

Overall survival is impacted by liver failure and comorbidities rather than etiology of cirrhosis in patients with Hepatocellular carcinoma detected during a surveillance program

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INTRODUCTION

Prevalence of underlying Alcohol-related Liver Disease (ALD) in patients with HCC

- Worldwide 6 to 70%
- France 37 to 72%

GBD Liver Cancer. JAMA Oncol 2017; 3(12): 1683-1691
Rosa I, et al. J Hepatol 2010;52:5231-5232

Impact of ALD on HCC characteristics

- Delayed diagnosis compared to HCC complicated HCV chronic hepatitis
 - outside a screening program
 - More advanced chronic liver disease
- Fewer therapeutic recourses

Buccini L et al. Aliment Pharmacol Ther 2016;43:385-399
Costentin CE, et al. Cancer 2018;124:1964-1972

AIM

To assess the impact of the etiology of the underlying liver disease (ALD, viral or mixt) in patients with HCC diagnosed within a systematic surveillance program, regarding :

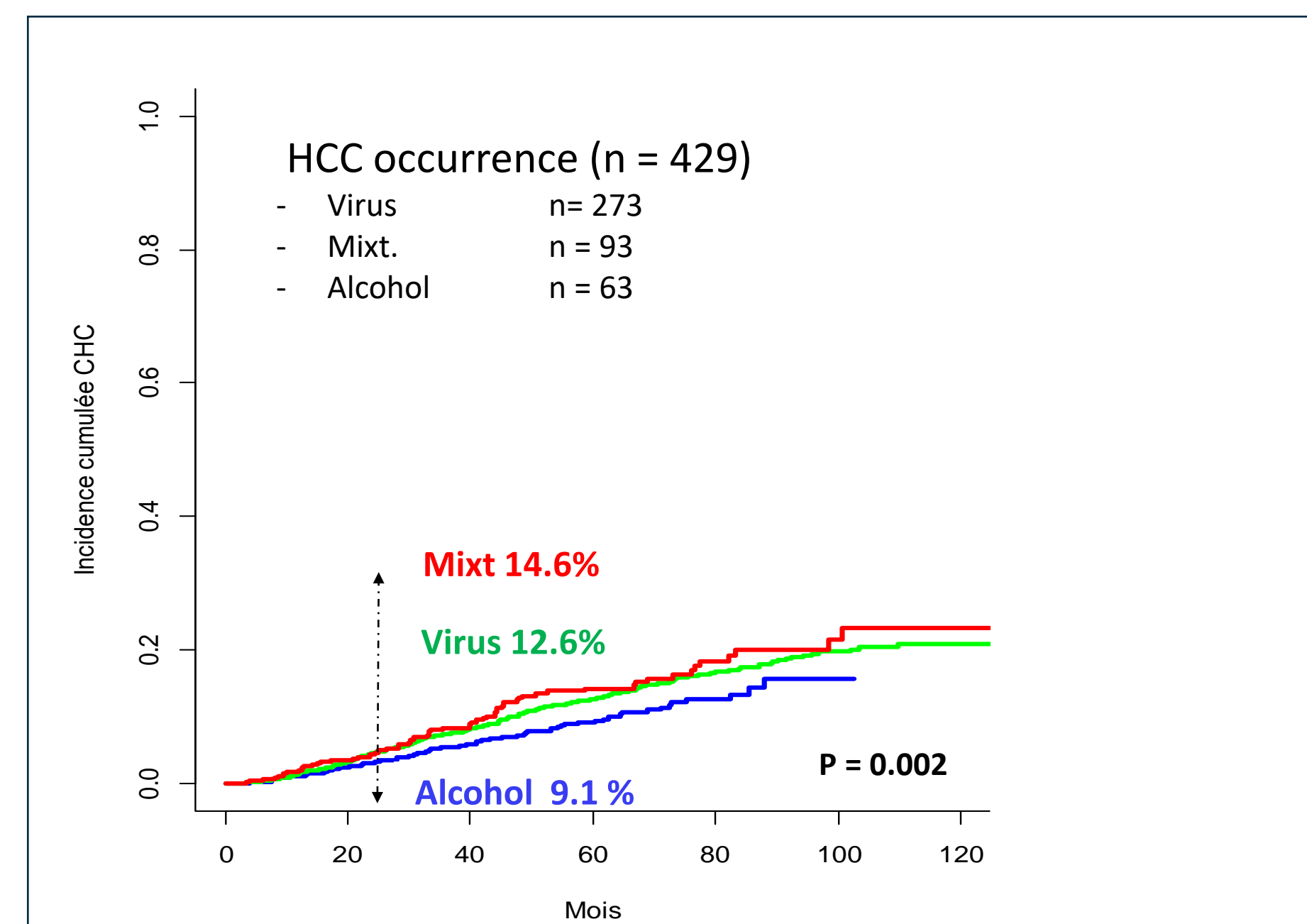
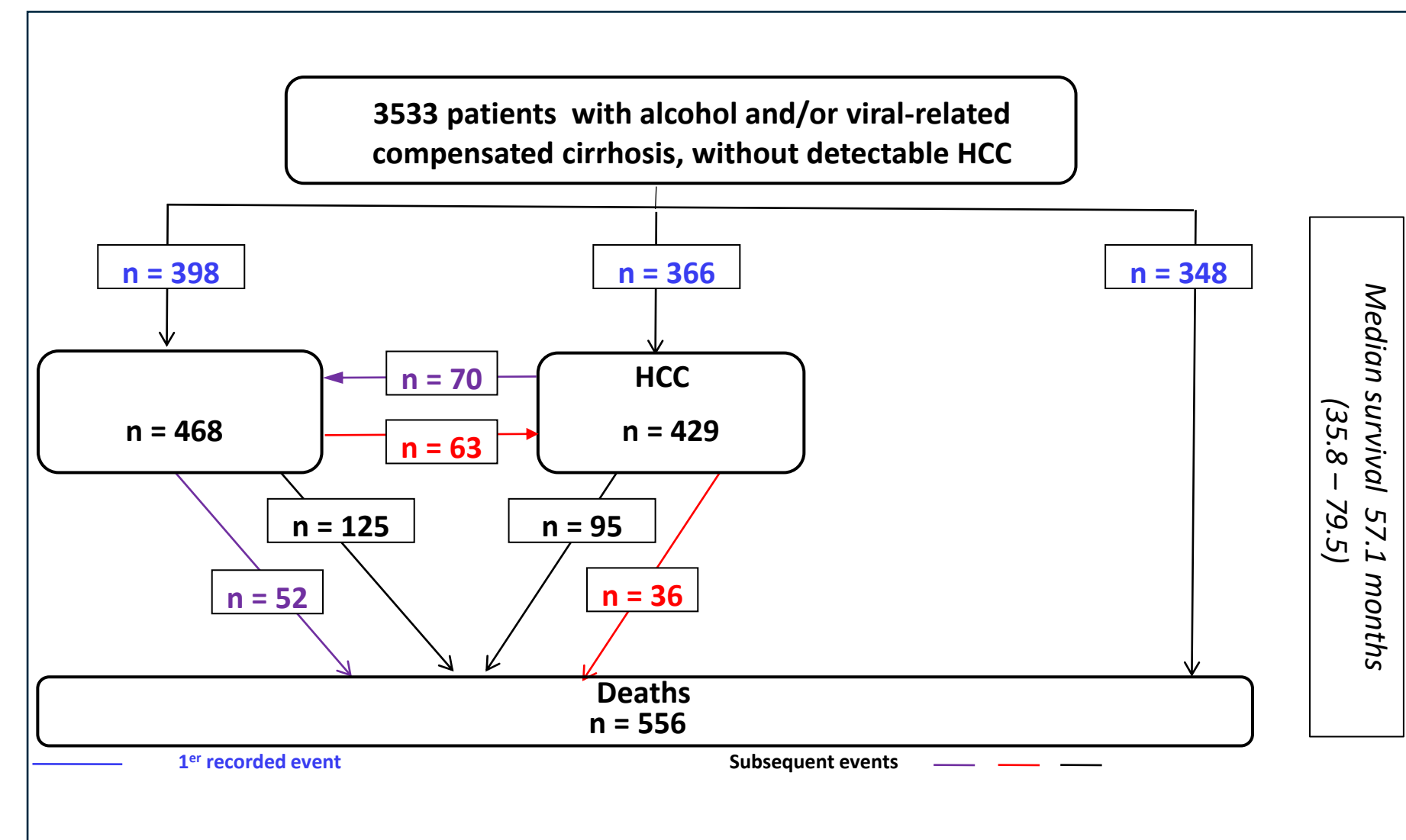
- Tumor characteristics
- Access to first treatment with curative intent
- Overall and liver-related survivals

PATIENTS

CHC 2000	ANRS CO12-CirVir	CIRRAL
Aim: To compare 2 periodicities of HCC screening in patients with cirrhosis	Aim: To describe natural history of virus related cirrhosis	Aim: To describe natural history of alcohol related cirrhosis
Criteria of inclusion : - Biopsy-proven cirrhosis - Child-Pugh A or B7 - No previous nor detectable HCC		
Causes of cirrhosis : Virus, Alcohol, Hemochromatosis, NASH	Causes of cirrhosis : Virus with or without alcohol	Cause of cirrhosis : Alcohol without virus
1278 patients included 43 tertiary centres in France and Belgium (2000-2006)	1671 patients included 35 tertiary French centres (2006-2012)	650 patients included 22 tertiary centres in France and Belgium (2012-2016)
1111 analyzable patients (520 Virus, 517 ALD, 175 Mixt)	1671 analyzable patients (1408 Virus, 265 Mixt)	650 analyzable patients
Median Follow-up: 47.5 months	Median Follow-up: 69.3 months	Median Follow-up: 69.3 months
114 HCC 101 decompensations 88 deaths without any event	357 HCC 262 decompensations 92 deaths without any event	68 HCC 105 decompensations 68 deaths without any event

N (%)	n	Total (n = 3533)	Alcohol (n = 1167)	Virus (n = 1926)	Mixt (n = 440)	p
Gender (M/F)	3533	2403/1108 (68%/32%)	790/363 (68%/32%)	1238/684 (64%/36%)	375/61 (86%/14%)	<10 ⁻⁴
Age (ans)	3522	55 (48; 64)	57 (50; 64)	56 (48; 65)	50 (45; 57)	<10 ⁻⁴
BMI (kg/m2)	3014	26 (23-29)	27 (24-30.5)	26 (23-29)	25 (23-28)	<10 ⁻⁴
Diabete (n)	2318	259 (11%)	146 (23%)	93 (7%)	20 (7.5%)	<10 ⁻⁴
Platelets (G/mm3)	3416	138 (98.8; 183)	139 (102-185)	140 (100-186)	125 (87-175)	0.0003
AFP (ng/mL)	3187	5 (3; 8)	4 (3-6)	5 (3-10)	6 (3-10)	<10 ⁻⁴
MELD	2536	8.3 (7.5; 9.4)	8.9 (7.8-10.9)	7.9 (7.5-8.9)	7.9 (7.5-9.0)	<10 ⁻⁴
Child-Pugh A	3255	3128 (96%)	924 (90%)	1808 (99%)	396 (98%)	<10 ⁻⁴
VIH +	3078	78 (2.5%)	2 (0.2%)	63 (3.4%)	13 (3.4%)	<10 ⁻⁴
HCV RNA+	2544	1333 (38%)	NA	1059 (55%)	274 (62%)	<10 ⁻⁴
HBV DNA+	1151	173 (5%)	NA	153 (8%)	20 (4.5%)	<10 ⁻⁴
Fibroscan (kPa)	1364	16.5 (10.5; 26.5)	24.5 (14-42)	14.5 (10-22)	17.5 (12-28)	<10 ⁻⁴

OUTCOME



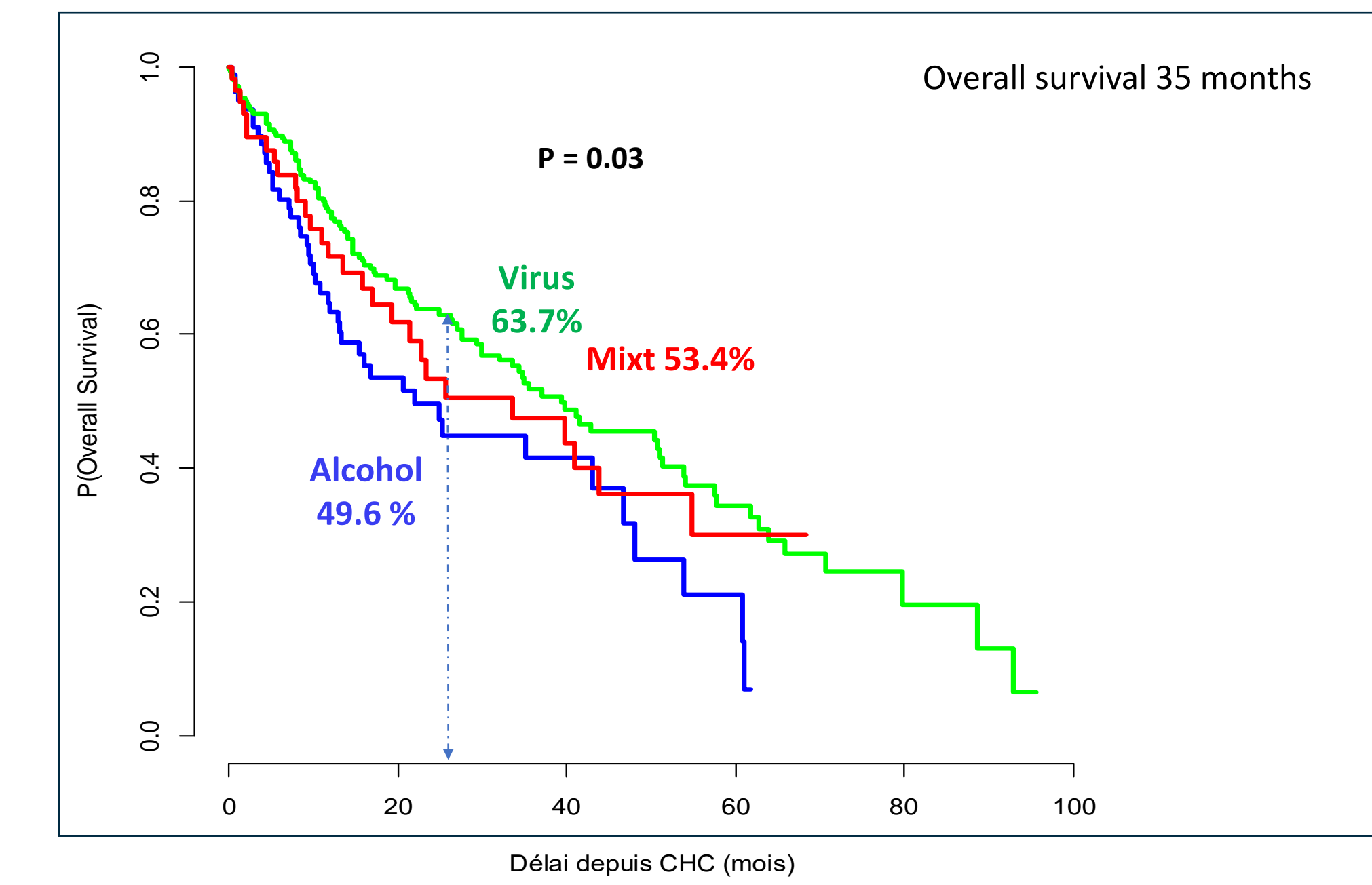
HCC CHARACTERISTICS

N (%)	Total (n = 429)	Virus (n = 273)	Alcohol + Mixt (n = 156)	p
Gender (M/F)	307/120 (72/28%)	178/94 (65/35%)	129/26 (83/17%)	0.0001
Age (years)	63 (55; 71)	64 (55; 72)	63 (55; 70)	0.26
Single nodule	245 (61%)	158 (61%)	87 (60%)	0.69
Size main nodule (mm)	20 (15; 26)	20 (15; 27)	19.5 (15; 25)	0.95
AFP (ng/mL)	10.5 (4; 87.5)	18 (5.5; 119)	8 (4; 57.5)	0.029
Portal thrombosis / metastasis	33 (9%) / 5 (3%)	18 (8%) / 2 (4%)	15 (12%) / 3 (3%)	0.41
Milan +	318 (74%)	207 (75%)	111 (72%)	0.34
Performance Status (0/1/2/3)	278/40/9/2	203/24/1/0	75/16/8/2	<10 ⁻⁴
Child-Pugh (A/B/C)	293/52/14	197/26/11	96/26/3	0.03
BCLC (0/A/B/C/D)	5/220/28/54/10	3/164/14/21/6	2/57/14/33/4	<10 ⁻⁴
Platelets (G/mm3)	111 (80; 154)	111 (80; 154)	111 (79; 170)	0.73

HCC TREATMENTS

	Total (n = 429)	Virus (n = 273)	Alcohol + Mixt (n = 156)	p
Resection	57 (13%)	40 (15%)	17 (11%)	0.33
Percutaneous Ablation	189 (44%)	116 (42%)	73 (47%)	0.45
Embolization	87 (20%)	54 (20%)	33 (22%)	0.81
Sorafenib	42 (10%)	25 (9%)	17 (11%)	0.64
Transplantation	32 (7%)	24 (9%)	8 (5%)	0.23

SURVIVAL AFTER HCC



PROGNOSTIC FACTORS

	HR	IC 95%	p
Size of the main nodule (mm)	1.02	1.01 - 1.03	< 0.0001
Child-Pugh B/ C	2.38	1.61 - 3.49	< 0.0001
BCLC B/C/D	2.97	1.97 - 4.50	< 0.0001

METHODS

•Analysis of individual data according to etiology of the underlying chronic liver disease (alcohol-related, viral or mixt) in patients with compensated cirrhosis enrolled 1 of the 3 prospective French cohorts

CHC 2000
ANRS CO12-CirVir
CIRRAL

Statistics:

- End point : 12/08/2019
- Methods: Kaplan-Meier
COX (multiple imputation / missing data)

CONCLUSIONS

HCC in patients with compensated cirrhosis included in a surveillance program :

- Has a higher incidence in case of virus-related or mixt cirrhosis
- Is associated with poorer liver function, worse general conditions and more advanced BCLC stage in alcoholic or mixt cirrhosis
- comes under the same therapeutic management whatever the cause of the underlying hepatopathy (Ablation 44%, Resection 13%)
- Is associated with a 35 months median survival without any prognosis impact of the cause of the underlying chronic liver disease

ACKNOWLEDGEMENTS

CHC 2000	CirVir anRS	CIRRAL
• GRETEL - 43 Centres français et Belges: Aix en Provence, Amiens, Angers, Besançon, Bicière, Bobigny, Bondy, Bordeaux, Caen, Clichy, Clermont-Ferrand, Créteil, Grenoble, Le Mans, Lille, Lyon, Marseille, Nancy, Nice, Paris-Cochin, Paris Institut Montsouris, Paris Pitié Salpêtrière, Paris-St Antoine, Paris-Tenon, Passac, Reims, Rouen, Rennes, St Laurent du Var, Suresnes, Toulouse, Tours	• 35 Centres: Aix en Provence, Amiens, Angers, Besançon, Bicière, Bobigny, Bondy, Bordeaux, Caen, Clichy, Clermont-Ferrand, Créteil, Grenoble, Le Mans, Lille, Lyon, Marseille, Nancy, Nice, Paris-Cochin, Paris Institut Montsouris, Paris Pitié Salpêtrière, Paris-St Antoine, Paris-Tenon, Passac, Reims, Rouen, Rennes, St Laurent du Var, Suresnes, Toulouse, Tours	• 22 Centres français et Belges: Amiens, Angers, Bobigny, Bondy, Bordeaux, Bruxelles, Caen, Clamart, Créteil CHC, Grenoble, Hôpital Saint-François, Lille, Nancy, Nantes, Nice, Montpellier, Paris-Cochin, Paris-Lariboisière, Paris-Pitié Salpêtrière, Paris-St Antoine, Paris-Tenon, Passac, Rouen, Rennes, Toulouse, Tours, Villejuif.
• Methodologie: SBIM - Paris-Saint Louis • Promotion: APHP	• Methodologie: département de statistiques, Mondor • Promotion: ANRS	• Methodologie: SBIM - Paris-Saint Louis • Promotion: APHP • Soutien financier: INCA, ARC, ANRS

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