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d'Infectiologie

Clermont-Ferrand
et l'interrégion Rhône-Alpes Auvergne

Du mercredi 12 au
vendredi 14 juin 2013
Polydome, centre d'expositions
et des congrès



Chez qui proposer aujourd'hui le traitement du VHC chez le coinfecté VIH?

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Vendredi 14 juin 2013



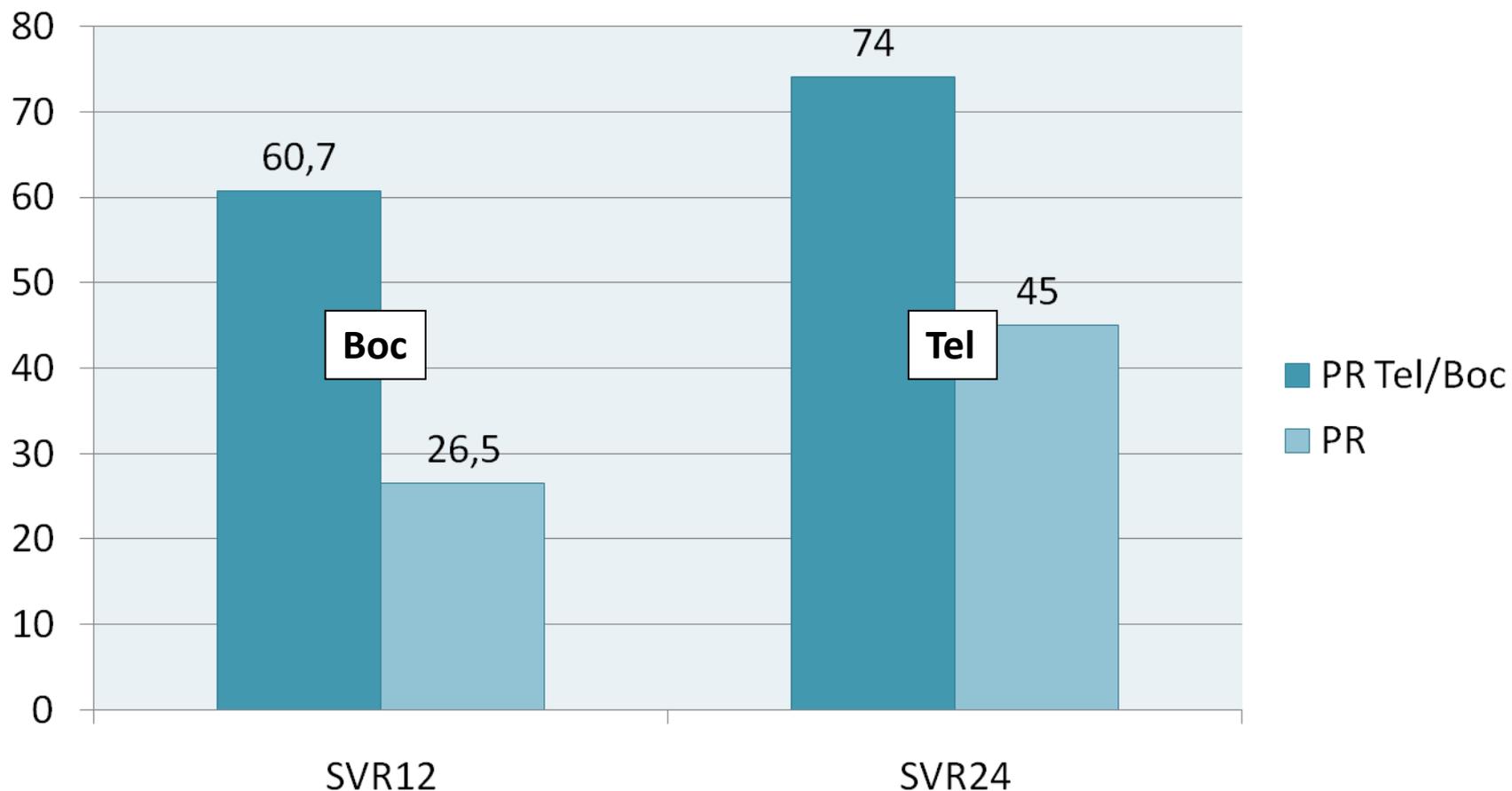
Stéphanie Dominguez

- **Board français et internationaux, workshop, consulting: Gilead, BMS, MSD, Roche, Janssen, ViiV, Abbvie**
- **Co-investigateur dans des études industrielles : Roche, MSD**

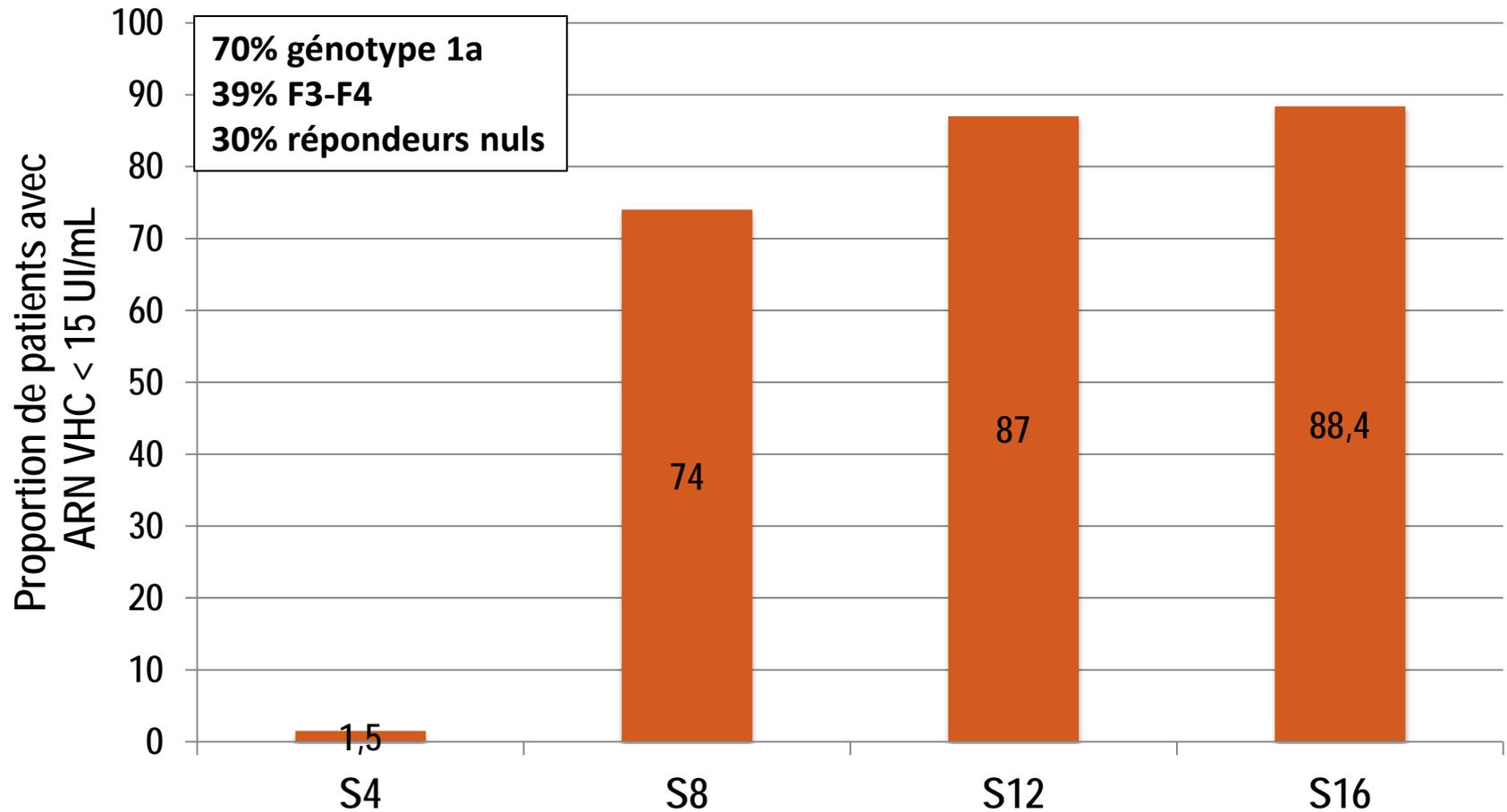
Vincent Mallet

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- **Co-investigateur dans des études industrielles : BMS, Roche, MSD, Boehringer Ingelheim, Tibotec, Vertex, Janssen, Abbott**

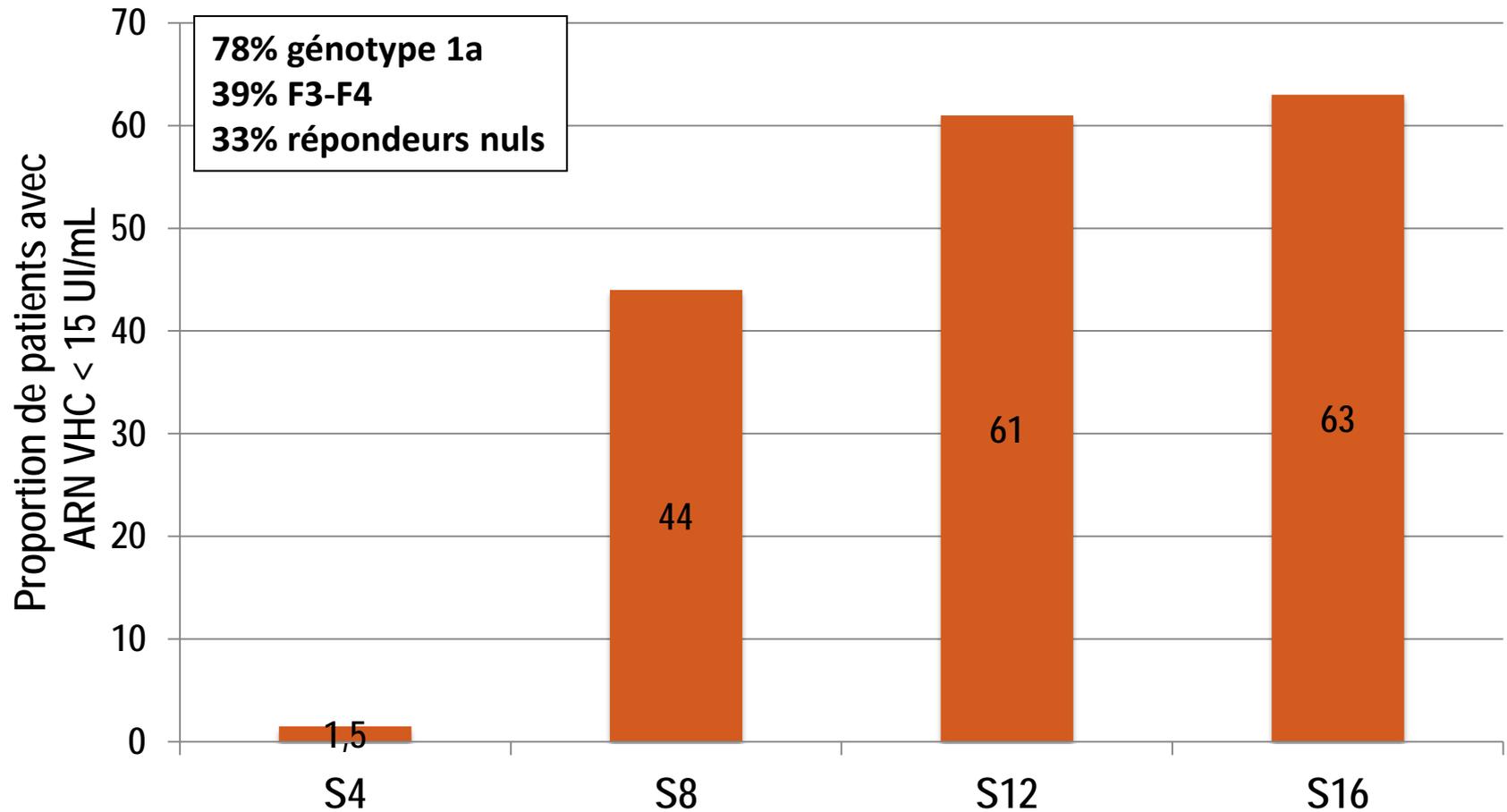
Previr efficacy in HIV/HCV naïve noncirrhotic patients



Malades en échec: ANRS TélapreVIH (n=69)

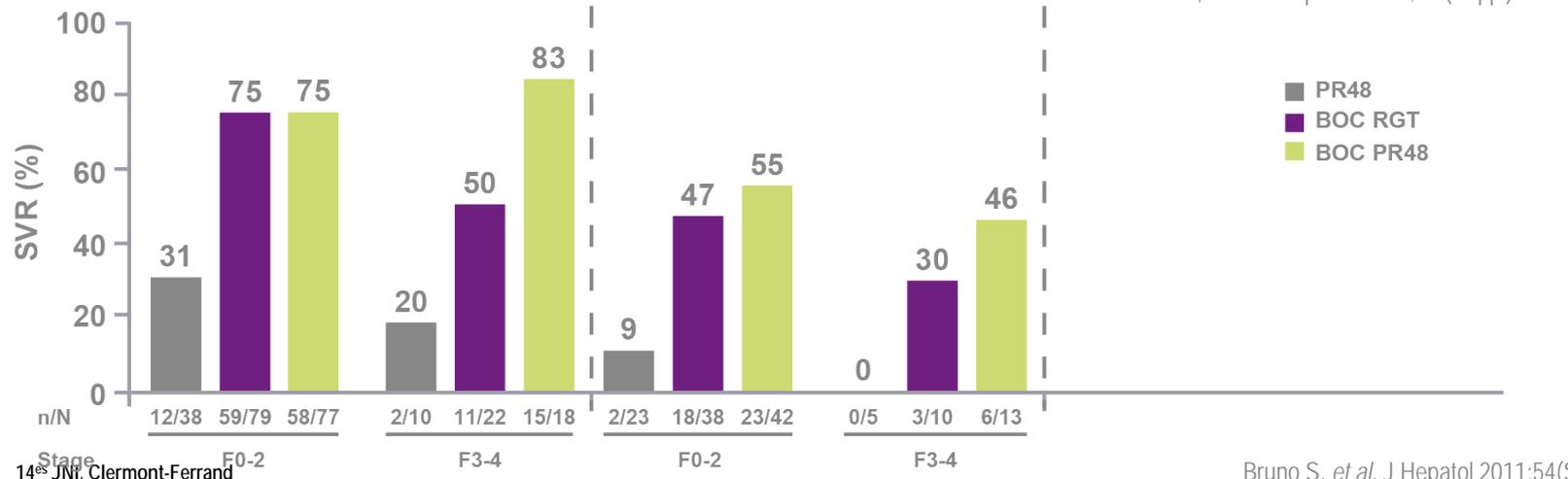
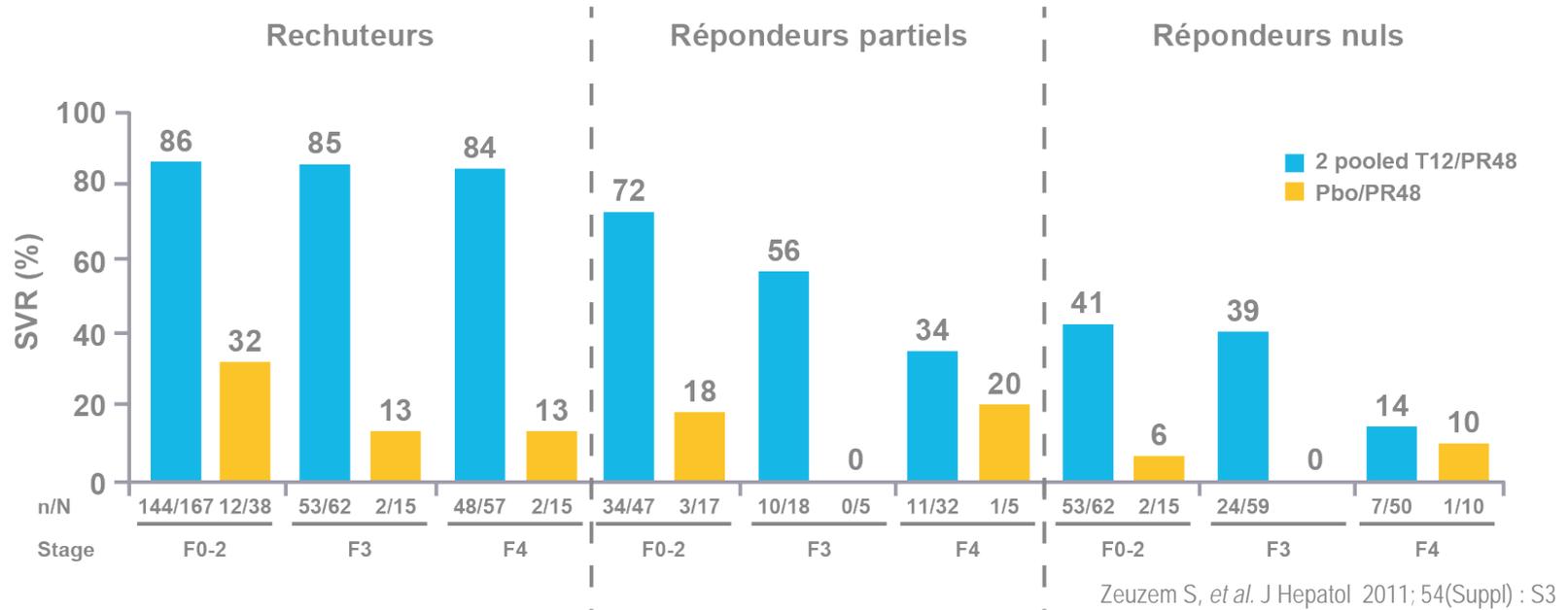


Malades en échec: ANRS BocépreVIH (n=64)



Facteurs prédictifs de réponse à la trithérapie

– Mono-infectés VHC



Prise de position SPILF/AFEF/SFLS pour les patients VIH POS / HCV POS (2013)

HCV RNA POS \pm ALT > N

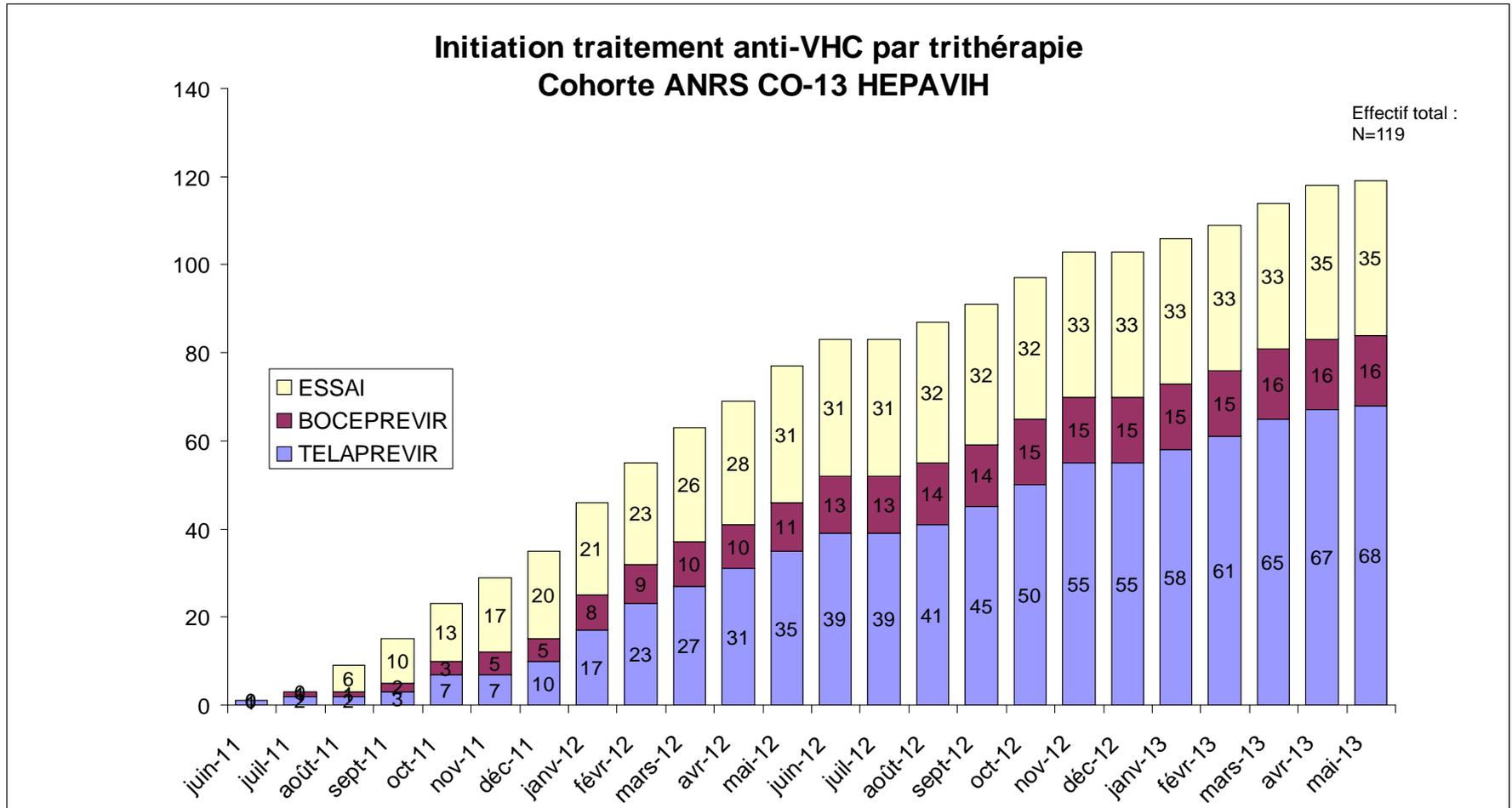
and

Fibrosis (Metavir)



Antiviral Rx
(PR or PR T/Boc for genotype-1)

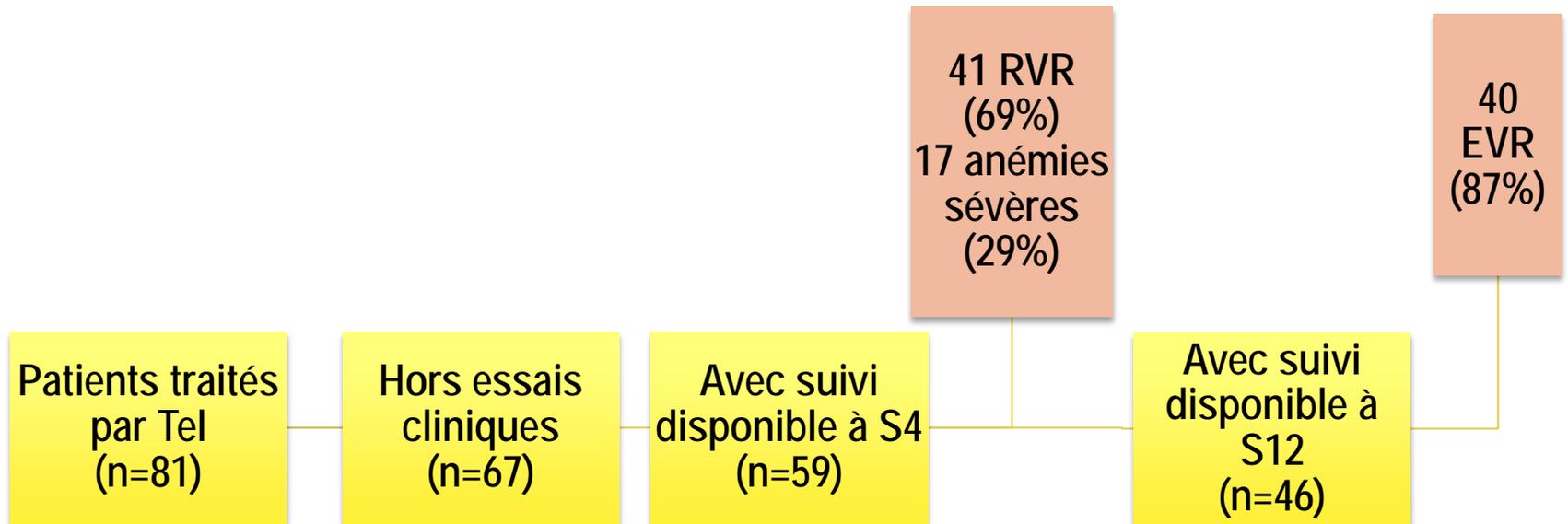
La trithérapie dans la cohorte HEPAVIH



Comparaison des patients ayant et n'ayant pas initié une trithérapie

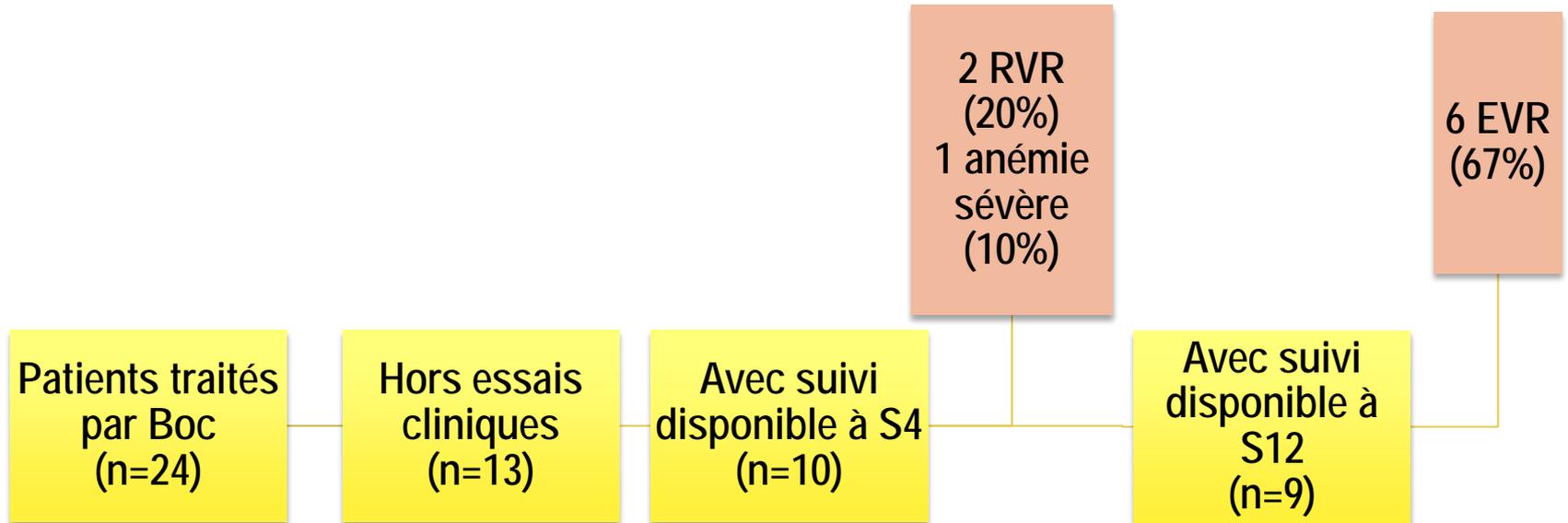
	Initiation d'une trithérapie anti-VHC, n=114	Pas de trithérapie anti-VHC *, n=206	p
Âge (années)	48 [43-52]	49 [46-53]	0,046
Hommes vs Femmes	85 (74,6)	145 (70,4)	0,440
CD4 (/mm³)	559 [392-747]	553 [380-780]	0,642
Patients avec ARN VIH < 50 copies/mL	95 (85,6)	174 (85,3)	0,890
Patients sous traitement ARV	113 (99,1)	196 (95,1)	0,105
Charge virale VHC (log₁₀ UI/mL)	6,2 [5,5-6,6]	6,4 [5,9-6,7]	0,017
Patients cirrhotiques	39 (34,2)	30 (14,6)	0,006
Score d'élasticité (KPa)	8,7 [5,9-15,4]	6,6 [5,1-9,1]	0,001
Traitement anti-VHC antérieur			<0,001
Naïfs	33 (28,9)	155 (75,2)	
En échec	81 (71,1)	51 (24,8)	

Accès au traitement — Telaprevir



RVR = ARN VHC indétectable à S4
EVR = ARN VHC indétectable à S12

Accès au traitement — Boceprevir



RVR = ARN VHC indétectable à S4
EVR = ARN VHC indétectable à S12

Bénéfice du traitement anti-VHC dans la cohorte HEPAVIH (2005-2012)

392 patients traités entre 2005 et 2012

226 patients sans FBS répétés ou avec FBS de mauvaise qualité

166 avec un FBS avant TTT et au moins 1 après la fin du TTT, de bonne qualité ($IQR \leq 30\%$)

5 avec RVS non disponible

161 avec RVS disponibles

1 avec CHC

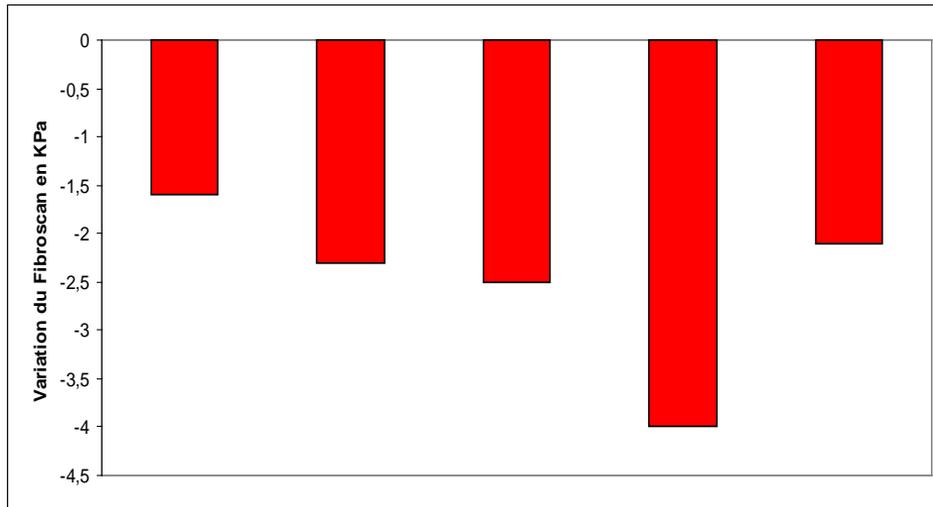
160 patients

Caractéristiques des populations à J0

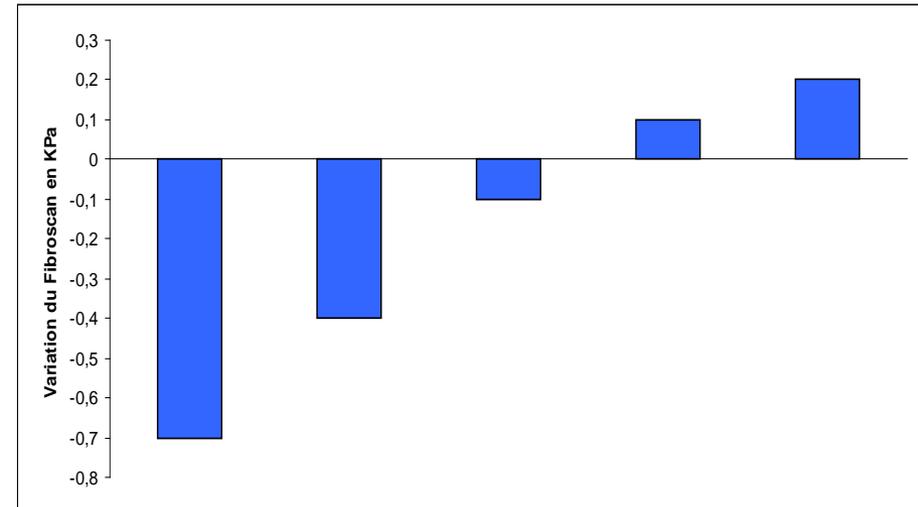
	Non RVS (N=91)	RVS (N=69)	Total	p
Age (année), médiane (Q1-Q3)	46 (44-49)	45 (43-49)	46 (43,5-49)	0,13
Sexe masculin, n(%)	60 (74,1)	46 (76,7)	106 (75,2)	0,93
CD4 (/mm ³)	497 (362-696)	454 (350-652)	486 (361-686)	0,51
Charge VIH indétectable	74 (82,2)	55 (82,1)	129 (82,2)	0,98
Plaquettes (Giga/l)	185 (141-234)	186 (152-235)	185 (143-234)	0,87
ASAT (UI/ML)	47 (39-68)	55 (39-94)	49 (39-78)	0,48
ALAT (UI/ML)	54,5 (39-75)	63 (39-110)	56 (39-89)	0,23
Alcool (3verres/j, 2verres/j)	15 (17,9)	3 (4,6)	18 (12,0)	0,01
Charge virale VHC (UI/ml)	6,2 (5,8-6,6)	6,0 (5,3-6,4)	6,1 (5,6-6,5)	0,007
Génotype VHC				<0,0001
1	67 (73,6)	31 (44,9)	98 (61,2)	
2	2 (2,2)	6 (8,7)	8 (5,0)	
3	8 (8,8)	24 (34,8)	32 (20,0)	
4	14 (15,4)	8 (11,6)	22 (13,8)	
Elasticité hépatique	8,7 (6,1-12,3)	7,9 (6,3-11,5)	8,4 (6,1-12,1)	0,43

Evolution de l'élasticité avant et après TTT chez un même patient

RVS



Non RVS

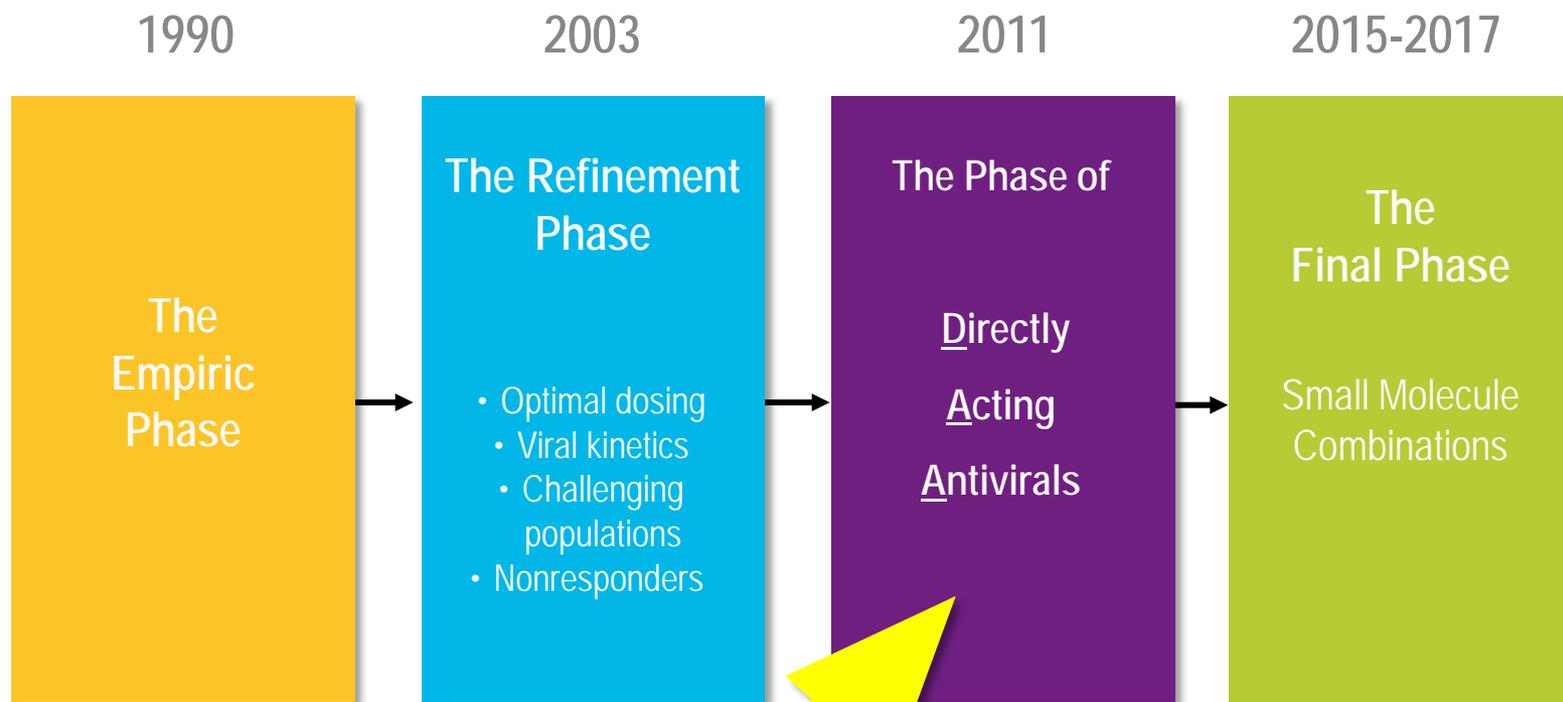


Suivi 1-2 ans 2-3 ans 3-4 ans 4-5 ans > 5 ans
P-value <0,0001 <0,0001 0,0005 0,05 0,06

Suivi 1-2 ans 2-3 ans 3-4 ans 4-5 ans > 5 ans
P-value 0,17 0,77 0,63 0,67 0,84

Suivi = délai entre le FBS avant et le FBS après la fin du TTT

VHC : la révolution thérapeutique est en marche



Vous êtes ici

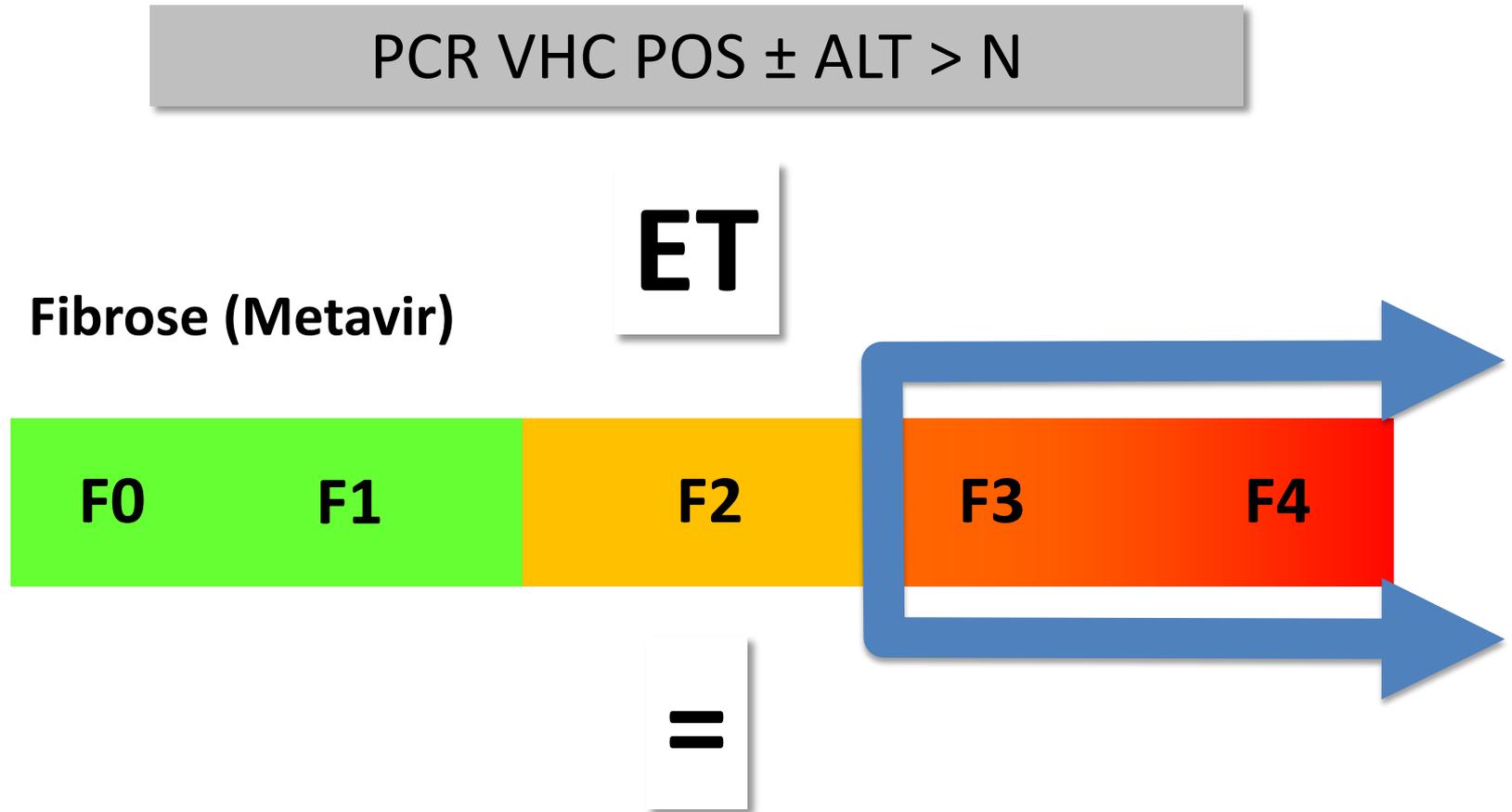
Des eaux plus calmes en vue



Combo orales

Des bateaux de compétition





**Traitement antiviral
(PR ou PR T/Boc en fonction du génotype)**

Est-il raisonnable d'attendre?



From: **Relationship of Liver Disease Stage and Antiviral Therapy With Liver-Related Events and Death in Adults Coinfected With HIV/HCV**

JAMA. 2012;308(4):370-378. doi:10.1001/jama.2012.7844

Table 2. Incidence Rates by METAVIR Stage

METAVIR Fibrosis Stage ^a	No. of Events	Person-Years ^b	Incidence Rate per 1000 Person-Years (95% CI) ^c
All outcomes: ESLD, HCC, or death			
F0	33	1396.3	23.63 (16.80-33.24)
F1	57	1568.8	36.33 (28.03-47.10)
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F4	31	390.3	79.43 (55.86-112.95)
Total	150	3888.3	38.58 (32.87-45.27)
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^cTests for trend were significant for all-cause outcomes ($P < .001$) and liver-related outcomes ($P < .001$).

Figure Legend:

Conclusion In this cohort of patients with HIV/HCV coinfection, hepatic fibrosis stage was independently associated with a composite outcome of ESLD, HCC, or death.

From: HIV, Age, and the Severity of Hepatitis C Virus–Related Liver Disease: A Cohort Study

Ann Intern Med. 2013;():. doi:10.7326/0003-4819-158-9-201305070-00604

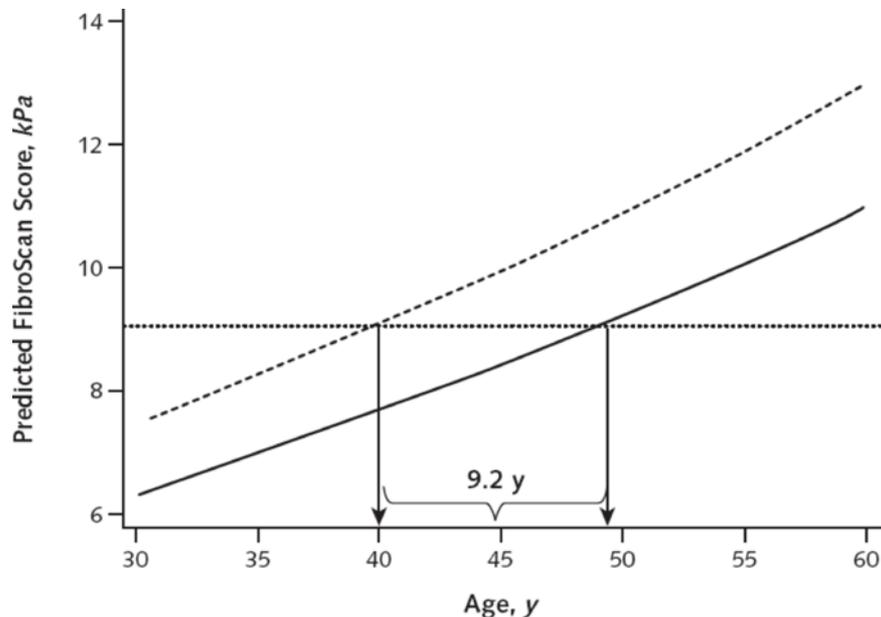


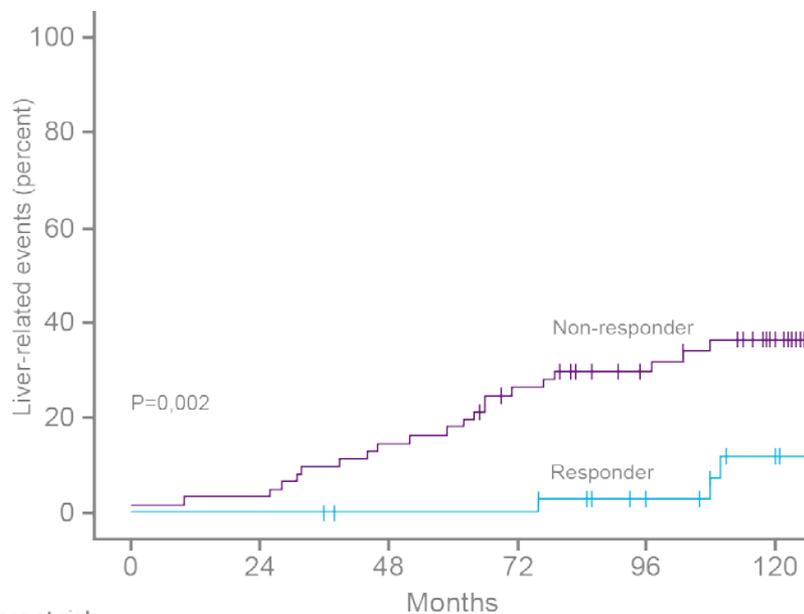
Figure Legend:

Liver fibrosis and age among persons coinfecting with HIV and HCV and those with only HCV.

For each age, predicted liver fibrosis scores were calculated using a regression equation that included the race, sex, alcohol use, body mass index, hepatitis B virus surface antigen level status, and HCV RNA level values for a representative participant (black overweight male who has no regular alcohol use, is hepatitis B virus surface antigen–negative, and has high HCV viral load) for persons coinfecting with HIV and HCV (dashed line) and for persons with only HCV (solid line). For example, a 40-year-old HIV and HCV coinfecting person with these characteristics was calculated to have a predicted FibroScan score of 9.04 kPa. For this same degree of fibrosis, the predicted age in a similar person but with only HCV was 49.2 years. Over the entire age range, the average difference in estimated age between persons coinfecting with HIV and HCV and those with only HCV was 9.2 years (90% coverage limit, 5.2 to 14.3 years). HCV = hepatitis C virus.

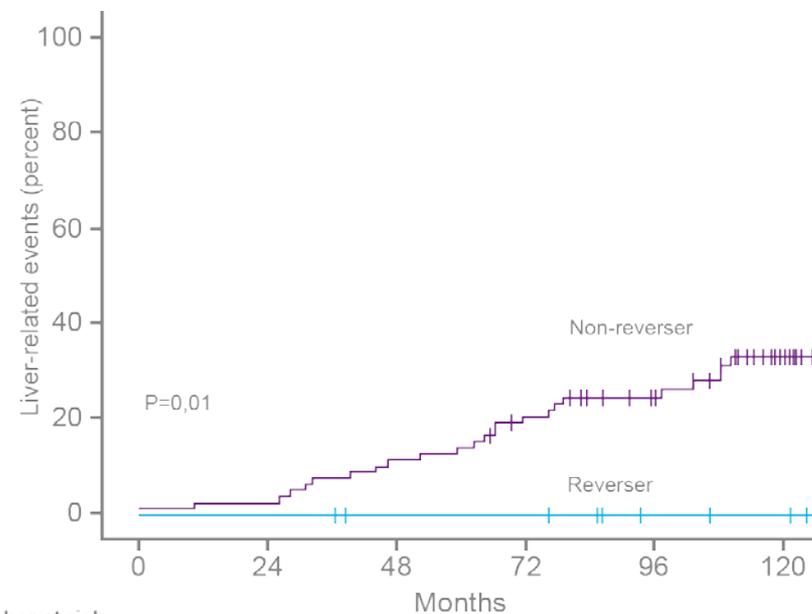
Incidence à 10 ans des événements hépatiques: Patients F3-F4

96 patients VHC
Score METAVIR F3-F4
Médiane de suivi 118 mois; EIQ=86-138 mois



Number at risk

	0	24	48	72	96	120
Non-responder	61	59	52	43	32	22
Responder	35	35	33	33	27	18



Number at risk

	0	24	48	72	96	120
Non-reverser	78	76	69	60	47	30
Reverser	18	18	16	16	12	10

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Regardez ici!

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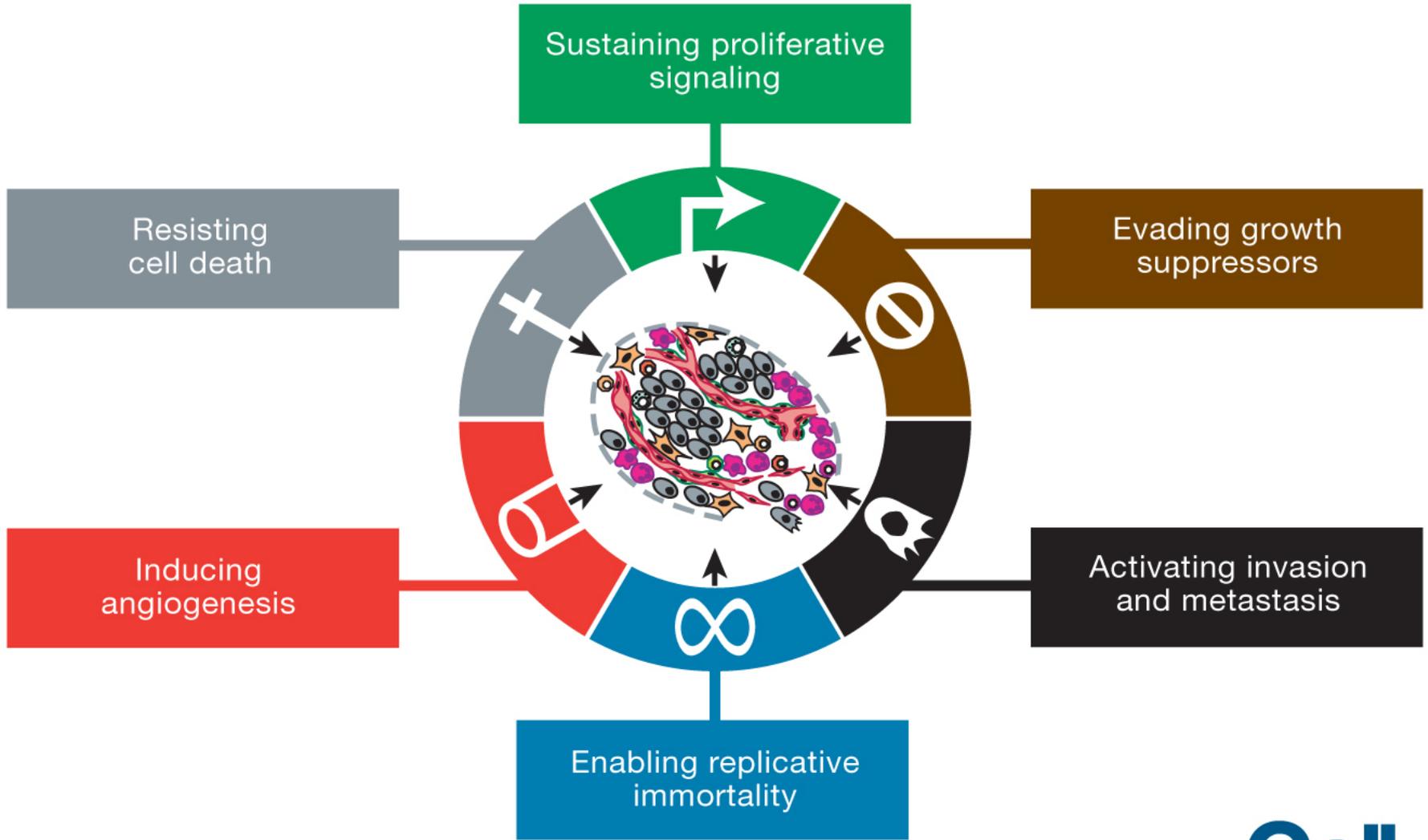
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Conclusion In this cohort of patients with HIV/HCV coinfection, hepatic fibrosis stage was independently associated with a composite outcome of ESLD, HCC, or death.

Femme de 51 ans; VIH avant 1987; Pas d'IO; ARV 1997; ATZ/TDF/FTC/RTV 2008; 300-350 CD4 (23%); ARN VIH NEG; Pas de syndrome métabolique; Alcool 30 g/j

- VHC G1, RR à PR (24 semaines) en 2005 (Metavir F2)
- Mars 2011: ALT 3N, PLQ NI, TP 90%, Bili T 86µmol/L, Alb N, Echo N, FT A3F4, FS 8,3 kPa
- Octobre 2012: CHC unifocal (5 cm), thrombose portale segmentaire, AFP 4859 UI
- Novembre 2012: Métastases pulmonaires multiples, AFP > 25.000 UI. Prise en charge palliative



Hanahan and Weinberg, 2011

Emerging Hallmarks

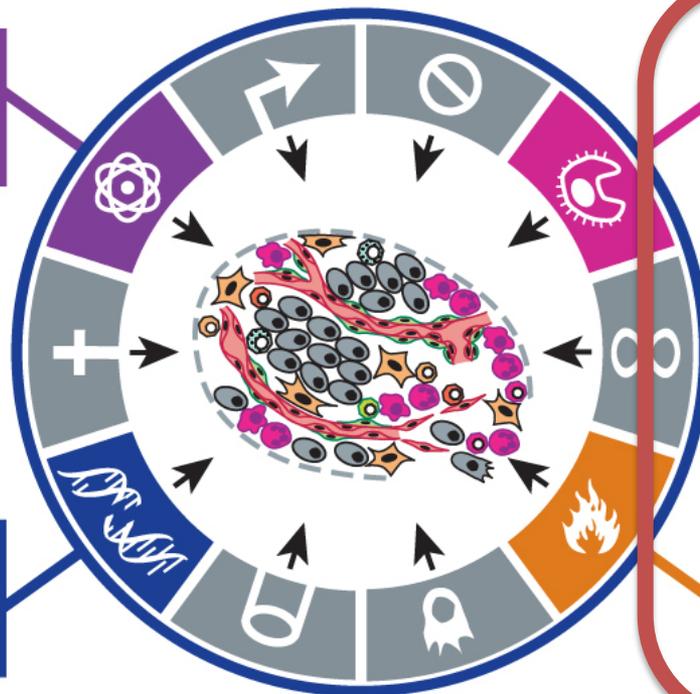
Deregulating cellular energetics

Avoiding immune destruction

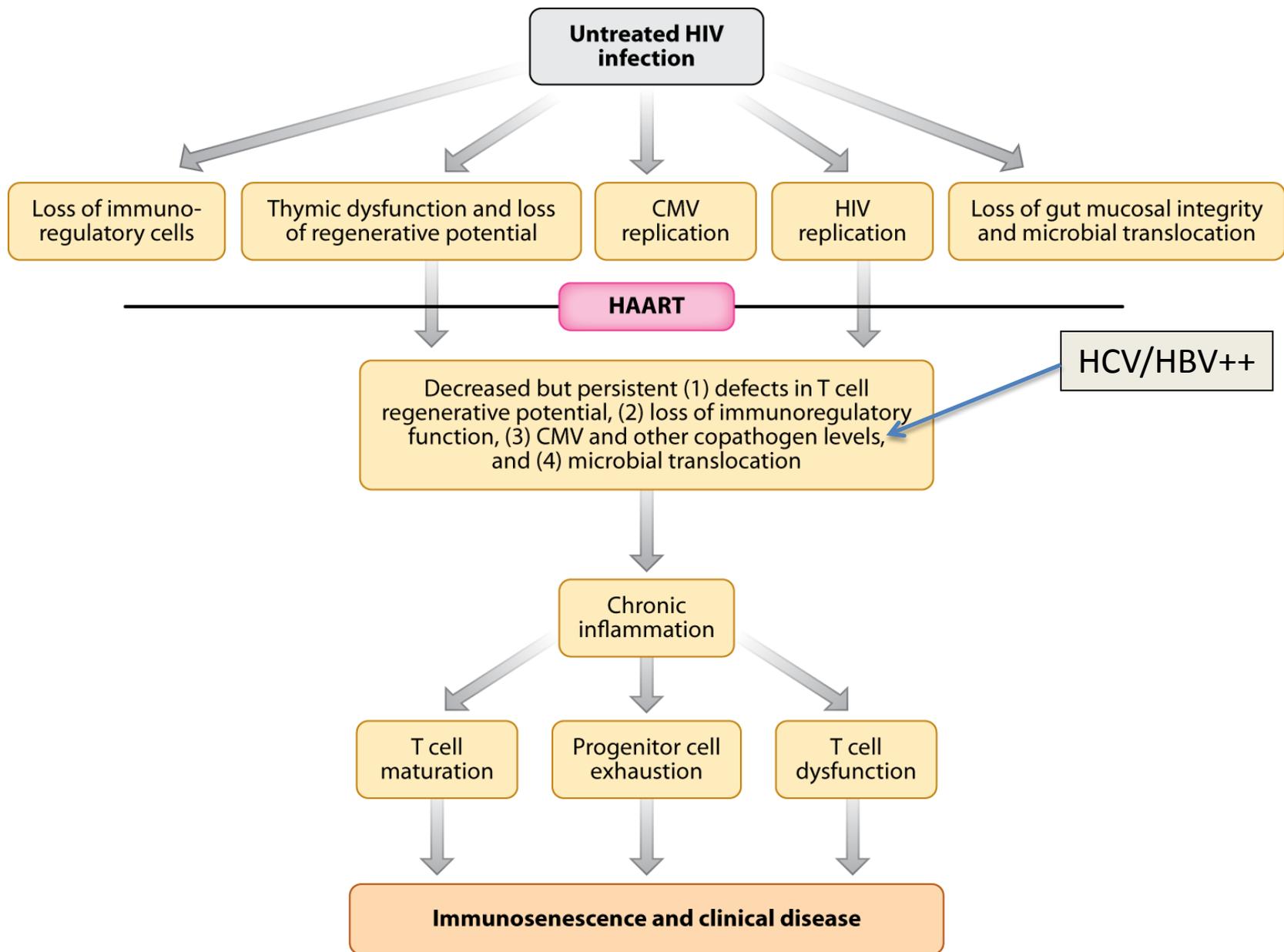
Genome instability and mutation

Tumor-promoting Inflammation

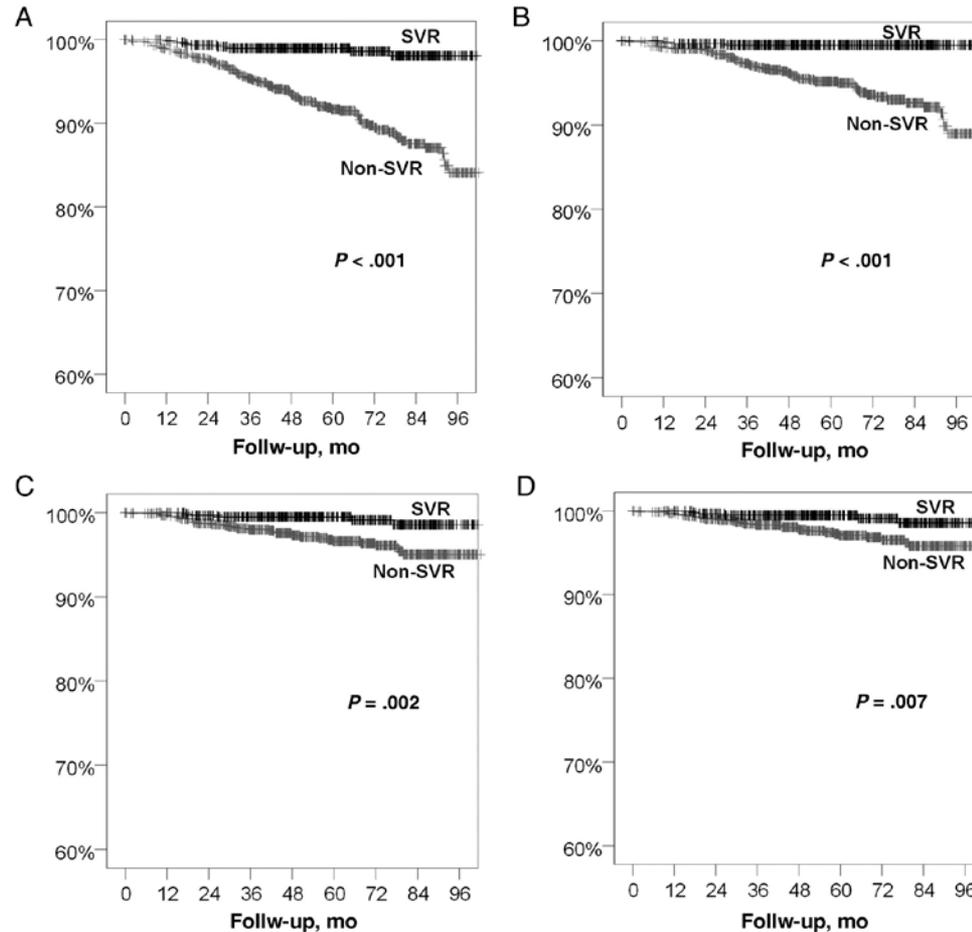
Enabling Characteristics



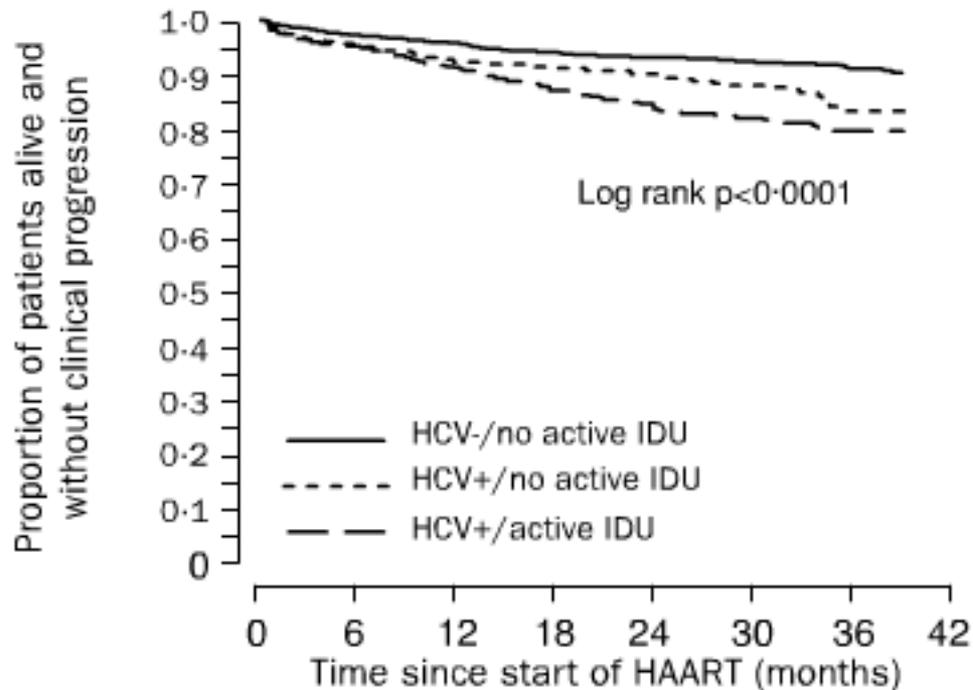
Hanahan and Weinberg, 2011



Kaplan-Meier curves showing the occurrence of overall deaths (A), liver-related deaths (B), non-liver related deaths (C), and non-liver-related, non-AIDS-related deaths (D) in 1599 patients coinfecting with human immunodeficiency virus and hepatitis C virus, with or without sustained virological response after therapy with interferon plus ribavirin.



Berenguer J et al. Clin Infect Dis. 2012;55:728-736



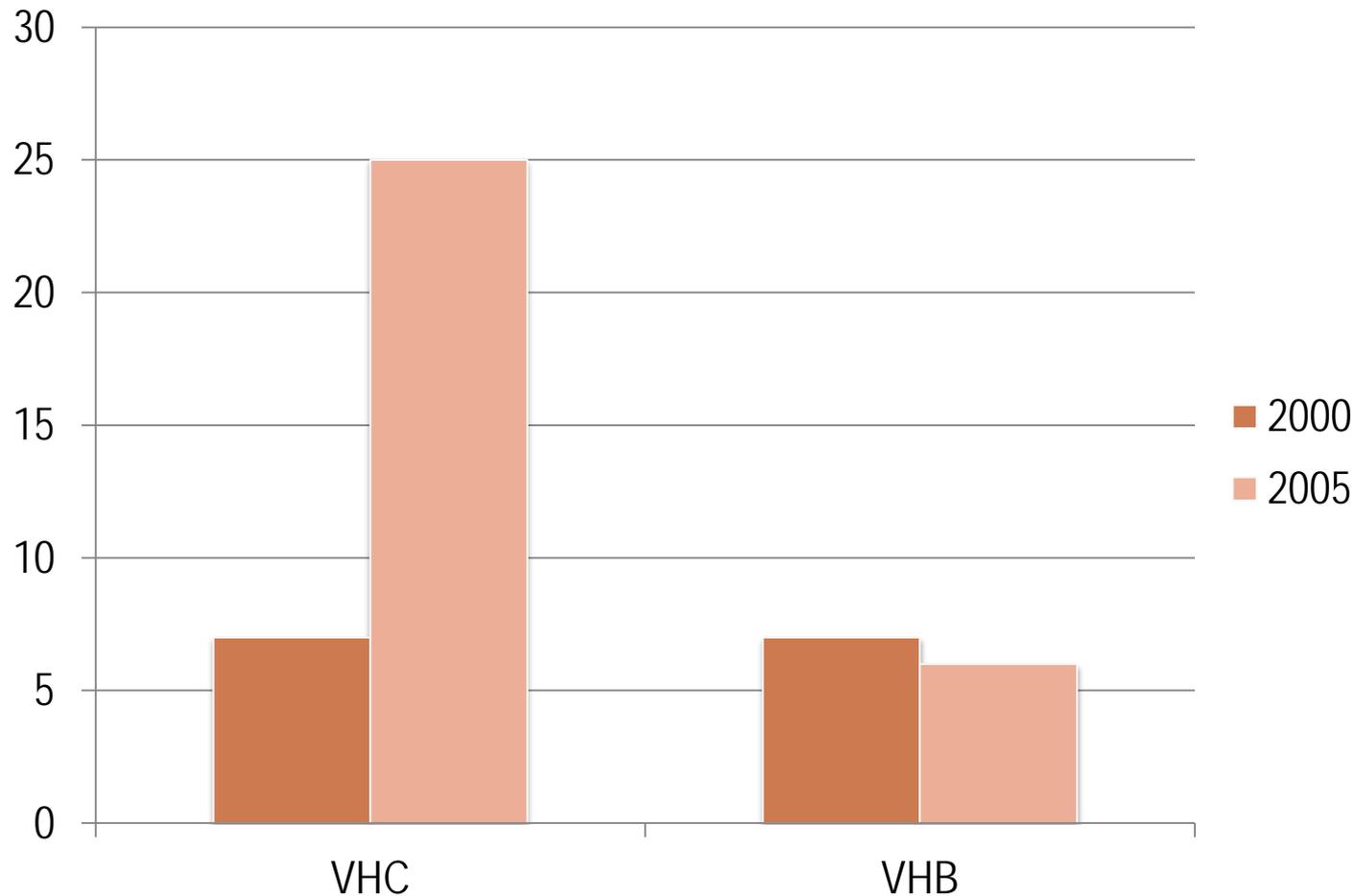
Numbers at risk

HCV-/no active IDU	1919	1473	1193	402
HCV+/no active IDU	552	418	355	118
HCV+/active IDU	605	442	388	92

Figure 1: Kaplan-Meier curves of the probability of remaining alive and free of new AIDS-defining illness

IDU=intravenous drug use. Three events that occurred among 93 HCV seronegative patients with active intravenous drug use are not represented.

Nombre de décès rapportés au CHC (cohorte Mortalité 2000-2005)



Conclusion: il faut traiter vite tous les patients VIH VHC

- Surtout ceux contaminés avant HAART
- VIH avant HAART
 - Sénescence immunitaire prématurée
 - Défaut de contrôle de la tumorigenèse
 - Vitesse de progression de la fibrose accrue
- L'éradication du VHC doit toujours être envisagée chez une personne VIH POS
- Poids des comorbidités (alcool) à prendre en compte

Quelle est la controverse?

- **Faut-il traiter les F0-F1?**
- Coût efficacité du traitement VHC pour tous?
- Quid des répondeurs nuls?

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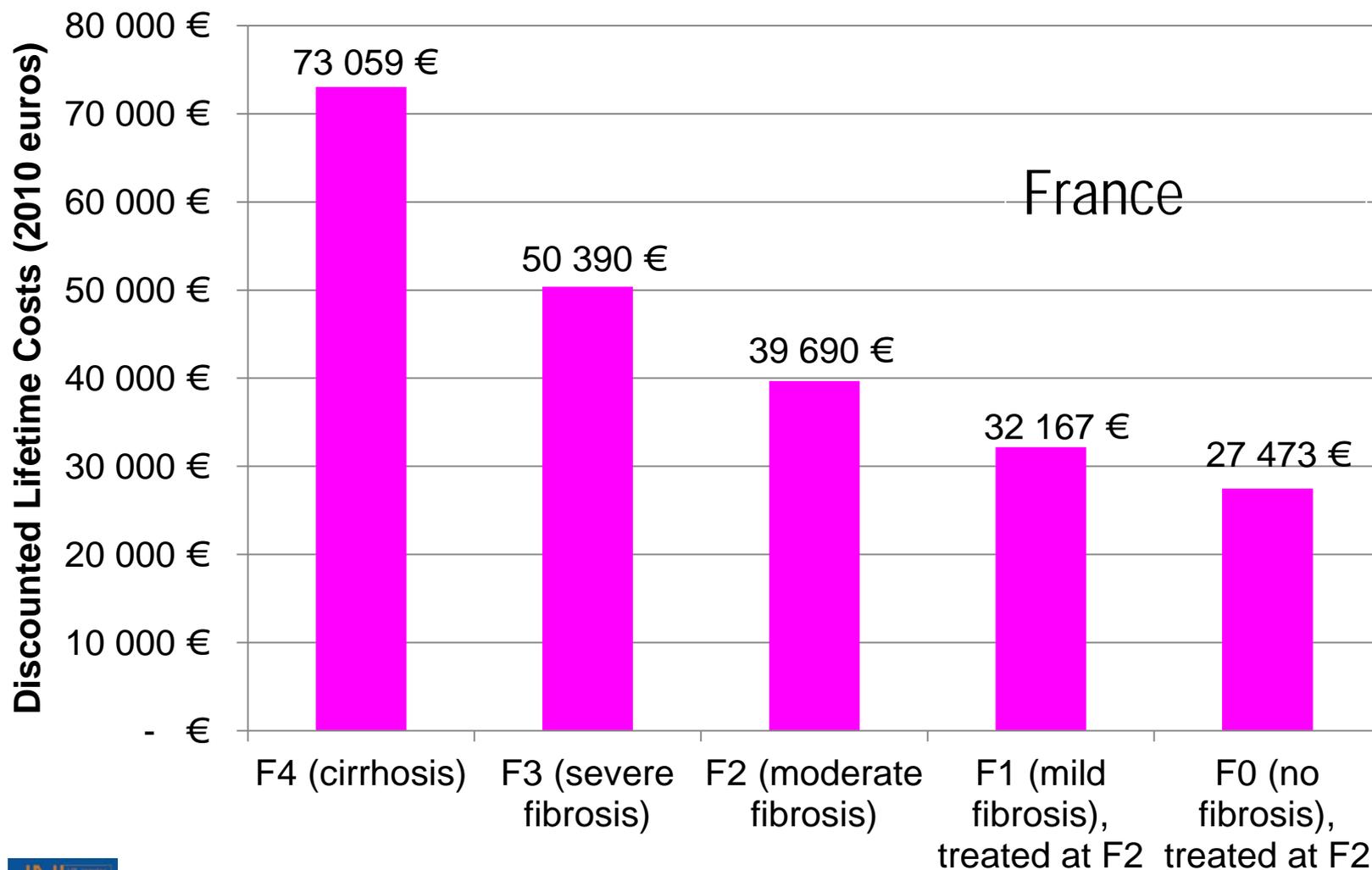
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Cout de la prise en charge d'un patient porteur d'une hépatite chronique C en fonction du stade de fibrose au diagnostic (Schwarzinger et al. Easl, 2013)

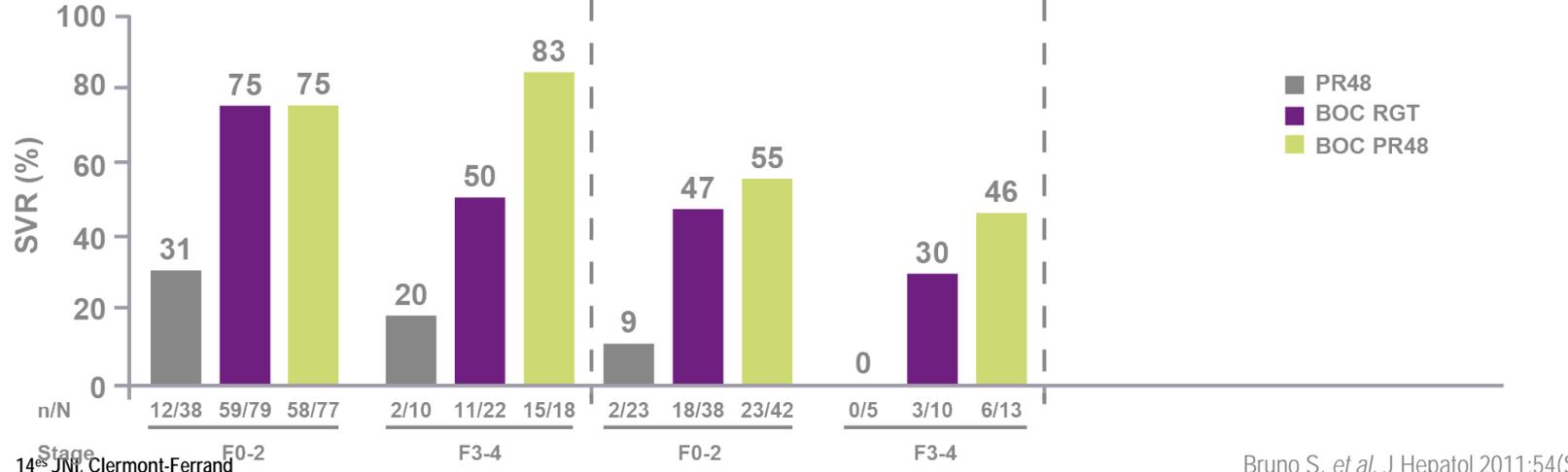
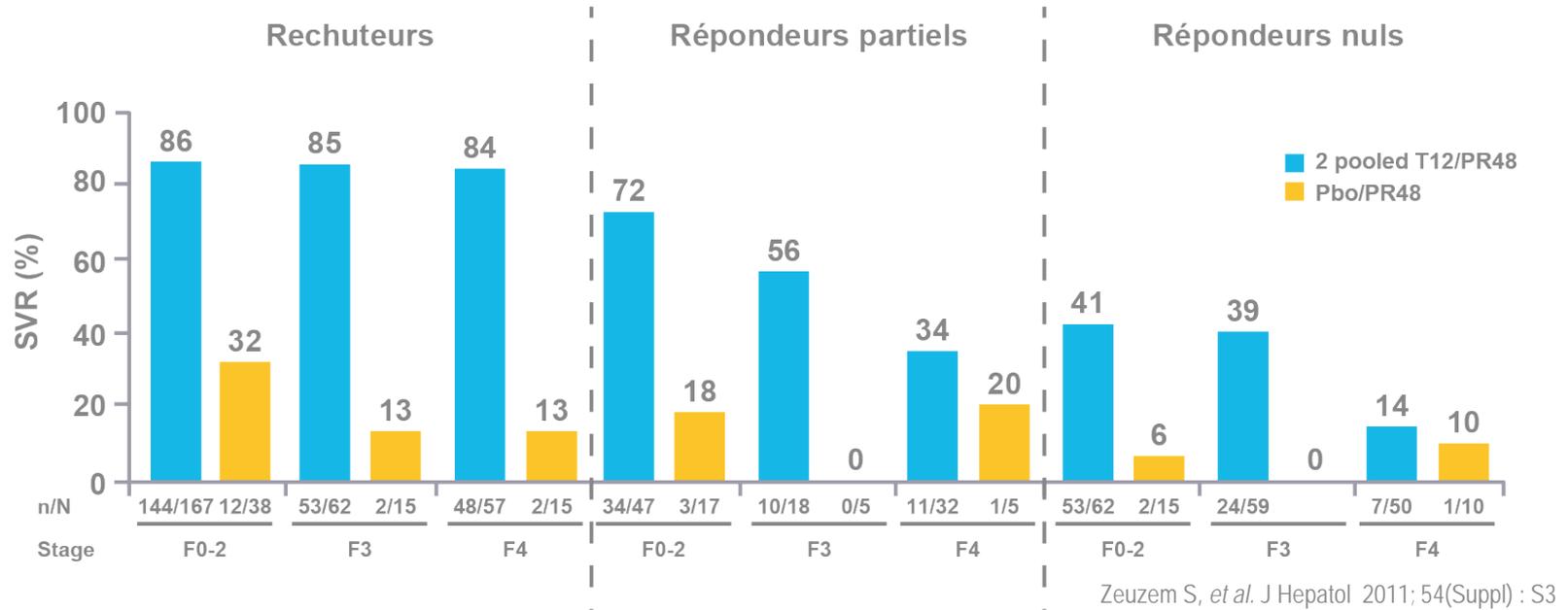


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