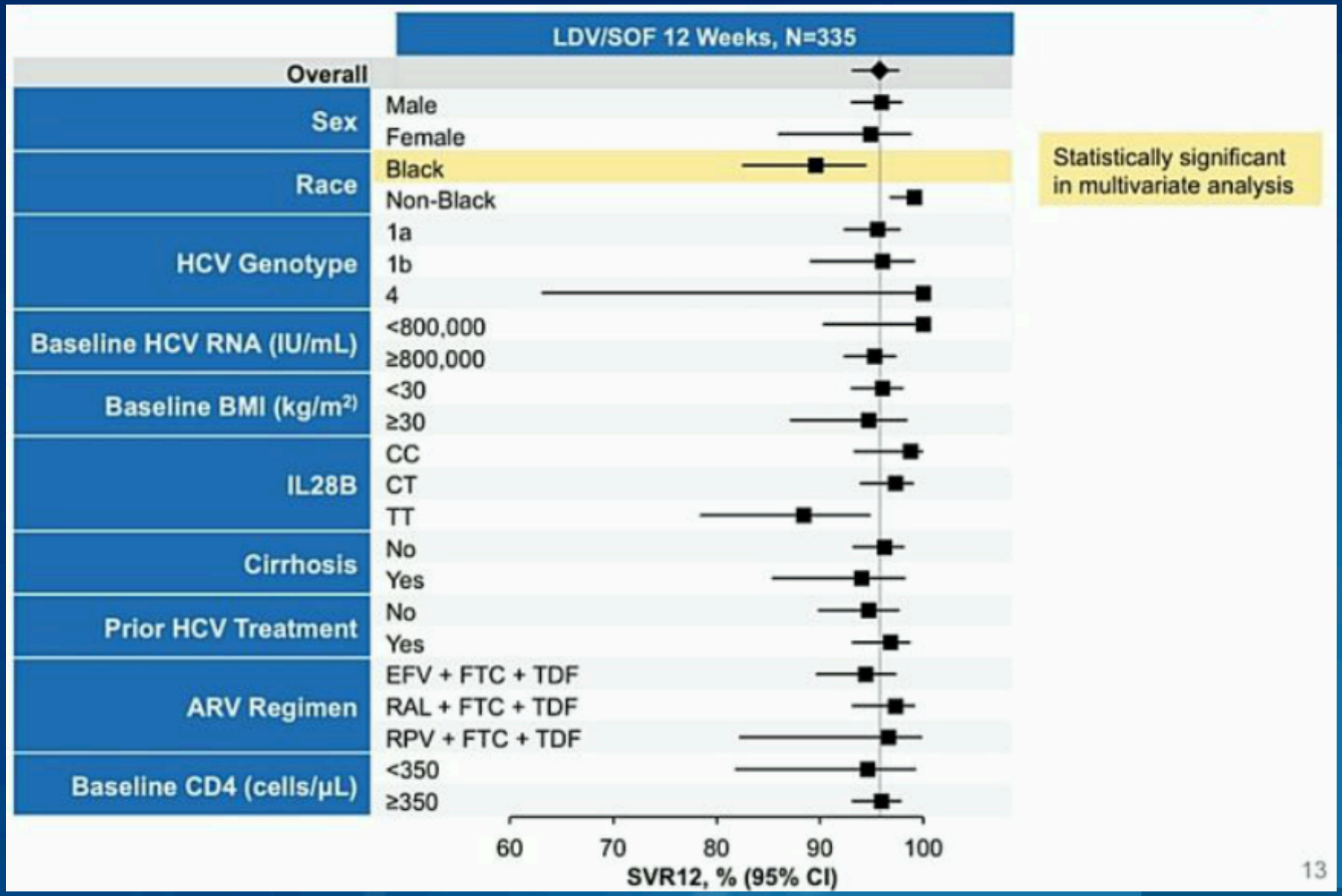
ION-4: Adverse Events (≥5%)

	LDV/SOF (n=335)
Serious adverse event Treatment DC due to AE	8 (2%) 0
Headache	83 (25%)
Fatigue	71 (21%)
Diarrhea	36 (11%)
Nausea	33 (10%)
Arthralgia	22 (7%)
Upper respiratory infection	18 (5%)

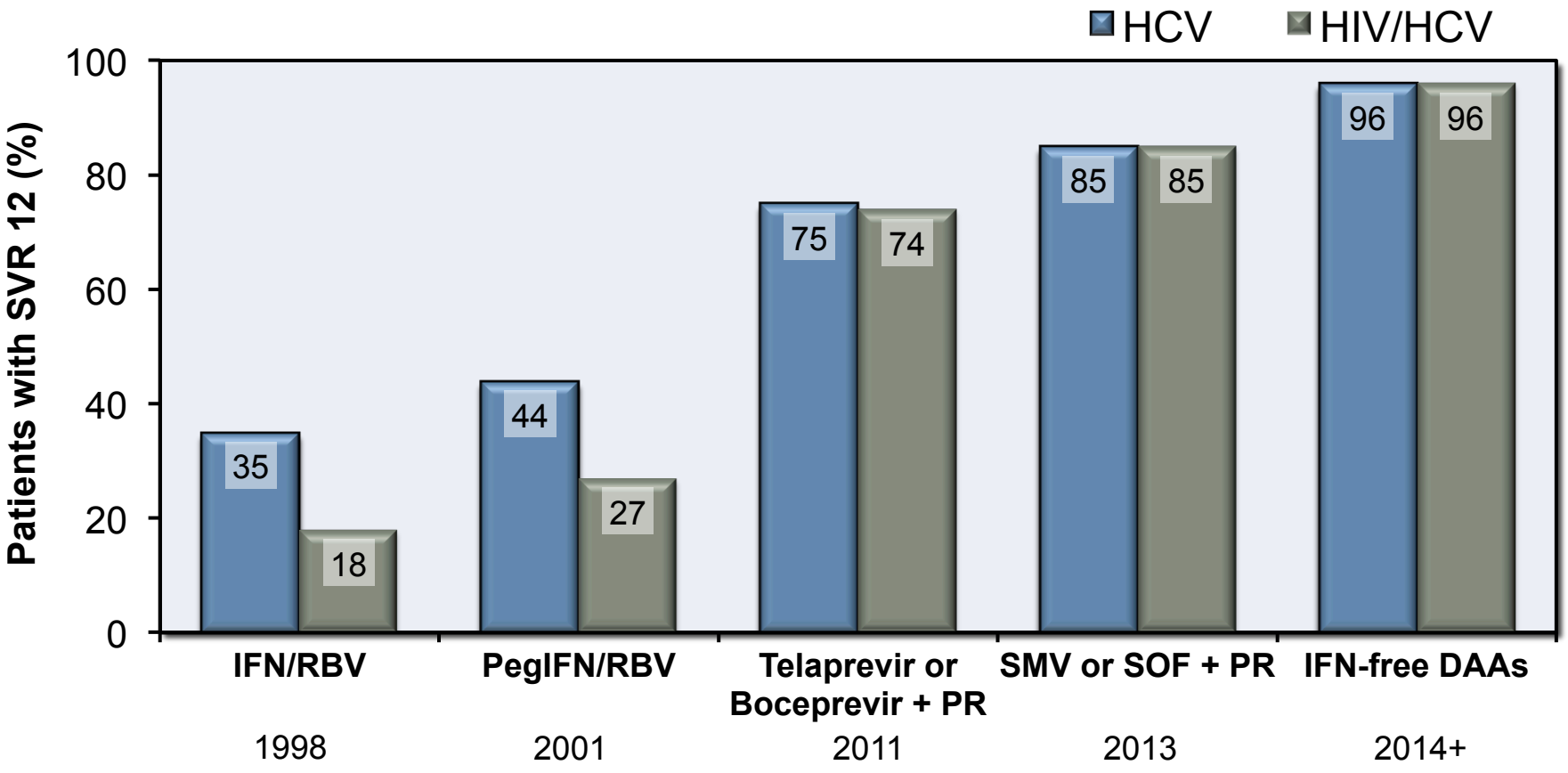
Note: n=4 (1%) patients had change in Cr ≥0.4 mg/dL.

ION-4: Subgroups



Naggie et. al. CROI 2015. Abstract 152LB.

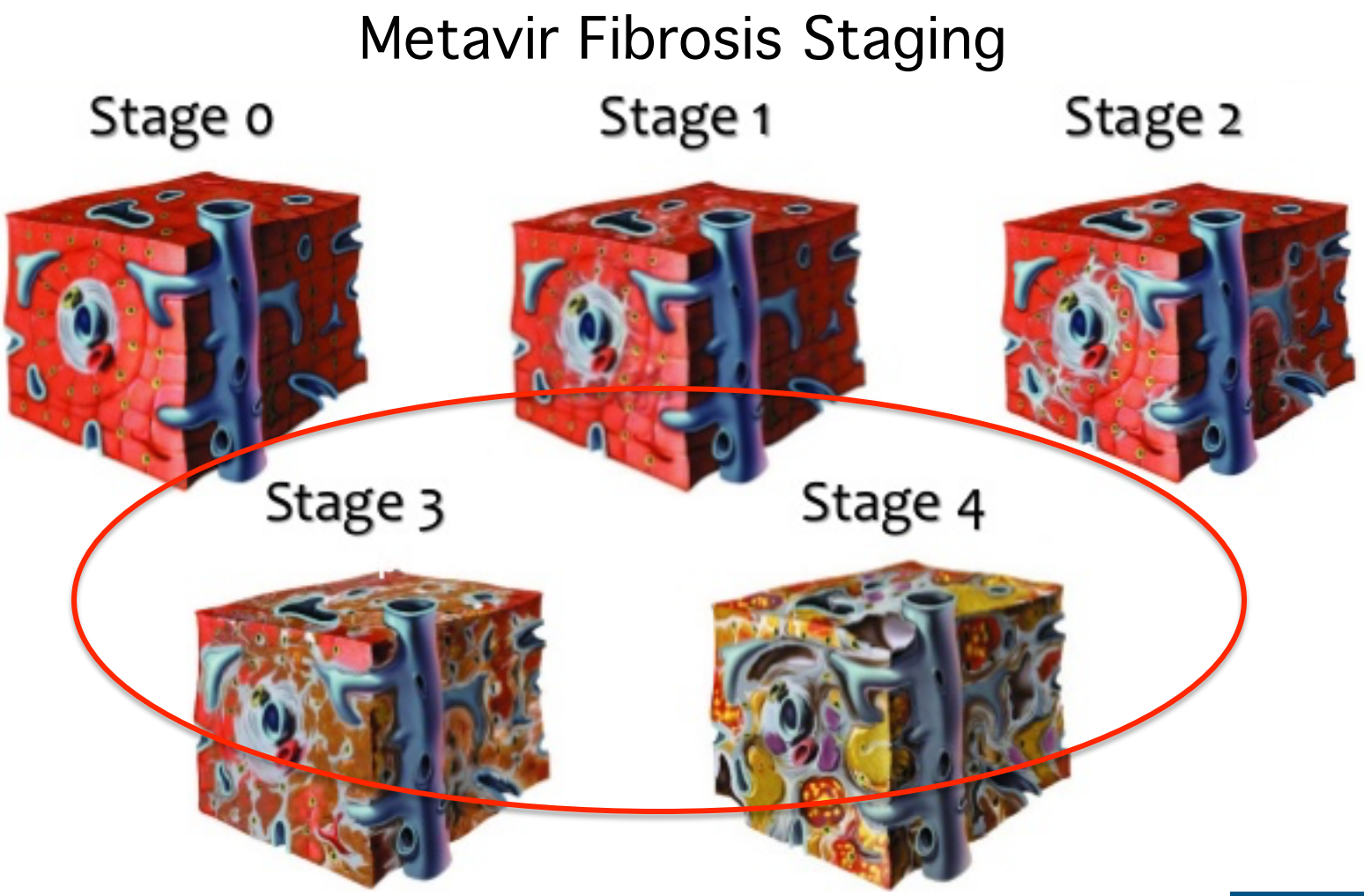
Milestones in HCV Treatment



Impact of Deferring HCV Therapy in HCV-HIV Co-infected Patients

Zahnd et. al. CROI 2015. Abstract 150.

Modeling the Impact of HCV Tx Deferral



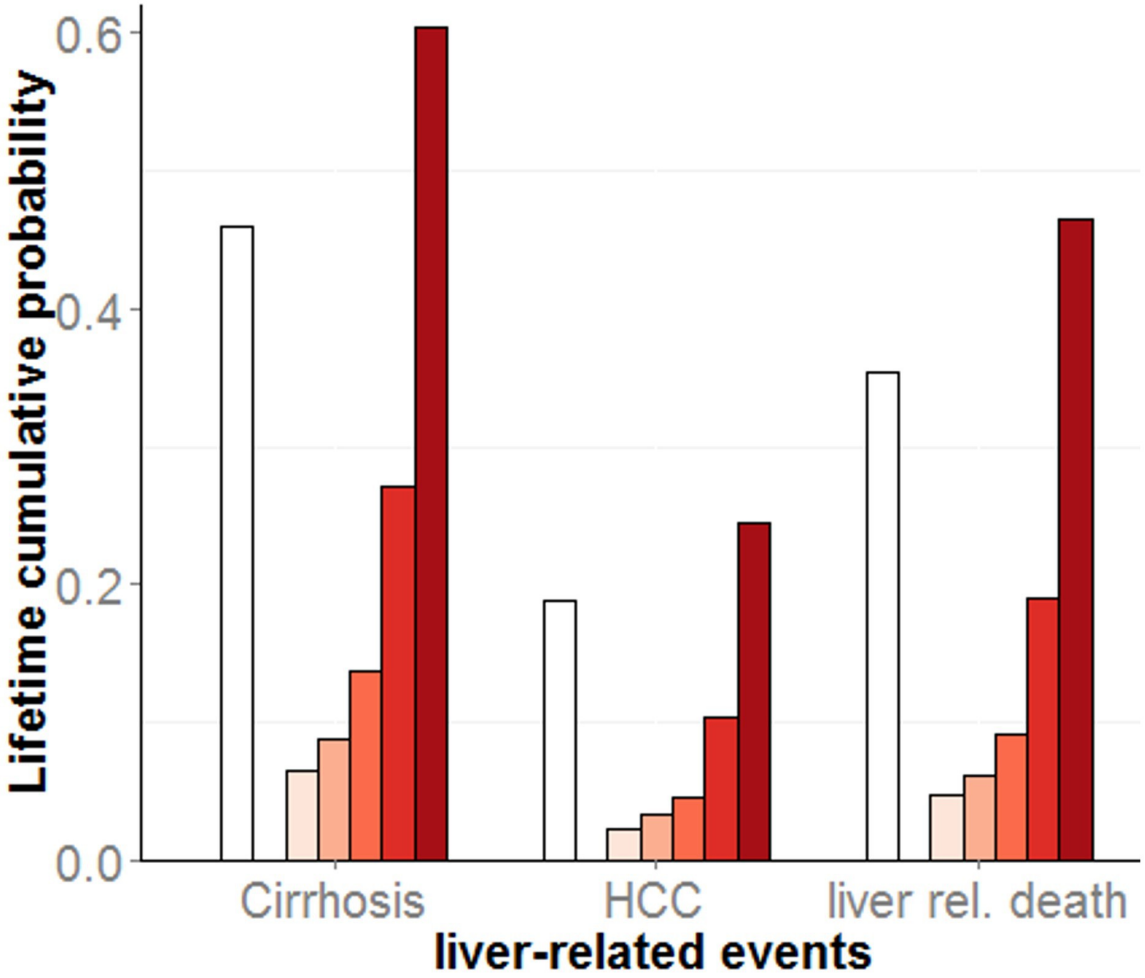
Zahnd et. al. CROI 2015. Abstract 150.

Modeling the Impact of HCV Tx Deferral

- Compared multiple scenarios:
  - "Historical"– Peg/RBV era
  - DAA very early – within 1 month of HCV diagnosis
  - DAA early – within 1 year of HCV diagnosis
  - DAA starts at F2, F3 or F4 disease
- Outcomes
  - Decompensated cirrhosis (DC), cancer (HCC), or liver-related death
  - Period of infectivity
- Assume successful HCV therapy will result in:
  - Liver fibrosis progression – 10-fold reduction
  - Risk of decompensated disease – 10-fold reduction
  - Risk of HCC – 2.6-fold reduction
- Additional assumptions
  - Peg/RBV uptake 60%, cure rate 40%
  - DAA uptake 100%, cure rate 90%

Zahnd et. al. CROI 2015. Abstract 150.

Modeling the Impact of HCV Tx Deferral



Scenario	Average time infectious (years)
Treat 1 month after diagnosis	5.11
Treat 1 year after diagnosis	5.80
Treat in F2	12.69
Treat in F3	16.36
Treat in F4	21.27

Treatment regimen

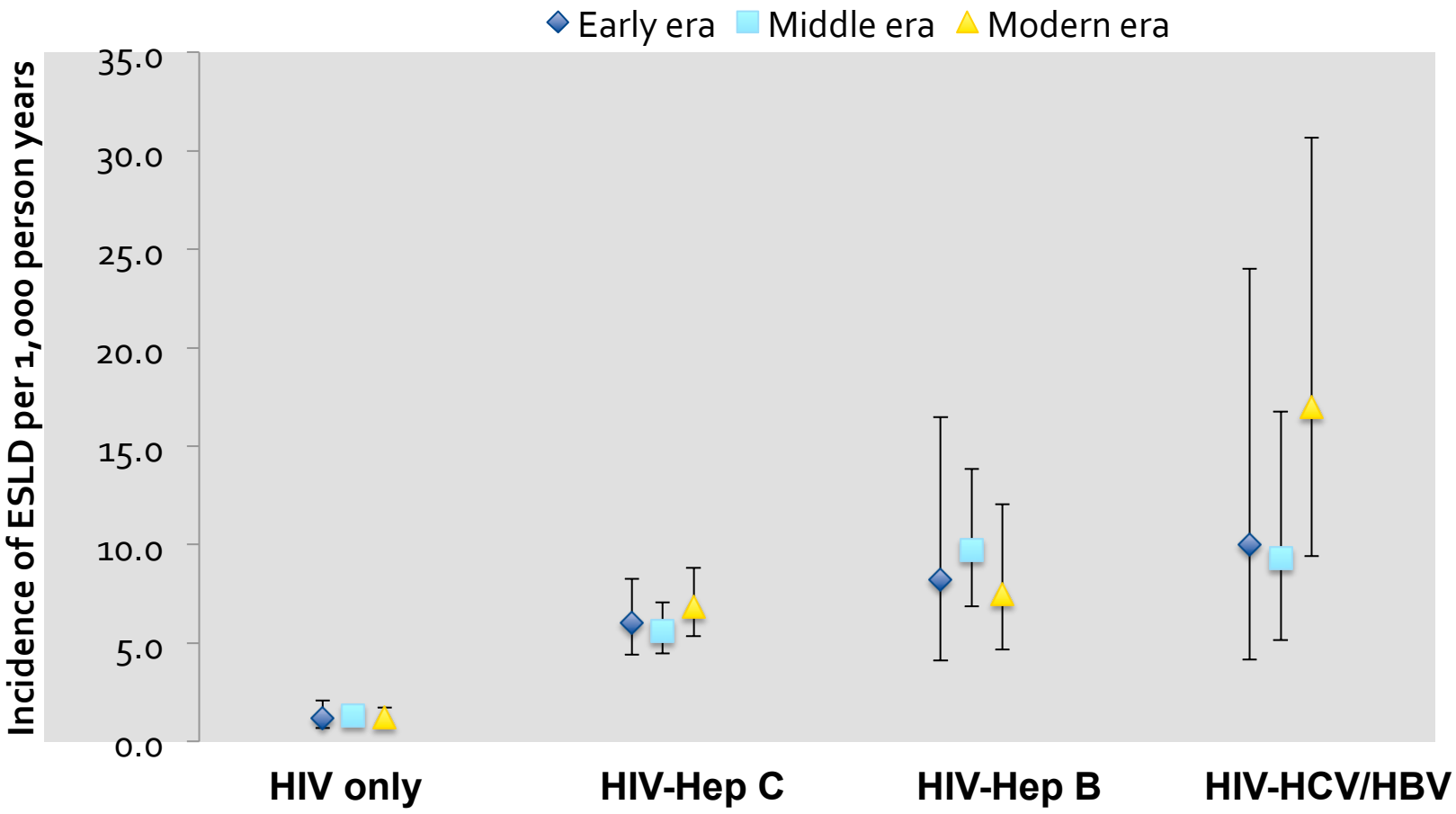
- SHCS
- Treat 1 month after diagnosis
- Treat 1 year after diagnosis
- Treat in F2
- Treat in F3
- Treat in F4

Zahnd et. al. CROI 2015. Abstract 150.

NA-ACCORD: End-stage Liver Disease in HIV-Hepatitis Co-infected Patients in the Modern ART Era

Klein et. al. CROI 2015. Abstract 638.

End-stage Liver Disease in NA-ACCORD



Klein, et. al. CROI 2015. Abstract 638.

Identifying and Prioritizing HCV Treatment in HCV-HIV Co-infected Patients: DC Cohort

Castel et. al. CROI 2015. Abstract 660.

Identifying & Prioritizing HCV Treatment for Coinfected Patients: DC Cohort

- Objective: To describe the prevalence & incidence of HCV and risk factors for disease progression & HCV transmission in a large urban cohort of HIV+ patients

Castel, et al. CROI 2015. Abstract 660.

Identifying & Prioritizing HCV Treatment for Coinfected Patients: DC Cohort

	HIV only (n=5614)	**Prevalent HCV** (n=865)	**Incident HCV** (n=198)	**P-value**
Male	73%	76%	80%	0.05
Race Black White Hispanic	 75% 15% 4.6%	 87% 9% 1.5%	 76% 15% 3.5%	 <0.001
Risk group MSM Heterosexual IDU	 41% 31% 2.5%	 16% 22% 35%	 36% 25% 19%	 <0.001
Insurance Private Public	 29% 65%	 14% 82%	 24% 70%	 <0.001
Mental health	34%	49%	42%	<0.001

Castel, et al. CROI 2015. Abstract 660.

Untreated HCV Patients (n=293)

IDSA/AASLD Treatment Category	N (%)
Highest Priority	
Advanced fibrosis or compensated cirrhosis (F3,F4) (defined by APRI (>1.0) or FIB4 scores (>3.25))	65 (22.2)
Organ transplant[1]	0 (0.0)
Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis)	2 (0.7)
Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis	9 (3.1)
Pts who meet any of the above criteria	**71 (24.2)**
High Priority	
Type 2 diabetes mellitus (insulin resistant)	44 (15.0)
Porphyria cutanea tarda	0 (0.0)
Pts meeting any of the above criteria not already in the highest risk group	**136 (46.4)**
Elevated Risk of HCV transmission	
Men who have sex with men (MSM) with high-risk sexual practices	92 (68.6)
Active injection drug users	87 (29.7)
Incarcerated persons[1]	0 (0.0)
Persons on long-term hemodialysis[1]	0 (0.0)
HCV-infected women of child-bearing potential wishing to get pregnant[1]	0 (0.0)
Pts who meet any of the above criteria and not already in the highest or high-risk groups	**47 (16.0)**

Over 86% HCV-infected patients in this HIV cohort met at least one AASLD/IDSA priority criteria for treatment

Castel, et al. CROI 2015. Abstract 660.

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Check out Bernard Fields lecture, “Hepatitis C: Light at the End of the Tunnel” by Dr. Charles Rice on CROI 2015 Webcast (Feb 23):
www.croiwebcasts.org