Public hearings

François Houÿez, 21 March 2012

Patients' interest for

PUBLIC HEARINGS ON MEDICINES IN EUROPE

Our expectations

Greater involvement of the public, moving away from comitology

Better understanding of regulatory decisions

(public explanation of an already made decision)

Participation in decision making by providing different insight (e.g. regulating access via the indication)

Selected own experience with public hearings @ FDA

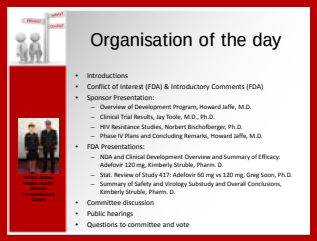
- 29 February 1996, Norvir®
- 14 July 1997, HIV RNA surrogate marker
- 1 November 1999, adefovir dipivoxil

Public contributions

Individual	Opinion	Interest disclosure	As	Contribution
Dr Burchett	In favour	Support for travel	Treating physician	10 children in EAP, 1 Fanconi syndrome
Dr Jones	In favour	Support for travel	Treating physician	24 adults in EAP, 4 stopped for nephrotoxicity
Dr Cimoch	In favour	Support for travel	Treating physician, researcher	55 adults in EAP, 2 stopped for severe nephrotoxicity
Dr Farthing	In favour	Support for travel, investigator and advisory board	Treating physician	130 adults in EAP, nephrotoxicity manageable
Dr Grossman	In favour	Support for travel, investigator	Treating physician	56 adults in EAP, nephrotoxicity = main reason to stop
Dr Hardy	In favour	Investigator	Treating physician, researcher	85 adults in EAP, 52 in CT. 1 Fanconi syndrome
Dr Margolis	In favour	Support for travel	Treating physician	82 adults in EAP, 5 with moderate renal toxicity
Dr McGowan	In favour	Support for travel	Treating physician	68 adults in EAP
Peter Hale	In favour	Undisclosed	Patient	Own experience with drug
William Bahlmann	In favour	Support for travel	Patient group	Let people have the choice
Max Delgato	In favour	Support for travel	Patient	Own experience
Timothy Christy	In favour	Support for travel	Patient	Own experience
Hosam Chreim	In favour	Support for travel	Patient	Own experience
Amy Sullivan	In favour	Support for travel	Investigator	27 in EAP
François Houÿez	against	Support for travel	Patient group	Unanimous vote in EATG membership
Michael Marco	against	none	Patient group	Statement explaining why
Jules Levin	Decided not to talk			

Lessons learned

- Opening the debates to the public brings in new issues
- Access issues may depend on the scientific committee's opinion (indication). Such issues are valid
- Being open to discuss them is a proof of mind-openness from scientific committees
- Yes, the contribution of the "public" during public hearing can have an impact
- Almost all speakers at the public hearing had received a grant from the applicant and were in favour of a positive opinion
- Presence of the company puts some pressure on the public
- The sequence applicant / FDA / committee discussion was very fruitful to realise there is no black/white situation
- The questions to committee were very useful to organise the day, to follow the logic of the discussions and the thinking


Organisation of the day

- Introductions
- Conflict of Interest (FDA) & Introductory Comments (FDA)
- Sponsor Presentation:
  - Overview of Development Program, Howard Jaffe, M.D.
  - Clinical Trial Results, Jay Tooke, M.D., Ph.D.
  - HIV Resistance Studies, Norbert Bischofberger, Ph.D.
  - Phase IV Plans and Concluding Remarks, Howard Jaffe, M.D.
- FDA Presentations:
  - NDA and Clinical Development Overview and Summary of Efficacy: Adefovir 120 mg, Kimberly Struble, Pharm. D.
  - Stat. Review of Study 417: Adefovir 60 mg vs 120 mg, Greg Soon, Ph.D.
  - Summary of Safety and Virology Substudy and Overall Conclusions, Kimberly Struble, Pharm. D.
- Committee discussion
- Public hearings
- Questions to committee and vote

Public hearings @ FDA

Pros

- Thesis, anti-thesis, discussion: well structured
- Agenda and questions: discussions remain focused
- Chairmanship: to the point
- 8.30 am to 5.30 pm: 7 hours
- Public can opt to keep silent or to make an address
- Public invited to talk only after case duly presented
- Public contributions can make a difference

Contras

- Public can diverge from the agenda
- Series of "own experience" by people invited by applicant who don't add much
- Pressure on the committee from the audience
- A quarter to half of the audience: stock analysts
- Applicant on stage

Decision based on evidences, but not made by robots

If I could speak for the committee, and please feel free to interrupt if you disagree, although I think there was split opinion on question one, I think the consensus of the committee is that there truly is something here with this drug; that the desire of this committee was to actually believe that there were efficacy data there and to see the data in a fashion that one could feel absolutely comfortable with....

... I see the issue here coming in with clear-cut demonstration of 60 mg efficacy data that the agency and the sponsor can agree on, such that if it comes before this committee again we have a clearer focus that there is something there. Some of us tried to see it but it was not fully clear to us.

IN EUROPE

For which cases?

Appeal procedure

- When case not clearly closed, impression of missed opportunity
- Risk of not authorising a yet effective product

High expectations from patients

- Unmet medical need but inconclusive evidence or safety issue
- New signal identified, important confirmatory studies or risk minimisation measures

Public concern

- Is [product] really as safe as they say?
- Discrepancy between actual risk and public fear
- Major media interest but controversial coverage

Divergence EMA / other agencies

- Within EU
- Across the world

Divergence EMA / HTA

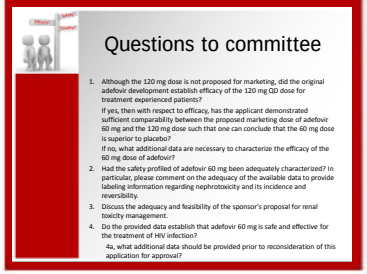
- Things can turn sour, from a political point of view, when that scenario happens, when the regulators say “yes this drug is safe and effective” and the payers say “Oh well but we won’t reimburse it”.

Who?

The « inquirers »	The « judges »	The « witnesses »	The « defendant »
Rapporteurs and/or EMA scientific staff Explain issues Counter-analysis	10-15 experts e.g. SAG & external experts	The public Patients Consumers Media Healthcare professionals	e.g. pharma. company, research institution, medical journal…

How?

- Not just safety
  - Expected benefits come in the discussion
  - E.g. Thalidomide victims/MM patients/ Peter Wijermans
- Public hearings
  - Public hearings: open to all <u>but</u>
    - Contributions should add something to the discussion
    - speakers during public phase could send written contribution ahead of the meeting (“filter”)
  - Meeting should be opened with a clear and understandable list of questions written to be understood by lay people (see questions to committee)
  - A “main thread” (fil conducteur) would be useful to guide the discussions

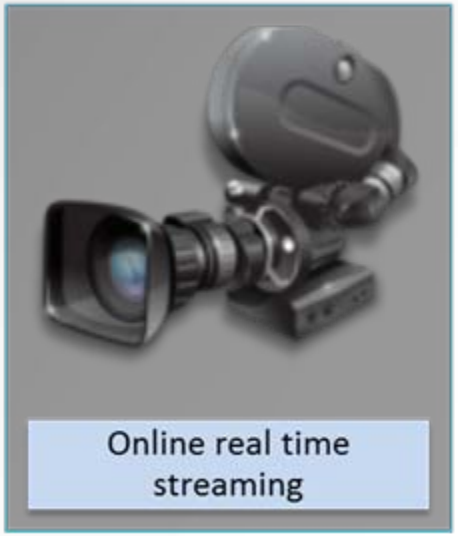

Questions to committee

1. Although the 120 mg dose is not proposed for marketing, did the original adefovir development establish efficacy of the 120 mg QD dose for treatment experienced patients?
   If yes, then with respect to efficacy, has the applicant demonstrated sufficient comparability between the proposed marketing dose of adefovir 60 mg and the 120 mg dose such that one can conclude that the 60 mg dose is superior to placebo?
   If no, what additional data are necessary to characterize the efficacy of the 60 mg dose of adefovir?
2. Had the safety profiled of adefovir 60 mg been adequately characterized? In particular, please comment on the adequacy of the available data to provide labeling information regarding nephrotoxicity and its incidence and reversibility.
3. Discuss the adequacy and feasibility of the sponsor's proposal for renal toxicity management.
4. Do the provided data establish that adefovir 60 mg is safe and effective for the treatment of HIV infection?
   4a, what additional data should be provided prior to reconsideration of this application for approval?

Ideas

Half presentations/ half discussions

Allow participants / questions from home



Online real time streaming

Decision / recommendation at the end of each meeting

The EU “touch”

Wherever the meeting takes place

- Have the EU flag + EMA flag/logo in the room
- The chair, or the co-chair should be from a different MS than the host country
- The introduction should make it clear this is a European meeting

Views in these slides are presenter's own views.
The presenter is currently working for the European Organisation for Rare Diseases (Eurordis), however his experience with FDA public hearings are anterior.