CLINICAL APPLICATIONS OF ANTIBODY AVIDITY AND IGM TESTING

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DIAGNOSIS OF ACUTE HEPATITIS C

Acute Viral Hepatitis C remains frequently undiagnosed because:

- the asymptomatic form of the disease prevails;
- the clinical presentation is similar to that of an acute exacerbation of Chronic Hepatitis C.

Reactivation of chronic HCV infection

194 patients with chronic HCV infection

Followed for 6.2 3.5 years

HCV reactivation in in 78 patients (40.2%)

43 patients showed only one episode of hepatonecrosis

35 patients had multiple episodes of hepatonecrosis

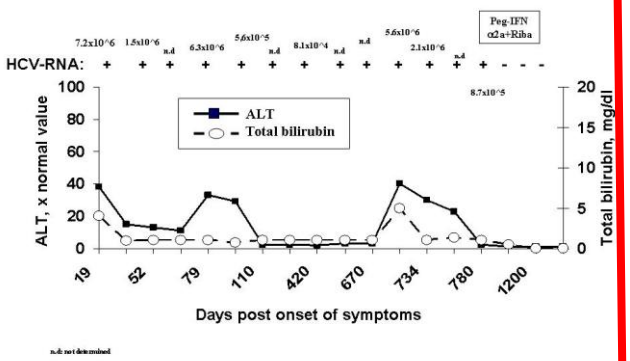
Liaw et al. J. Hepatology, 1996

Virological and Epitope Evolution of HCV Infection from Acute Hepatitis C to Subsequent Episodes of HCV-Related Acute Liver Cell Necrosis

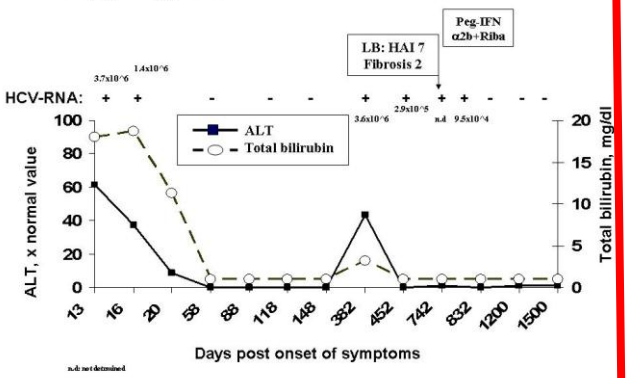
E. Sagnelli, C. Argentini, D. Genovese, M. Pisaturo, N. Coppola, S. Taffon,

Infection 2009;37:344-8

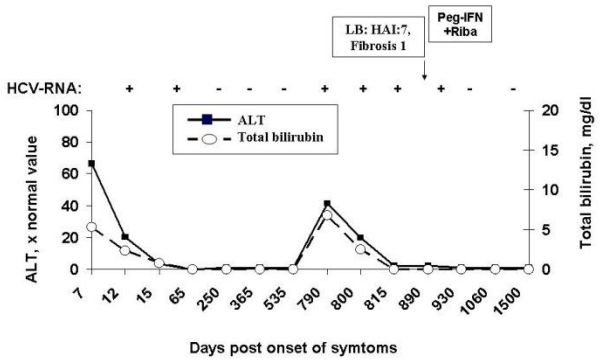
Patient 1, IVDU, genotype 3a

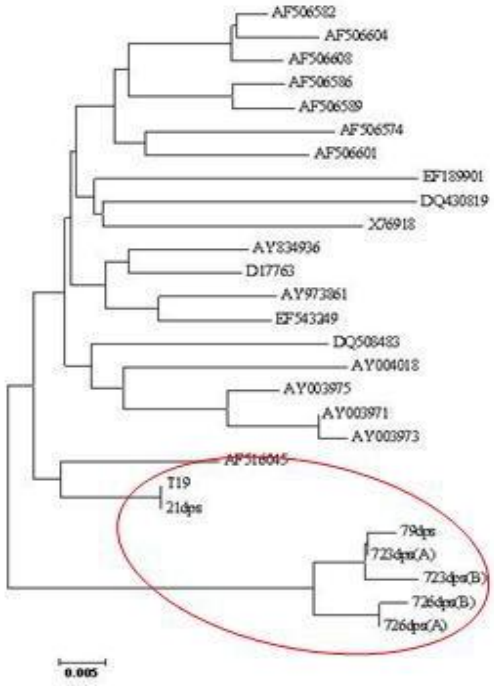


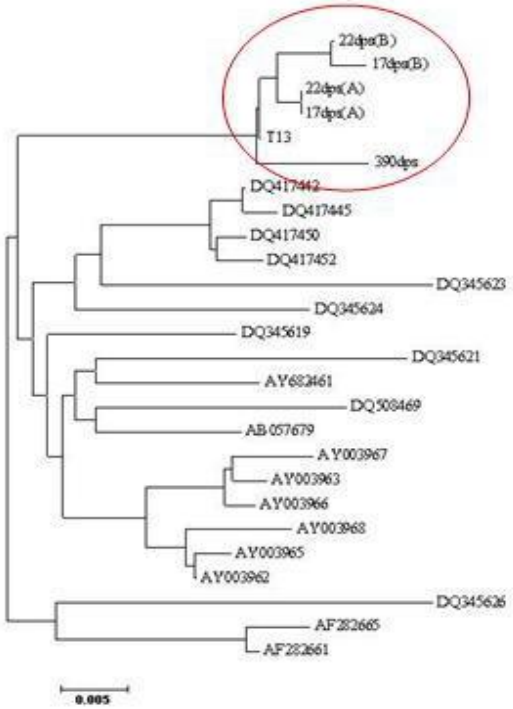
Patient 2, genotype 1b



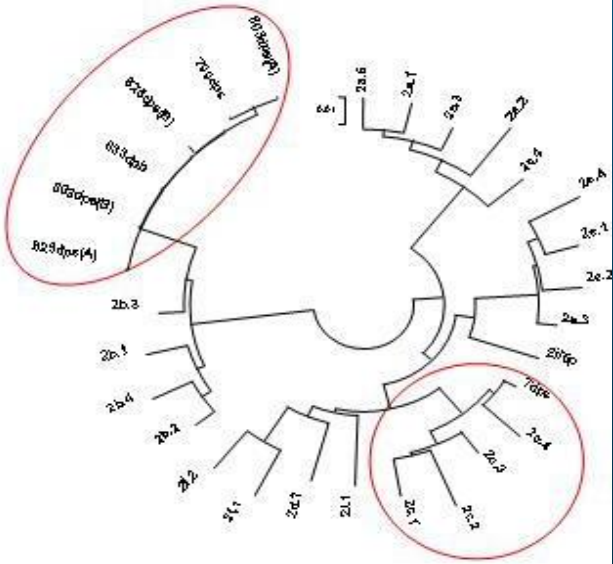
Patient 3, TD, genotype 2c







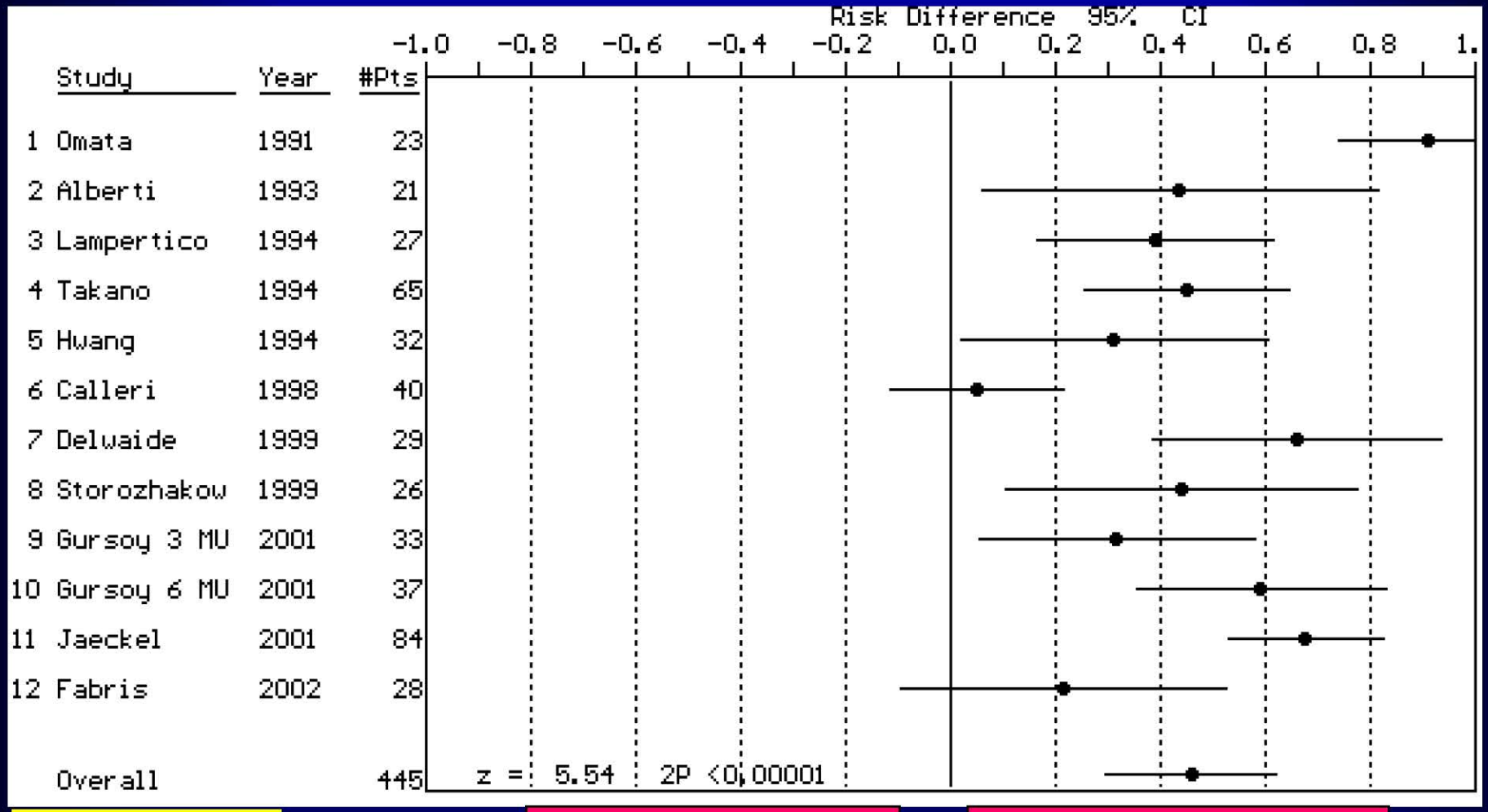
HCV gen 2b



HCV gen 2c

Meta-analysis of 12 controlled trials of standard IFN monotherapy

SUSTAINED VIROLOGICAL RESPONSE

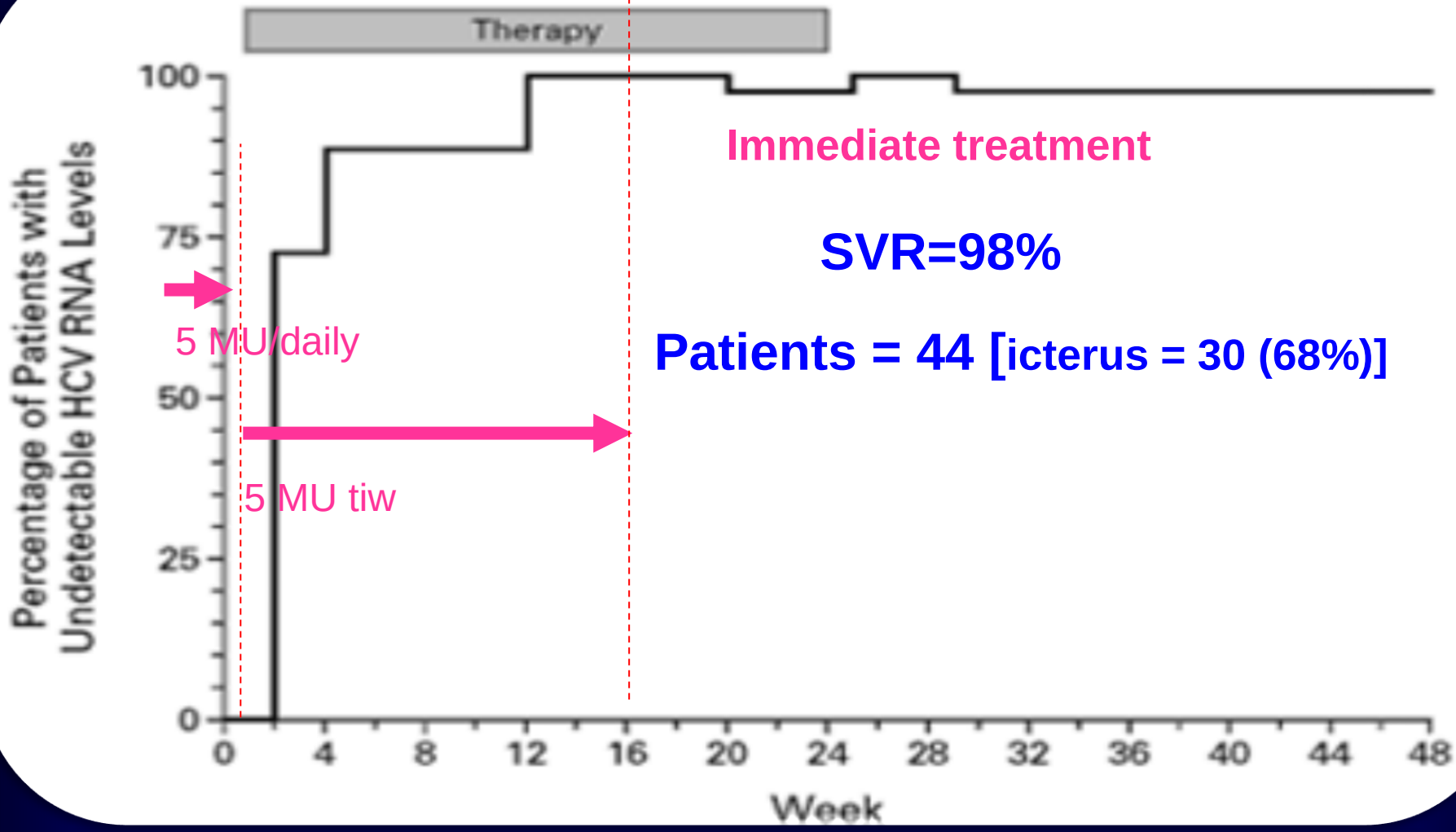


RD: +49.0%
NNT: 2

FAVOR CONTROL | **FAVOR TREATMENT**

Licata et al. J Hepatol 2003

Treatment of Acute Hepatitis C: INF Alfa-2b



Immediate treatment

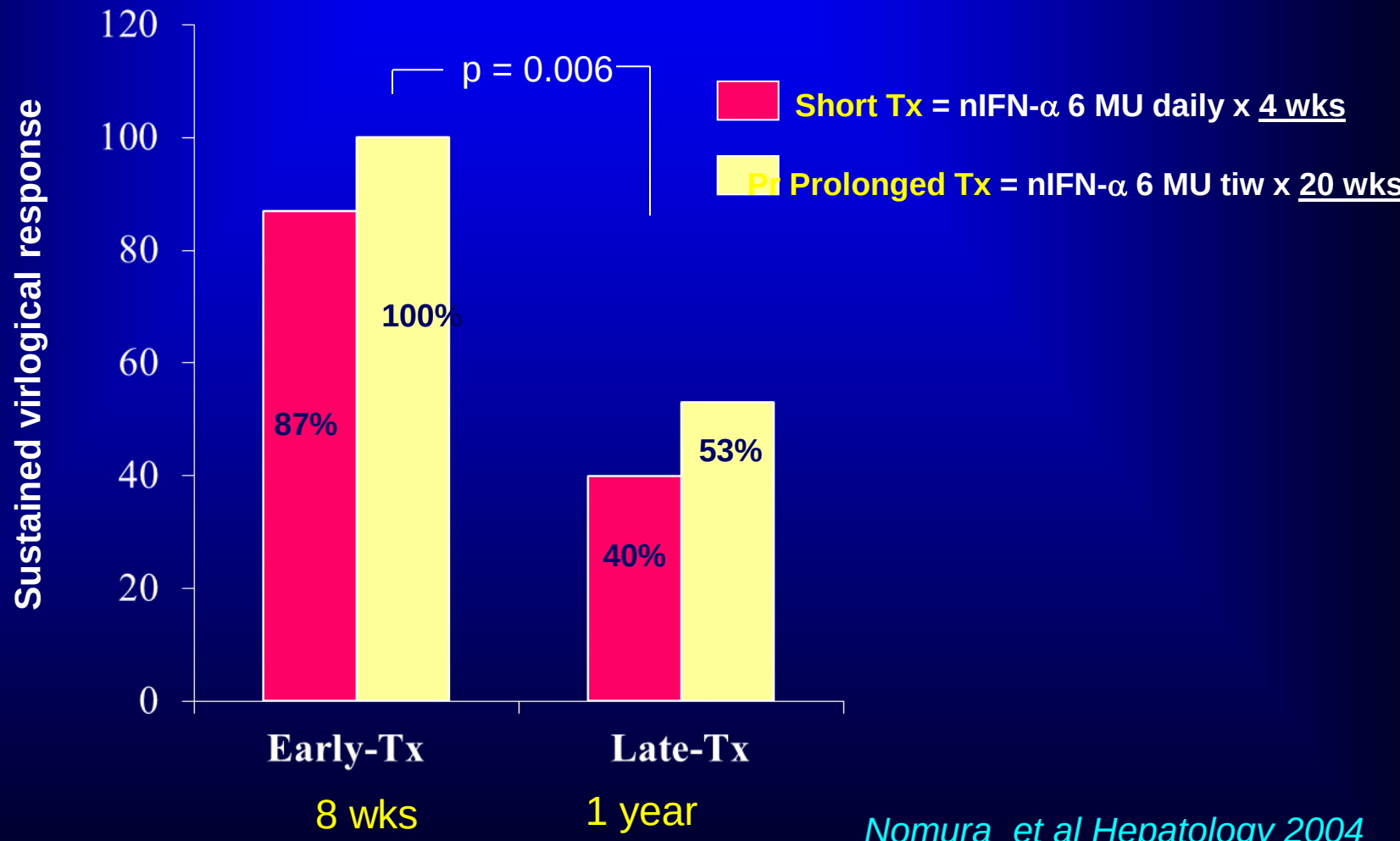
SVR=98%

Patients = 44 [icterus = 30 (68%)]

Jaeckel et al., NEJM, 2001

Early versus late IFN-α Therapy

34 pts with AHC → after 8 wks 30 pts still viremic → randomization



Nomura et al Hepatology 2004

Diagnosis of acute hepatitis C (AHC): seroconversion to anti-HCV positive

(documented in a minority of patients in the clinical practice)

First observation	Subsequent observations
Anti-HCV negative	anti-HCV positive
Normal AMT	AMT > v.n.x 5
HCV-RNA Positive/ negative	HCV-RNA positive

A RELEVANT CLINICAL PROBLEM: to distinguish AH-C from reactivation of CH-C

ELSEVIER

J Hepatol. 2005 May;42(5):646-51.

Journal of Hepatology

www.elsevier.com/locate/jhep

Diagnosis of HCV related acute hepatitis by serial determination of IgM anti-HCV titres

Evangelista Sagnelli[1,2,*], Nicola Coppola[1,2], Cecilia Marrocco[2], Giancarlo Coviello[1], Martina Battaglia[1,2], Vincenzo Messina[1], Giovanni Rossi[1,2], Caterina Sagnelli[2], Carlo Scolastico[2], Pietro Filippini[2]

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ELSEVIER

J Clin Virol. 2007 Oct;40(2):110-5

JOURNAL OF CLINICAL VIROLOGY

www.elsevier.com/locate/jcv

Anti-HCV IgG avidity index in acute hepatitis C

Nicola Coppola[a], Raffaella Pisapia[a], Cecilia Marrocco[a], Salvatore Martini[a,b], Luisa Maria Vatiero[a,b], Vincenzo Messina[b], Gilda Tonziello[a,b], Caterina Sagnelli[a], Pietro Filippini[a], Felice Piccinino[a], Evangelista Sagnelli[a,b,*]

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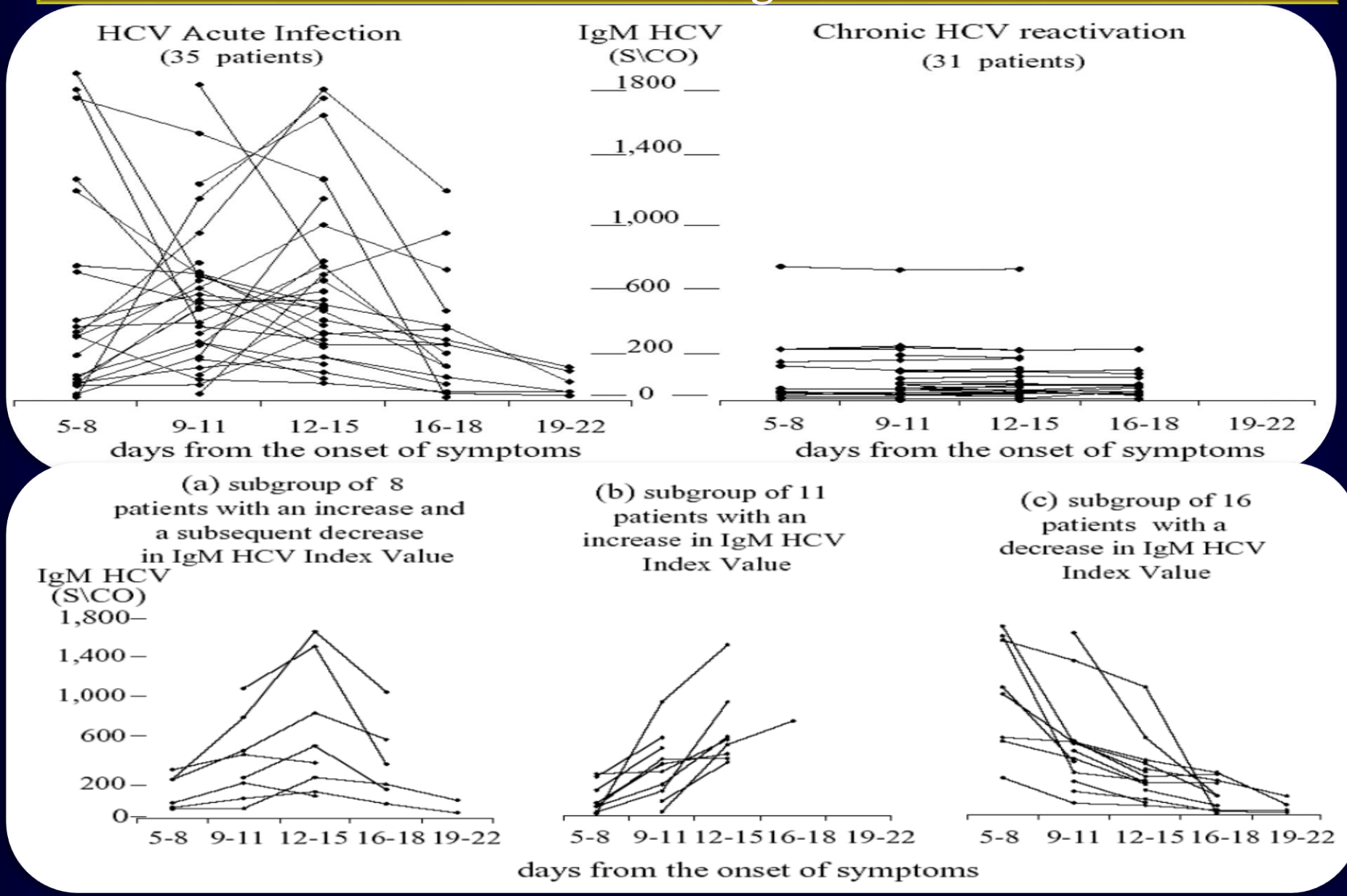
[b] *Division of Infectious Diseases, Azienda Ospedaliera Sant'Anna e San Sebastiano, Caserta, Italy*

PATIENTS INVESTIGATED

- Symptomatic AHC patients, diagnosed on the bases of seroconversion to Anti-HCV positive.
- Symptomatic patients with acute exacerbation of CHC, diagnosed on the bases of persistence of anti HCV in serum from at least one year before reactivation.

Diagnosis of Hepatitis C Virus related acute hepatitis by serial determination of IgM anti-HCV titer



Sagnelli E, et all. J Hepatol 2005

Anti HCV IgG avidity index in acute hepatitis C

AHC group
40 patients with AHC

Pair-mached

CHC group
40 patients with CHC symptom-free

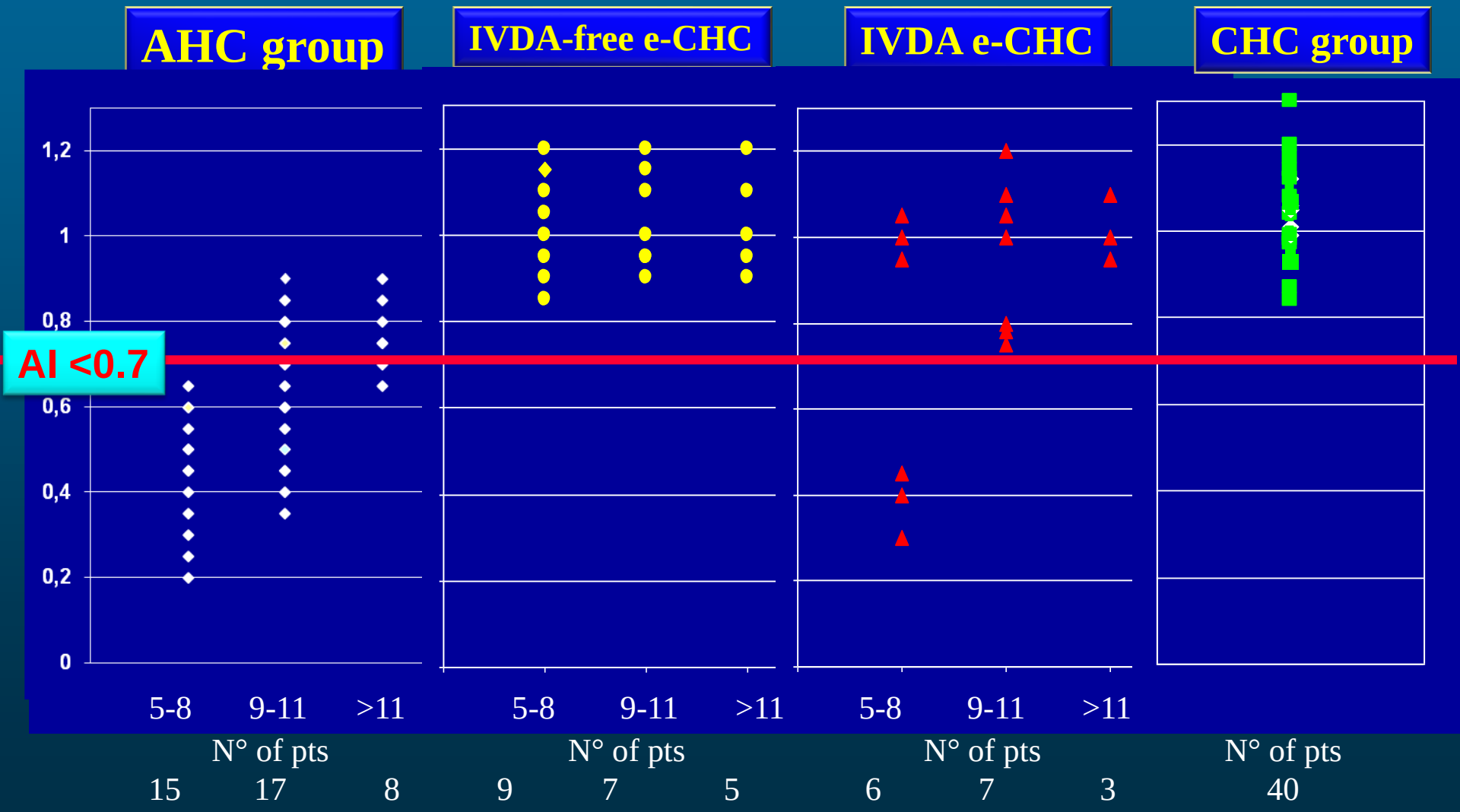
37 patients with r-CHC (a-e-CHC group)

21 patients with a-e-CHC IVDA free

16 patients patients with a-e-CHC IVDA

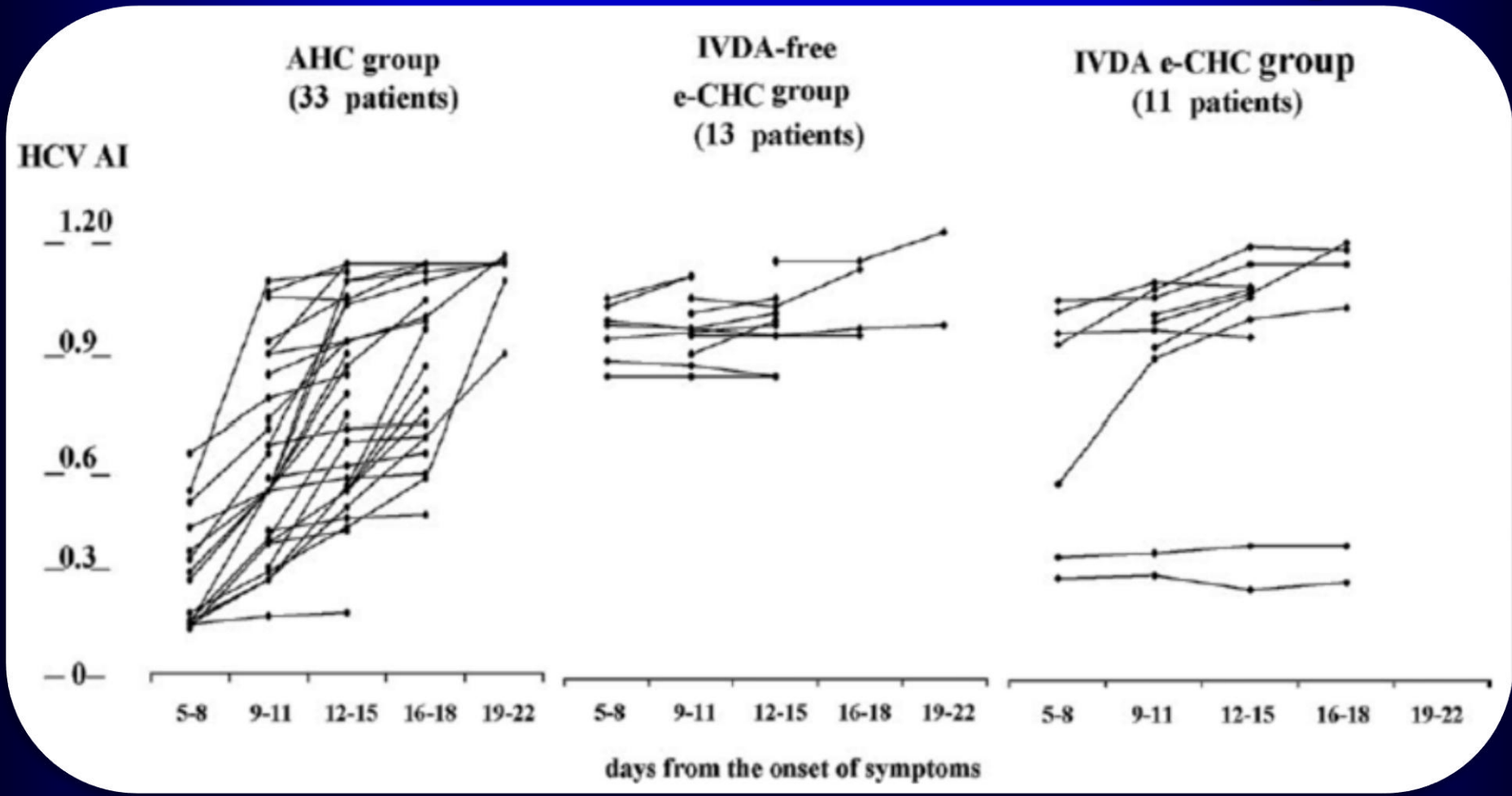
Results

The baseline Avidity Index of anti-HCV IgG in the three groups of patients according to the day from the onset of symptoms



Acute Hepatitis C: anti-HCV IgG avidity

Dynamics of HCV AI values in acute phase of diseases in patients with AHC and a-e-CHC with at least two serum samples



Improvement in the aetiological diagnosis of acute hepatitis C: A diagnostic protocol based on the anti-HCV-IgM titre and IgG Avidity Index

AHC group
45 patients with AHC

a-e-CHC group
36 patients with e-CHC without active intravenous drug addiction

HCV-IgM titers and HCV-AI for a correct diagnosis on a single serum sample

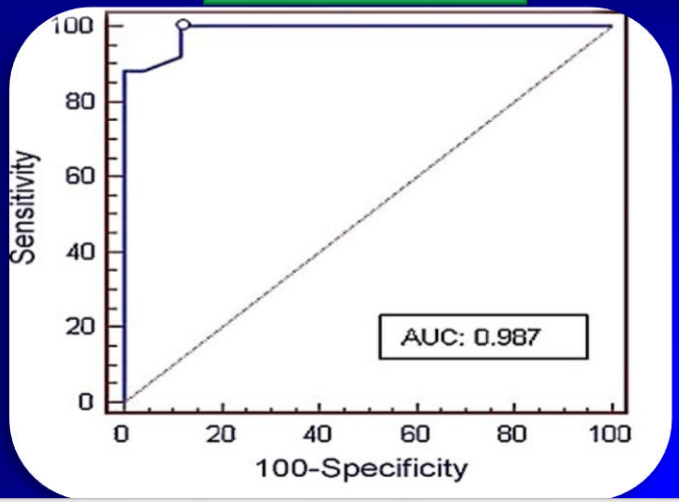
For each test specific cut-off values at 4 selected checking points were established during the observation :
- for the HCV-IgM assay the highest value in e-CHC +5%
- for HCV-AI assay the lowest value in e-CHC -5%.

N. Coppola, et al. J Clin Virol46,2009.222–229

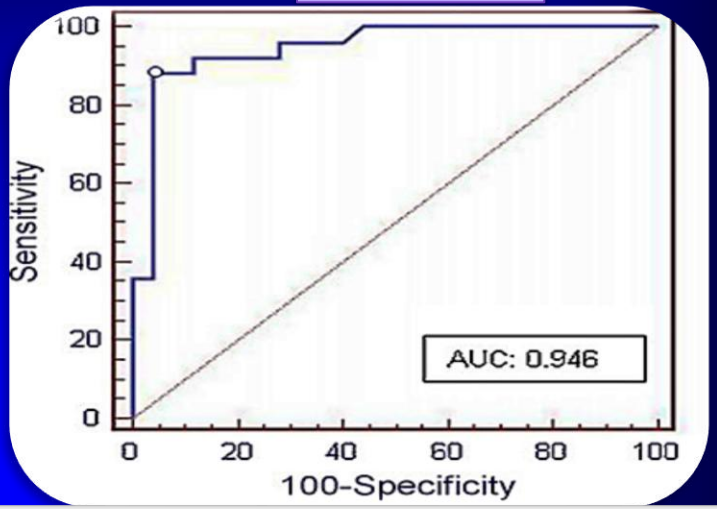
ROC curves and related AUC of the HCV-IgM and HCV-AI assays at different checking points during the course of illness

< 10 days

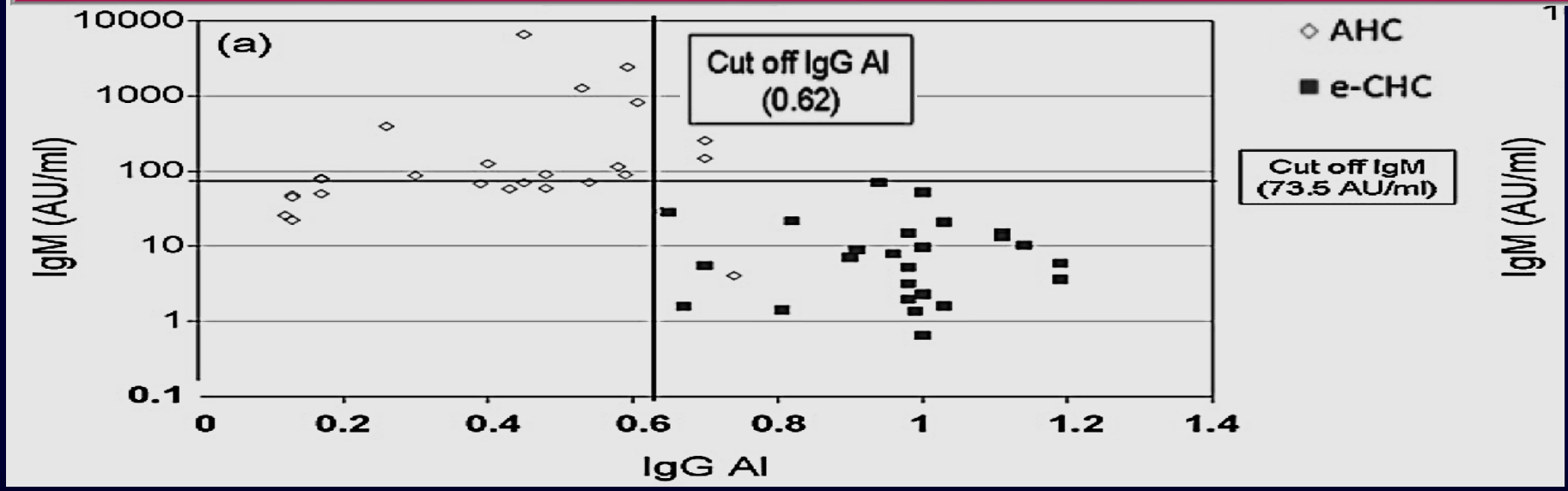
IgG avidity

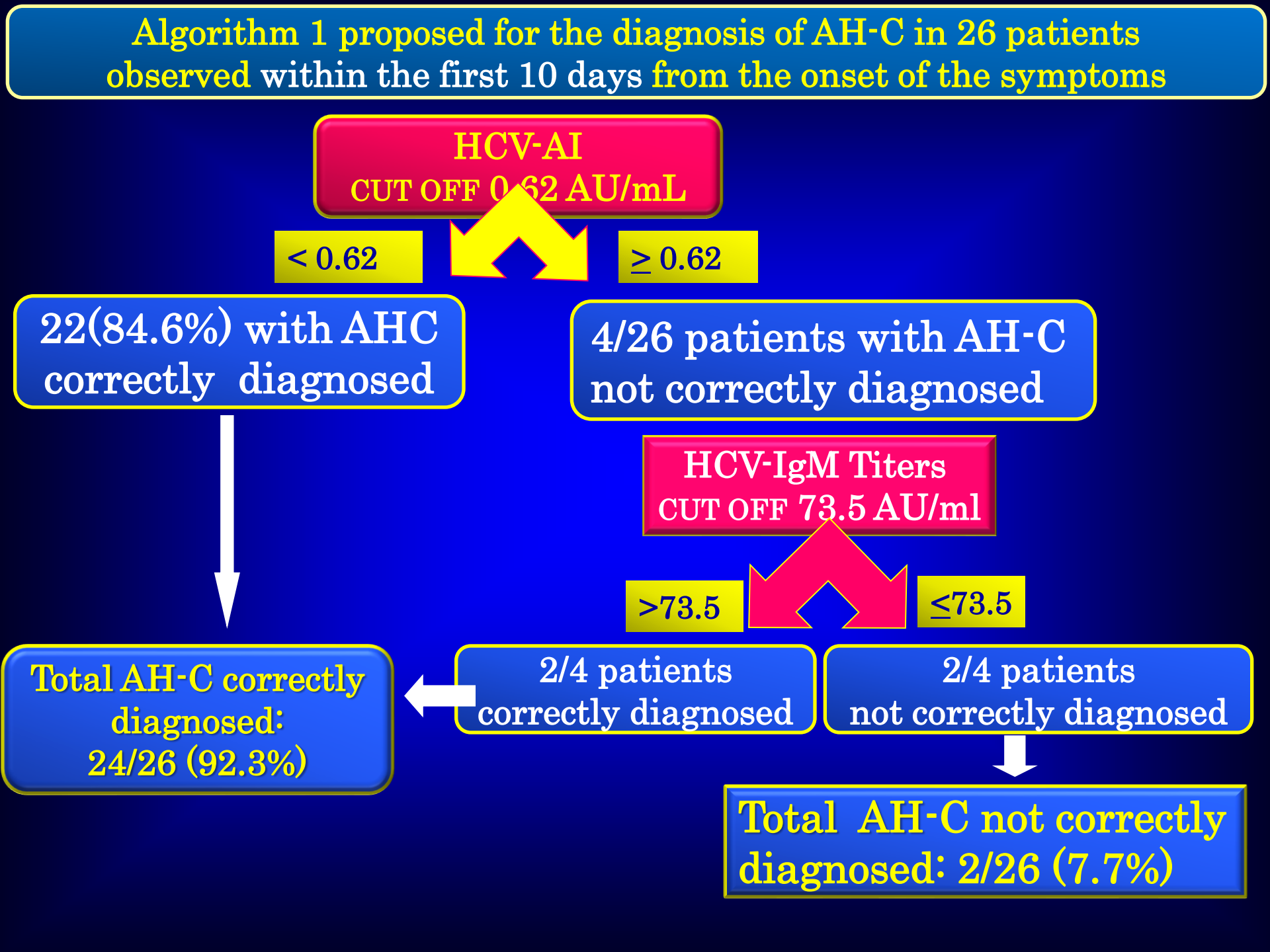


IgM titer



Distribution of patients with AH-C or ae-CH-C according to the results of both HCV-AI and HCV-IgM assays obtained ≤10 days

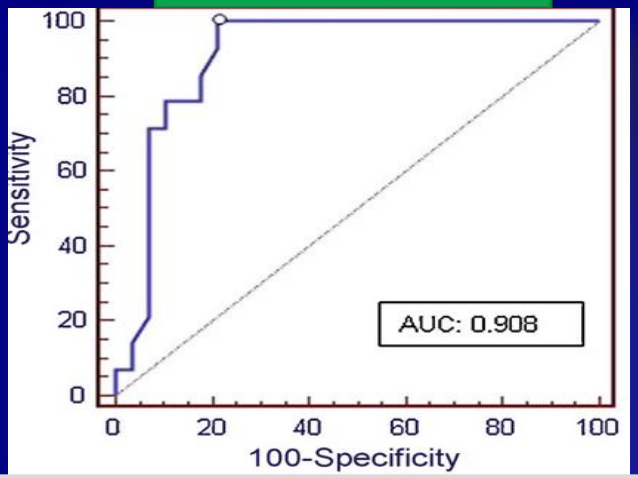



Algorithm 1 proposed for the diagnosis of AH-C in 26 patients observed within the first 10 days from the onset of the symptoms
HCV-AI
CUT OFF 0.62 AU/mL
< 0.62
≥ 0.62
22(84.6%) with AHC correctly diagnosed
4/26 patients with AH-C not correctly diagnosed
HCV-IgM Titers
CUT OFF 73.5 AU/ml
>73.5
≤73.5
Total AH-C correctly diagnosed: 24/26 (92.3%)
2/4 patients correctly diagnosed
2/4 patients not correctly diagnosed
Total AH-C not correctly diagnosed: 2/26 (7.7%)

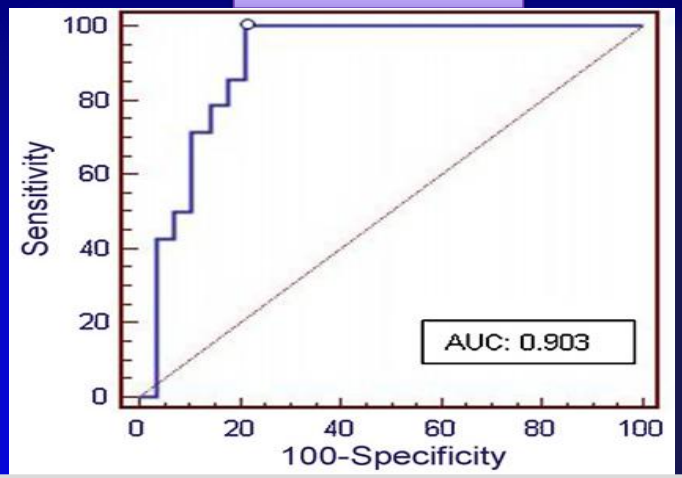
ROC curves and related AUC of the HCV-IgM and HCV-AI assays at different checking points during the course of illness

11-15 days

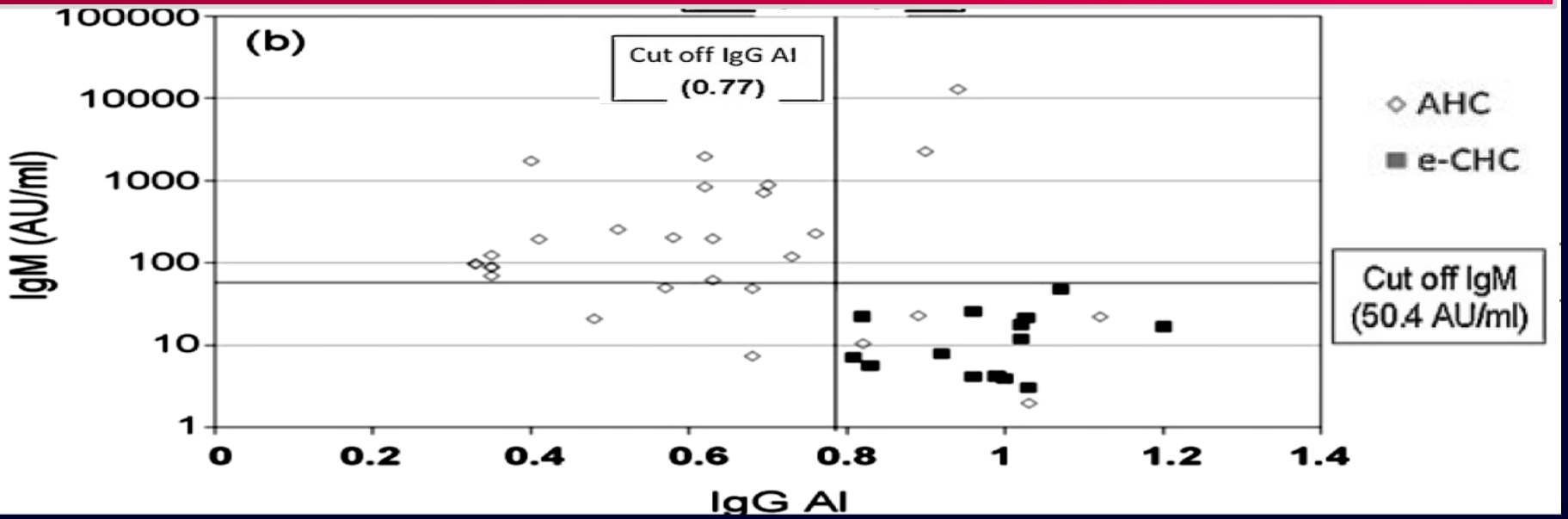
IgG avidity

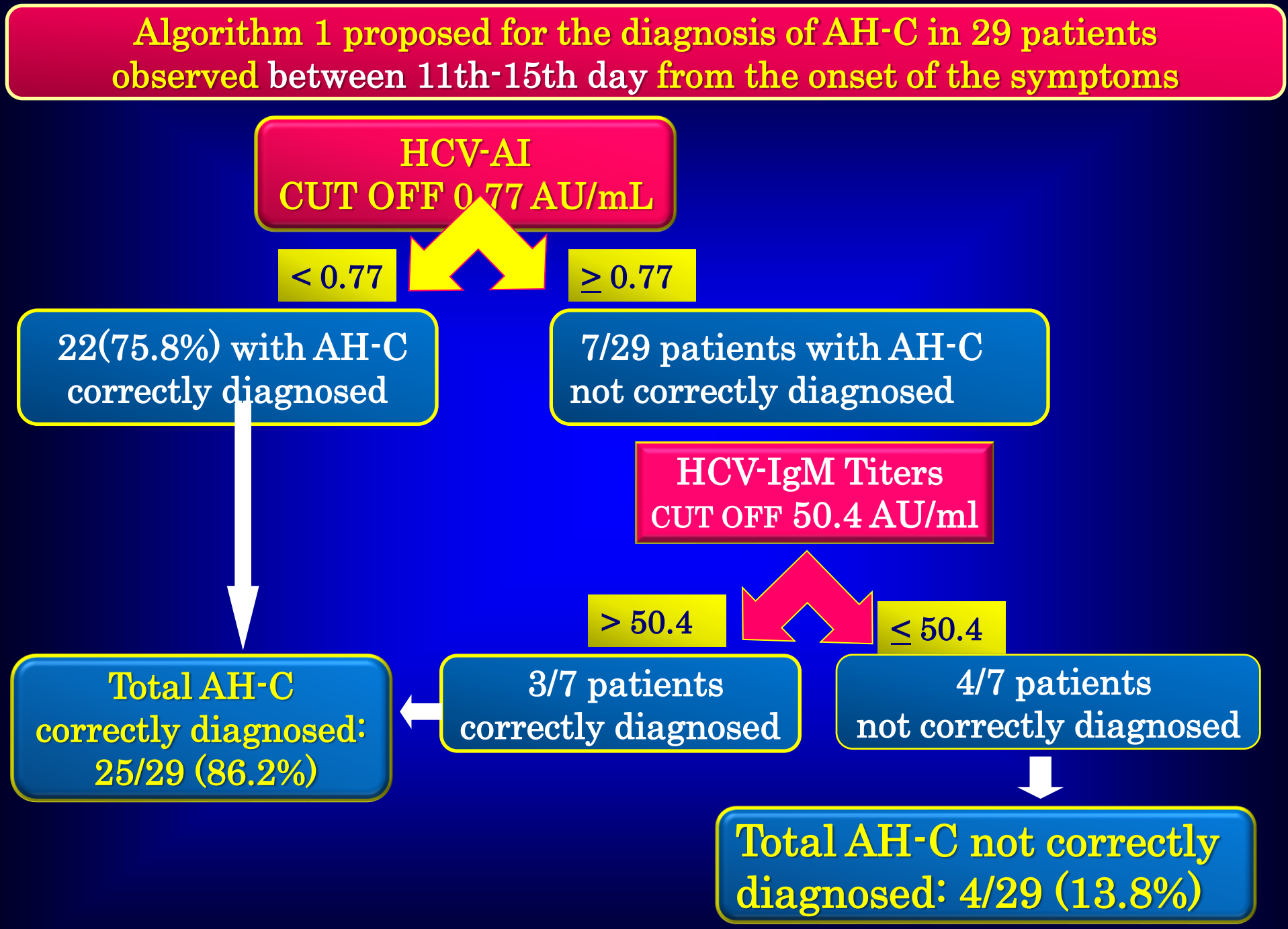


IgM titer



Distribution of patients with AH-C or ae-CH-C according to the results of both HCV-AI and HCV-IgM assays obtained from 11 to 15 days

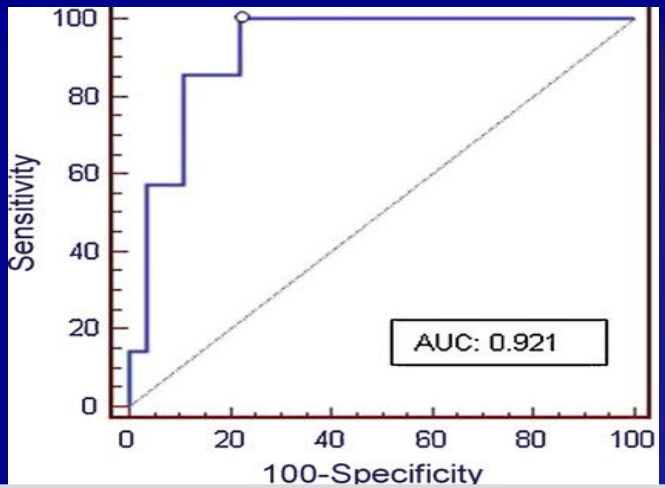



Algorithm 1 proposed for the diagnosis of AH-C in 29 patients observed between 11th-15th day from the onset of the symptoms
HCV-AI
CUT OFF 0.77 AU/mL
< 0.77
≥ 0.77
22(75.8%) with AH-C correctly diagnosed
7/29 patients with AH-C not correctly diagnosed
HCV-IgM Titers
CUT OFF 50.4 AU/ml
> 50.4
≤ 50.4
Total AH-C correctly diagnosed: 25/29 (86.2%)
3/7 patients correctly diagnosed
4/7 patients not correctly diagnosed
Total AH-C not correctly diagnosed: 4/29 (13.8%)

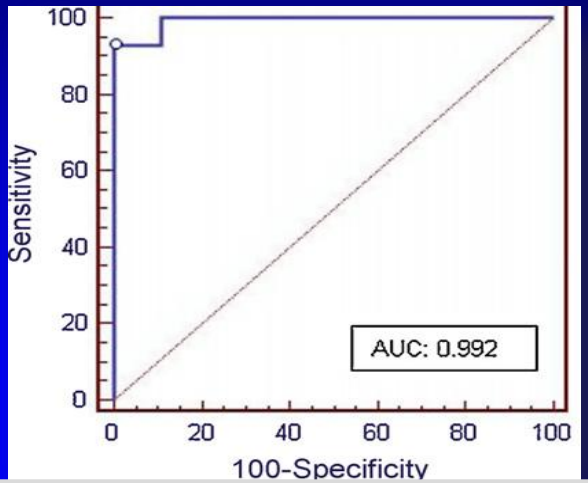
ROC curves and related AUC of the HCV-IgM and HCV-AI assays at different checking points during the course of illness

16-20 days

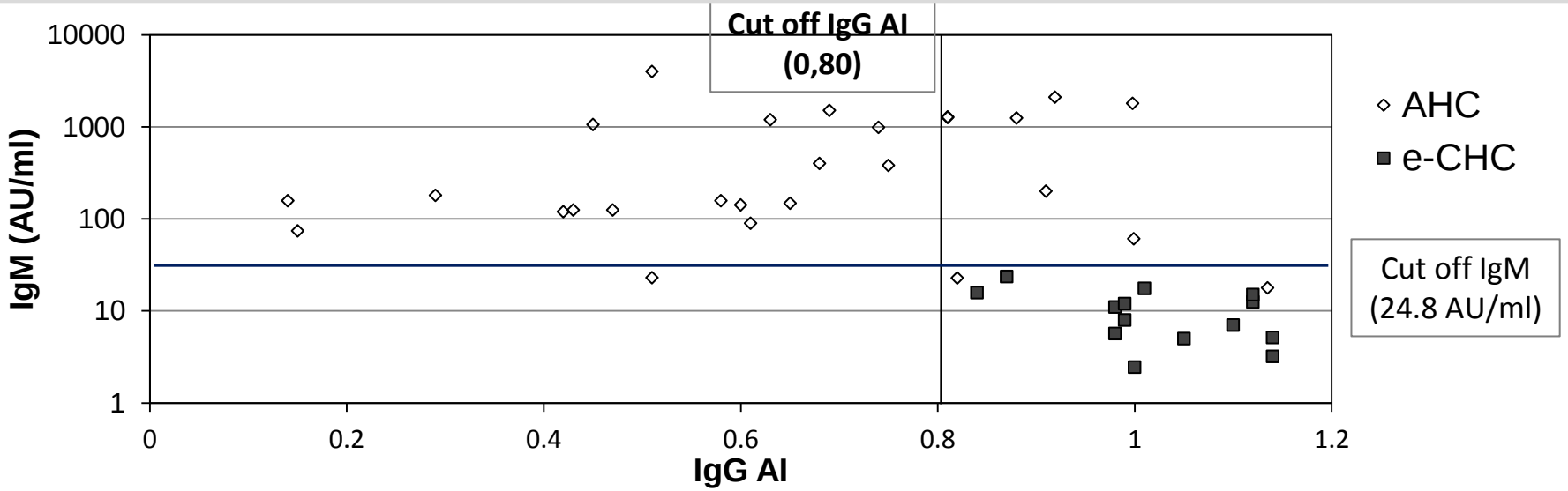
IgG avidity



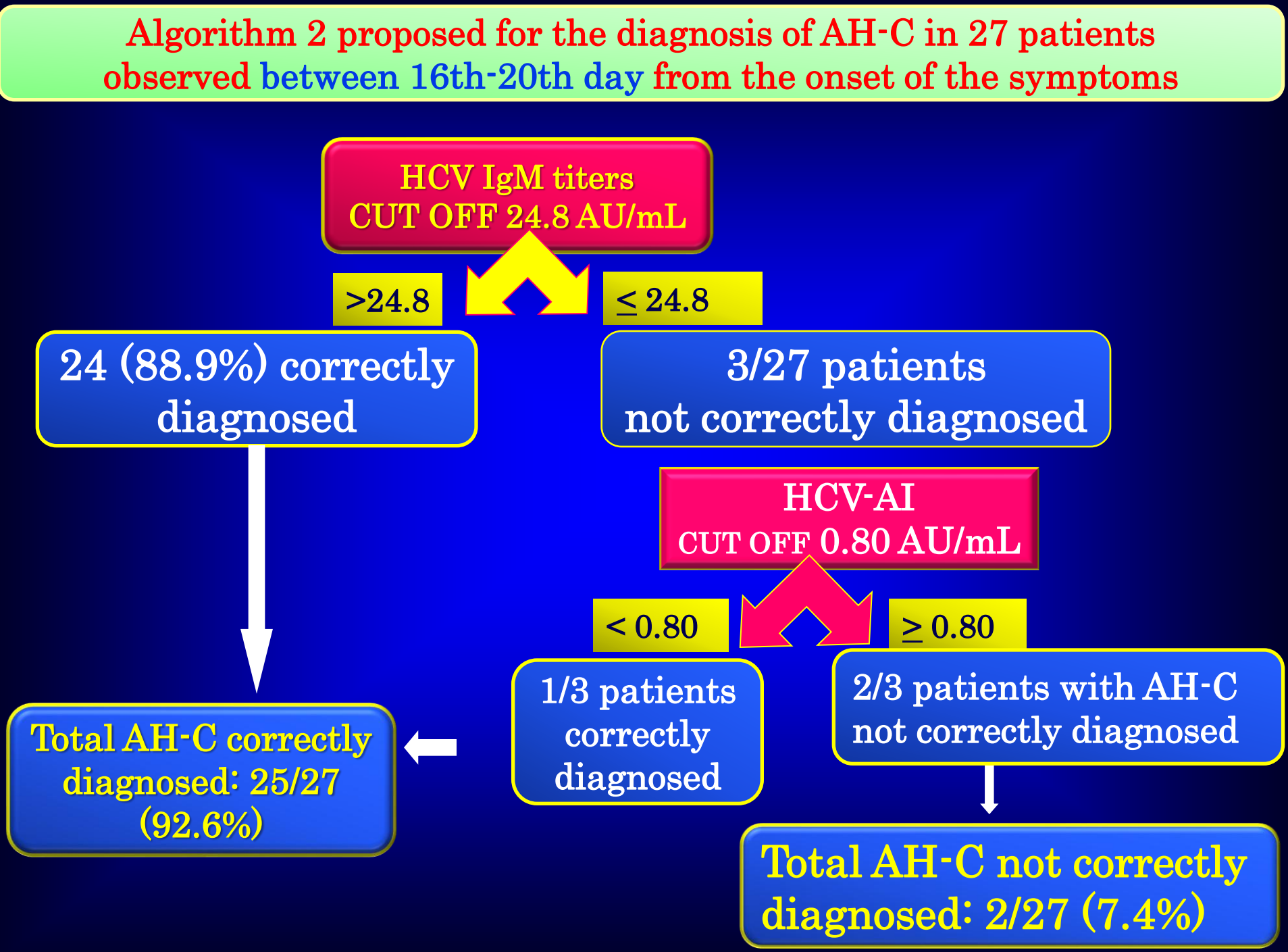
IgM titer



Distribution of patients with AH-C or ae-CH-C according to the results of both HCV-AI and HCV-IgM assays obtained from 16 to 20 days

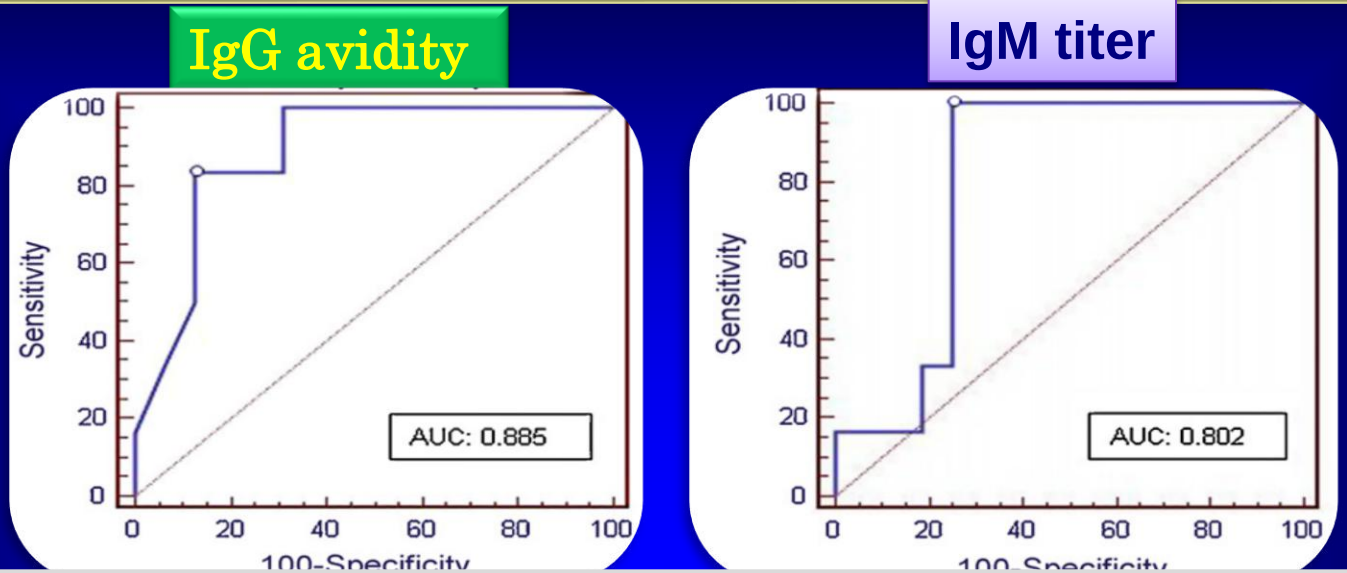


Algorithm 2 proposed for the diagnosis of AH-C in 27 patients observed between 16th-20th day from the onset of the symptoms



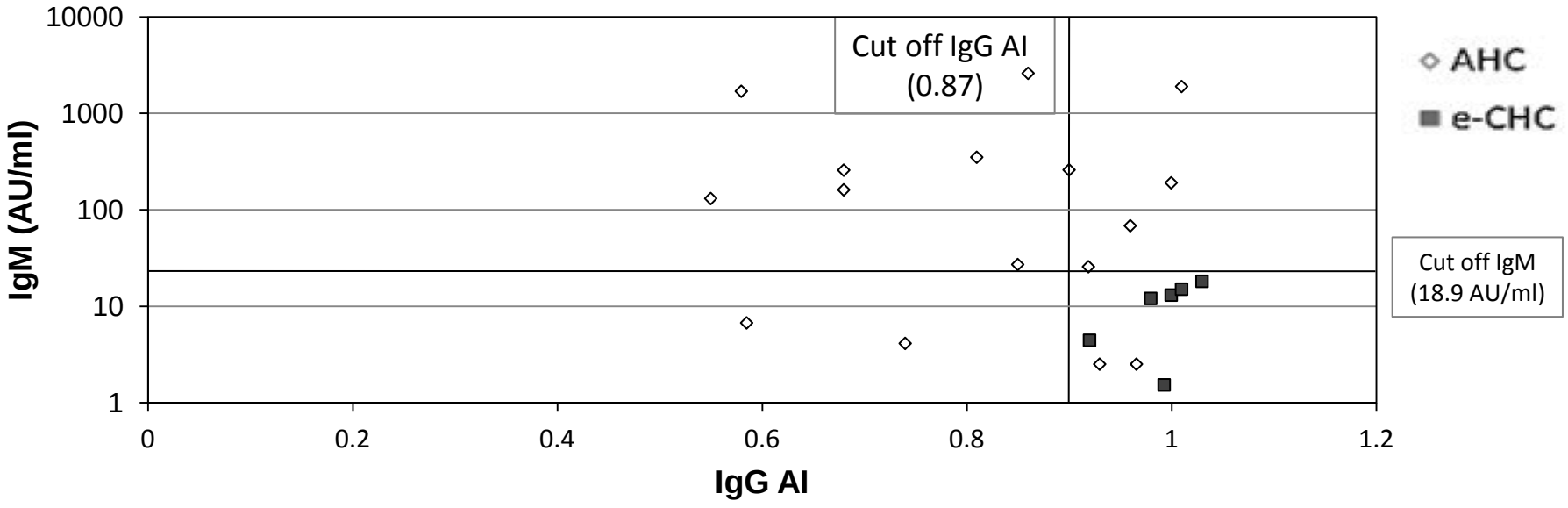
ROC curves and related AUC of the HCV-IgM and HCV-AI assays at different checking points during the course of illness

> 20 days

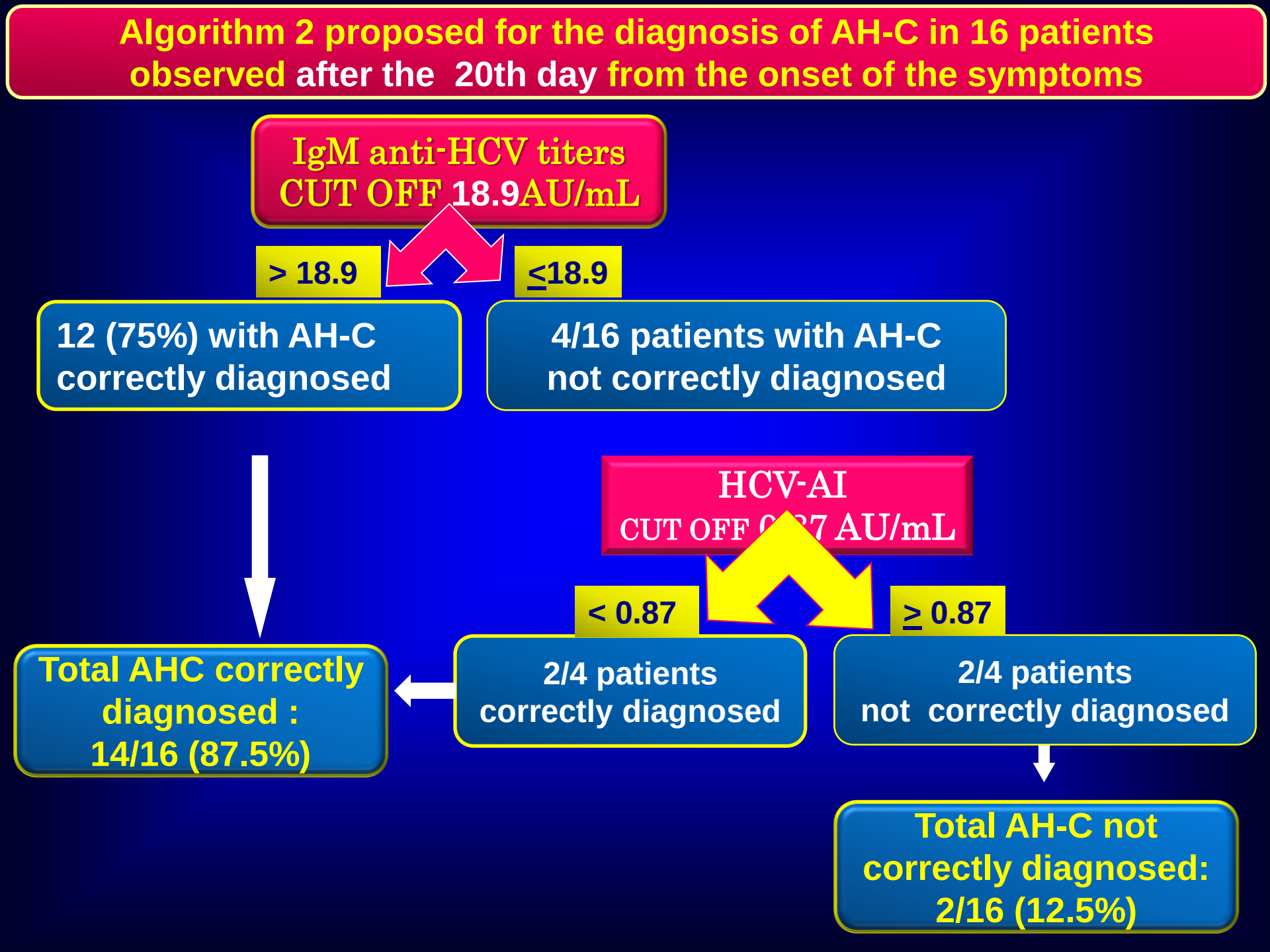


Distribution of each patient with AH-C or ae-CHC according to the results of both HCV-AI and HCV-IgM assays obtained >20 days

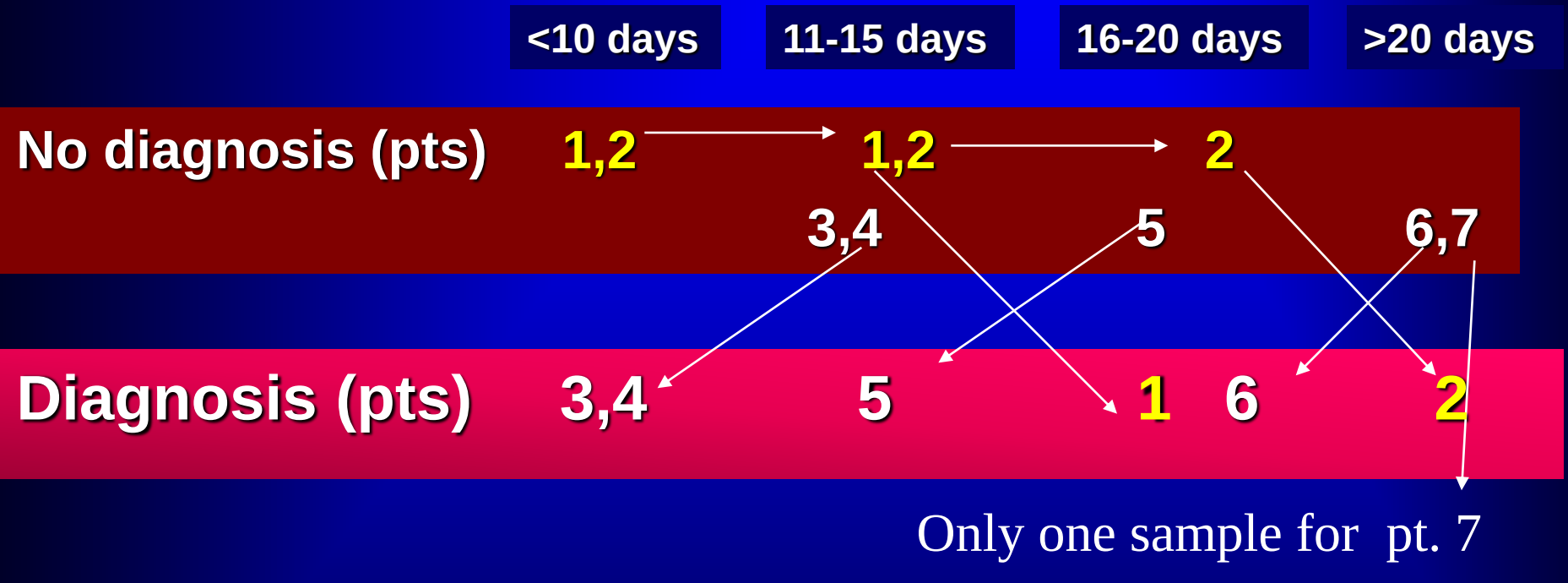
Fig 2 d



Algorithm 2 proposed for the diagnosis of AH-C in 16 patients observed after the 20th day from the onset of the symptoms



7 Patients not correctly diagnosed at different time



Only one sample for pt. 7

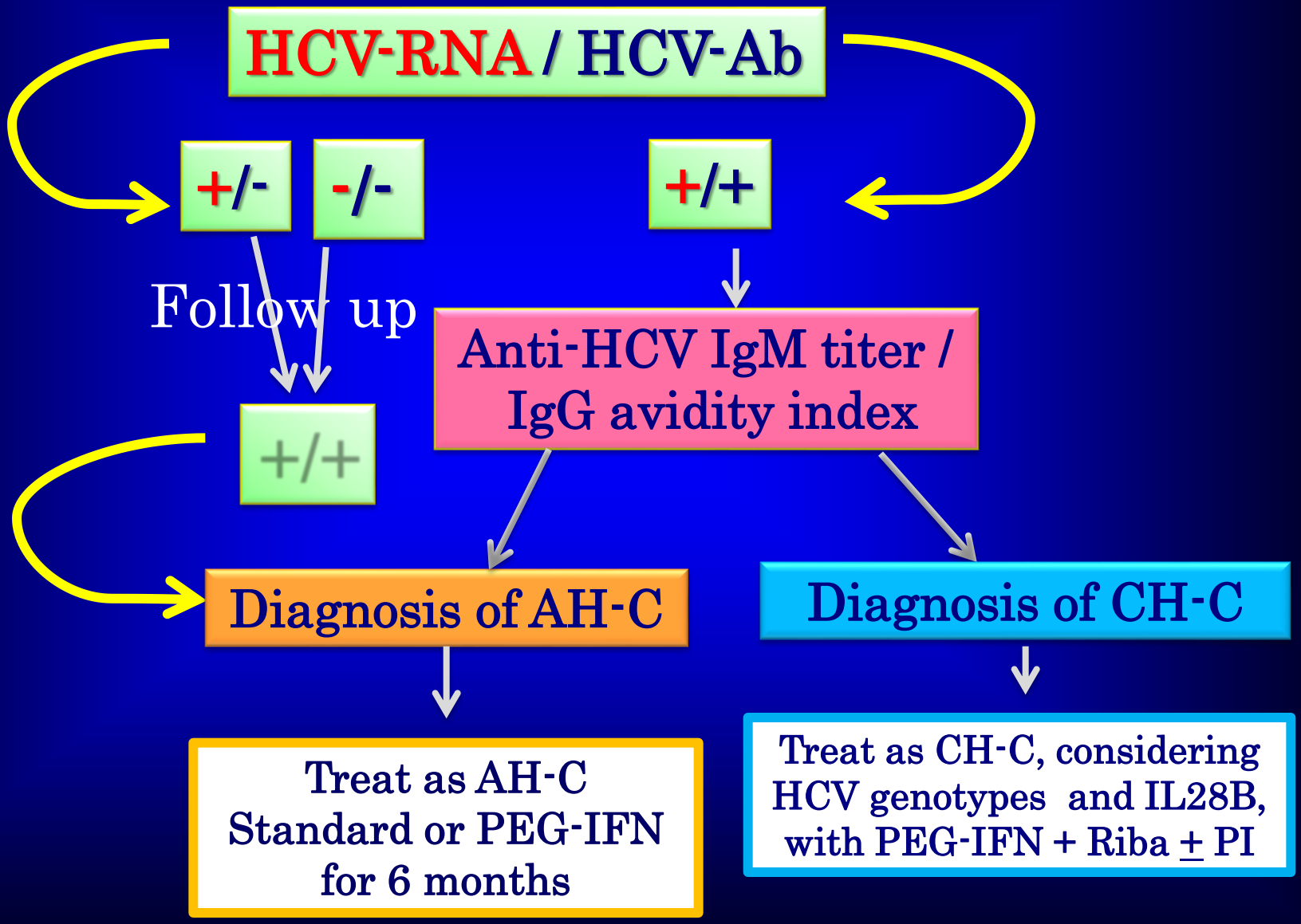
- **Of the 7 patients not correctly diagnosed at one of the 4 selected checking points, 6 were correctly diagnosed at the previous or subsequent checking point**
- **44/45 (97.8%) patients were correctly diagnosed**

Consideration

Our studies demonstrates the possibility to diagnose symptomatic AH-C in nearly 90% of patients with documented seroconversion to anti-HCV positivity by determining IgM titer and IgG avidity index in a single serum sample.

Asymptomatic patients with acute hepatitis C should be identified in anti-HCV negative persons at risk of acquiring HCV infection by periodic controls including physical examination, AMT determination and anti-HCV screening.

Symptomatic/Asymptomatic persons with no sign of advanced liver disease and occasional AMT > 200UI/ml

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