Regulatory process to involve patients in discussion on CT endpoints

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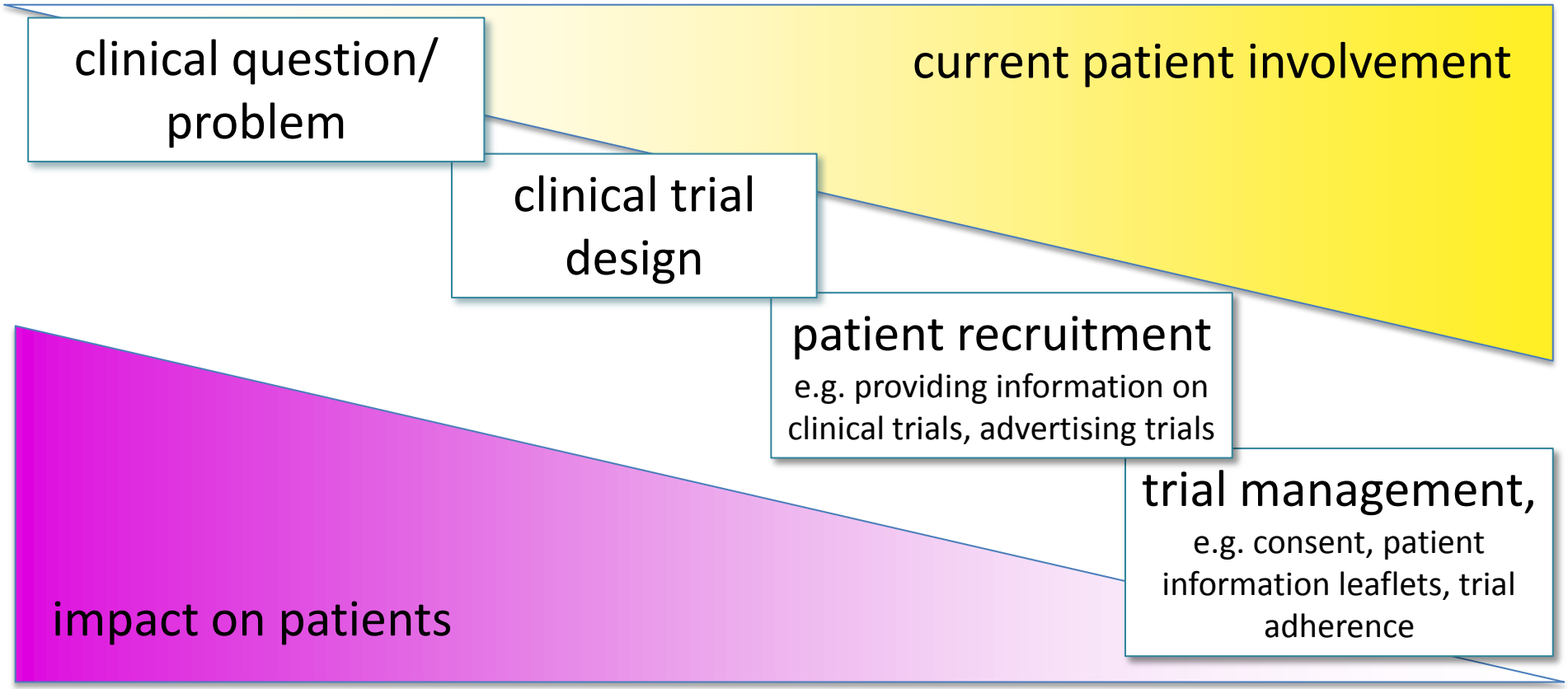
Bettina Ryll, MD/PhD, Melanoma Patient Network Europe, MPNE
EORTC patient course 2014

Where to get involved?

[in clinical trials]



doing the right thing ⟷ doing things right

What can patients add to the methodology?

Endpoint	Regulatory Evidence	Advantages	Disadvantages
OS **OS**	Clinical benefit for regular approval	•Universally accepted •Direct measure of benefit •Easily measured •Precisely measured	•Larger studies •May be affected by crossover therapy and sequential therapy •Includes non-cancer deaths
PROs **PROs**	Clinical benefit for regular approval	•Patient perspective of direct clinical benefit	• Blinding is often difficult •Data are frequently missing or incomplete •Clinical significance of small changes is unknown •Multiple analyses •Lack of validated instruments
DFS **DFS**	Surrogate for accelerated approval or regular approval*	• Smaller sample size and shorter follow-up necessary compared with survival studies	• Not statistically validated as surrogate for survival in all settings •Not precisely measured; subject to assessment bias, particularly in open-label studies •Definitions vary among studies
ORR	Surrogate for accelerated approval or regular approval*	• Can be assessed in single-arm studies •Assessed earlier and in smaller studies compared with survival studies •Effect attributable to drug, not natural history	Not a direct measure of benefit •Not a comprehensive measure of drug activity •Only a su of patients who benefit
CR **CR**	Surrogate for accelerated approval or regular approval*	• Can be assessed in single-arm studies •Durable complete responses can represent clinical benefit •Assessed earlier and in smaller studies compared with survival studies	Not a direct measure of benefit in all cases •Not a comprehensive measure of drug activity •Small subset of patients with benefit
PFS or TTP **PFS**	Surrogate for accelerated approval or regular approval*	•Smaller sample size and shorter follow-up necessary compared with survival studies •Measurement of stable disease included •Not affected by crossover or subsequent therapies •Generally based on objective and quantitative assessment	•Not statistically validated as surrogate for survival in all settings •Not precisely measured; subject to assessment bias particularly in open-label studies •Definitions vary among studies •Frequent radiological or other assessments •Involves balanced timing of assessments among treatment arms

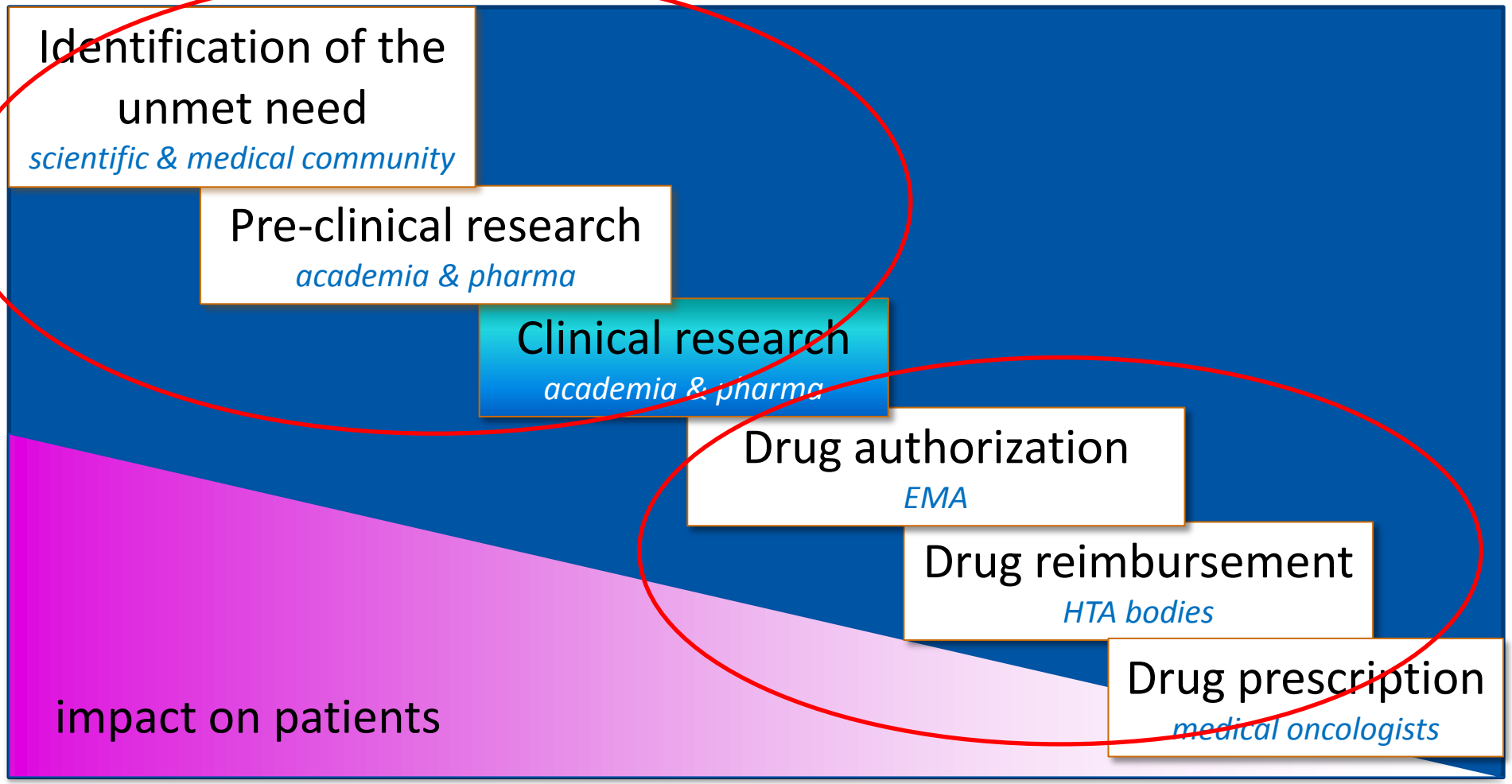
What 4 months is worth?

Direct patient perspective

Surrogate endpoints

+ PROs?

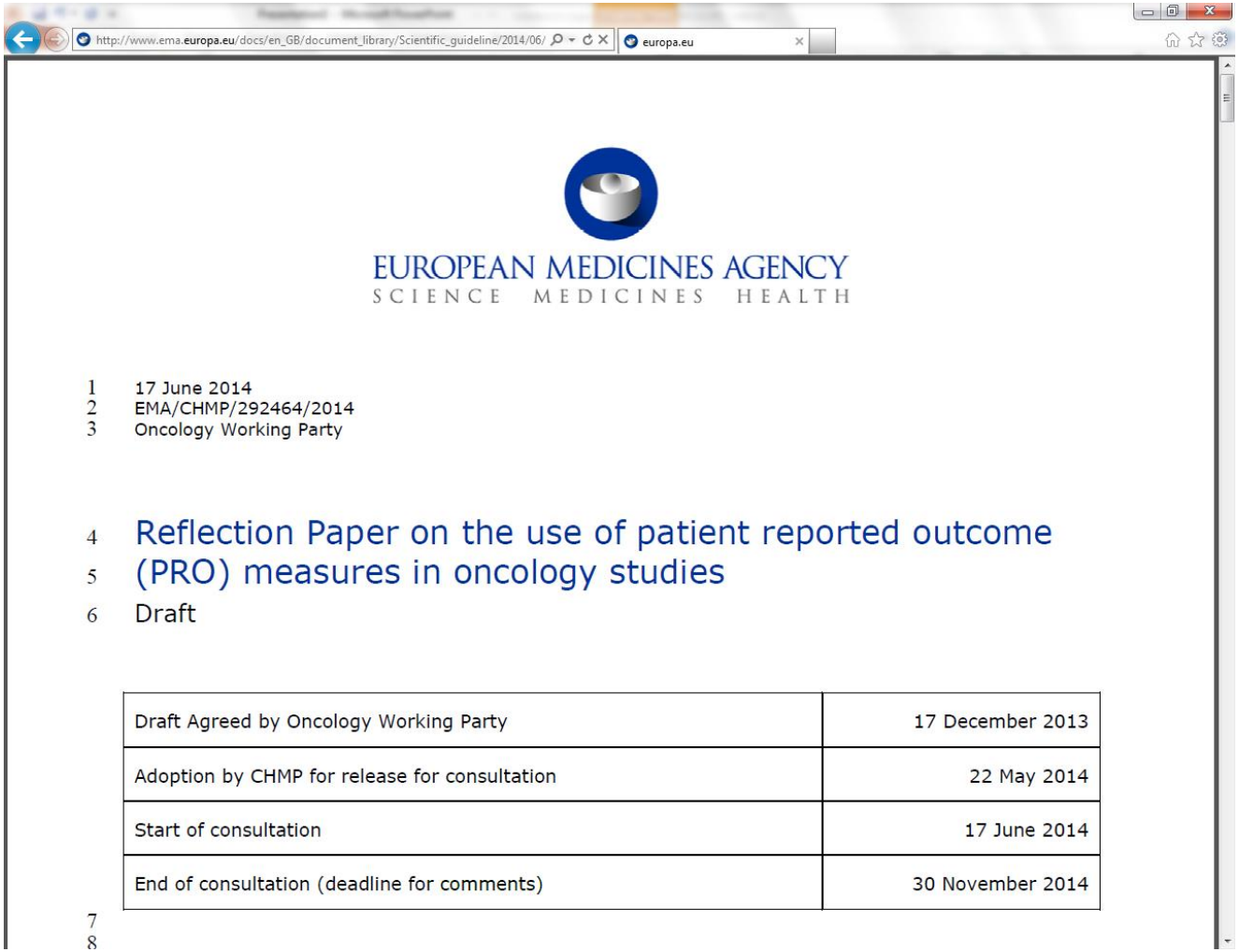
Where to get involved? [drug development]



Patients and consumers involvement within EMA

- Patient organisations are represented within:
  - some of EMA scientific committees
  - EMA management board
- Patients also:
  - take part in scientific advisory groups;
  - respond to specific requests from the Agency's committees and working parties;
  - reviewing information on medicines prepared by the Agency;
  - are being involved in the preparation of guidelines;
  - regularly take part in Agency conferences and workshops.

Currently under consultation



http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/06/ europa.eu

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 June 2014
EMA/CHMP/292464/2014
Oncology Working Party

Reflection Paper on the use of patient reported outcome (PRO) measures in oncology studies

Draft

Draft Agreed by Oncology Working Party	17 December 2013
Adoption by CHMP for release for consultation	22 May 2014
Start of consultation	17 June 2014
End of consultation (deadline for comments)	30 November 2014

Patient involvement with HTA

EPF survey conclusions (2013):

- **HTA agencies:** very few HTA agencies currently involve and integrate patients' perspectives in their work; the question of the exact stage of HTA where patient engagement is needed or is most useful is still being debated though the need to improve patient involvement is recognized.
- **HTA appraisal committees and decision makers:** the bodies or institutions in charge of decision making on health technologies admit not to always do it. And often when there is some form of patient involvement this is not done in a systematic, comprehensive and meaningful way.
- **Patient organisations :** patient organisations are poorly or not involved in both aspects of HTA and decision-making.

Patient involvement in clinical trials

- Clinical trials regulation requires inclusion of lay persons & in particular patient representatives in the review panel
  - Finalised trial review
  - Comments rather than through involvement
  - Too late in the process

Earlier involvement is essential

Patient early involvement in clinical research

- Cultural differences within EU -> different “services” available
  - UK PPI:
    - commenting on research proposals/applications
    - as co-applicants on a research project
    - involvement in identifying research priorities
    - helping inform the design of data collection tools (piloting a questionnaire)
    - as members of a project advisory or steering group
    - commenting and developing patient information leaflets
  - FR cancer league panel:
    - patient information review
    - newsletter
  - ES, PL -> little involvement

Patient involvement within EORTC

- co-organisation of events & exchange of speakers
- coordinated policy actions & common position statements
- review of patient information
  - english template: all EORTC led trials
  - nationally adapted versions: all UK & FR + case by case
- members of executive project boards or steering group e.g SPECTA
- member of EORTC IRB
- support development & validation of PRO measure tools
- attend [some] group meetings
- bringing new research questions to EORTC

Some perceived challenges

- Is patient view representative of the community?
  - expert patients vs “naïf” patients
- Is it [not] biased by industry influence?
- What type of evidence patients can provide?
- Which instruments to use?
- What is the value of individual patient stories?
- Measuring facts *versus* sharing emotions
- ….

Barriers to optimal patient involvement

- getting an interface between organizations with benevolent members with heterogeneous background
  &
  heavily regulated highly professionalized clinical research environment
- lack of funding and infrastructure
- accusations of non-independency *vis-à-vis* of industry
- lack of training
  - EUPATI
  - EORTC patient course
  - …

Future needs and perspectives

- Generalize patient involvement at all stages
- Establish/clarify rules of engagement with patients
- Clarify the scope of public-private partnership
- Further support patient organization's infrastructure
- Develop and maintain appropriate training tools
  - for patient organisations and patients willing to engage
  - for academia & industry on rules and mechanisms of engagement

TAKE HOME MESSAGE

..I now have a different sense of what in life is really important…

We took up hiking about a year after my husband was diagnosed with metastatic prostate cancer in October 2003. ... During the past three years, we have climbed some of the most challenging mountains in the White Mountains. ...

…This experience has changed my perception of things…

You would never think it's important until you experience this yourself