

DÉFIS ET PERSPECTIVES DANS L'HÉPATITE B

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- 1 L'HÉPATITE B ET LE CHC une tragédie africaine
- 2 OBSTACLES ET DEFIS : le blocus paradoxal du diagnostic virologique
- 3 PERSPECTIVES
- 4 TRAITEMENT

NEWS FEATURE · 05 DECEMBER 2018 · CORRECTION 19 DECEMBER 2018

The silent epidemic killing more people than HIV, malaria or TB

Viral hepatitis is on the rise. Tackling hepatitis B in Africa is key to fighting back.

Ian Graber-Stiehl



AFRICA'S SILENT EPIDEMIC

Hepatitis now kills more people worldwide than HIV, tuberculosis or malaria. Tackling the hepatitis B virus in Africa is key to fighting back.

BY IAN GRABER-STIEHL

Nuru was prepared for the worst when she went to get screened for HIV eight years ago. After caring for her mother in Uganda, who died as a result of the virus, Nuru moved to the United Kingdom to study, and decided to take her health into her own hands. “I was ready to be told I had HIV,” she says. “I felt, ‘That’s okay. I’ve looked up to my mother’.” What she didn’t expect was to be diagnosed with a different viral infection altogether: hepatitis B. “The way the health worker delivered it to me, it was like, ‘It’s worse than HIV. I was confused, I was suicidal,’” says Nuru (who asked that her real name not be used for this article). “I just didn’t understand what it was because no one ever talks about hep B — they talk about HIV. That’s well researched, it’s well talked about, well documented. It’s all over the television. But hep B is not.”

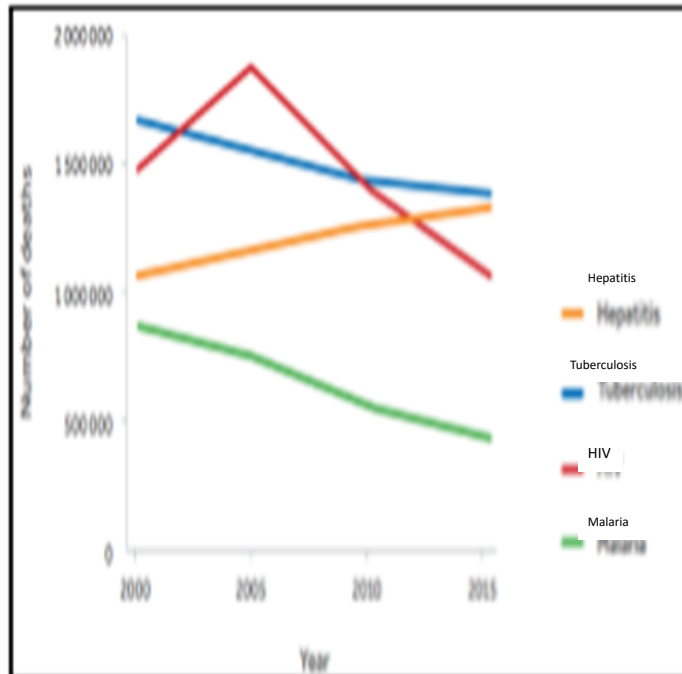
The hepatitis B virus (HBV), which spreads through blood and bodily fluids and invades liver cells, is thought to kill just under 1 million people every year around the world, mostly from cancer or scarring (cirrhosis) of the liver. HBV is less likely to be fatal than HIV, and many people who carry the virus don’t have symptoms. But because more than 250 million people live with chronic HBV infections, more than 7 times the number with HIV, its global death toll now rivals that of the more-feared virus.

Hepatitis — or liver inflammation — is caused by a number of viruses, but types B and C are associated with the most deaths. In 2016, the most recent year for which estimates are available, the number of deaths worldwide from viral hepatitis rose to 1.4 million, outstripping those from tuberculosis, HIV or malaria individually (see “The burden of hepatitis B”).

This is despite the fact that HBV infection can be prevented by vaccination early in childhood and treated with the same antiretroviral drugs used to combat HIV. “HIV has been an acute pandemic with resources thrown at it. That’s a completely different picture than hep B, which has travelled with humankind for tens of thousands of years — and by dint of that invisible carriage, has never had that injection of political advocacy, funding, energy and education that’s gone into HIV,” says Philippa Matthews, an immunologist at the University of Oxford,

SHUTTERSTOCK

Le fardeau sanitaire mondial de l'hépatite virale et du cancer du foie



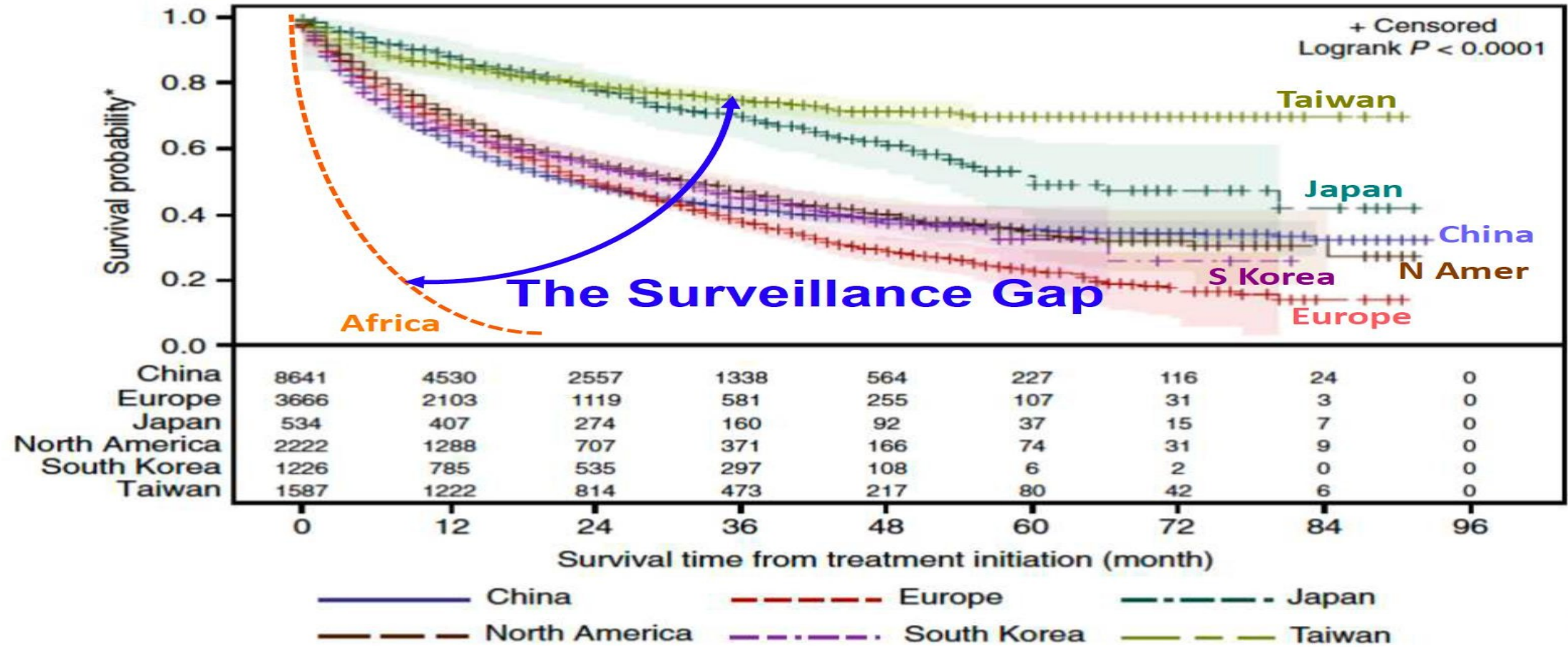
- Mortality from viral hepatitis has increased by 22% since 2000

- ❑ 257 millions de porteurs chronique de HBV dans le monde : **60 millions en Afrique**
- ❑ 1,34 million décès/an du aux complications
 - ❑ **136 000 en Afrique**
- ❑ **La couverture vaccinale reste très insuffisante**
- ❑ Les thérapies antivirales ralentissent la maladie mais ne la guérissent pas
- ❑ **Moins de 5% de patients traités**

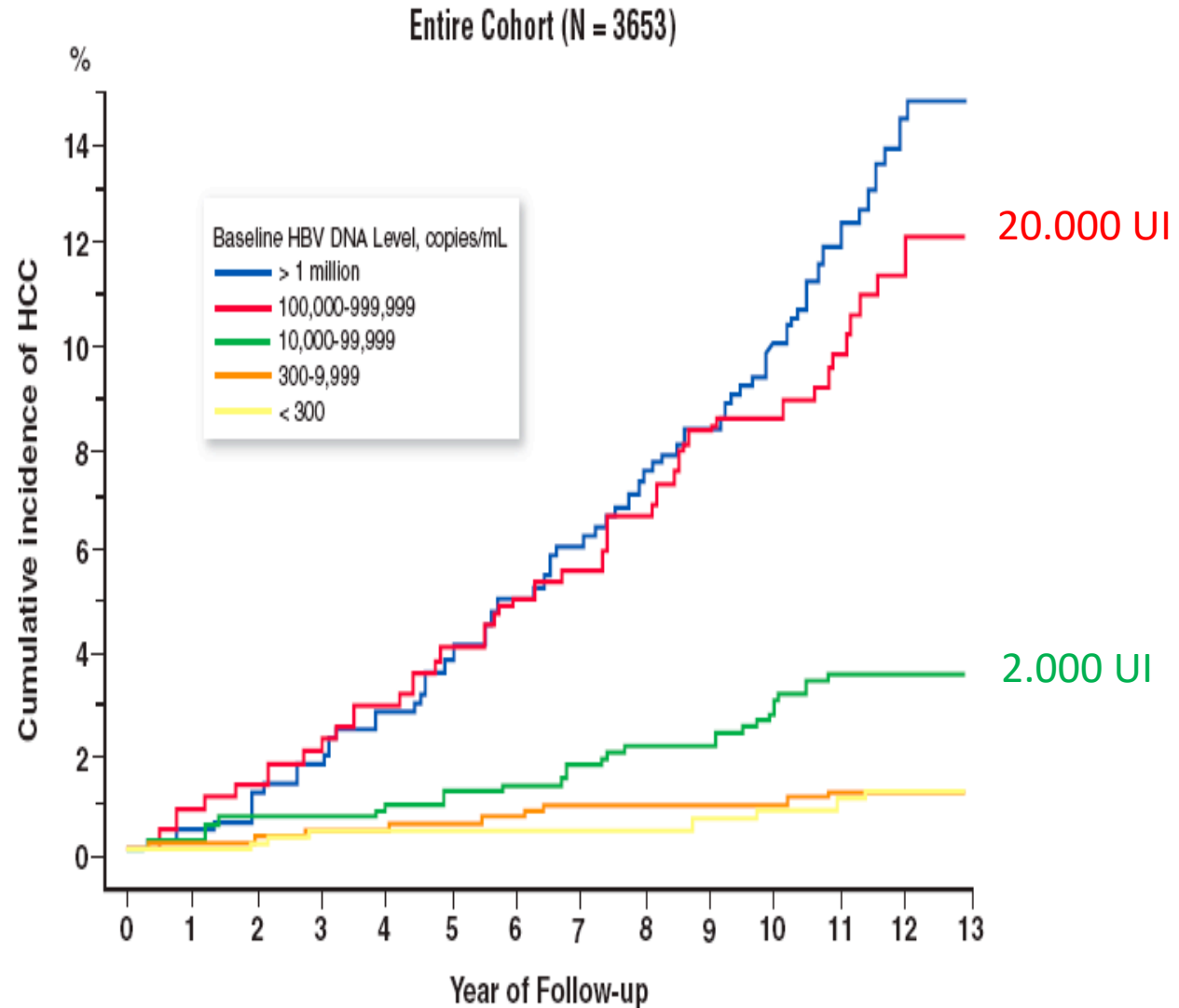
La mortalité liée au HBV dépasse celles de HIV, TB and malaria

Programmes de surveillance du CHC

L Roberts; Liver Int 2015; 35(9): 2155



La charge virale : « turbine » de la progression vers le CHC



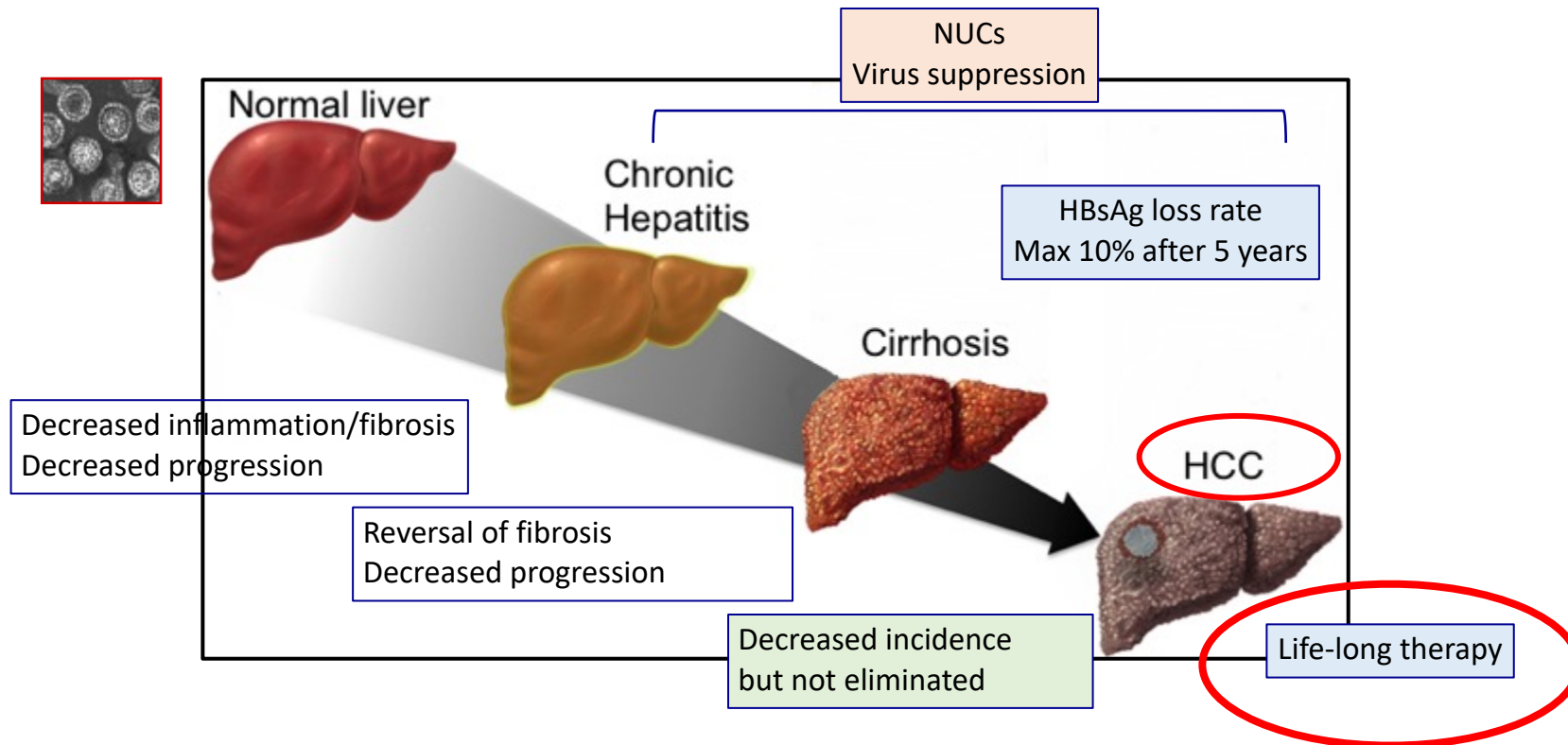
Chen et al; JAMA 2006

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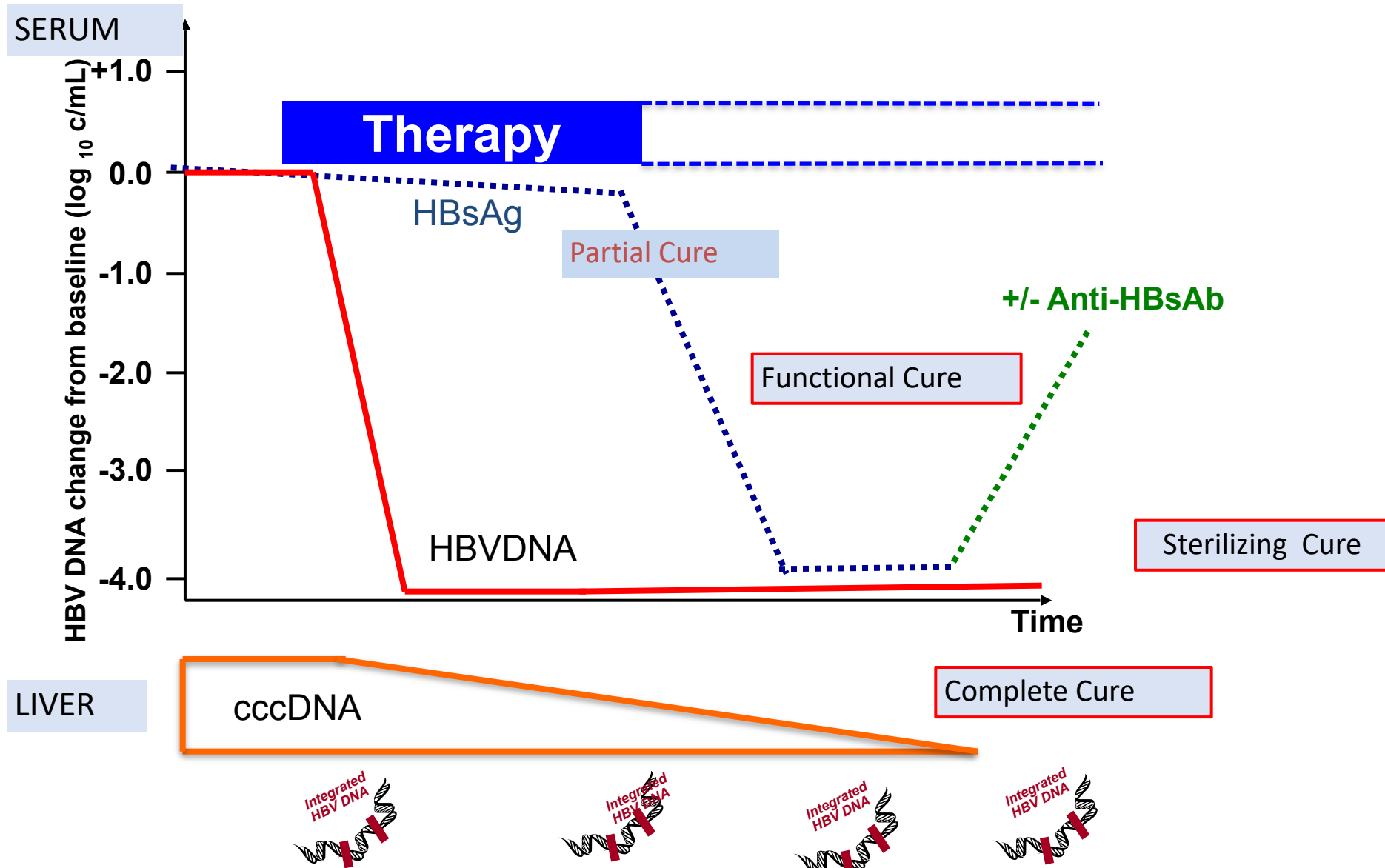
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Traitements actuels:
suppression virale et contrôle durable de la maladie

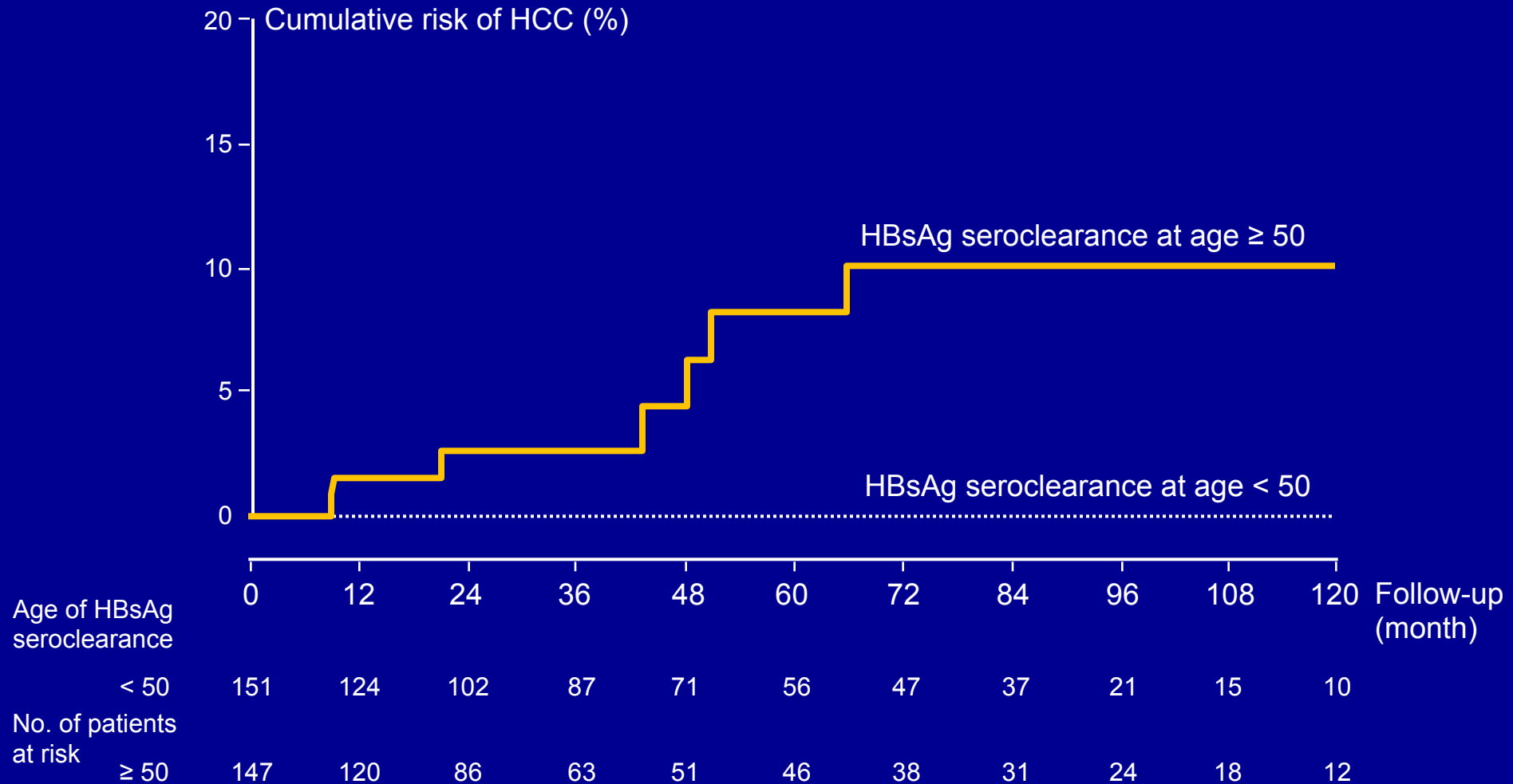
(Pourquoi ne pas traiter plus de patients?)



Que voulons nous?



Elimination de l'AgHBs et reduction du risque de CHC



Development of a simple score based on HBeAg and ALT for selecting patients for HBV treatment in Africa

Yusuke Shimakawa^{1,*}, Ramou Njie², Gibril Ndow^{3,4}, Muriel Vray^{1,5}, Papa Saliou Mbaye⁶, Philippe Bonnard⁷, Roger Sombié⁸, Jean Nana⁹, Vincent Leroy⁹, Julie Bottero¹⁰, Patrick Ingiliz¹¹, Gerrit Post^{11,12}, Bakary Sanneh¹³, Ignatius Baldeh¹³, Penda Suso³, Amie Ceesay³, Adam Jeng³, Harr Freeya Njai³, Shevanthi Nayagam⁴, Umberto D'Alessandro³, Isabelle Chemin¹⁴, Maimuna Mendy¹⁵, Mark Thursz⁴, Maud Lemoine^{4,*}

• Simple score

- Pour sélectionner les patients éligibles au traitement antiviral
- **S'affranchit de l'HBV DNA** et du Fibroscan
- Composé des marqueurs usuels et peu coûteux

- Age, sex
- HBeAg
- AST, ALT, GGT, ALP
- Albumin, total bilirubin
- Platelet count

Diagnostic check up

Essential

- AgHb
- Ag
- V
- A
- A
- A
- Fi
- Écho abdominale

minimal cost
68 750 F
126,5 \$

Maximal cost
142 200 F
261,6 \$

Optimal (Essential+)

- AgHb
- Ag
- An
- TP, e
- NF
- Cre
- Gly

minimal cost
128 750 F
237 \$

Maximal cost
262 200 F
482,4 \$

Difficultés rencontrées

- Inaccurate registration of patients

Positive points

- Lack of
National strategic plan on HBV
Tenofovir is available : 4 € per month
- High
ALT : 2 – 6 €
HBeAg : 4,4 – 19 €
- ✓ HBV
- ✓ FibroScan[®] : 45 €
- ✓ FibroMeter[®] : 100 €

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Infection HBV en Afrique de l'Ouest, impact en Santé Publique : **PREvention Of Liver FIBrosis and Cancer in Africa** **(PROLIFICA)**

❑ Launching “PROLIFICA 2” (<http://www.prolifica.africa/>)

Lancet Glob Health. 2016 Aug;4(8):e559-67. doi: 10.1016/S2214-109X(16)30130-9.

Acceptability and feasibility of a screen-and-treat programme for hepatitis B virus infection in The Gambia: the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) study.

Lemoine M¹, Shimakawa Y², Njie R³, Taal M⁴, Ndow G¹, Chemin I⁵, Ghosh S⁵, Njai HF⁶, Jeng A⁶, Sow A⁷, Toure-Kane C⁷, Mboup S⁷, Suso P⁶, Tamba S⁶, Jatta A⁶, Sarr L⁶, Kambi A⁶, Stanger W⁸, Nayagam S⁸, Howell J⁸, Mpabanzi L⁹, Nyan O¹⁰, Corrah T⁶, Whittle H¹¹, Taylor-Robinson SD⁸, D'Alessandro U⁶, Mendy M³, Thursz MR¹²; PROLIFICA investigators.

Lancet Glob Health. 2016 Aug;4(8):e568-78. doi: 10.1016/S2214-109X(16)30101-2.

Cost-effectiveness of community-based screening and treatment for chronic hepatitis B in The Gambia: an economic modelling analysis.

Nayagam S¹, Conteh L², Sicuri E³, Shimakawa Y⁴, Suso P⁵, Tamba S⁵, Njie R⁶, Njai H⁵, Lemoine M⁷, Hallett TB⁸, Thursz M⁹.

J Hepatol. 2018 Jun 18. pii: S0168-8278(18)32102-0. doi: 10.1016/j.jhep.2018.05.024. [Epub ahead of print]

Development of a simple score based on HBeAg and ALT for selecting patients for HBV treatment in Africa.

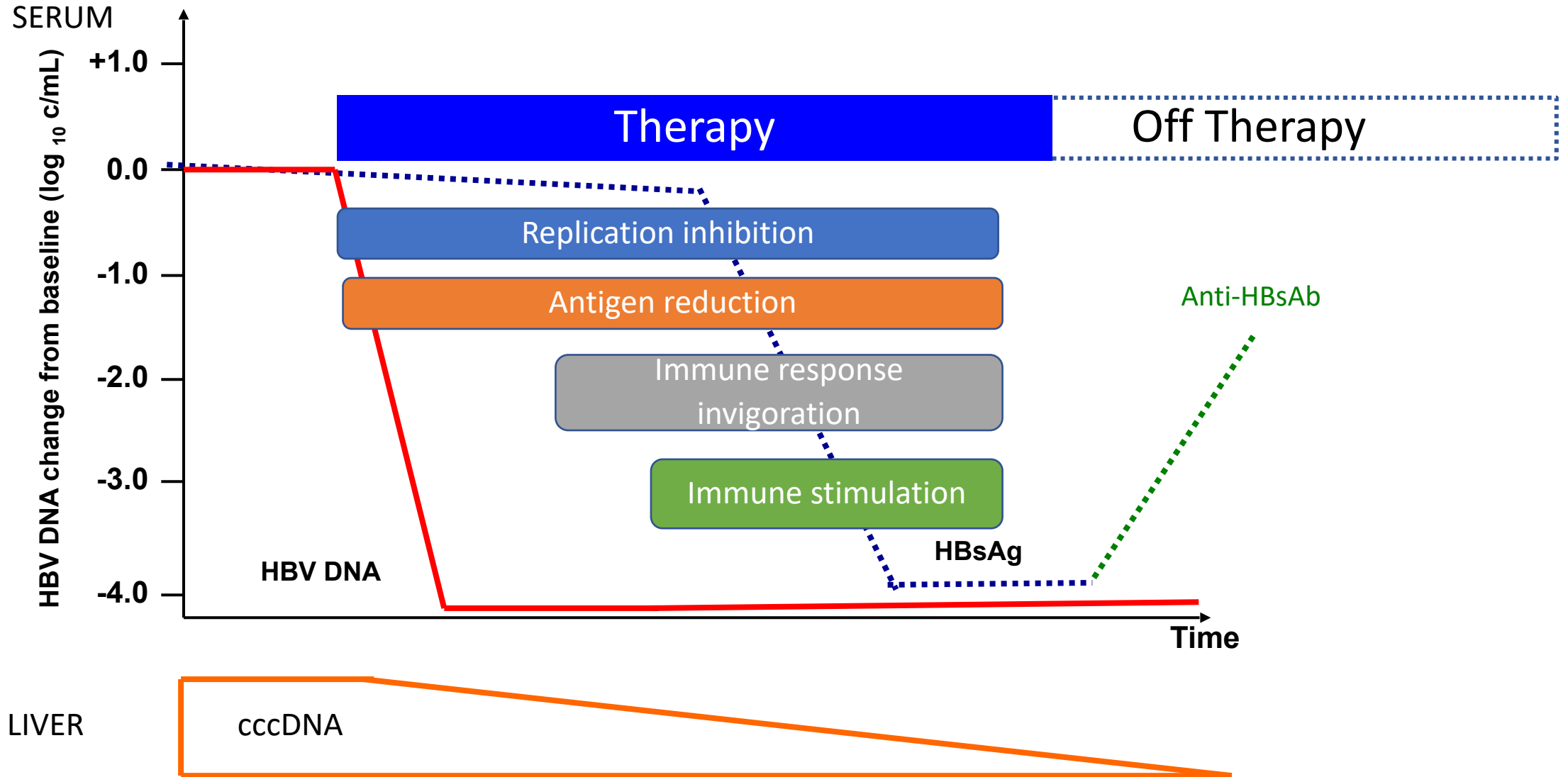
Shimakawa Y¹, Njie R², Ndow G³, Vray M⁴, Mbaye PS⁵, Bonnard P⁶, Sombié R⁷, Nana J⁸, Leroy V⁸, Bottero J⁹, Ingiliz P¹⁰, Post G¹¹, Sanneh B¹², Baldeh I¹², Suso P¹³, Ceasay A¹³, Jeng A¹³, Njai HF¹³, Nayagam S¹⁴, D'Alessandro U¹³, Chemin I¹⁵, Mendy M¹⁶, Thursz M¹⁴, Lemoine M¹⁷.



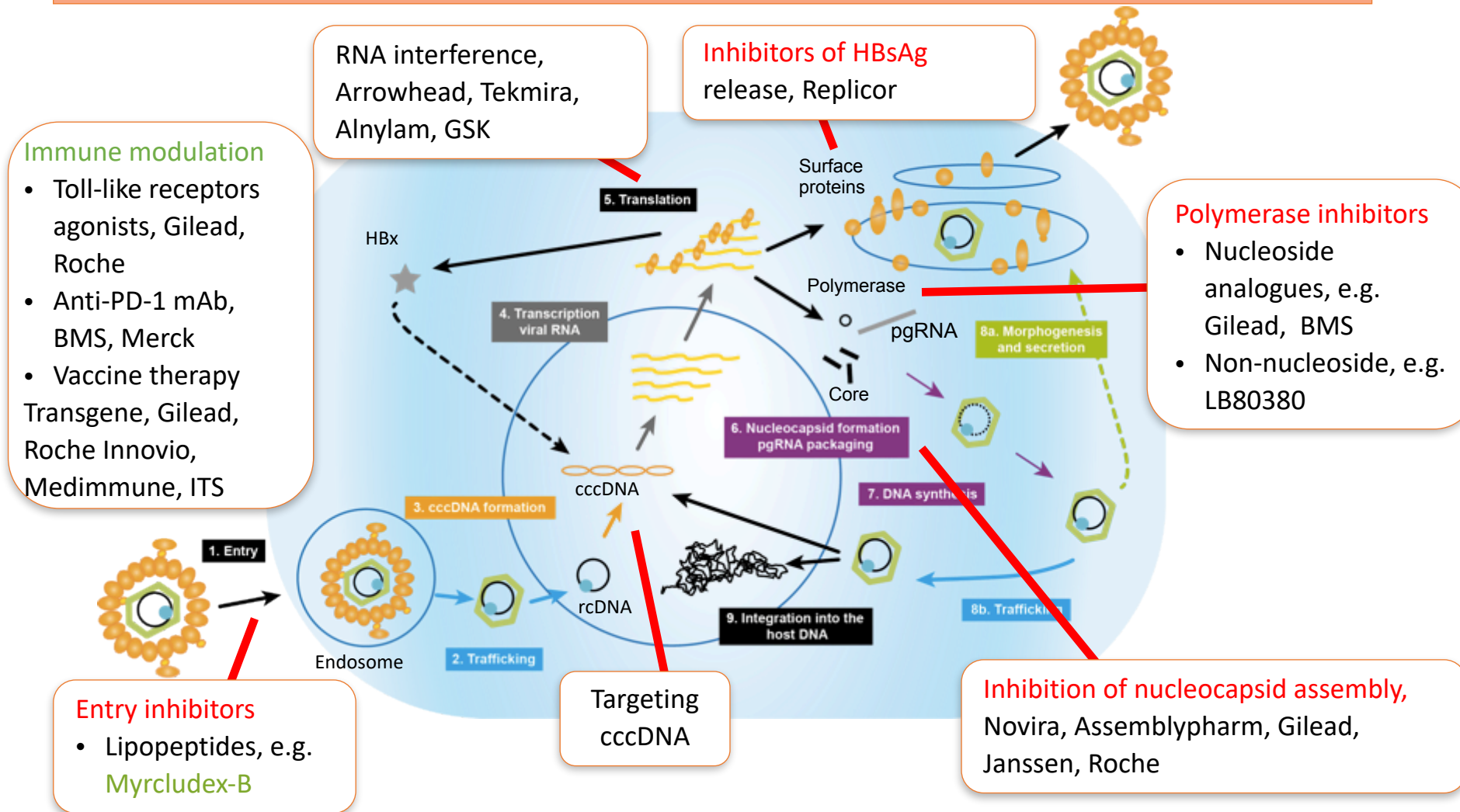
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Essais cliniques : nouveaux concepts de traitements combinés



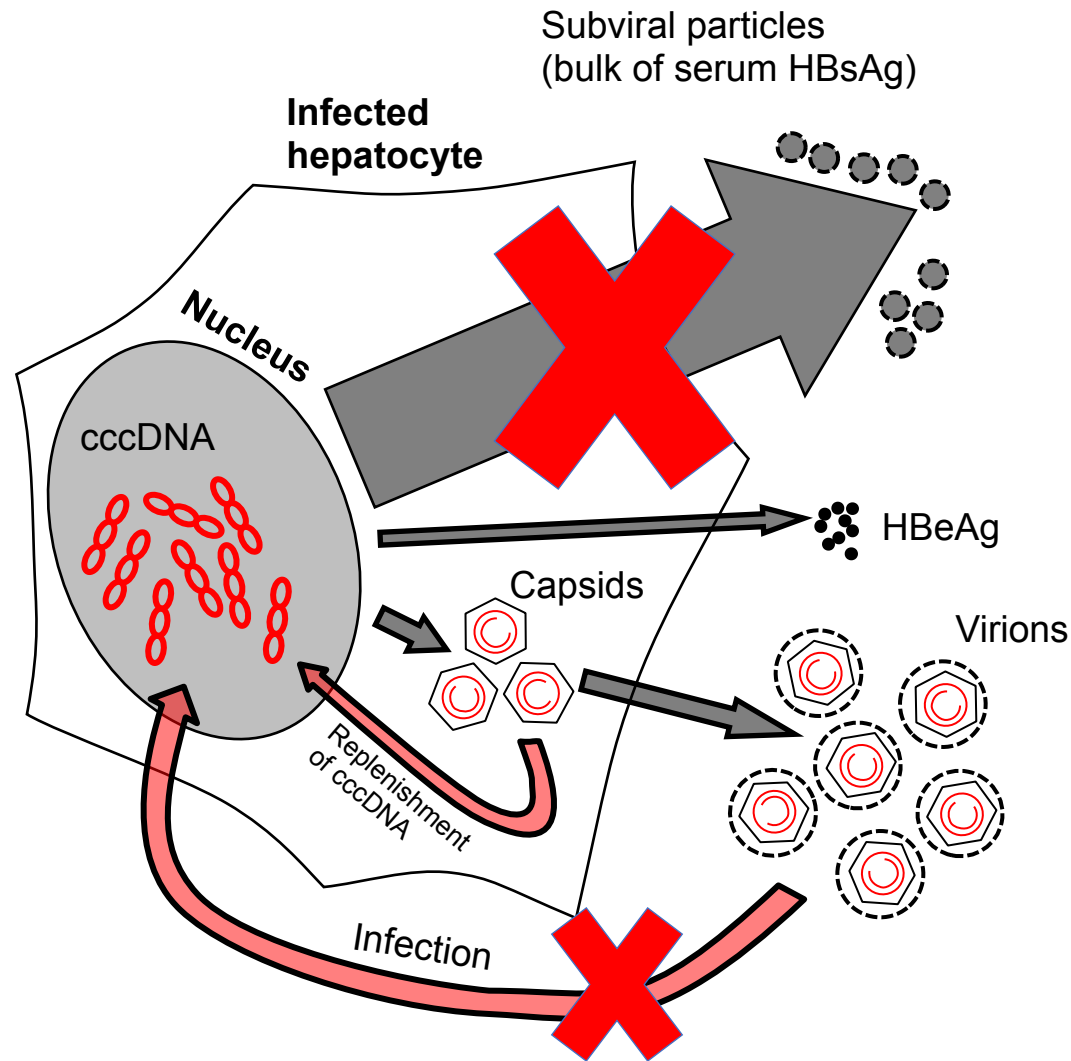
Futur : viser des cibles multiples



Development stage: **preclinical**, **clinical**

Zoulim F, et al. Antiviral Res 2012;96(2):256–9; HBF Drug Watch, Available at: http://www.hepb.org/professionals/hbf_drug_watch.htm.

Les NAPs bloquent la libération des particules subvirales (replicor)



L'AgHBs est la clé :

Sequesters anti-HBs
Suppresses innate immunity
Suppresses T-cell proliferation
Suppresses cytokine signaling

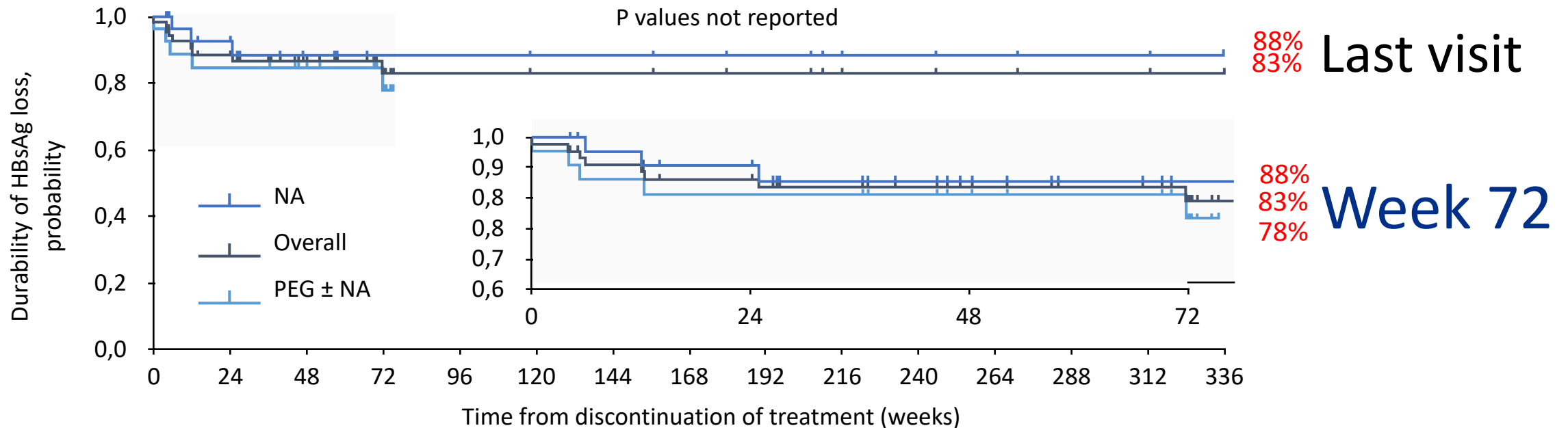
Invalidates immunotherapy

**L'élimination de l'AgHBs
est indispensable
à des SVR élevées**

Persistence de la négativation de l'antigène HBs après NUC / PEG

Etude rétrospective de 1,381 CHB patients#

Estimated Probability of Durable HBsAg Loss to Last Study Visit and to Week 72 in Patients with Confirmed HBsAg Loss (n=55) and HBsAg Seroreversion (n=8)



L'espoir de guérison du VHB

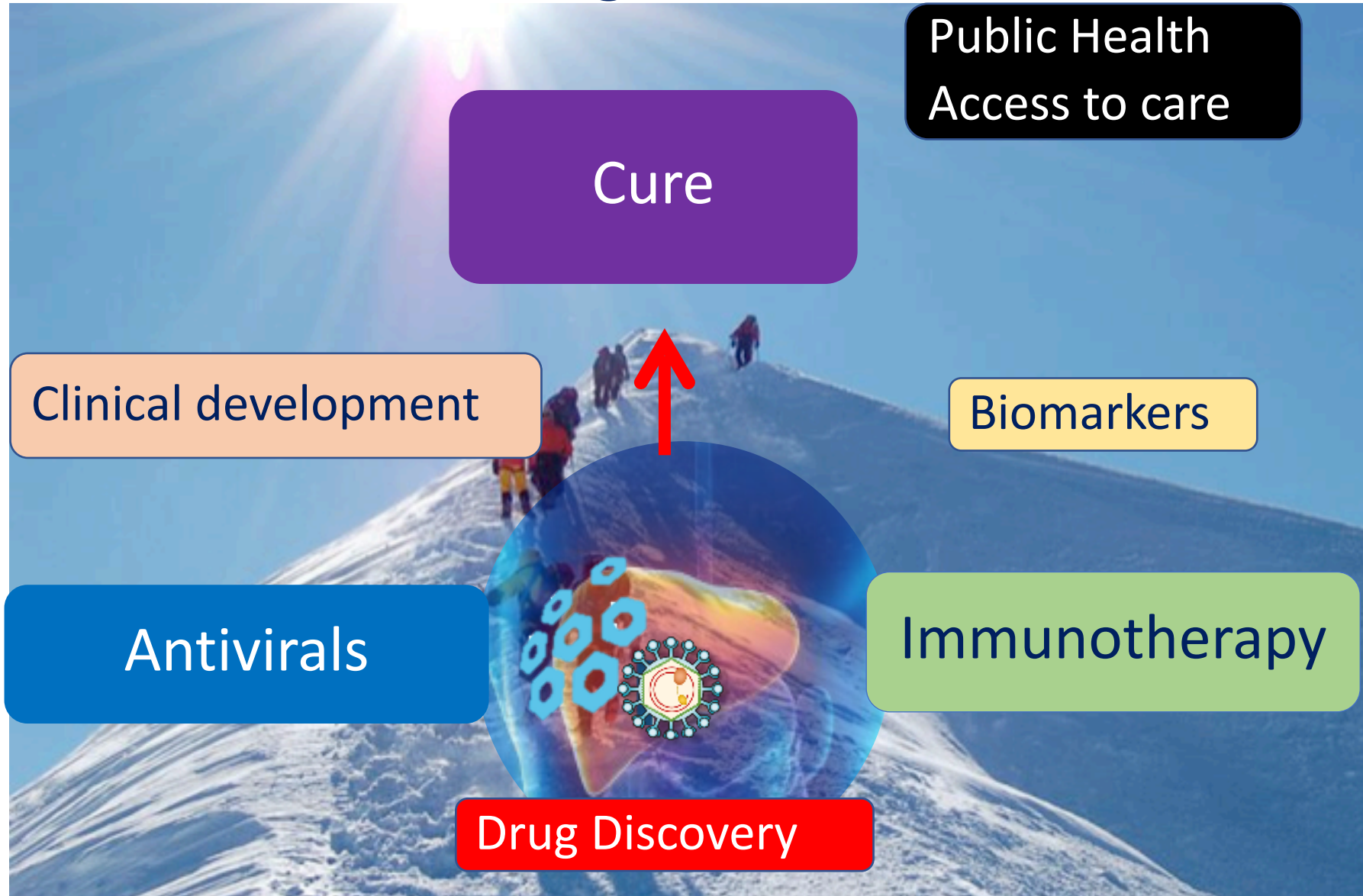
dans les 5-7 ans

doit inciter à traiter bien plus tôt

tous les malades à risque de fibrose et de CHC

YES WE CAN !

HBV cure: An attainable goal within the next decade !



LES EQUIPES



Remerciements
Professeur Roger SOMBIE
Professeur Fabien ZOULIM