

Prise en charge thérapeutique de l'hépatite C chronique

Cas cliniques commentés

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Cas Clinique 1

- B. Oum el Kheir, F. de 42ans, G2P2
- 28/02/2009: Ac anti HCV + (asthénie persistante)
- PCR VHC positive,
- Ex. Physique normal, BMI 21
- FNS, ALT, TSH, AFP Nles, cryoglobulinémie (-), test de grossesse (-)
- Echographie Nle

Cas Clinique 1 (suite a)

- Charge virale avant traitement: 2 800 000UI/MI
- Serotype 2
- Fibrotest : A2 F1
- Début du traitement par Interféron pégylé alpha 2a 180µg/s + 4cp Ribavirine **16/03/2009**
- Visites à 2, 4 et 8 semaines, à 8 semaines aménorrhée, test de grossesse positif (sous contraceptifs oraux)

Cas Clinique 1 (suite b)

- Arrêter la grossesse ?
- Poursuivre grossesse mais arrêt interféron et ribavirine ?
- Poursuivre traitement et grossesse ?

The Ribavirin Pregnancy Registry: Findings after 5 years of enrollment, 2003-2009.

Birth Defects Res A Clin Mol Teratol. 2010 Jul;88(7):551-9. [Roberts SS](#), and al.

- INTRODUCTION: Ribavirin is contraindicated in pregnancy (FDA Pregnancy Category X) and in men whose partners may become pregnant. In 2003, the Ribavirin Pregnancy Registry was established to monitor pregnancy exposures to ribavirin and to evaluate the potential human teratogenicity of prenatal exposure.
- METHODS: This voluntary registry enrolls pregnant women who have been exposed to ribavirin during pregnancy or during the six months prior to conception either directly, by taking ribavirin, or indirectly through sexual contact with a man taking ribavirin. Women are followed until delivery; live born infants are followed for one year. The Registry aims to enroll 131 live births following direct (maternal) exposure to ribavirin and 131 live births following indirect (male) exposures.
- RESULTS: After more than five years of operation, the Registry has enrolled 49 live births with direct exposure and 69 live births following indirect exposure. Six outcomes with birth defects have been reported. All were among live born infants: torticollis (2), hypospadias (1), polydactyly and a neonatal tooth (1), glucose-6-phosphate dehydrogenase deficiency (1), ventricular septal defect and cyst of 4th ventricle of the brain (1). Three received direct exposures ([6.1% (95% CI: 1.2, 16.9)], three were exposed indirectly [4.3% (95% CI: 0.9, 12.2)]).
- CONCLUSIONS: Although current enrollment is far short of the required sample size, preliminary findings have not detected a signal indicating human teratogenicity for ribavirin. However, findings must be interpreted with caution concerning direct or indirect prenatal ribavirin exposures.

Cas Clinique 1 (suite c)

Décision

- Interruption thérapeutique de la grossesse
- Reprise 1 mois plus tard de la bithérapie pour une durée de 6mois
- Réponse virologique soutenue
- Exiger, contrôler, la contraception la femme et l'homme
- ?? Double contraception
- Contraception appliquée jusqu'à 6mois après la fin du traitement

Cas clinique 2

- A. Derradji, H. de 48ans, Agriculteur
- 10/06/2007: HCV + PCR (+)
(dépistage familial; femme HCV +, PCR + traitée)
- BMI 43 (140 kg pour 182cm), TA nle
- FNS, TP, B. lipidique, glycémie, TSHu Normales
- ALAT 1,5xN
- Charge virale C: 2 550 000UI/ML
- Génotype 1b

Cas clinique (2 suite a)

- Echographie: Foie hyperéchogène
- PBF: A1/F2
- Fibrotest A1-A2 /F1-F2

Cas clinique (2 suite b)

- **Début du traitement 14/11/2007**

PEG-INF alfa-2a 180 microg ?????? / semaine

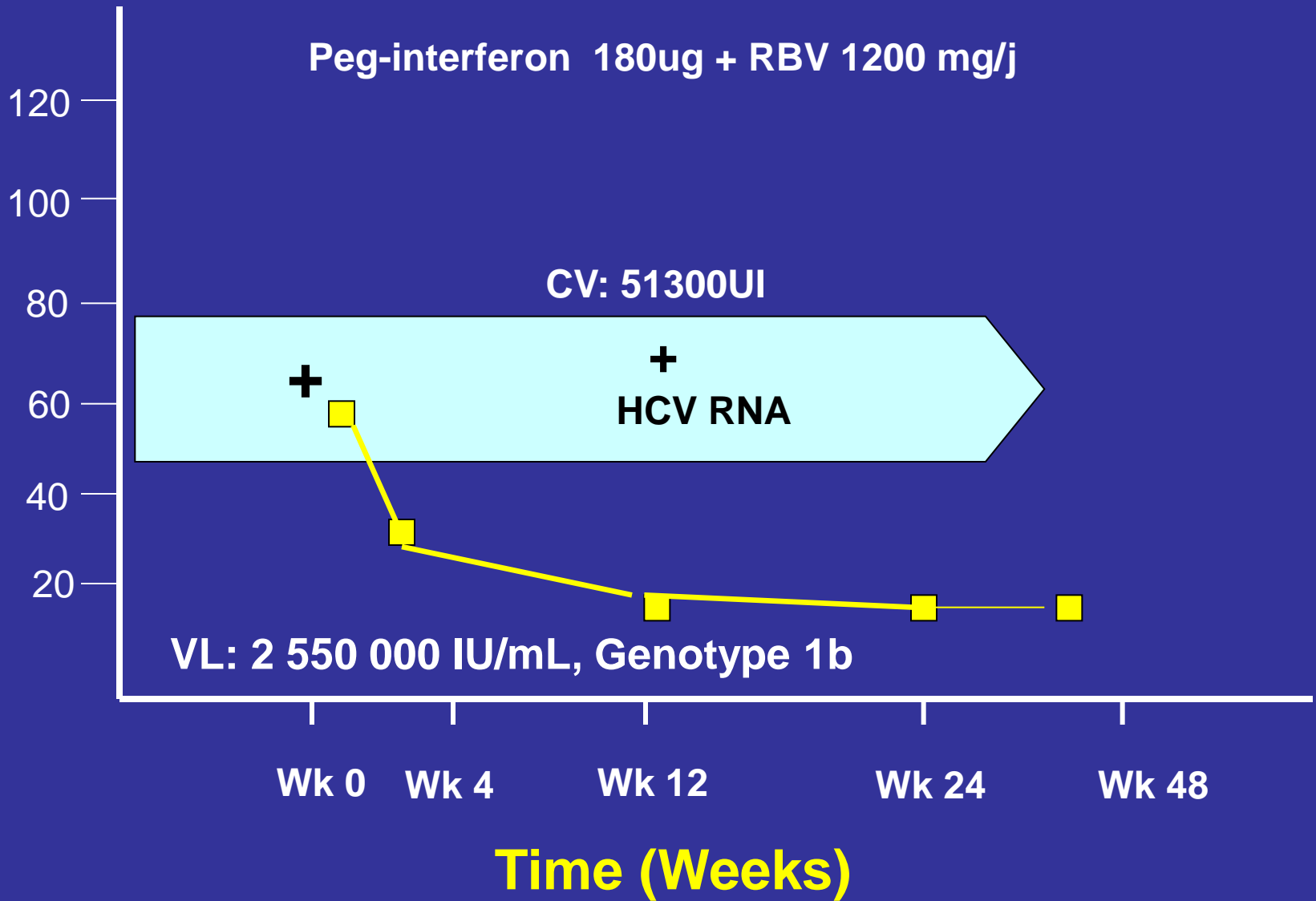
PEG-INF alfa-2b ??????

+ RBV (????? Dose....)

48 semaines ??????????

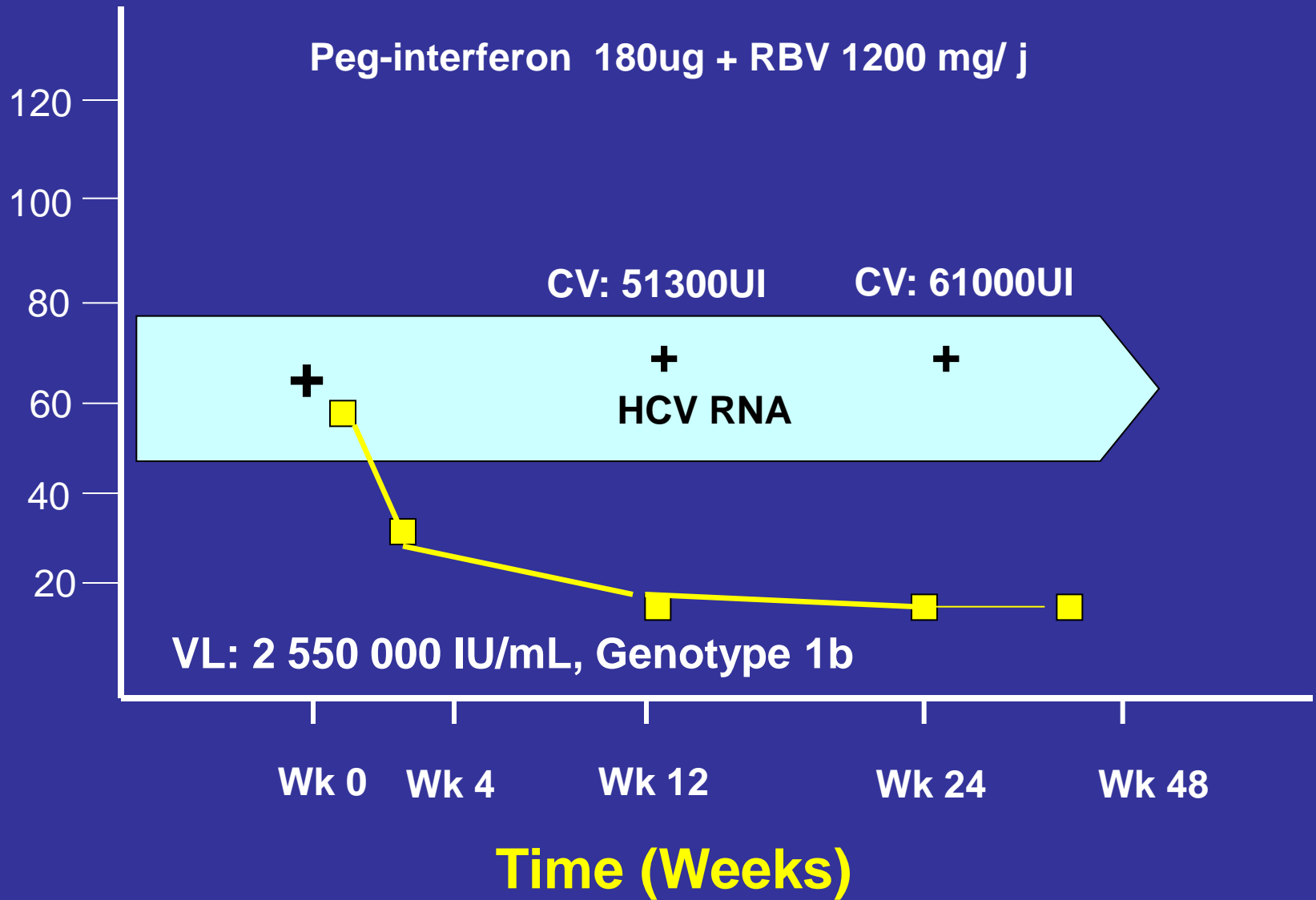
Cs clinique 2

ALT



Cs clinique 2

ALT



Cas clinique 2 (suite c)

- PCR virale C + à 6 mois
- Arrêt du traitement: Non répondeur
- Evolution: (-) 10kg
 - ALAT: 1xLSN
 - CV: 4 830 000UI/mL (PCR TaqMan 19/1/10)
- Trithérapie, amaigrissement ++

AASLD 2009

- Nouvelle échelle de dosage RBV :

— 800mg/j	< 65kg
— 1000mg/j	65-85kg
— 1200mg/j	86-105kg
— 1400mg/j	>105kg

Management of HCV in Patients With Obesity

Key Data

Epidemic in the US, common among persons with HCV infection
High BMI > 30 is associated with lower SVR rates
Insight into causes
 Obesity is an active inflammatory state
 Insulin resistance
 Presence of steatosis
 Increased fibrosis

HCV Management Strategies in Obese Patients

Fixed dosing vs weight-based dosing
 Can more interferon overcome impact of higher BMI?
Weight loss program BEFORE hepatitis C treatment
 Diet, exercise, surgery
Insulin-sensitizing agents have been studied but remain experimental

PROGRESS Study Final Results

HCV genotype 1 patients with high viral load and high body weight achieve lower SVR rates

1175 G1 patients with baseline viral load $\geq 400\,000$ IU and body weight ≥ 85 kg randomised to either

A- 48wk-180mcg/wk PEG-INF + RBV 1200mg/d

B- 48wk-180mcg/wk PEG-INF + RBV 1400/1600 mg/d

C-12wk-360mcg/wk PEG-INF + 36 wk 180mcg/wk + RBV 1200mg/d

D-12wk-360mcg/wk PEG-INF + 36 wk 180mcg/wk + RBV 1400/1600 mg/d

Résultat

- PEG à forte dose (ou dose d'induction) 360 μ g / 3 mois + 1400 à 1600 mg RBV selon le poids > à 85 ou > à 95 kg

Pas d'avantage sur la RVS 38 à 44%

Pas de bénéfice de l'induction sur la RVS

Cas clinique 3

- D. Salima, F. de 23ans, en insuffisance rénale terminale
- En hémodialyse 3x / semaine
- Transplantation rénale prévue
- Évaluation avant transplantation faite

Investigations

- Hb = 10gm/dl
- GB = 11000
- Plaq = 350000
- T. Billi = 12
- ALT = 78
- AST = 89
- PAL = 150
- Albuminémie = 38
- TP 100%
- Echographie Nle
- Anti HCV +
- RNA VHC + en PCR
- Génotype 1a

Comment évaluer l'atteinte hépatique ?

- PBF
- Fibrotest
- Fibroscan
- Fibrotest + fibroscan

Comment évaluer l'atteinte hépatique ?

- PBF: A2 F1

Hématome sous cutané

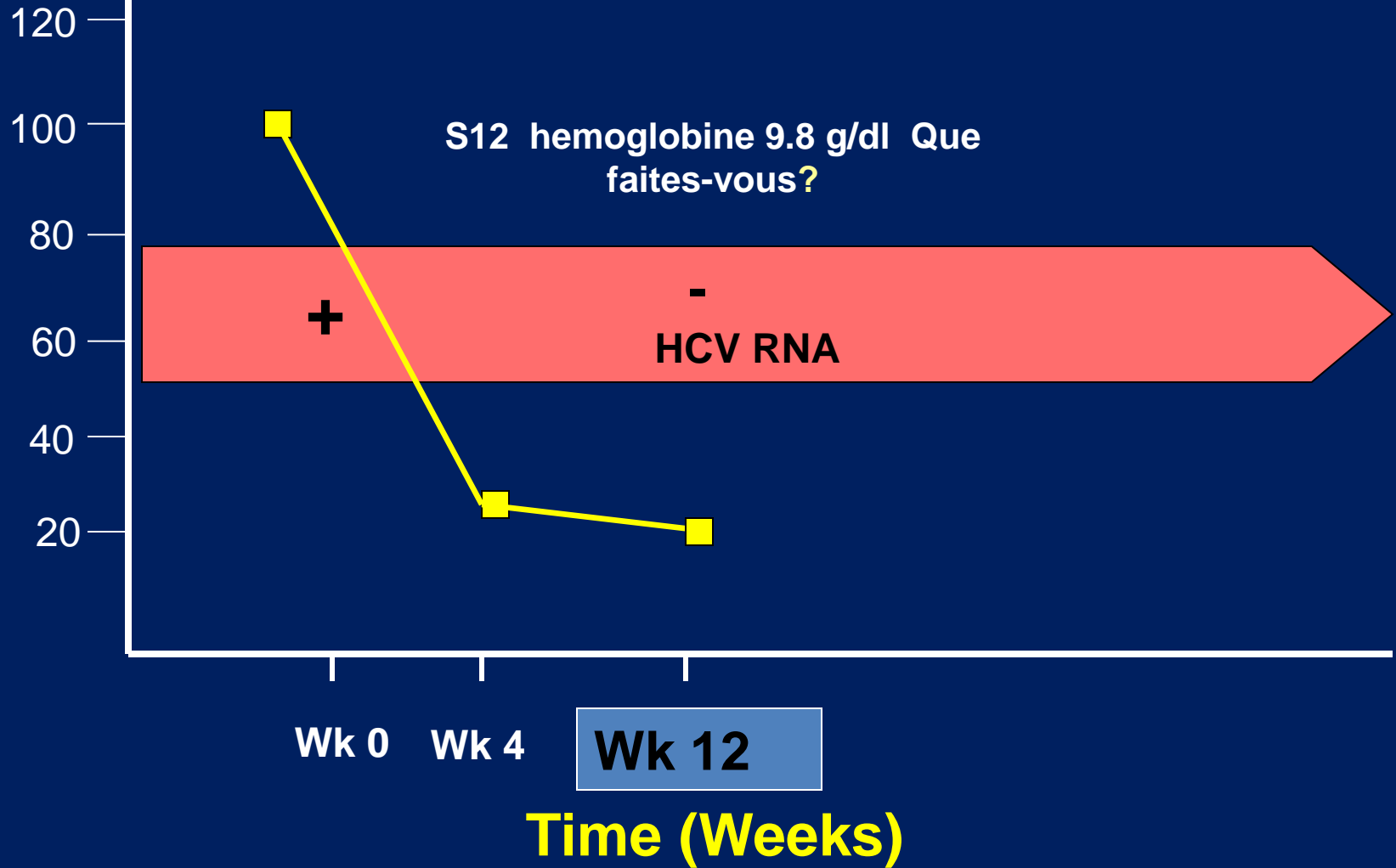
- Charge virale c avant traitement 1340 000 UI/ML
(PCR en temps réel TaqMan)

Que faire ?

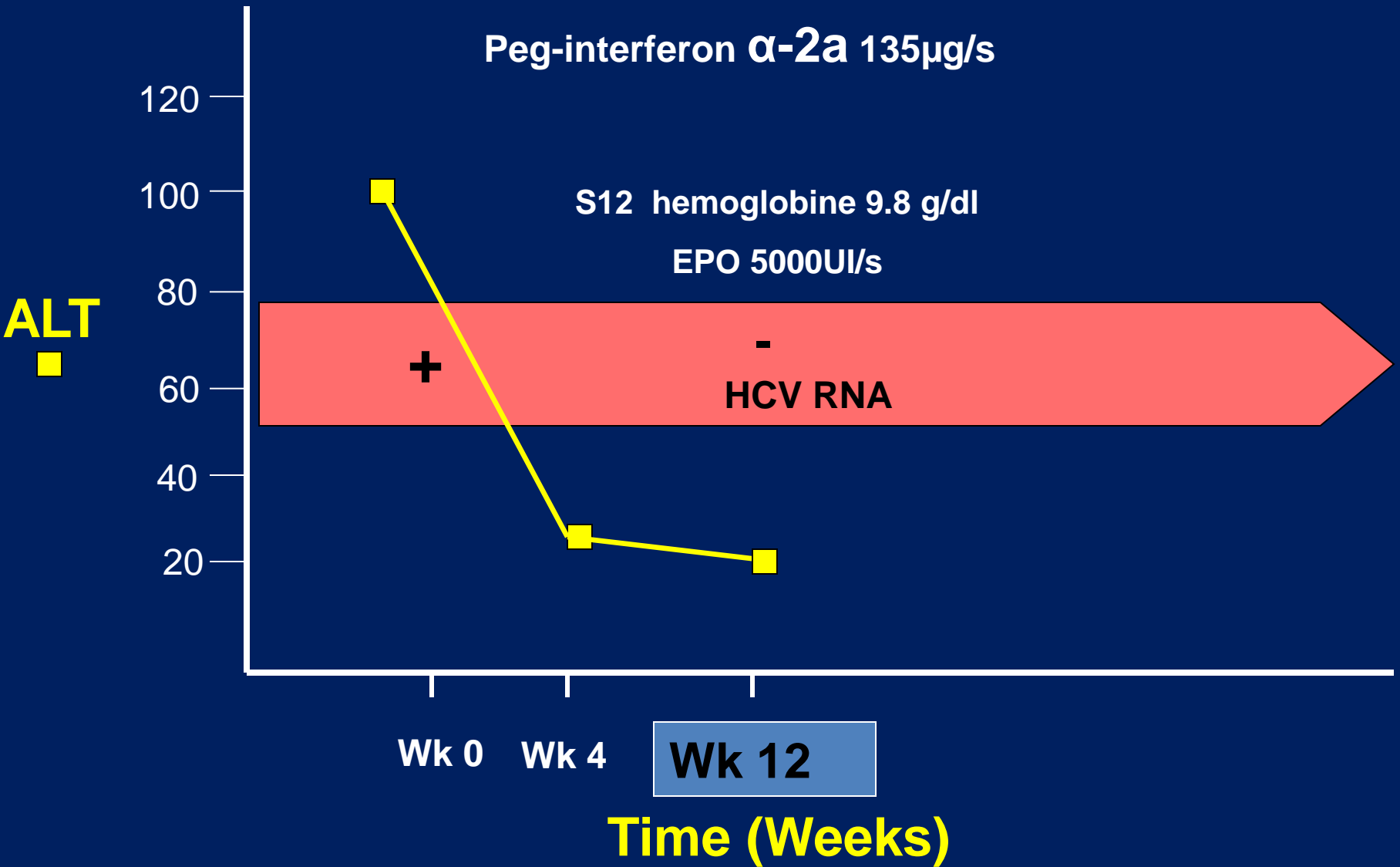
- Traiter avant la transplantation ?
- Usage de la RBV au cours d'une IR chez une patiente en hémodialyse ?
- Monitoring sous traitement ?

Cas clinique 3

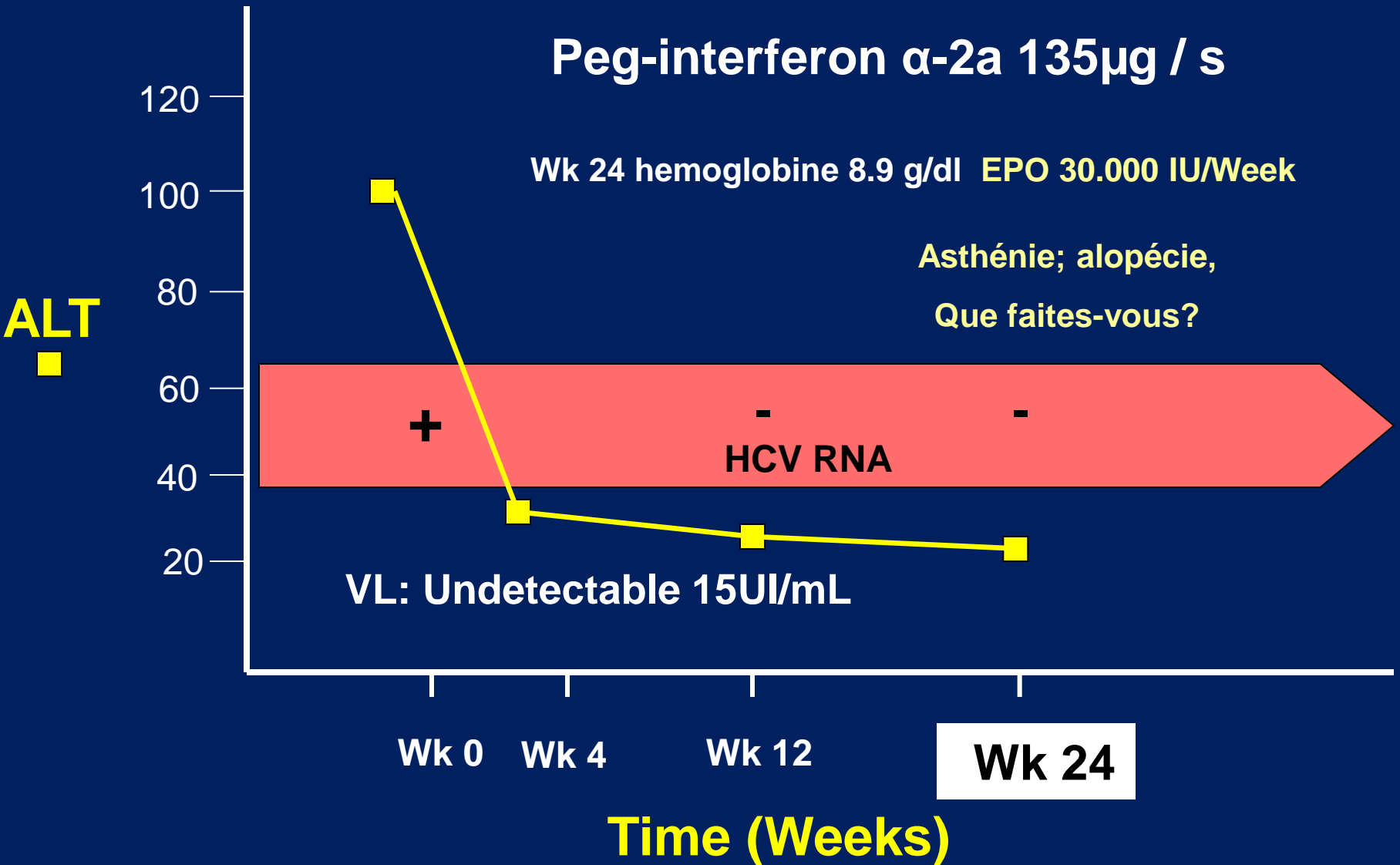
Peg-interferon α -2a 135 μ g/s 11/02/2007



Cas clinique 3



Cas clinique 3



Cas clinique 3

- Traitement INF PEG 135 μ g /S seul poursuivi à 48 semaines
- Réponse virologique soutenue (RVS)
- PCR VHC négative (RH 1529/10 du 26/9/10 < 12UI/ML)
- Greffe rénale prévue

Patients With Renal Disease: Summary of Recommendations (I)

Description	GFR, mL/min*1.73 m ²	Recommended Treatment
Kidney damage with normal or increased GFR	≥ 90	Routine combination therapy
Kidney damage with mildly decreased GFR	60-90	
Moderately decreased GFR	30-59	PegIFN alfa-2b 1 µg/kg/wk or pegIFN alfa-2a 135 µg/wk + RBV 200-800 mg/day (starting with lowest dose and increasing if adverse effects manageable)
Severely decreased GFR	15-29	
Kidney failure	< 15	
Dialysis		Standard IFN 3 mU 3x/wk or pegIFN alfa-2b 1 µg/kg/wk or pegIFN alfa-2a 135 µg/wk ± markedly reduced daily RBV dose*

*Controversial.

HCV Therapy in Patients With Kidney Disease

- Kidney important for catabolism and filtration of both IFN and RBV
 - Reduced doses warranted
- Standard IFN vs pegIFN for persons with kidney failure
 - Reduced excretion of pegIFN
 - Higher rate of adverse events with pegIFN vs standard IFN
 - Management of adverse events more difficult with pegIFN vs standard IFN

Cas clinique 4

- B. Nora., 26 ans,
- 05/06/2007: VHC +, bilan pré-op d'une lithiase VB
- ATCD: Asthme
- A l'admission: BMI : 20,5 (42kg / 149cm) TA 12/6
- GS: O+ FNS, TP, glycémie N, Bil T, B. Rénal, ALT N,
- Pas de coinfection VHB, HIV
- PCR VHC positive, CV= 21643 UI/ML (Taqman),
- Sérotype 1
- PBF échoguidée: A1 F1

Cas clinique 4 (suite b)

- Suivi clinique et ALAT / 3 à 6 mois
- 02/11/10
 - Ischémie progressive des doigts depuis 20j
 - Gangrène sèche indolore des doigts + ulcérations
- Ex neurologique nl , bilan biologique normal
- Cryoglobulinémie négative,
- Doppler artériel, capillaroscopie : NI









Merci

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