



PATIENTS MET WITH THE
EUROPEAN MEDICINES
AGENCY FOR THE FIRST TIME

16 April 1996

17-May-96 15:43

0171-627 3101

NAM Publications

Keith Alcorn → Rodya Troyke

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NOTES FROM A MEETING BETWEEN THE CPMP OF THE EMEA AND REPRESENTATIVES OF THE EATG.

London - April 16, 1996

Present for the EATG : Keith Alcorn (National AIDS Manual, London), Raffi Babakhanian (Treatment Action Taskforce, London), Arnulfo Gonzalez (director, EATG, Spain), François Houyez (Treatment Committee, ACTUP Paris), Stéphane Korsia (director, EATG; AIDES, Paris), Hans-Josef Linkens (Executive Director, EATG; Deutsche AIDS Hilfe, Berlin).



May/June 1996

EUROPEAN AIDS TREATMENT NEWS

Combination therapies p 32

Interview with Dr. Charles Boucher

European drug regulation p 36

EMEA and EATG

The National AIDS Manual p 47

Community information services

Readers survey 1995 p 49

How readers replied

Vancouver or bust p 52

What to look for, where to act

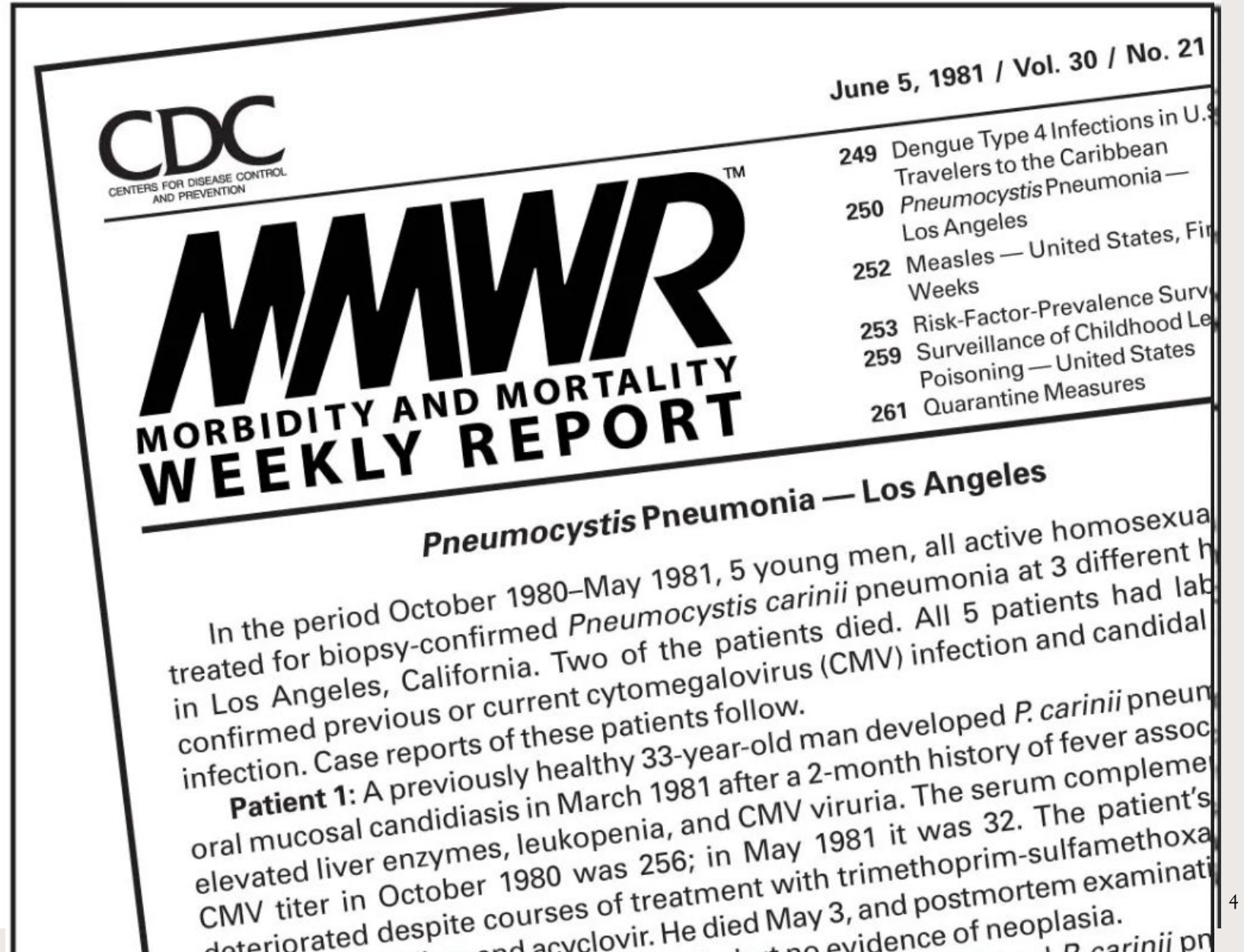
plus: ...News, News, News

Volume 5
Number 3



1981
It all started

FIGURE. *MMWR* report on *Pneumocystis pneumonia* in five previously healthy young men in Los Angeles — June 5, 1981



1983 Denver Principles of Patient Advocacy





1983 HIV
DISCOVERED
BY FRANÇOISE
BARRÉ
SINOUSSE



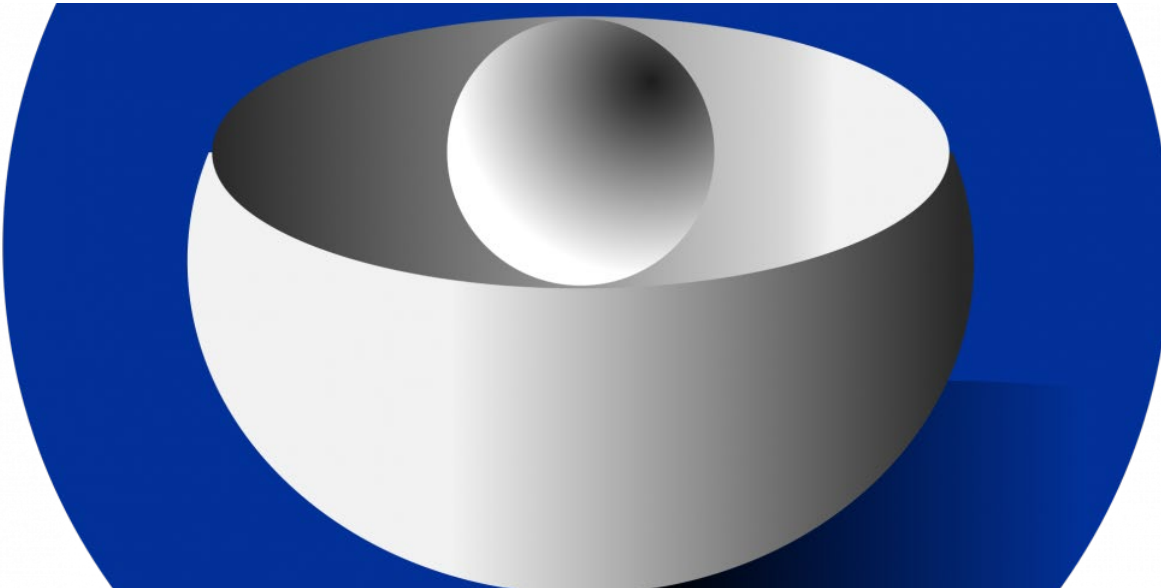
1988
March
on the
FDA

AND THEN CAME HIV VIRAL LOAD

- Polymerase Chain Reaction invented in 1983
- Measure of the number of virus in the blood (per mm³)
 - *First (1994): prognostic factor (million copies, hundreds of thousands, tenths of thousands): the higher the number, the faster you evolved to AIDS / death*
 - *Soon after: does this number decrease with an effective treatment?*
 - *Most clinicians involved in research activities were using it (exploratory phase)*
- 1996: the relation between viral load reduction, treatment, and clinical benefit shown at AIDS CROI conference
- EATG had just commented on EMEA “Points to Consider for the Evaluation of HIV Products”
- Prof Jean-Michel Alexandre took this opportunity to suggest a meeting with CPMP, avoiding a discussion on Norvir® evaluation



*With a high quality
dialogue, patients and
regulators can only agree*



trt5

**GRUPE INTERASSOCIATIF
TRAITEMENTS & RECHERCHE THÉRAPEUTIQUE**



European
AIDS Treatment
Group

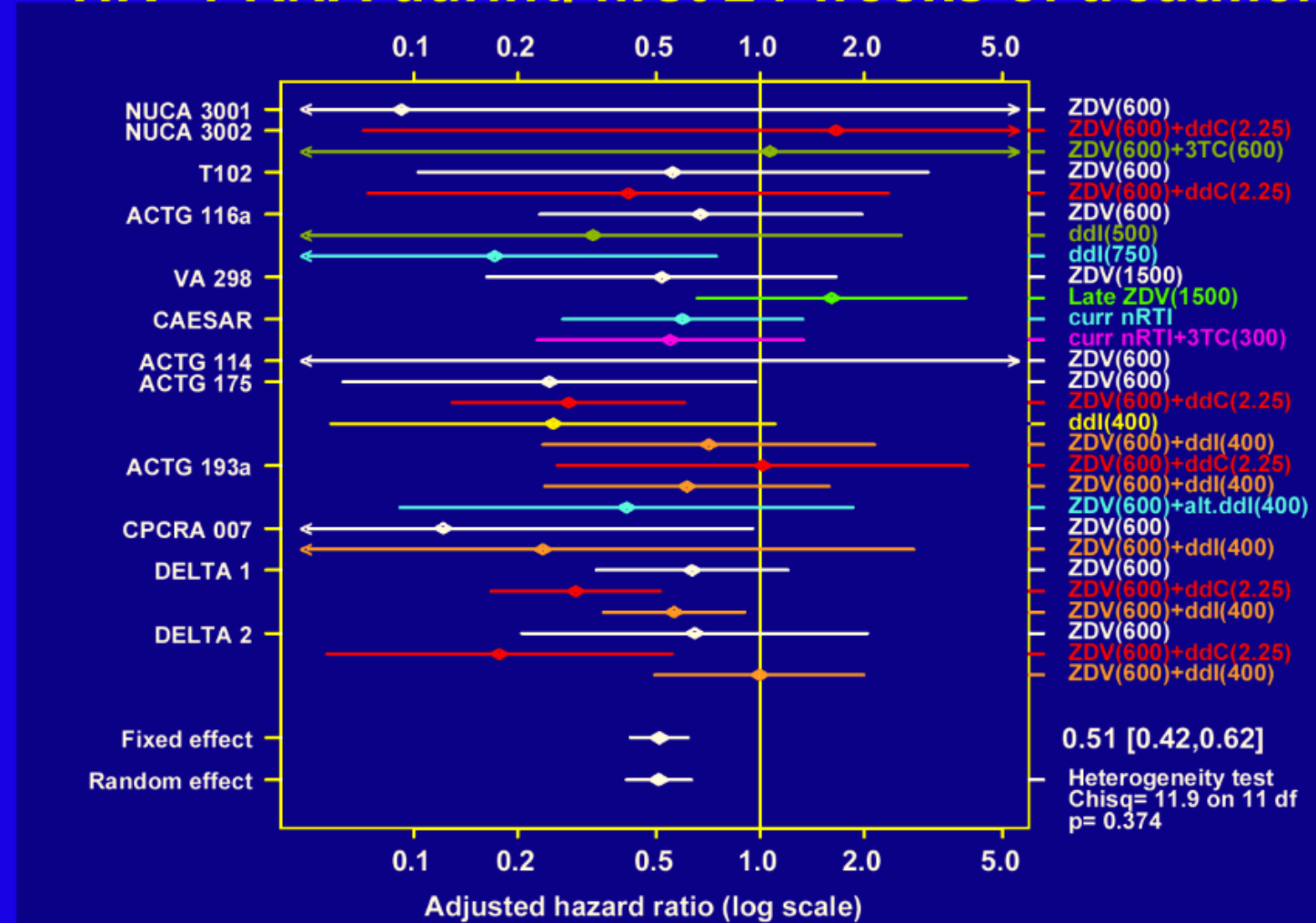
Estimated Hazard Ratio for Progression to AIDS/Death by Treatment (for each 1 log₁₀ reduction in HIV-1 RNA during first 24 weeks of treatment)

HSMCG Meta-Analysis

- All 16 trials with HIV-1 RNA measured and involving one class of drugs (NRTIs)
- Markers: Change in HIV-1 RNA and CD4 cell count over 24 weeks
- **Clinical endpoint: Progression to AIDS/death over 2 years**

- 13,045 patients
- 3369 (26%) developed AIDS or died
- 3,146 patients with HIV-1 RNA measurements (often done retrospectively using stored specimens)

[ref: HSMCG. Aids Research and Human Retroviruses, 2000]



IMPACT ON CPMP MEMBERS

- Diverging views among them
 - Chair: *“CPMP members are determined to row together, but maybe not to the same shore. Difficulty is validation. There is no consensus on that point among CPMP members”, our credibility is at stake*
 - *Some willing to approve products based on viral load (“under exceptional circumstances”)*
 - *“Points to Consider” not binding enough. Not clear enough on the use of viral load for regulatory purposes, industry lacking guidance*
- FDA, 14 July 1997: Public Hearing on the role of HIV RNA as surrogate marker
- EATG took part and advised EMEA for its own scientific workshop
- 1997: Points to Consider amended, with the use of HIV RNA as surrogate marker
- 1999: second FDA workshop on the validation of HIV viral load (always a dynamic process)

EPILOGUE

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EMA organised a scientific workshop in September 1997 and changed the evaluation guidelines. Duration of clinical trials for HIV dropped from **156-208 weeks (3-4 years) to 16-24 weeks (4-6 months)**

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London - April 16, 1996

Viracept®: 1st HIV product approved with no mortality or new AIDS cases data (January 1998)

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Abacavir

Glaxo Wellcome

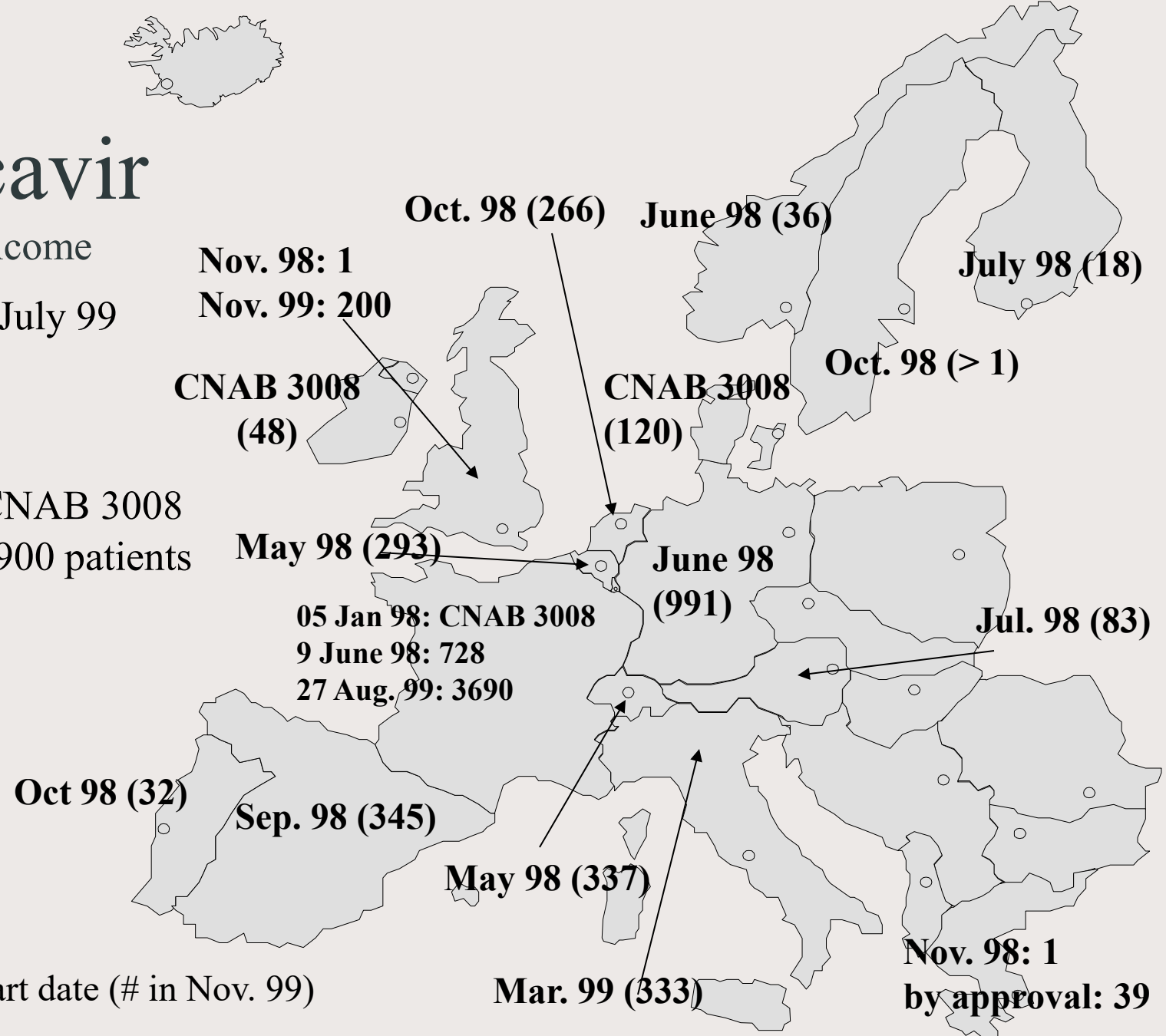
EU approval: July 99

USA

Summer 97: CNAB 3008

March 98: EAP 1900 patients

MM YY (n): start date (# in Nov. 99)



THANK YOU!