

The place of Pegylated IFN in HBV therapeutic

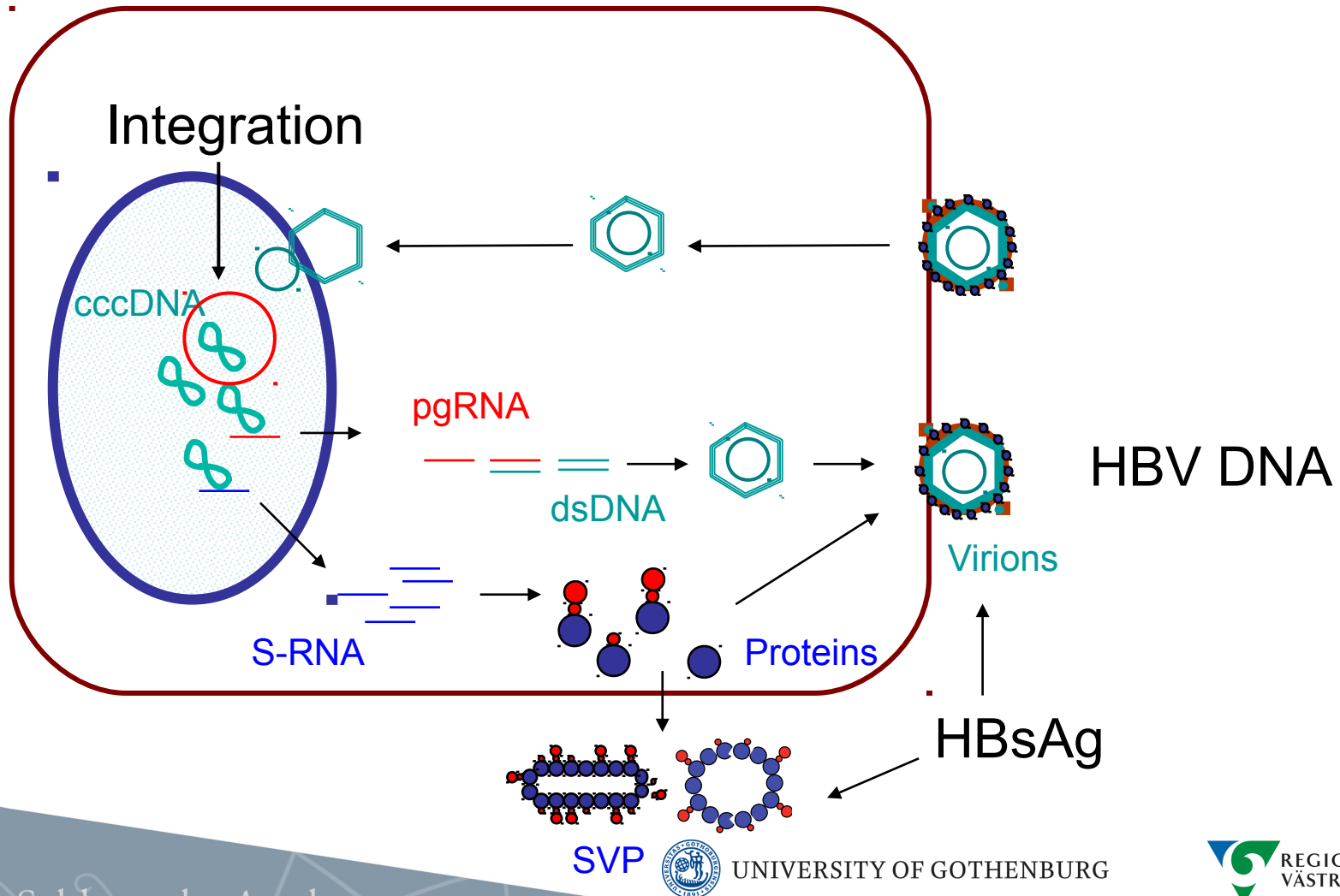
Simon Larsson, M.D., Ph.D.
University of Gothenburg
Sahlgrenska University Hospital
Gothenburg, Sweden

The Sahlgrenska Academy

Chronic HBV infection

- 240 million patients worldwide
- Cirrhosis and HCC
- Vaccine
- Rarely cured

Replication of HBV



HBV-infection - Natural history

HBeAg+

HBV DNA
>10⁸ copies/mL

HBsAg
10⁵ IU/mL

HBeAg-

HBV DNA
~10⁴ copies/mL

HBsAg
10³ IU/mL

Treatment indications in HBV

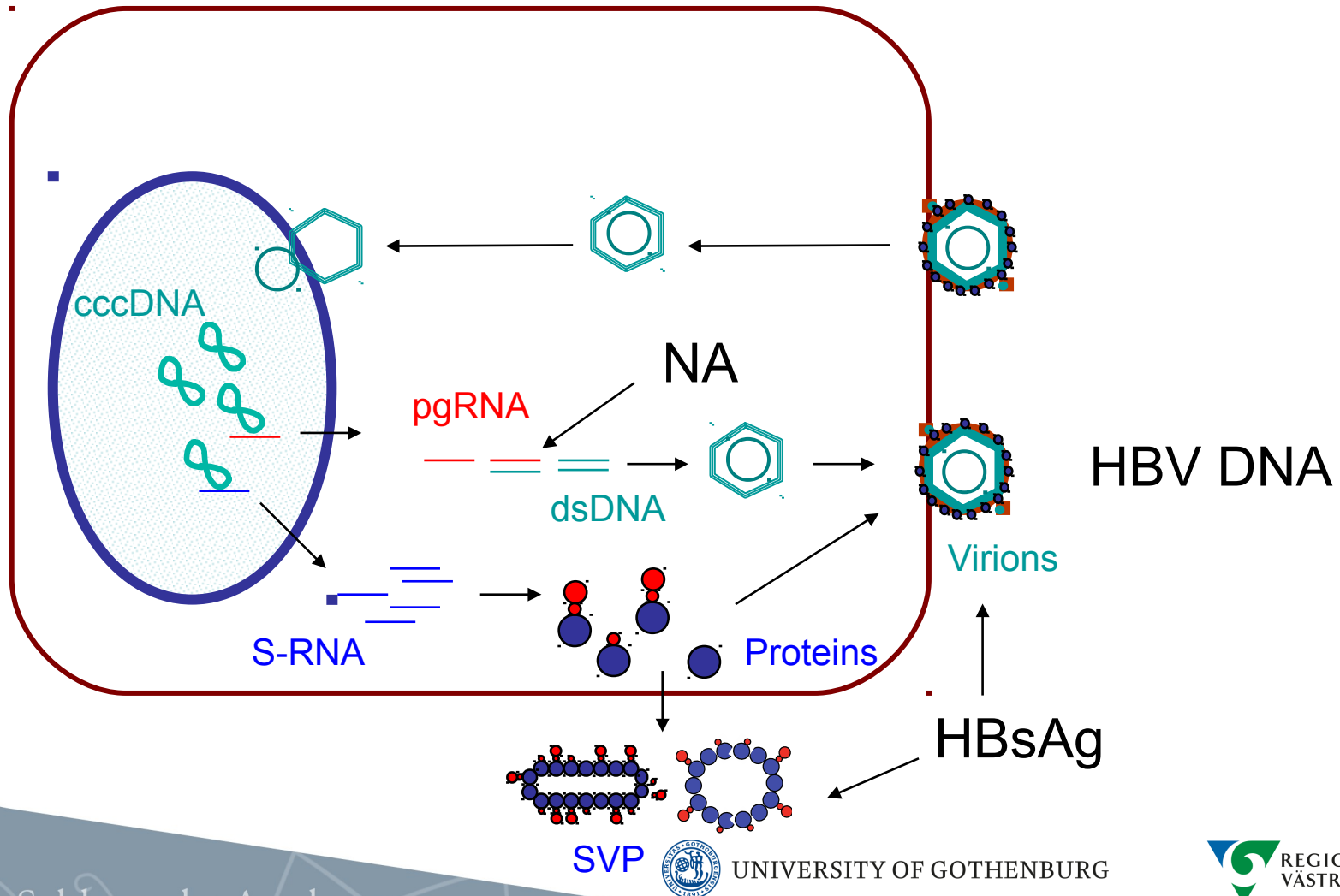
- Serum HBV DNA levels
- Serum ALT levels
- Severity of liver disease
 - Liver biopsy
 - Fibroscan

HBV treatment options

Nucleos(t)ide analogues: tenofovir,
entecavir

Pegylated Interferon

NAs in HBV infection



NAs in HBV infection

- Potent antiviral effect
- Few side effects
- Oral administration
- Indefinite duration
- Risk of resistance
- Unknown long-term safety

Peg-IFN in HBV infection

- Immunomodulatory
- Antiviral effects (cccDNA elimination?)

Peg-IFN in HBV infection

- Finite duration
- No resistance
- Higher rates of seroconversion (HBe/HBs)
- Moderate antiviral effect
- Side effects and adverse events
- Subcutaneous injections

End-points for Peg-IFN in HBV

- HBeAg seroconversion
- SVR (HBV DNA <2000 IU/ml, normal ALT)
- HBsAg-loss

Clinical Case

- male, born 1983
- Vertical transmission at birth
- HBs+, HBe+, genotype D
- 2/7 brothers and sisters also HBs+, HBe+

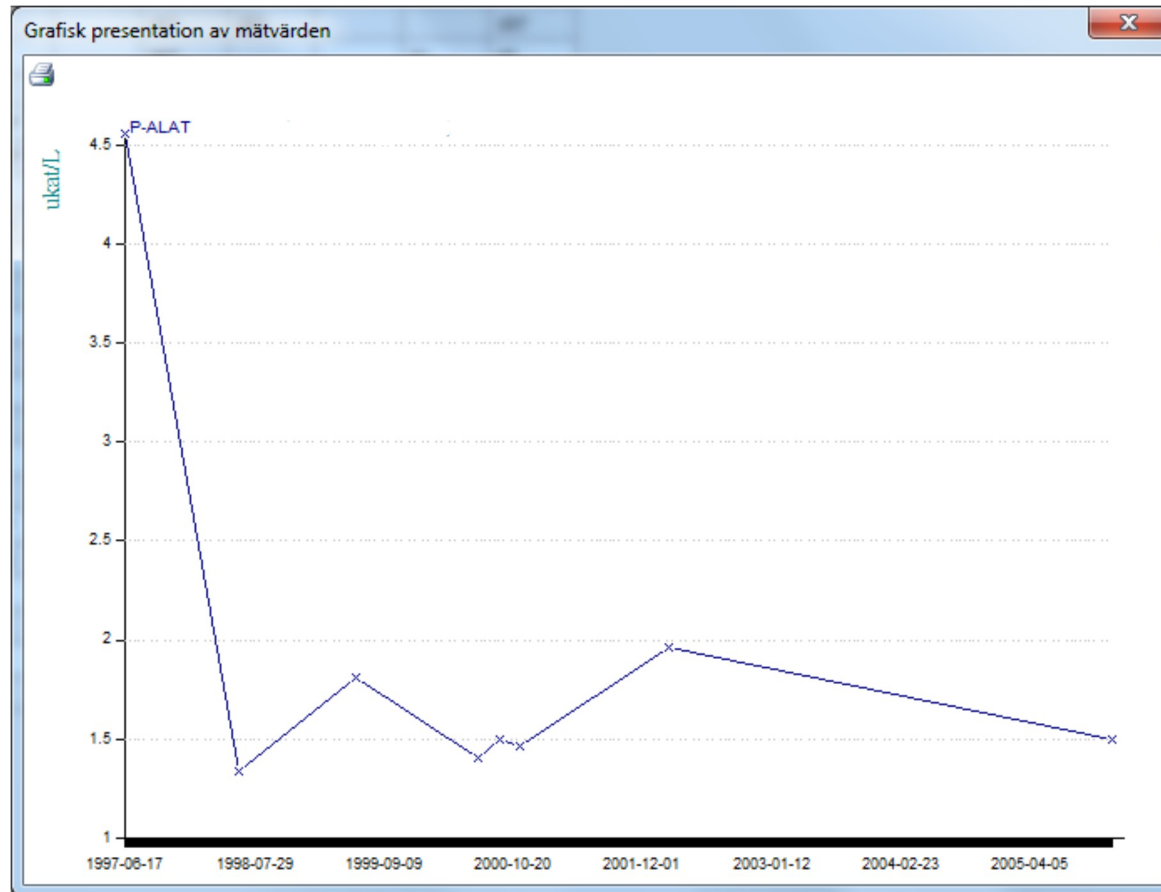
Clinical Case

- Sees doctor once a year
- Normal ALT, high levels of HBV DNA
- August 1998: anti-HBe +, HBe-
- 1999: transferred to clinic of infectious diseases

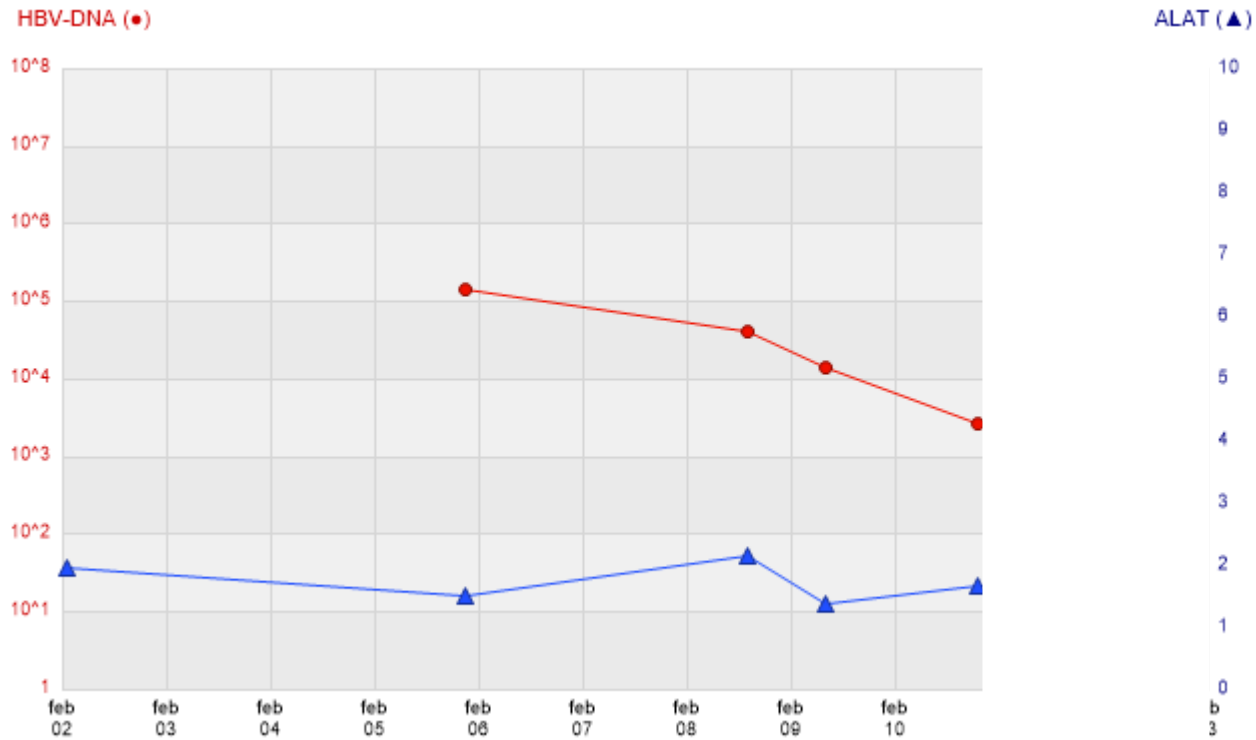
Clinical Case

- July 1999: HBV DNA negative
- Liver biopsy Sep 2000: Infl 1, Fibrosis 1
- November 2000: HBV DNA positive
- Persistently elevated ALT, 1.3-2 X ULN

Clinical Case



Clinical Case



Clinical Case

- Fibroscan April 2009: kPa 6.9 (but difficult due to subcutaneous fat)
- Considered to be F1/F2
- 2009-2010: treatment discussion
- Patient wants Pegylated Interferon

Clinical Case

- Starts treatment May 2011
- Pegasys 180 mg, 1 inj/week
- HBV DNA 1200 IU/ml
- HBsAg 440 IU/ml

Clinical Case

	W0
HBV DNA	1200
HBsAg	440
anti-HBs	-

Clinical Case

	W0	W4
HBV DNA	1200	22
HBsAg	440	552
anti-HBs	-	-

Clinical Case

	W0	W4	W10
HBV DNA	1200	22	<20
HBsAg	440	552	102
anti-HBs	-	-	-

Clinical Case

	W0	W4	W10	W24
HBV DNA	1200	22	<20	neg
HBsAg	440	552	102	neg
anti-HBs	-	-	-	-

Clinical Case

	W0	W4	W10	W24	W28
HBV DNA	1200	22	<20	neg	neg
HBsAg	440	552	102	neg	neg
anti-HBs	-	-	-	-	+

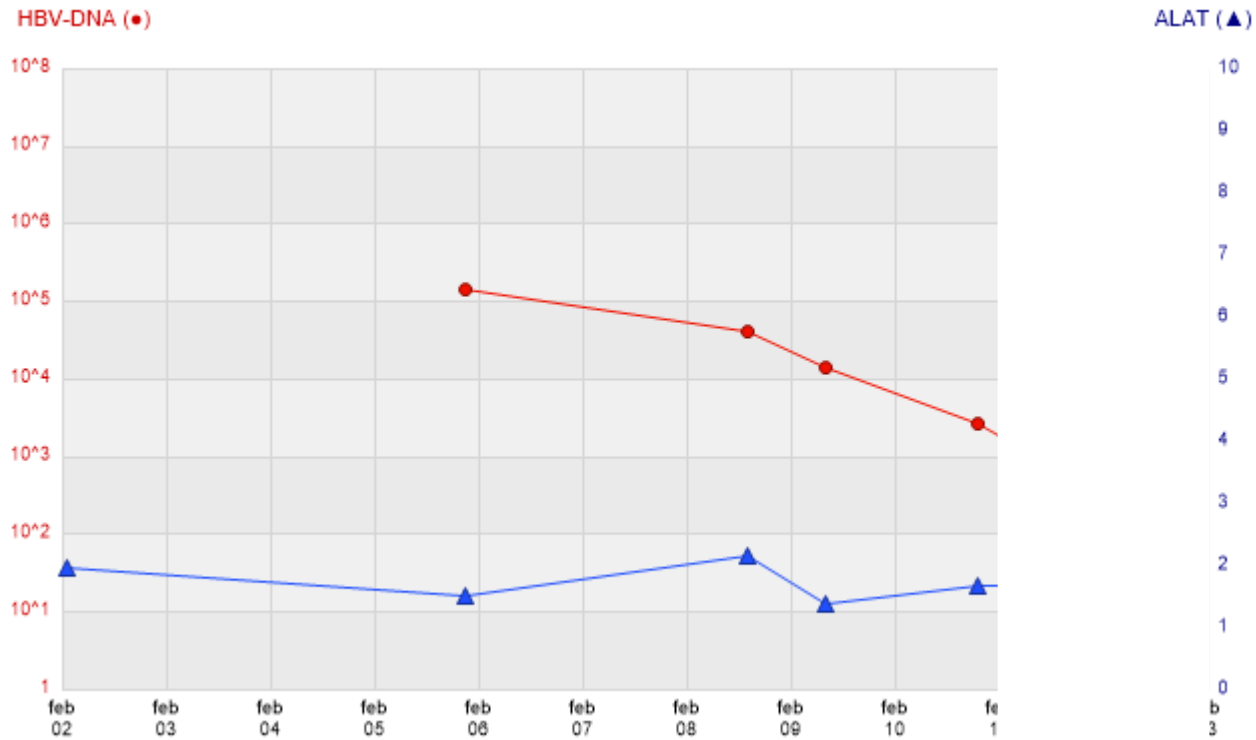
Clinical Case

	W0	W4	W10	W24	W28	W32
HBV DNA	1200	22	<20	neg	neg	neg
HBsAg	440	552	102	neg	neg	neg
anti-HBs	-	-	-	-	+	+

Clinical Case

	W0	W4	W10	W24	W28	W32	W36
HBV DNA	1200	22	<20	neg	neg	neg	neg
HBsAg	440	552	102	neg	neg	neg	neg
anti-HBs	-	-	-	-	+	+	+

Clinical Case



Clinical Case

- Side effects: muscle pain, headache, fever, fatigue
- Interrupt treatment? Patient wants to continue
- dose reduction at W8 -> 135 mg

Clinical Case

- HBs- in week 24, 28, 32
- Treatment discontinued week 36
- Follow-up: HBV DNA neg, anti-HBs +
- November 2011: anti-HBs titer 6.8 IU/mL
- January 2013: anti-HBs titer 616 IU/mL

Clinical Case - summary

- HBeAg negative patient
- HBsAg negative after 24 w peg IFN
- Anti-HBs at week 28

Clinical Case – Q & A

- Treat HBeAg- patients with Peg-IFN?
- When?
- Who to treat?
- What to consider?
- Follow-up?

