Petit panorama des activités de la Commission Hépatologie

Bertrand Hanslik
Montpellier

La Commission Hépato du Cregg

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2002 : Le Forum d'Hépatologie Libérale
2008 : Les Webconfs
2011 : Les Minutes Vidéos

30 membres

Les minutes vidéos

Les « minutes vidéos » de la Commission

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Poster LB-8

OPTIMIZE Trial: Noninferiority of Twice-daily Telaprevir Versus Administration Every 8 Hours in Treatment-naïve, Genotype 1 HCV-infected Patients

Maria Buti,[1] Kosh Agarwal,[2] Yves Horsmans,[3] William Sievert,[4] Ewa Janczewska,[5] Stefan Zeuzem,[6] Lisa Nyberg,[7] Robert S Brown Jr,[8] Christophe Hezode,[9] Mario Rizzetto,[10] Raymundo Parana,[11] Sandra De Meyer,[12] Donghan Luo,[13] James Witek[13]

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Introduction

- The NS3•4A protease inhibitor telaprevir (TVR, T) in combination with peginterferon alfa (Peg-IFN, P) and ribavirin (RBV, R)[1,2] is approved for the treatment of chronic genotype 1 hepatitis C virus (HCV) infection in adults with compensated liver disease.
- The ADVANCE study (NCT00672626) in treatment-naïve patients evaluated the efficacy and safety of either 8 or 12 weeks of TVR every 8 hours (q8h) in combination with 24 or 48 weeks of PR compared with PR for 48 weeks[3]
  - Sustained virologic response (SVR) was achieved by 79% of 12 week TVR-treated patients compared with 46% of patients in the PR only arm.[3]
- ILLUMINATE (NCT00759043) evaluated the safety and efficacy of 24 weeks and 48 weeks of TVR-based treatment in patients who achieved extended rapid viral response (eRVR):
  - The overall SVR rate was 74%, the 24-week treatment duration was noninferior to the 48-week regimen for patients with an eRVR (SVR 92% versus 90%, respectively, 95% confidence interval [CI], 4–8%).[1,4]
- The Phase II C208 clinical trial (NCT00528528) investigated the efficacy of TVR 750 mg given q8h or TVR 1125 mg every 12 hours (q12h; twice daily [bid])[5]
  - SVR rates were similar between groups with ≥80% of patients achieving SVR regardless of the TVR dosing frequency.
- The OPTIMIZE study is the first Phase III trial to investigate the use of TVR bid versus TVR q8h in combination with PR.

Methods

Study Design

- The OPTIMIZE trial was a randomized, open-label, multicenter, Phase III trial in treatment-naïve patients with genotype 1 chronic HCV infection (NCT01241760).
- Patients were randomized into two treatment groups: TVR 750 mg q8h or TVR 1125 mg bid in combination with PR (Figure 1).
- All patients received 12 weeks of treatment with TVR in combination with PR at standard doses (Figure 1). At Week 12, TVR dosing ended and patients continued on PR treatment only. If a patient achieved an HVR+ (HCV RNA <25 IU/mL, target not detected at Week 4 of treatment), the total treatment duration was 24 weeks. Otherwise the total treatment duration was 48 weeks.

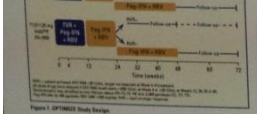

Figure 1. OPTIMIZE Study Design.

- To minimize the risk of accumulation of mutations in patients without an adequate antiviral response and for consistency with standard guidelines for the treatment of genotype 1 chronic HCV infection, HCV RNA results were monitored to determine if treatment and procedural modifications should be made for individual patients
  - TVR was stopped if HCV RNA levels were >1000 IU/mL at Week 4 or ≥25 IU/mL at Weeks 12, 24, 32 or 40.
- On-treatment virologic failure was defined as patients who met a virologic stopping rule or experienced viral breakthrough.
- Randomization was stratified by histologic status (no/mild fibrosis and portal fibrosis [e.g. Metavir F0–F2; Ishak score ≤3] and IL28B (rs12979860) genotype (CC, CT or TT).

Study Objectives

- The primary objective of the OPTIMIZE trial was to demonstrate noninferiority in SVR12 (defined as plasma HCV RNA levels <25 IU/mL 12 weeks after the last planned dose of study drug) with TVR bid dosing compared with q8h dosing in combination with PR in treatment-naïve patients with genotype 1 chronic HCV infection.
- Secondary objectives were to evaluate:
  - The tolerability and safety of TVR when administered as 750 mg q8h or 1125 mg bid in combination with PR
  - The effect of IL28B genotype on viral response
  - The pharmacokinetics of TVR, Peg-IFN-alfa-2a and RBV, and pharmacokinetic-pharmacodynamic relationships for safety and efficacy
  - The changes from baseline in the amino acid sequence of the HCV NS3•4A region.

Analysis Methods

- Full analysis set: all randomized patients who received at least one dose of the study medication (TVR).
- Per-protocol analysis set: all randomized patients who received at least one dose of the study medication (TVR) and who did not report a major protocol deviation that could significantly impact efficacy evaluation.
- The primary efficacy analysis was conducted on both the full analysis and per-protocol analysis sets, with the full analysis set as the primary analysis set (intention-to-treat). The per-protocol analysis set was used to provide supportive efficacy analysis of the primary efficacy endpoint.
- Noninferiority testing to reject the null hypothesis that TVR bid dosing was inferior to TVR q8h dosing for the primary efficacy endpoint was conducted using the confidence interval (CI) approach. The noninferiority of bid dosing would be established if the lower limit of the 2-sided 95% CI of the observed treatment difference for the primary endpoint between TVR bid and q8h dosing was greater than the prespecified noninferiority margin of −11%.

Results

Patient Disposition and Baseline Characteristics

- A total of 744 patients were randomized of which 740 patients were treated and represent the overall population for the full analysis set. Patient disposition is shown in Table 1.

Table 1. Patient Disposition.

Parameter, n	T12PR8q/PR (N=371)	T12PR12q/PR (N=369)	All patients (N=740)
Screened	–	–	984
Not randomized – not treated	–	–	140
Randomized – not treated	1	3	4
Randomized – treated (full analysis set)	371	369	740
Per-protocol analysis set	357	355	712

- Baseline characteristics of the 740 randomized and treated patients are shown in Table 2.

Efficacy

- SVR12 was 74% in the T12bid/PR group versus 73% in the T12q8h/PR group (Figure 2).
  - The difference between T12bid/PR and T12q8h/PR was 1.5% with a 95% CI: −4.9 to 12.0
  - The lower limit of the 95% CI (−4.9%) was well above the predetermined noninferiority margin of −11% and thus establishes the noninferiority of T12bid/PR to T12q8h/PR. Per-protocol analysis further supported the noninferiority (76% versus 75% in SVR12 for T12bid/PR and T12q8h/PR, respectively).

Table 2. Patient Baseline Characteristics.

Characteristic	T12q8h/PR (N=371)	T12bid/PR (N=369)	All patients (N=740)
Age, mean years (SD)	48 (11)	48 (11)	48 (11)
BMI, mean kg/m² (SD)	27 (5)	26 (5)	27 (5)
Male sex, n (%)	235 (63)	209 (57)	444 (60)
Race, n (%)			
Asian	6 (2)	10 (3)	16 (2)
Black or African American	15 (4)	20 (5)	35 (5)
Multiple*	3 (<1)	6 (2)	9 (1)
White	347 (94)	333 (90)	680 (92)
Region			
Europe	192 (52)	179 (48)	371 (50)
North America	126 (34)	137 (37)	263 (36)
Other	53 (14)	53 (14)	106 (14)
Baseline Log₁₀ HCV RNA,† mean IU/mL (SD)	6.48 (<1)	6.48 (<1)	6.49 (<1)
Baseline HCV RNA,† n (%)			
<800000 IU/mL	54 (15)	57 (15)	111 (15)
≥800000 IU/mL	317 (85)	312 (85)	629 (85)
HCV genotype subtype,† n (%)			
1a	209 (56)	210 (57)	419 (57)
1b	160 (43)	157 (43)	317 (43)
IL28B genotype, n (%)			
CC	106 (29)	105 (29)	211 (29)
CT	208 (56)	206 (56)	414 (56)
TT	57 (15)	58 (16)	115 (16)
Liver fibrosis status, n (%)			
F0–F2	298 (72)	294 (72)	592 (72)
F3–F4	153 (28)	155 (28)	308 (28)
Stage of fibrosis,† n (%)			
No cirrhosis (F0–F3)	321 (87)	315 (85)	636 (86)
Cirrhosis (F4)	49 (13)	54 (15)	103 (14)

*Multiple race = patients who identified with more than one race
†HCV RNA levels were measured with the use of COBAS® TaqMan® HCV assay (v2.0, Roche).
HCV genotype and subtype were determined using the HCV assay.
‡To assess liver fibrosis status, patients underwent liver biopsy (pre-screen, cirrhosis [Metavir F4, Ishak >5], bridging fibrosis [Metavir F3, Ishak ≥3], portal fibrosis [Metavir F1, Ishak 1], and minimal or no fibrosis [Metavir F0–F1, Ishak 0–2]); one patient in the bid arm was missing individual fibrosis stage assessment.
BMI = body mass index; SD = standard deviation

Figure 2. SVR12 in the T12bid/PR Group, T12q8h/PR Group and All Patients.

- Subgroup analyses for liver fibrosis stage and IL28B genotype showed similar SVR12 outcomes for T12bid/PR and T12q8h/PR (Figure 3a and 3b)
  - In cirrhotic patients, SVR12 rates were 54% and 49% for T12bid/PR and T12q8h/PR, respectively
  - In non-cirrhotic patients, SVR12 rates were 78% and 77% for T12bid/PR and T12q8h/PR, respectively.
- Subgroup analyses for a spectrum of baseline characteristics showed similar SVR12 outcomes for T12bid/PR and T12q8h/PR (Figure 4).
- Total treatment duration was determined at Week 4 by RVR status. RVR was similar between T12bid/PR (80%) and T12q8h/PR (67%)
  - Overall, approximately two-thirds of patients were eligible for the shortened treatment duration of 24 weeks of total therapy.
  - SVR rates in RVR+ patients were 86% and 85% for T12bid/PR and T12q8h/PR, respectively
  - SVR rates in RVR− patients were 47% and 47% for T12bid/PR and T12q8h/PR, respectively.
- The extended RVR rates (eRVR, <25 IU/mL, target not detectable at Week 4 and Week 12) were 66% and 63% for T12bid/PR and T12q8h/PR, respectively.

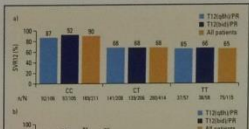

Figure 3. SVR12 in the T12bid/PR Group, T12q8h/PR Group and All Patients by a) IL28B Genotype and b) Liver Disease Status.

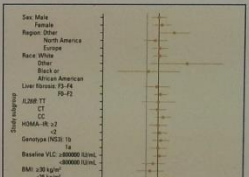

Figure 4. SVR12 in the T12bid/PR Group, T12q8h/PR Group According to Baseline Subgroup.

Treatment Outcome

- Treatment outcome was similar between the T12bid/PR and T12q8h/PR arms with relapse seen in 8% versus 7% of patients, respectively (Table 3).

Table 3. Treatment Outcome Classification.

Treatment outcome, n (%)	T12q8h/PR (N=371)	T12bid/PR (N=369)	All patients (N=740)
SVR12	270 (73)	274 (74)	544 (74)
Relapse*	19/350 (7)	23/330 (8)	42/680 (7)
On-treatment virologic failure†	36 (10)	30 (10)	74 (10)
Other	46 (12)	34 (9)	80 (11)

*Assessed in Patients with HCV RNA <25 IU/mL at the planned end of treatment.
†Patients who met a virologic stopping rule or experienced viral breakthrough

Safety and Tolerability

- During the TVR treatment phase, T12bid/PR showed a similar safety profile to T12q8h/PR (Table 4).
- The incidences of adverse events of special interest defined using a special search category were similar between the two treatment groups during the TVR treatment phase (Table 4).

Table 4. Adverse Events During the TVR Treatment Phase.

Adverse event, n (%)	T12q8h/PR (N=371)	T12bid/PR (N=369)	All patients (N=740)
Any adverse event	367 (99)	360 (98)	727 (98)
Serious adverse event	35 (9)	28 (8)	63 (8)
Death*	1 (<1%)	0	1 (<1%)
Any Grade ≥3 adverse event	139 (38)	156 (42)	295 (40)
Grade ≥3 anemia SSC	70 (19)	95 (26)	165 (22)
Grade ≥3 rash SSC	22 (6)	18 (5)	40 (5)
Any Grade 4 adverse event	24 (7)	23 (6)	47 (6)
Any adverse event leading to permanent discontinuation of TVR	68 (19)	57 (15)	125 (17)
Any treatment-related adverse event considered possibly related to TVR†	335 (90)	344 (93)	679 (92)
Most frequent adverse events‡			
Fatigue	137 (40)	173 (47)	310 (41)
Pruritus SSC	171 (46)	170 (46)	341 (46)
Anemia SSC	162 (44)	187 (49)	349 (46)
Nausea	142 (38)	128 (35)	270 (37)
Rash SSC	138 (54)	189 (51)	368 (52)
Headache	107 (29)	87 (24)	194 (26)

*One patient died during the study of a brain neoplasm; the brain neoplasm was considered not related to TVR or Peg-IFN-alfa-2a and RBV by the investigator.
†Considered at least possibly related to TVR by an investigator.
‡Adverse events occurring in >20% in all patients in any group.
SSC = special search category; grouped adverse event terms representing similar medical concepts, used to ensure that each patient with an event included within a predefined special search category was counted but counted only once.

Conclusions

- SVR12 rates for TVR 1125 mg bid were noninferior to TVR 750 mg q8h (74% versus 73%, respectively)
  - 28% of patients enrolled had advanced fibrosis (bridging and cirrhosis), 71% had non-CC IL28B genotype and 85% had HCV RNA ≥800000 IU/mL.
- SVR12 outcomes for T12bid/PR and T12q8h/PR were similar regardless of liver fibrosis status and IL28B genotype.
- RVR and eRVR rates were similar in both arms
  - The majority (two-thirds) of patients were eligible to receive 24 weeks, total duration of therapy.
- The safety and tolerability profile of T12bid/PR and T12q8h/PR was similar between treatment groups.
- Similar SVR and adverse event rates achieved with 1125 mg bid TVR and 750 mg q8h TVR offers the potential of a simplified dosing regimen for genotype 1 HCV-infected patients.

References

1. INCIVEK® (t) Summary of Product Characteristics. Vienna: Tergeist, Thomas. EMEA, 2011.
2. INCIVEK® Package Insert. Cambridge, MA: Vertex Pharmaceuticals Incorporated. 2012.
3. Jacobson IM, et al. N Engl J Med 2011; 364:2405–16.
4. Manns M P et al. Gastroenterol 2011; 140:839–48.

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The authors have the following conflict of interest to declare: **Maria Buti** has been a clinical investigator, speaker and/or consultant for Gilead, Janssen and Vertex. **Kosh Agarwal** has received grant support from Novartis, Gilead and Vertex. **Yves Horsmans** has been a clinical investigator for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **William Sievert** has been a clinical investigator for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **Ewa Janczewska** has been a clinical investigator and/or consultant for Janssen and Roche. **Stefan Zeuzem** has been a clinical investigator for Abbott, Bayer, Gilead, Janssen, Novartis, Pharmasset, Roche, Tibotec and Vertex. **Lisa Nyberg** has been a clinical investigator for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **Robert S Brown Jr.** has been a clinical investigator and/or consultant for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **Christophe Hezode** has been a clinical investigator and/or consultant for Janssen. **Robert S Brown Jr.** has been a clinical investigator and/or consultant for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **Mario Rizzetto** has been a clinical investigator and/or consultant for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **Raymundo Parana** has been a clinical investigator and/or consultant for Gilead, Janssen, Novartis, Pharmasset, Tibotec and Vertex. **Sandra De Meyer**, **Donghan Luo** and **James Witek** are employees of Janssen Pharmaceuticals.

Supported by Tibotec/Janssen Pharmaceuticals and Vertex Pharmaceuticals Incorporated.

Presented at the 63rd Annual Meeting of the American Association for the Study of Liver Diseases, Boston, MA, USA, November 9–13 2012

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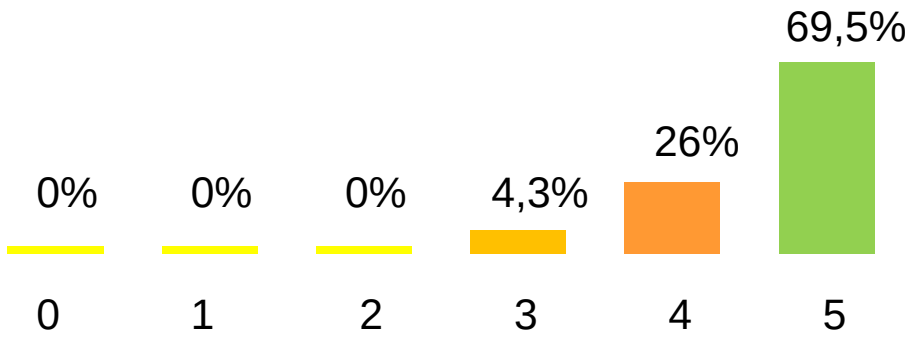

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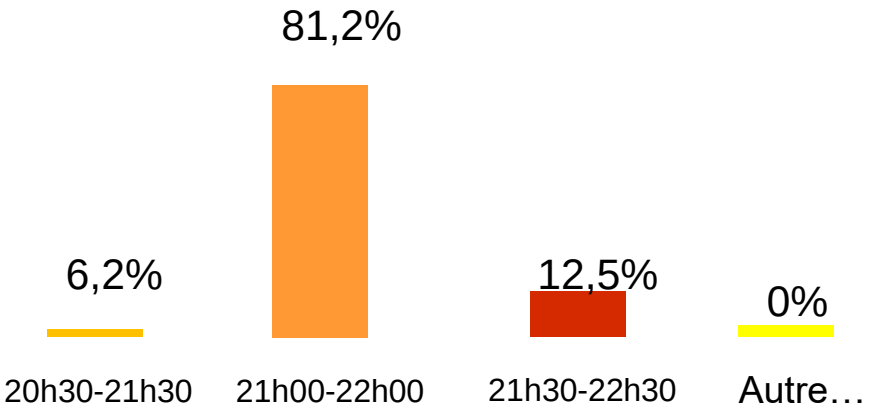

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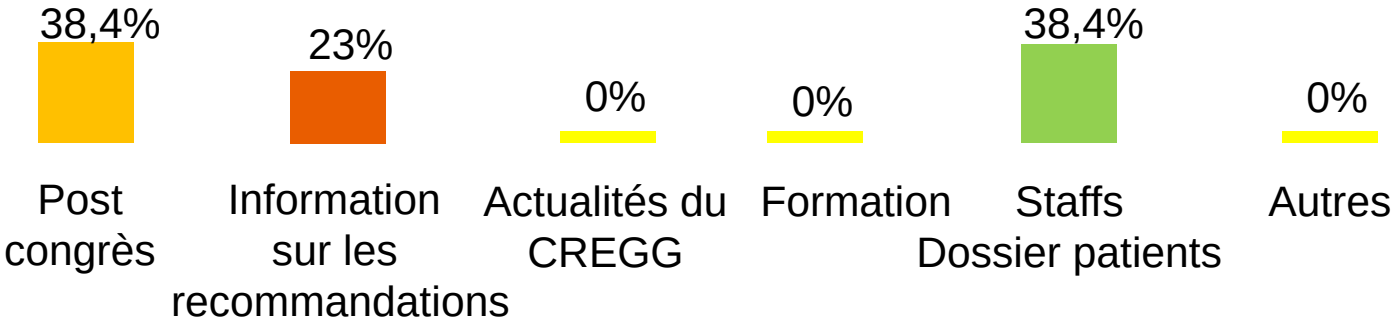

L'aventure des nouvelles molécules dans l'hépatite C

TRILIB : Trithérapie avec antiprotéases de 1ère génération en secteur libéral: expérience chez les 300 premiers patients traités pour hépatite chronique C

Hanslik B. [1], Bresson-Hadni S. [2], Fontanges T. [3], Orsini M. [4], Louvet H. [5], Delasalle P. [6], Antoni M. [7], Toulemonde P. [8], Beorchia S. [9], Baesjou S. [10], Boyer N. [11], Liautard J. [12], Bonny C. [13], Cuissard L. [14], Castelnau C. [15], Ouzan D. [16].

Objectifs: Evaluer l'efficacité des traitements PR+IP en pratique libérale. Méthodo: 15 HGE libéraux.
Résultats: 300 premiers patients traités dès Avril 2011, 273 dossiers exploitables, et 76% des patients avec une RVS disponible.

Les patients

	n (%)
Age	48 ans
Sexe (M/F)	162/111 (59/41)
IMC > 25	150 (55)
Diabète	31 (12)
Troubles psy	
G	
CV	
IL28B	75/91 (82%)
Fibrose sévère (F3/F4)	192 (70%)
Cirrhose (Child A)	91 (33%)
Pré-traités	188 (69%)
dont RR + NR répondeurs	45 (29%)

Les traitements

	n (%)
Télaprévir / Bocéprévir	172/101 (63/37)
Education thérapeutique ...dont éducation	
	174 (64)
...EPO / transfusions	92 (53) / 6 (3,6)
EI cutanés *Grades 3*	103 (37%) *6 patients*
Arrêt traitement pour EI	34 (12)
Décompensation cirrhotique *décès*	8 (3) *2 patients**

...dans le secteur libéral, des circuits de prise en charge sont opérationnels pour répondre à la demande croissante d'accès aux soins des patients...

RVS 12 et 24

	Globale	
	n/N	%
RVS 12	157/238	66
RVS 24	138/206	67
	F0/F1/F2	
	n/N	%
RVS 12	57/74	77
RVS 24	51/66	77
	F3/F4	
	n/N	%
RVS 12	100/164	61
RVS 24	87/140	62

	Naïfs	
	n/N	%
RVS 12	54/72	75
RVS 24	48/60	80
	Prétraités	
	n/N	%
RVS 12	103/166	62
RVS 24	90/146	62

Seul un ATCD de NR à un ttt antérieur était associé à un échec

B. Hanslik, S. Bresson Hadni, T. Fontanges et al, AFEF 2013 CA-02

Cohorte AVDLib
des cabinets libéraux CREGG

RS-1903

Viral hepatitis

Hepatitis C - clinical (Therapy)

SAFETY AND EFFICACY OF SOFOSBUVIR CONTAINING REGIMENS FOR HEPATITIS C: COMMUNITY TREATMENT OF A REAL WORLD POPULATION WITH ADVANCED LIVER FIBROSIS

Denis Ouzan*[1], Thierry Fontanges[2], Guillaume Pénaranda[3], Hadni[6],
Patricia Cerdan[7], Nathalie Boyer[8], Corinne
Corinne Bonny[13], Pierre (Club
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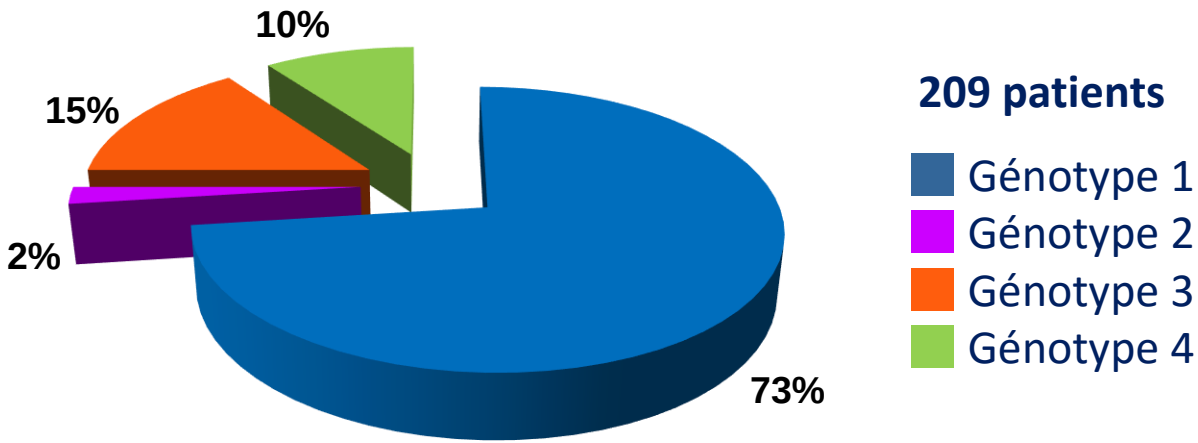
Langue [15]Private Practice, Montpellier, France

L'objectif d'AVDLIB 1 est d'évaluer les résultats obtenus par ces traitements de mars à septembre 2014 en secteur libéral

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER

Vienne, 2015

Cohorte AVDLIB des cabinets libéraux CREGG
Caractéristiques des 209 patients inclus

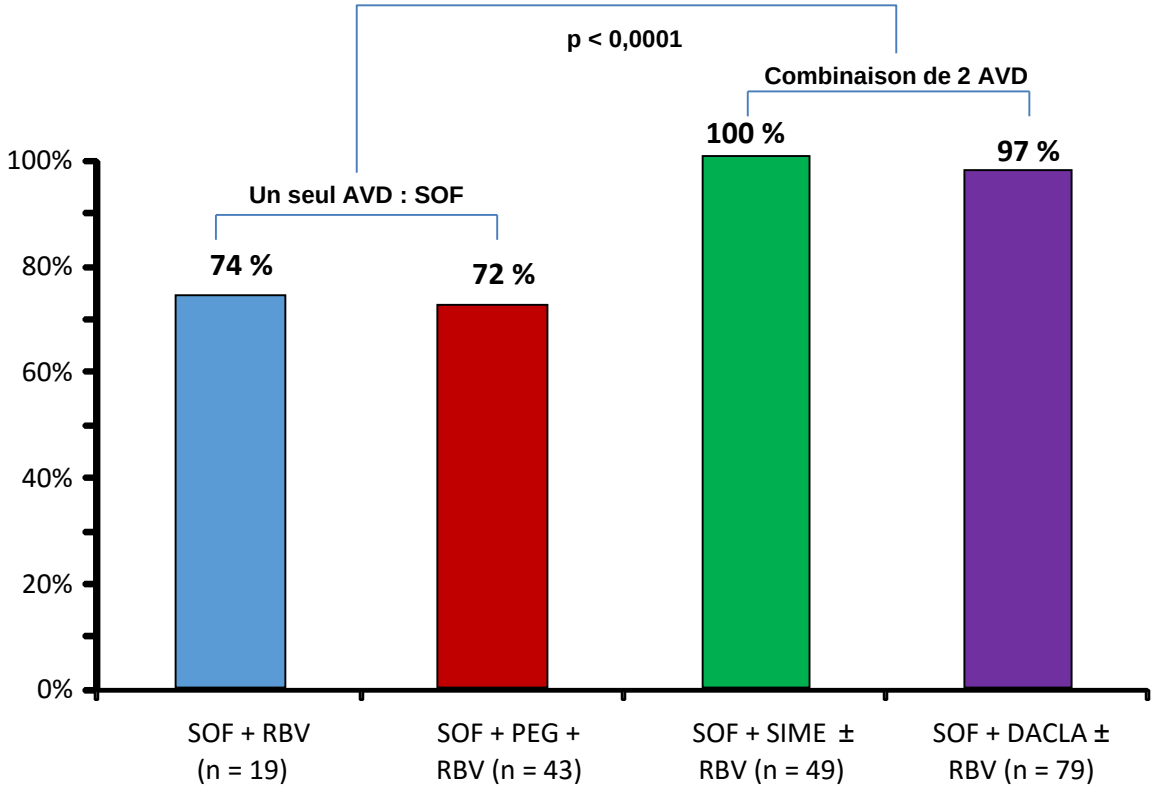


- Mai à novembre 2014
- Age moyen : 43 ± 13 ans
- Sex ratio: 58% hommes
- Comorbidités : 18 % patients

- F3 34%
- F4 66% (Child A: 91%, B: 9%)
- Prétraités 79%
- Coinfectés 5%

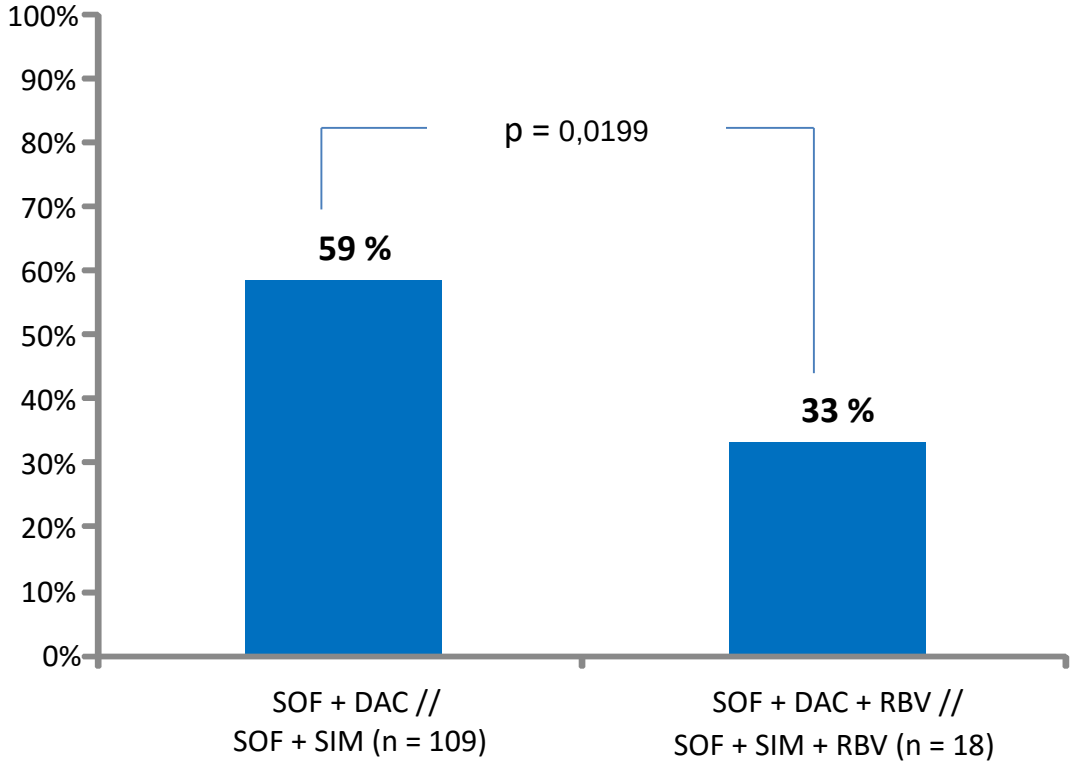
D. Ouzan, P. Delasalle et al. AFEF 2015 actualisé

AVDLIB 1 (2014) : RVS12 en fonction du traitement chez 190 patients F3 et F4



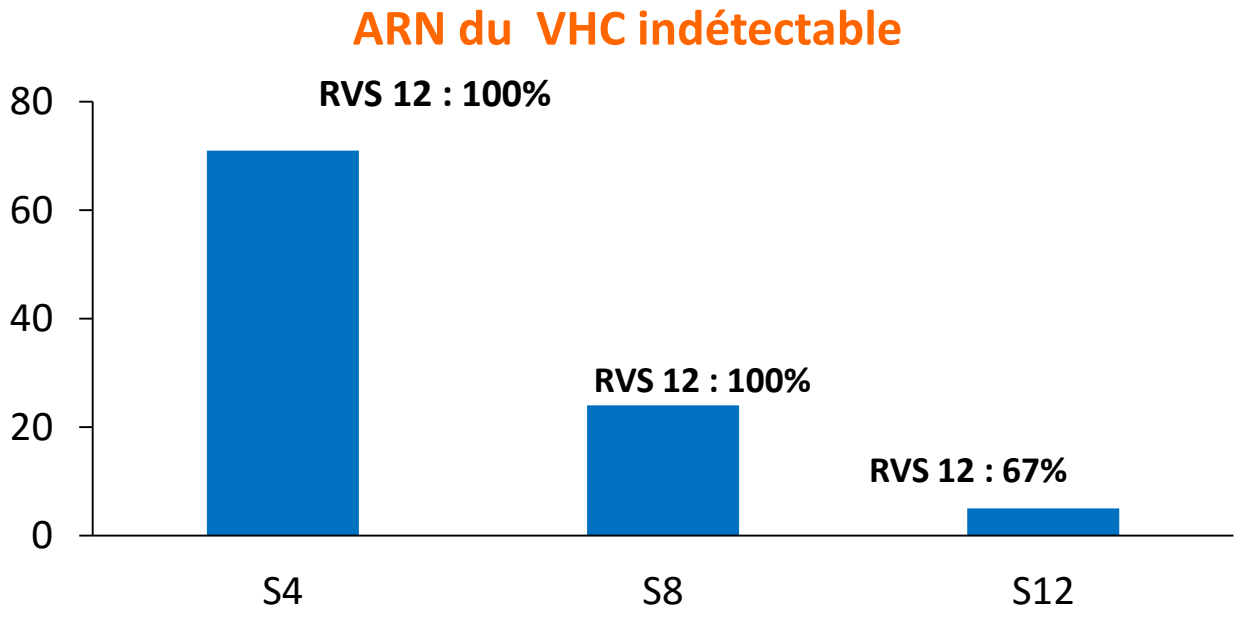
D OUZAN et al AFEF Toulouse 2015

AVDLIB 1 : vie Normale sous traitement et ribavirine



D OUZAN et al AFEF Toulouse 2015

La réponse sous traitement et RVS 12 chez les 125 patients traités par SOF + DAC ou SOF + SIM



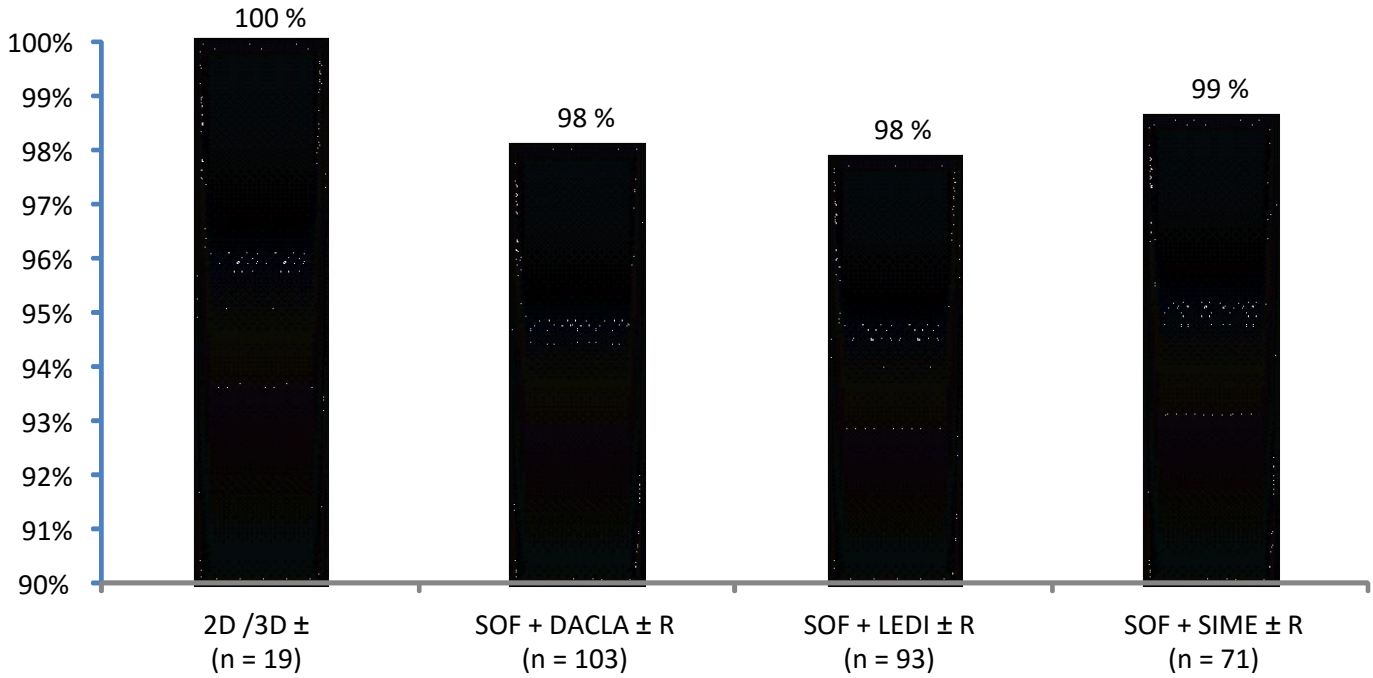
- Après traitement corrélation complète entre RVS4 et RVS12

D OUZAN et al AFEF Toulouse 2015

AVDLIB 1 et 2 : RVS12 chez 286 patients traités par une association d'AVD

DO

CREGG
Club de Réflexion des Cabinets et Groupes d'Hépato-Gastroentérologie



D OUZAN et al JFHOD 2016 soumis

Les webstaffs

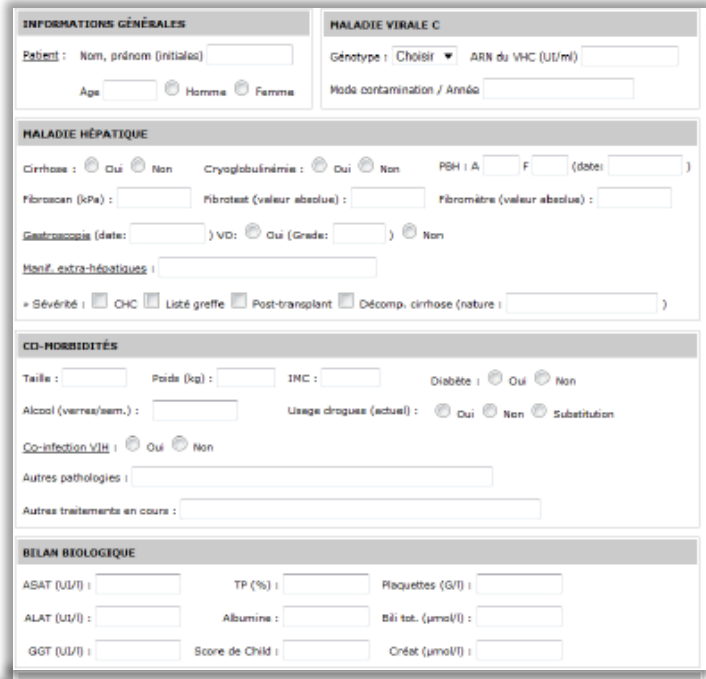
Création d'un WebStaff - Avril 2014

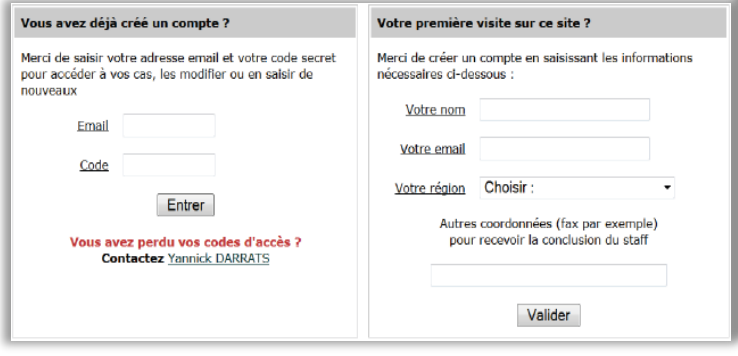
Le WebStaff de la Commission Hépatologie du CREGG, sur Internet

- en direct, avec vidéo & son & slides
- accessible de n'importe où, sur PC, Mac et Smartphones
- avec des mini-présentations contextuelles (interactions, résistances, rein…)

Développement Web

- **Février 2015**
  Mise en place d'une interface web sécurisée de saisie des fiches
- Saisie des fiches en ligne





Recommandations AFEF juin 2015

DO

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	< F4		F4		Cirrhose Child B	Echecs AVD
1	Naïf	Echec PEG-Riba +/- T-B	Naïf	Echec PEG-Riba +/- T-B	Naïf & prétraités	Echec Sof-Riba +/- Peg (Options selon génotype)
	Sof-sime 12s (G1b)(A)	Sof-sim 12s (G1b échec P/R) (B)	Sof-dacla + R 12s (C)	Sof-dacla + R 12s (C)	Sof-dacla + R 12s (B)	Sof-sime +R 24s (AE)
	Sof-dacla 12s (A)	Sof-dacla 12s (A)	Sof-dacla 24s (A)	Sof-dacla 24s (A)	Sof-dacla 24s (AE)	Sof-dac +R 24s (AE)
	Sof-ledi 12s (A)	Sof-ledi 12s (A)	Sof-ledi + R 12s (A)	Sof-ledi + R 12s (A)	Sof-ledi + Riba 12s (B)	Sof-ledi +Riba 12s (B)
	3D + Riba (G1a) 12s (A)	3D + Riba (G1a échec P/R) 12s (A)	Sof-ledi 24s (A)	Sof-ledi 24s (A)	Sof-ledi 24s (AE)	3D + Riba 24s (AE)
	3D (G1b) 12s (A)	3D (G1b échec P/R) 12s (A)	3D + Riba 12s (A)	3D + Riba (G1a échec P/R) 24s (A)		Sof- P/R (G2)
	Grazoprevir-elbasvir 12s (A)	Grazoprevir-elbasvir + Riba 12s (A)	Grazoprevir-elbasvir + R 12s (A)	3D + R (G1b échec P/R) 12s (A)		Echec Sof-Sim
	Dac-asuna-beclabuvir +R (G1a) 12s (A)		Dacla-asuna-beclabuvir +R (G1a) 12s (A)	Grazoprevir-elbasvir + R 16s (C)		Sof-dac +R 24s (AE)
	Dacla-asuna-beclabuvir (G1b) 12s (A)	Dacla-asuna-beclabuvir (G1b échec P/R) 12s (C)	Dacla-asuna-beclabuvir (G1b) 12s (A)			Sof-ledi +Riba 12s (AE)
	Sof-GS5816 12s (B)	Sof-GS5816 12s (B)	Sof-GS5816 12s (B)			Echec Sof-Dac Echec Sof-Ledi
2	Naïf	EchecPEG-Riba	Naïf	EchecPEG-Riba	Naïf & prétraités	
	Sof-Riba 12s (A)	Sof + Riba 12 s (C)	Sof + Riba 12s (A)	Sof + Riba 24s (C)	Sof-dacla 24s (AE)	Sof-sim +R 24s(G1G4)(AE)
		Sof-dacla 12s (AE)		Sof-dacla 12s (AE)		Sof + P/R 12 s (G3)(AE)
3	Naïf & prétraités		Naïf & prétraités		Naïf & prétraités	Echec 3D
	Sof-dacla 12s (B)		Sof + P/R 12 s (B)		Sof-dacla +R 24s (AE)	aucune donnée
	Sof-GS5816 12s (B)		Sof-dacla + Riba 24s (B)			
			Sof-GS5816 + Riba 12s (B)			
4	Naïf & prétraités	Naïfs seuls	Naïf & prétraités		Naïf & prétraités	
	Sof-sime 12s (C)	Grazo-elbasvir 12s (C)	Sof-sime + R 12s (C)		Sof-dacla +R 12s (C)	
	Sof-dacla 12s (C)	Sof-GS5816 12s (C)	Sof-sime 24s (C)		Sof-dacla 24s (AE)	
	Sof-ledi 12s (B)		Sof-dacla + R 12s (C)		Sof-ledi +Riba 24s (C)	
	2D + Riba 12s (A)		Sof-dacla 24s (C)			
			Sof-ledi + R 12s (AE)			
5 et 6	Naïf & prétraités		Naïf & prétraités			
	Sof-dacla 12s (AE)		Sof-dacla + R 12s (AE)			
	Sof-ledi 12s (B)		Sof-dacla 24s (AE)			
	Cut-offs tests de fibrose F3 : FS > 9,5 kPa FT > 0,59 FM > 0,63 F4 : FS > 12,5 kPa FT > 0,74 FM > 0,85		Sof-ledi + R 12s (C)			
			Sof-ledi 24s (C)			
			Stratégie 12s : si arrêt Riba, prolonger traitement jusqu'à 24s			

(A) Preuve scientifique établie (études phase 3, méta-analyses, grandes cohortes multicentriques)
(B) Présomption scientifique (essais randomisés faible puissance, phases 2, cohortes monocentriques)
(C) Faible niveau de preuve (études cas-témoins, rétrospectives...)
(AE) pas d'études,accord entre experts

B. Hanslik (disponible sur demande à bhanslik@wanadoo.fr)

CREGG
Club de Réflexion des Cabinets et Groupes d'Hépato-Gastroentérologie
Thierry Fontanges
(Bourgoin-Jallieu)
Nathalie Boyer
(Paris)
Bertrand Hentzik
(Montpellier)

CREGG

WebStaff Commission Hépatologie

v 30-06-2015-web

Informations générales :

Nom, prénom (initiales) : Année naissance ou âge : ☐ Homme ☐ Femme

Médecin présentant le dossier : Région :

Coordonnées *(mail ou fax, lisible : important pour recevoir la conclusion du staff)* :

Téléphone portable (*important si besoin de précisions pour discuter le dossier)* :

Maladie virale C :

Génotype ☐ 1 ☐ 1a ☐ 1b ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ autre ARN du VHC (UI/ml)

Mode de contamination/année :

Maladie hépatique :

Cirrhose : ☐ oui ☐ non Cryoglobulinémie : ☐ oui ☐ non PBH : A F (date :)

Fibroscan (en kPa) : Fibrotest (val. absolue) : Fibromètre (val. absolue) :

Gastroscopie (date :) → VO : ☐ oui (grade :) ☐ non

Sévérité : ☐ CHC ☐ listé greffe ☐ post transplant ☐ décomp. cirrhose, nature :

Co-morbidités :

Taille : Poids (kg) : IMC : Diabète : ☐ oui ☐ non

Alcool (verres/sem.) : Usage drogues (actuel) : ☐ oui ☐ non ☐ substitution

Co-inf. VIH : ☐ non ☐ oui CD4 (/mm^3) : ARN VIH (UI/ml) : Traitement ARV:

Autres pathologies :

Autre(s) traitement(s) en cours (vérification des interactions) :

ASAT (UI/l)		TP (%)		Plaquettes (G/l)	
ALAT (UI/l)		Albumine		Bili tot. (µmol/l)	
GGT (UI/l)		Score de Child		Créat (µmol/l)	

Statut thérapeutique de la maladie : ☐ non traitée antérieurement ☐ déjà traitée

Traitements(s) antérieur(s) déjà réalisé(s)	Durée (semaines)	Réponse
PEG-IFN + ribavirine		
Inhibiteur de protéase (bocé. ou téla.) + PEG + riba.		
AVD actuels (lesquels ?) :		
Autre :		

Prise en charge thérapeutique propsée (plusieurs propositions sont possibles) :

○ Sofosbuvir (Sovaldi®) + Ribavirine
○ 12 sem ○ 12 s + PegIFN ○ 24 sem

○ Paritaprévir/rito/ombitasvir (Viekirax®) + Dasabuvir (Exviera®)
○ 12 sem ○ 12 s + Riba ○ 24 sem ○ 24 s + Riba

○ Sofosbuvir (Sovaldi®) + Siméprévir (Olysio®)
○ 12 sem ○ 12 s + Riba ○ 24 sem ○ 24 s + Riba

○ Paritaprévir/rito/ombitasvir (Viekirax®)
○ 12 s + Riba ○ 24 sem ○ 24 s + Riba

○ Sofosbuvir (Sovaldi®) + Daclatasvir (Daklinza®)
○ 12 sem ○ 12 s + Riba ○ 24 sem ○ 24 s + Riba

Autre proposition ou question :

○ Sofosbuvir® + Lédipasvir (Harvoni®)
○ 8 sem ○ 12 sem ○ 12 s + Riba ○ 24 sem ○ 24 s + Riba

Stade retenu fibrose	
F0-F1	○
F2	○
F2 sévère	○
F3	○
F4	○

Evolution	
RVS 12	○
Rechute	○
a eu EIG	○
AT	○
PDV	○

Synthèse Sept 2014 - Juillet 2015

Fiches traitées

433

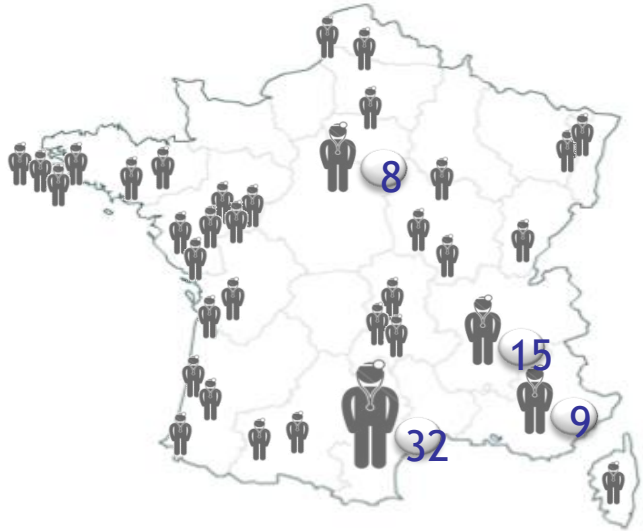
Spectateurs différents

192

Nombre d'HGE différents envoyant des fiches

130

Origine des fiches



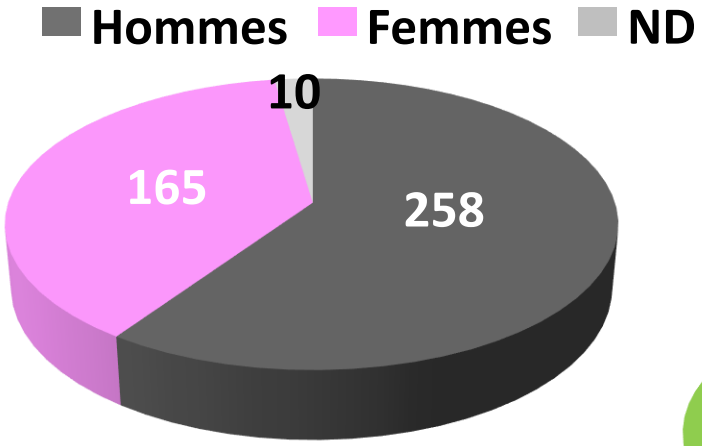
Réunion

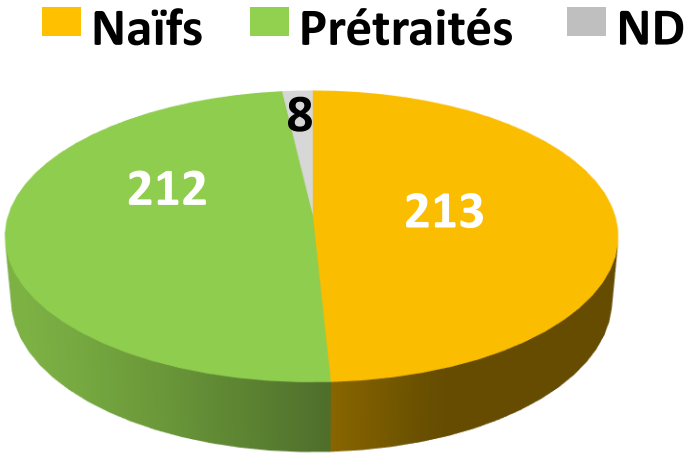
Martinique

Guadeloupe

Webstaff 2015

Sexe, Statut traitement





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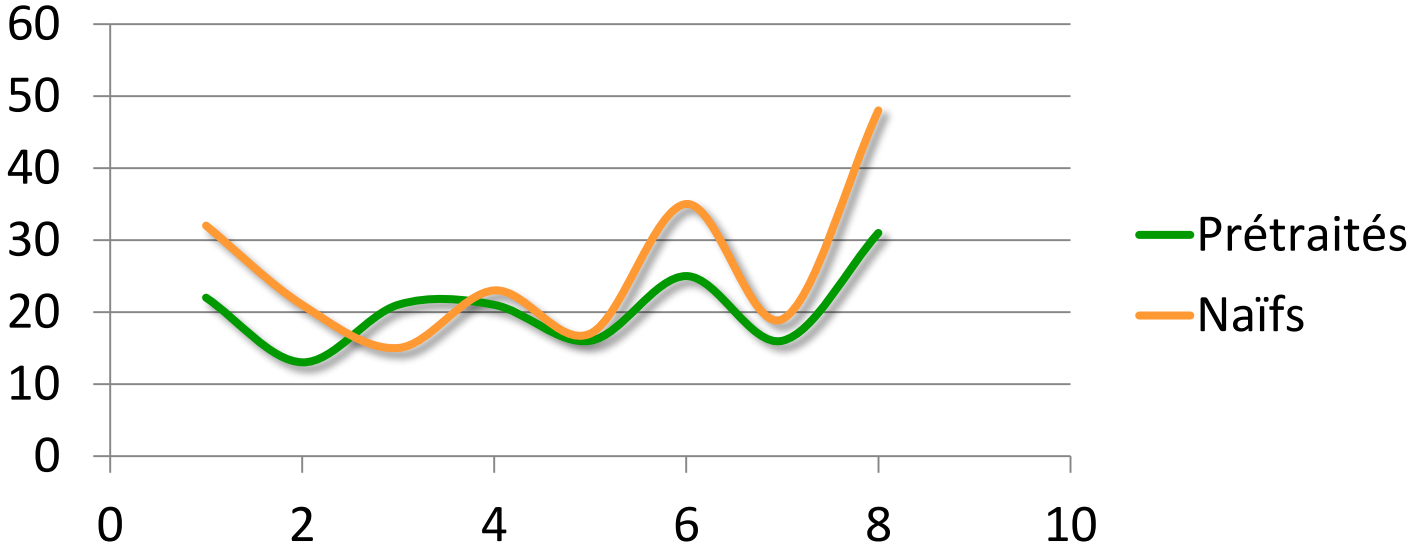
Répartition naïfs/échecs



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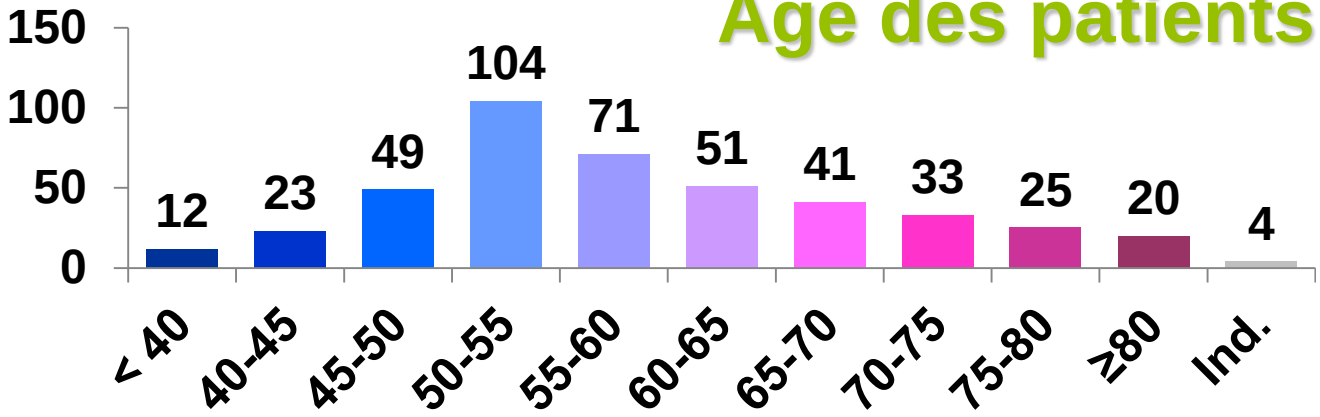
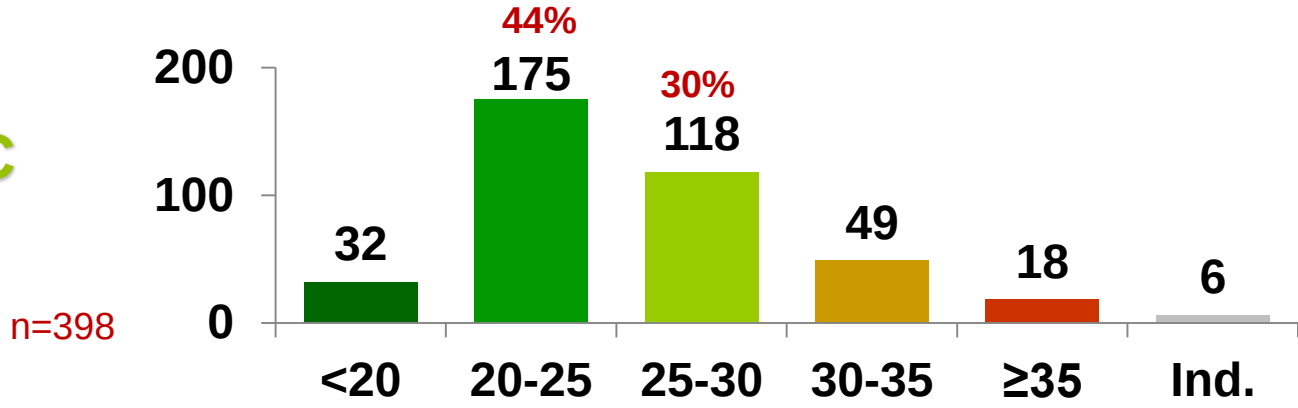
Age des patients

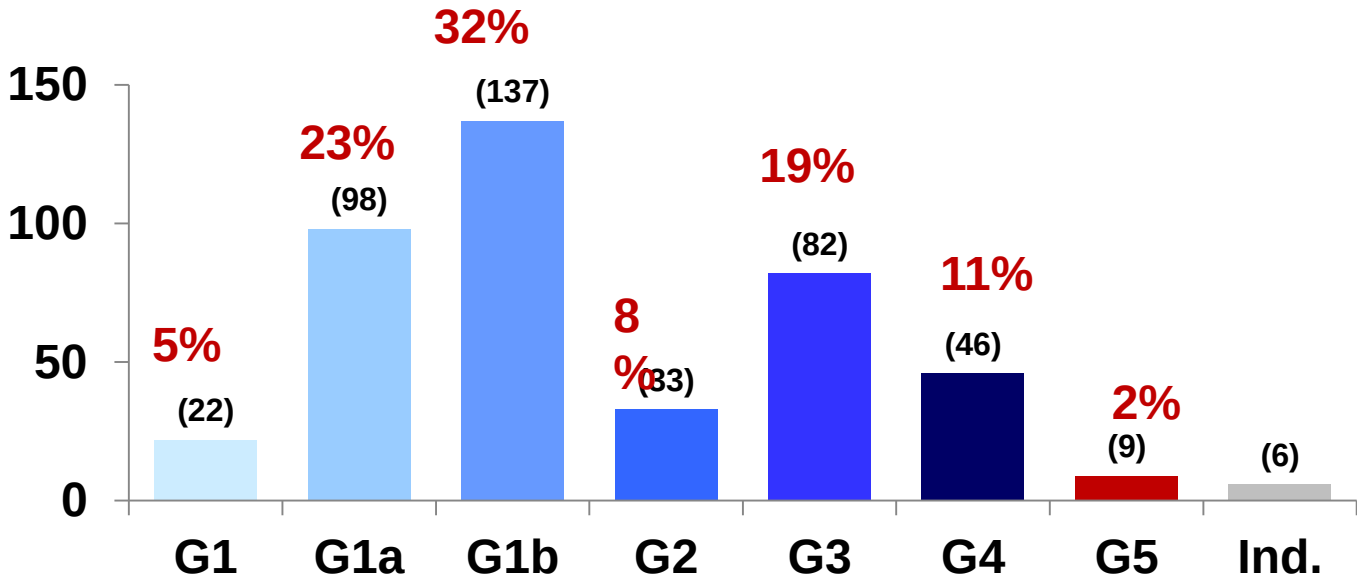


IMC



Webstaff 2015

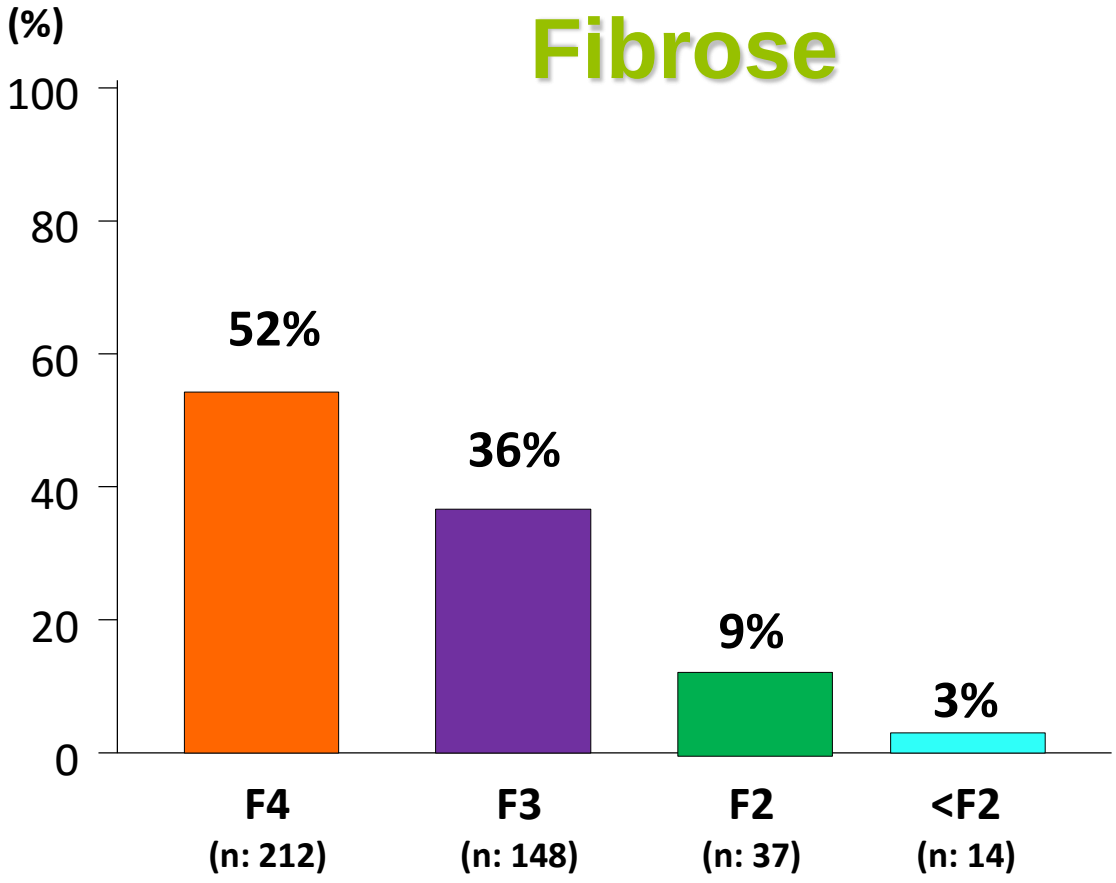
Génotype



n=433

Webstaff 2015

Fibrose



Arrêté n° : 2015 – 1831

Objet : RCP ambulatoire experte déposée par le CREGG (Club de réflexion des cabinets et groupes d'hépato-gastroentérologie)

Demande de création de Réunions de Concertation Pluridisciplinaires pour les traitements des personnes porteuses d'infection chronique par le virus de l'hépatite C.

Dans le cadre de l'instruction du 30 avril 2015, et sur la base des éléments de votre dossier je vous accorde la reconnaissance de votre RCP ambulatoire.
La prise en charge des patients par votre association telle que l'a étudiée la commission d'instruction, répond au cadre réglementaire en vigueur.

Je vous rappelle que la reconnaissance de votre RCP ne donne pas lieu à un financement dédié de l'Agence.

Je vous remercie de bien vouloir m'adresser régulièrement un bilan d'activité.
Mes services restent à votre disposition pour toutes questions.

Je vous prie d'agréer, Docteur, l'expression de mes salutations distinguées.

Dominique MARCHAND
Directrice Générale par intérim

DECIDE :

Article 1 : la demande présentée par le CREGG représenté par le Docteur HANSLIK Bertrand, ,ayant pour objet la demande de création de RCP hépatite C est acceptée.

Article 2 : la liste régionale des RCP hépatite C ainsi consolidée sera transmise au Ministère et fera l'objet d'une publication sur le site internet de l'ARS, conformément aux dispositions de la lettre d'instruction susvisée.

Montpellier, le

Dominique MARCHAND
Directrice Générale par Intérim

Prochaine réunion
« RCP experte CREGG »

Mercredi 9 décembre 2015 – 21h

Participez !
Traitez vos patients !

D’autres collaborations

Et d'autres choses encore…

Représentations actives dans les différentes instances :

CA AFEF
Rapport Dhumeaux
CA SNFGE
Rédaction des Recos AFEF (Hépatite C)

Préparation d'un recueil didactique de cas rares en hépatologie sur clé USB

Et le FORUM annuel !

AFFICHES 2015

Pharmacies

Etablissements

de soin

Urgences

Cabinets d'anesthésie

PITAL PASTEUR
HÉPATITE B et C, VIH
FAITES VOUS DÉPISTER !
LES TESTS SONT REMBOURSÉS PAR LA SÉCURITÉ SOCIALE
www.hepatite06.fr
RHECCA
CORE VIH
Bristol-Myers Squibb
abbvie
GILEAD
MSD
VILLE DE NICE

Inactive HBV carriers and immunotolerant patients: Results of a practice survey on the knowledge of French hepatogastroenterologists working in primary referral hospitals or in private practice?

Xavier Causse[a], Jean-François Cadranel[b], Pascal Potier[a], Jacques Denis[c], Christophe Renou[d], Bertrand Hanslik[e], Patrick Delasalle[f], on behalf of CREGG and ANGH

ENQUETE -MINUTE CFHTP-ANGH-CREGG : utilisation de l'albumine en Hépatologie en dehors de protocoles thérapeutiques

Titre :	Evaluation des recommandations pour la pratique clinique de la ponction biopsie hépatique. Résultats d'une étude multicentrique
Auteurs/Adresses :	JF Cadranel (1), JB Nousbaum (2), B Hanslik (3), ANGH; AFEF; CREGG (1) CREIL; (2) BREST; (3) MONTPELLIER.

73èmes journées de l'AFEF

ObservatoiRe des modalités de prescription de l'acide ursodésoxycholique (AUDC) dans la prise en charge des ChoLEstases (ORACLE) : premiers résultats

Auteurs : B. Hanslik, JP. Bronowicki, O. Chazouillères, S. Erlinger, H. Hagège, F. Henri, P. Mathurin, A. Pariente

Cohorte de surveillance des porteurs inactifs de l'antigène HBs (AgHBs)
PIBAC (Porteurs Inactifs du B Angh Cregg)

Xavier Causse (1), Pascal Potier (1), Si Nafa Si Ahmed (1), Thierry Fontanges (2), Jean-François Cadranel (3), Christophe Renou (4), Anne-Marie Roque-Afonso (5), Sophie Jacquot (6), Isabelle Rosa (7), Jean Henrion (8) et l'ANGH

Déficit en LAL*

T.Fontanges

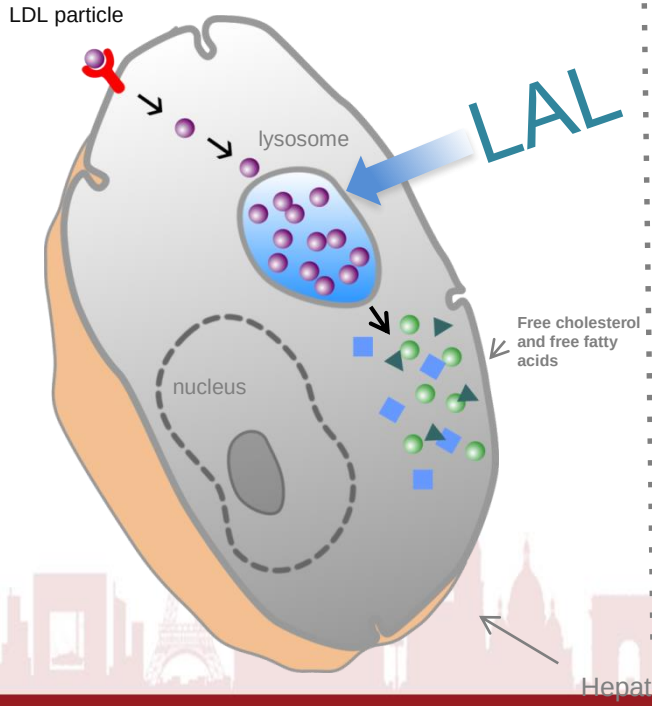
*Lipase acide Lysosomale

De quoi s'agit –il ?

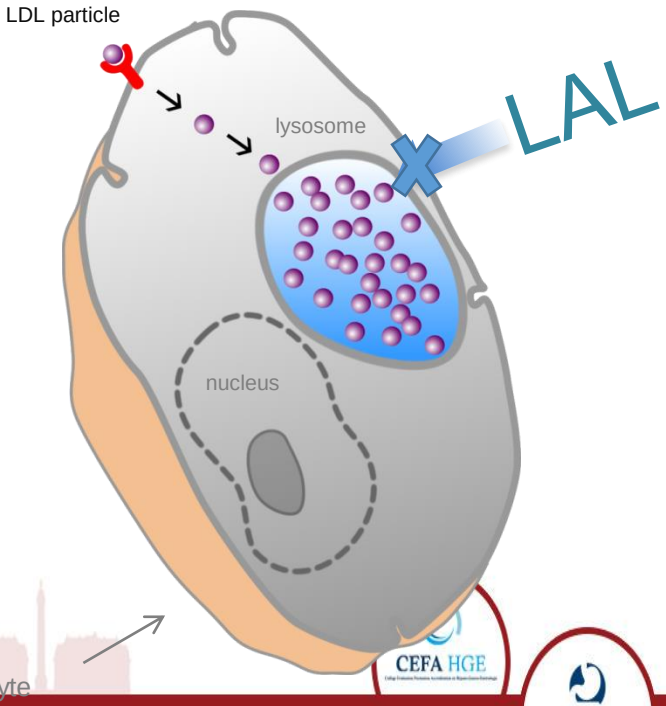
- Maladie autosomique récessive responsable d'une dyslipémie
- Mutation du gène régulateur de la production de LAL (gène LIPA situé sur le chromosome 10)
- La LAL hydrolyse les AG libres et le cholestérol
- La conséquence est l'accumulation de lipides dans les cellules hépatiques (mais aussi les surrénales et les macrophages)

Lysosomal Acid Lipase (LAL)

Healthy Individuals



LAL Deficiency Patients

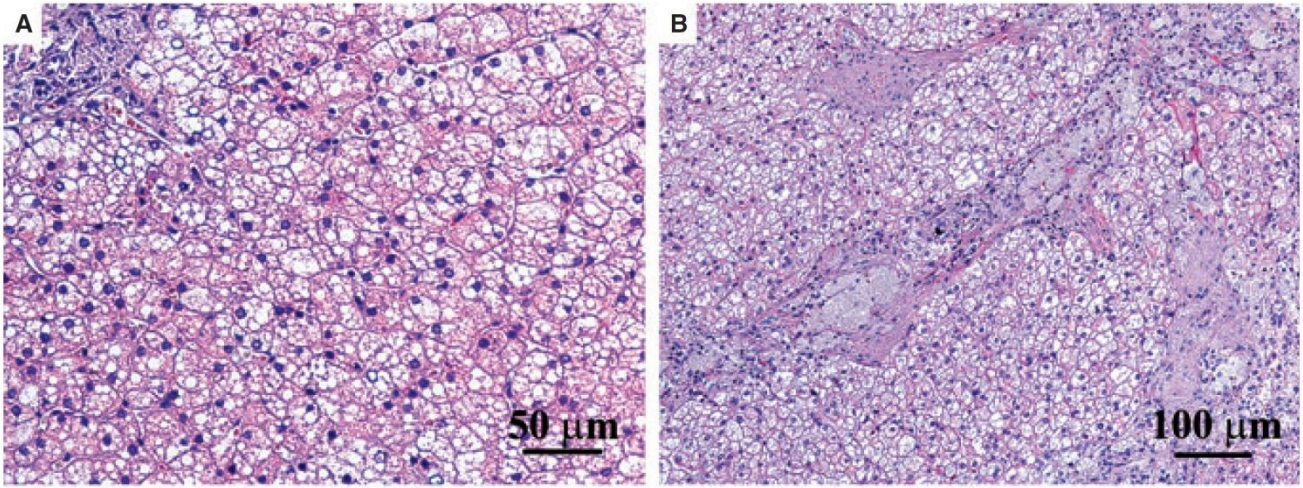


Hepatocyte

Microvesicular steatosis is a common feature of LAL D

Uniform microvesicular steatosis in the early stage of the disease (A)

leading to fibrosis with further progression of the disease (B; adult form)



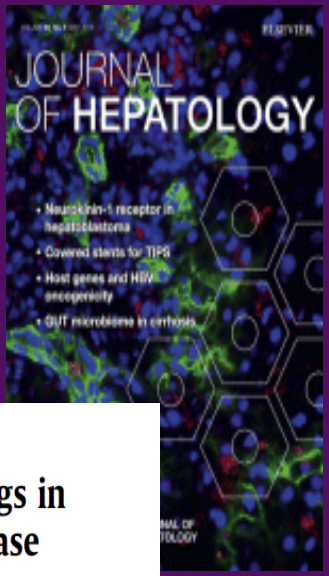
Haematoxylin and Eosin stain

Hůlková H, et al. *Histopathology*. 2012;60:1107-13.

Bernstein *et al.*

Journal of Hepatology

February 2013



Cholesteryl ester storage disease: Review of the findings in 135 reported patients with an underdiagnosed disease

Donna L. Bernstein[1], Helena Hülkova[2], Martin G. Bialer[1], Robert J. Desnick[3,*]

[1]*Division of Medical Genetics, North Shore-Long Island Jewish Health System, 1554 Northern Boulevard, Suite 204, Manhasset, NY 11030, United States;* [2]*Institute of Inherited Metabolic Disorders, Charles University, 1st Faculty of Medicine and The General Teaching Hospital, Prague, Czech Republic;* [3]*Department of Genetics & Genomic Sciences, Mount Sinai School of Medicine, Box 1498, Fifth Avenue at 100th Street, New York, NY 10029, United States*

Quelles conséquences ?

- Chez le nouveau-né (1/1500 000) : forme mortelle
- Chez l'adulte (1/200 000): tableau « plus banal » de stéatose microvésiculaire hépatique et de manifestations cardiovasculaires (athérome)

Quand y penser ?

- Taux élevé de LDL et bas de HDL cholestérol et le plus souvent taux augmenté de triglycérides … **mais sans syndrome métabolique**
- Cytolyse hépatique
- Stéatose échographique
- Cirrhose non étiquetée
- Athérome précoce

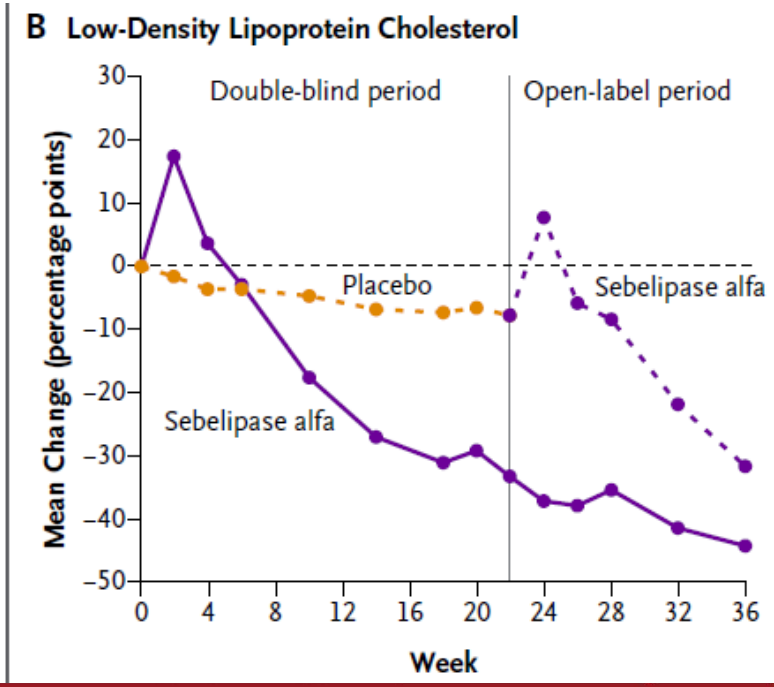
Pourquoi ce dépistage ?

- Essayer de différencier cette affection de la NASH
- Un traitement existe : la Sebélipase alfa !
- Etude prospective en cours

Etude ARISE - **Effects of Sebelipase Alfa on Levels of LDL**

Sebelipase alfa

Placebo

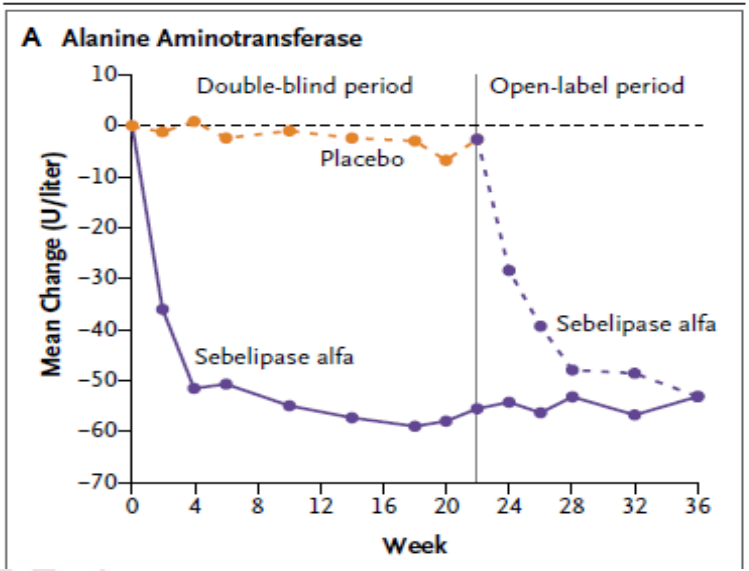


Burton BK, et al. *N Engl J Med*. 2015;373(11):1010-1020.

Etude ARISE - **Effects of Sebelipase Alfa on Levels of ALAT**

Sebelipase alfa

Placebo



Burton BK, et al. *N Engl J Med*. 2015;373(11):1010-1020.

A simple Blood Test to diagnose LAL D

Development of Dry Blood Spot Assay allows for easy testing

- The biochemical diagnostic is **an enzyme activity assay**
- LAL activity is determined via an LAL-specific inhibitor (LALISTAT 2)
- Patients with LAL D have very little to no LAL enzyme activity
- Allows for the possibility of testing high-risk populations

Hamilton J, et al.. *Clin Chim Acta.* 2012;413:1207-10.

Projet
Etude prospective CREGGAL

Début des inclusions : janvier 2016
Fin des inclusions : juin 2016

Objectif :

Quelle est la prévalence du déficit en LAL dans une population de sujets suivis par des HGE de ville ?

Critères d'inclusion
Stéatose échographique (surbrillance)
+
Cytolyse hépatique (ASAT/ALAT >N)
+
Dyslipidémie (traitée ou non)
+
Absence de diabète ++ (traité ou non)
+
IMC indifférent

Test buvard déficit en LAL (DBS)

Etes vous intéressé ?

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