EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Scientific Advisory Groups (SAG)

Experience and impact of patient involvement

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Training session for patients and consumers involved in EMA activities
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“Our expectations”

EUROPEAN MEDICINES AGENCY

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)

‘Permanent’ patient representatives on some EMA committees but not CHMP

Modified from François Houÿez

When to convene a SAG?

- Expected major public health interest where public controversy might be expected (e.g.: first-in-class)
- Substantial disagreement between rapporteurs on clinical aspects
- Controversial issues (e.g., high impact on health care professionals, the public and other stakeholders)
- Complex technical aspects, rare diseases
- Risk minimisation measures affecting the clinical practice
- Design and feasibility of a clinical trial
- Major post-authorisation safety issues

Procedural Advice for CHMP on the need to convene a Scientific Advisory Group (SAG) or *Ad Hoc* Expert Meeting (EMA/CHMP/551508/2010)

Typical Questions for SAG (Oncology)

- Benefit-risk negative or marginally positive
- Clinical meaningfulness of benefits
- Clinical impact of risks
- Need for further studies
- Biologic rationale to support findings
- Guidelines

Company – CHMP – SAG Communication

CHMP

SAG

Company

Company presents (open part of SAG meeting)

Scientific Advisory Groups (EMA/CHMP) vs. Advisory Committees (US FDA)

- Many similarities
  - overall concept, structure, experts
- Key differences

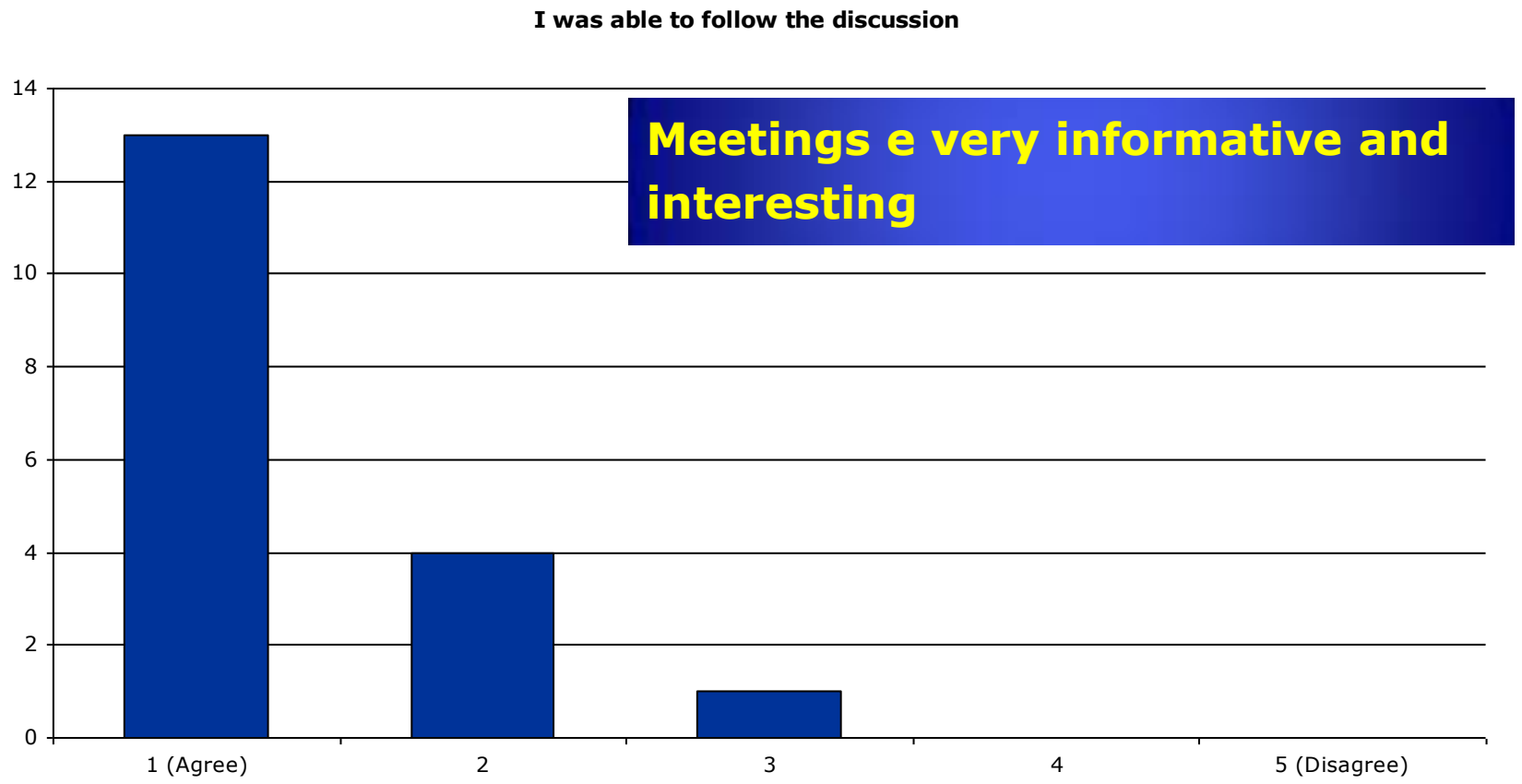
FDA: public meetings (recorded, transcript, media)	EMA: not public (but reflected in EPAR)
FDA: generally longer timelines (sponsors' backgrounder submitted 48 days prior meeting)	EMA: more flexible (min. 2 weeks notice)

Patient representatives involvement in SAGs

- Statistics for 2013
  - 18/22 (82%) SAG meetings had one or two patient representatives
- Some myths
  - Patients contribution will have little impact
  - Discussion too technical for patients to contribute

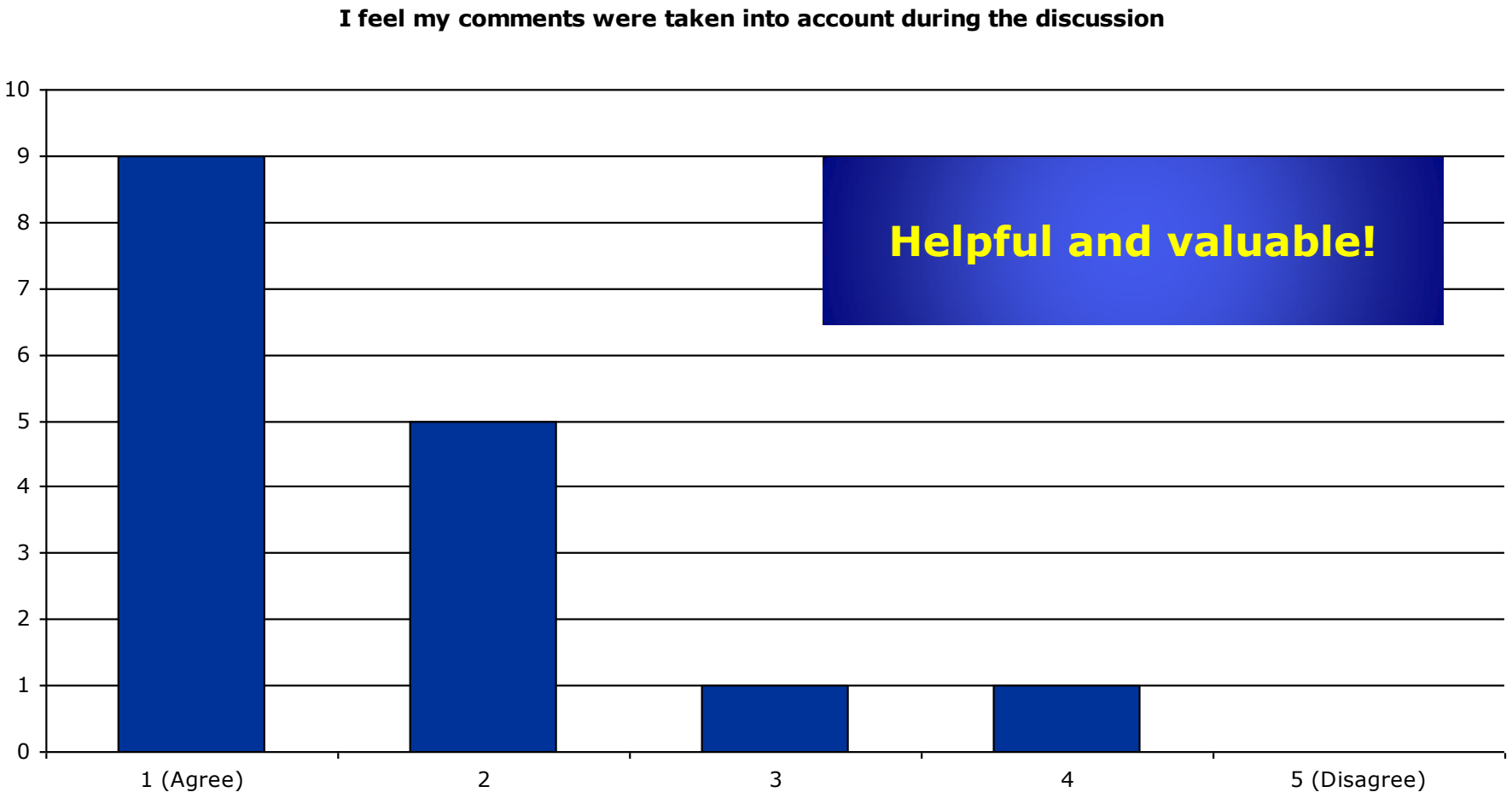
➢ 2011 Survey

Are patients able to follow the discussion?



7 EMA (2011) Outcome report on pilot phase for participation of patient representatives in Scientific Advisory Group (SAG) meetings.

Are patients' views taken into account?



8 EMA (2011) Outcome report on pilot phase for participation of patient representatives in Scientific Advisory Group (SAG) meetings.

Chairpersons and rapporteurs

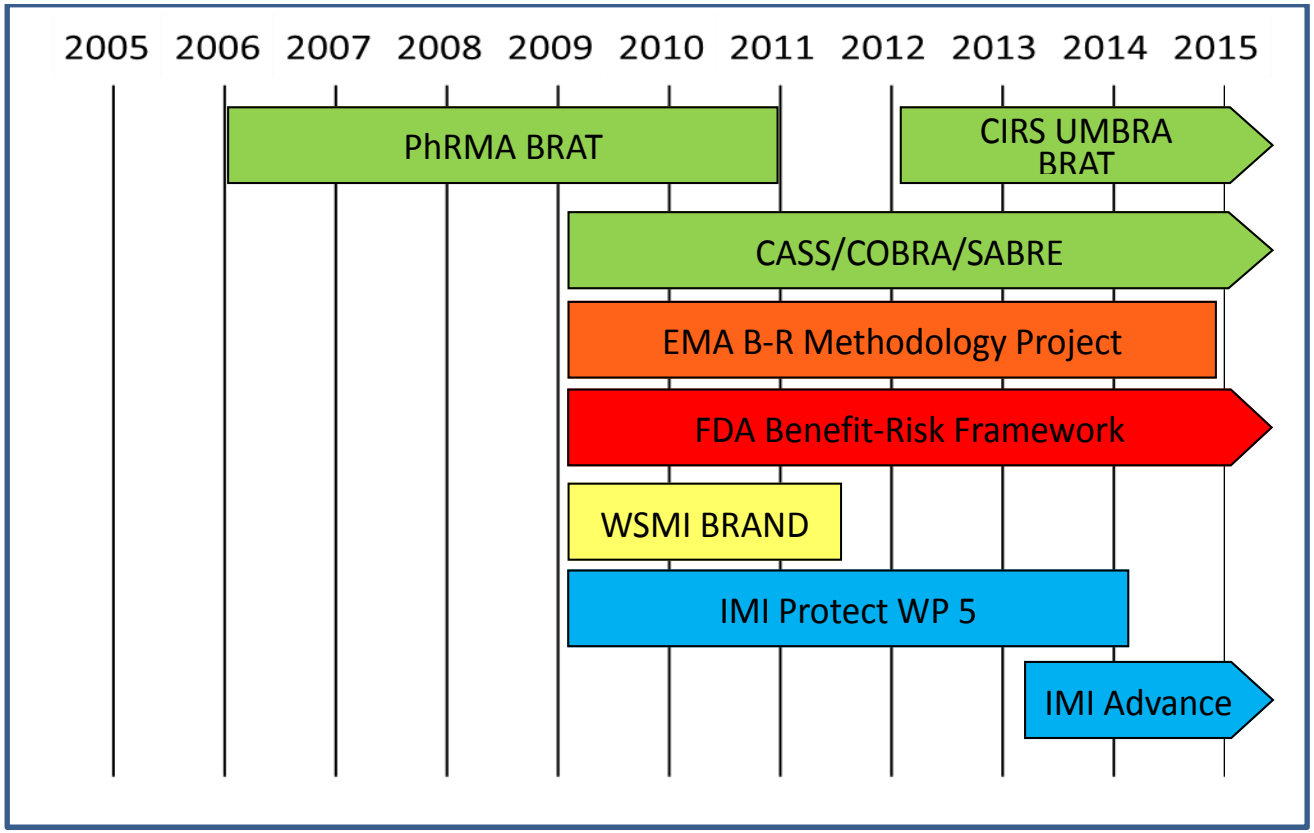
The overall impression is that the **patient contribution is variable**, and can depend on the type of questions addressed during the SAG and on the individual patient who attended;

On the whole, the assessment of contribution ranged from being beneficial (able to obtain patient views with **an actual impact on the outcome**) to having no actual impact;

In all cases **patients were well integrated in the dynamic of the SAGs** and the meetings ran smoothly.

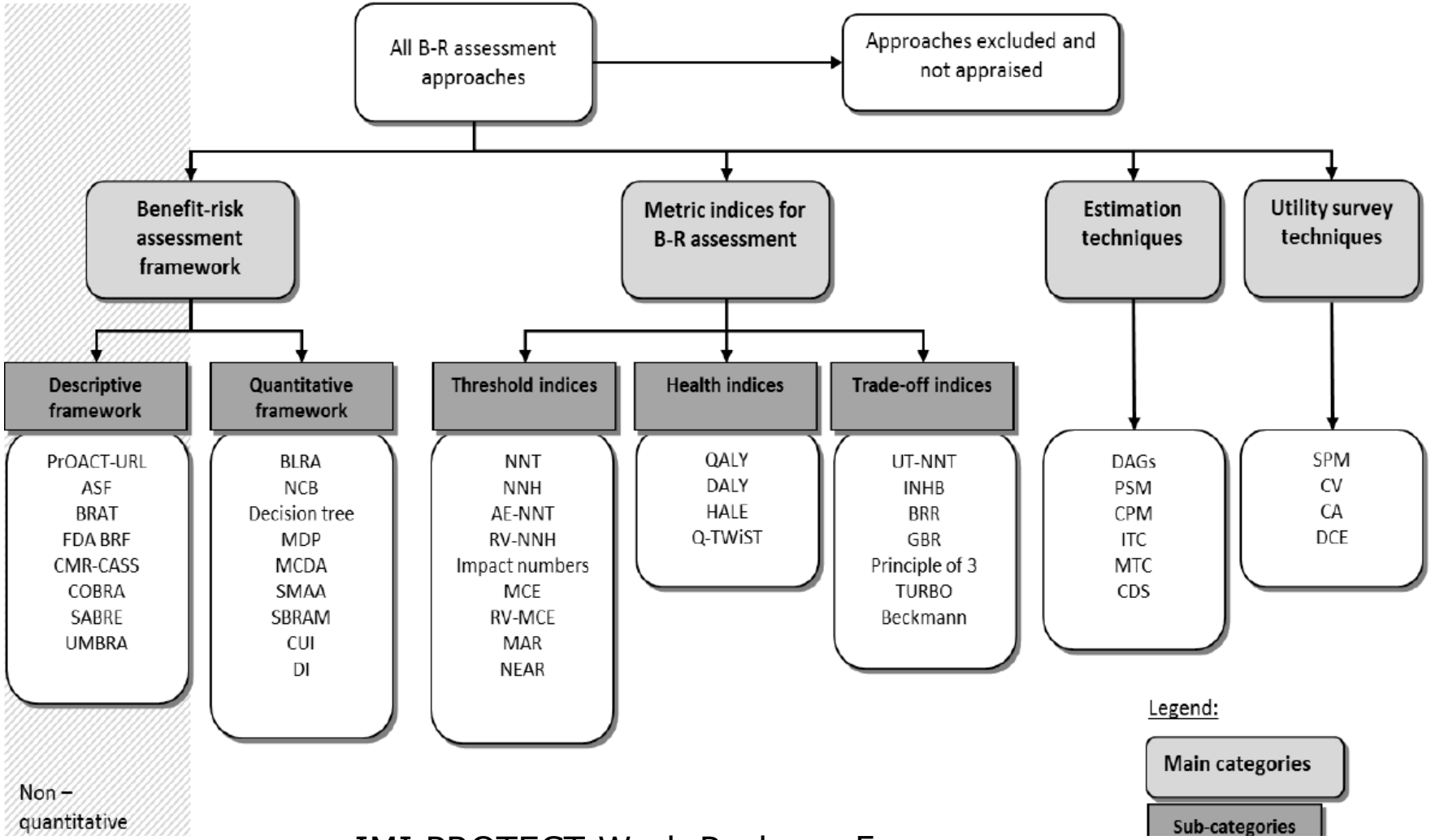
EMA (2011) Outcome report on pilot phase for participation of patient representatives in Scientific Advisory Group (SAG) meetings.

Historical perspective on benefit-risk initiatives



(Modified from M. Ouwens *et al., ESFPI/PSI Benefit-Risk Special Interest Group* meeting 2013.) Abbreviations: CMR, Centre for Medicines Research International Institute for Regulatory Science; CIRS, Centre for Innovation in Regulatory Science; UMBRA, Unified Methodologies for Benefit-Risk Assessment; EMA, European Medicines Agency; CASS Taskforce of representatives from Health Canada, Australia's Therapeutic Goods Administration, Swissmedic and the Singapore Health Science Authority; COBRA, Consortium on Benefit-Risk Assessment; PhRMA BRAT: Pharmaceutical Research and Manufacturers of America Benefit-Risk Action Team; BRAND, Benefit-Risk Assessment for Nonprescription Drugs; IMI PROTECT, Innovative Medicine Initiative "Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium"; Advance, "Accelerated development of vaccine benefit-risk collaboration in Europe".

Benefit-risk assessment toolkit



Different views about quantitative methods

Against	In favour
Require more effort	Easy to update
Does not reflect mental process	Intuition can lead to error and bias
Highly subjective	No more subjective than any other decision-making strategy Subjectivity is handled explicitly
"Black box"	Easily understood, transparent
High precision is unattainable	Uncertainty can be managed explicitly
Oversimplification ("single number")	A single number summary is an abuse of the model
Whose values? The authority of the decision-makers will be questioned	Impact of different inputs (e.g., from patients) can be explored. Regulator's decisions can be scrutinised.

MCDA to elicit stakeholder's preferences based on regulators' assessment

EMA workshop with PCWP and HCPWP (26 February 2014)

Separate, parallel exercise with patient jury and healthcare professionals jury

Two hours to build 2 models using MCDA (MACBETH - Measuring Attractiveness by a Categorical Based Evaluation Technique)

Hypothetical example:

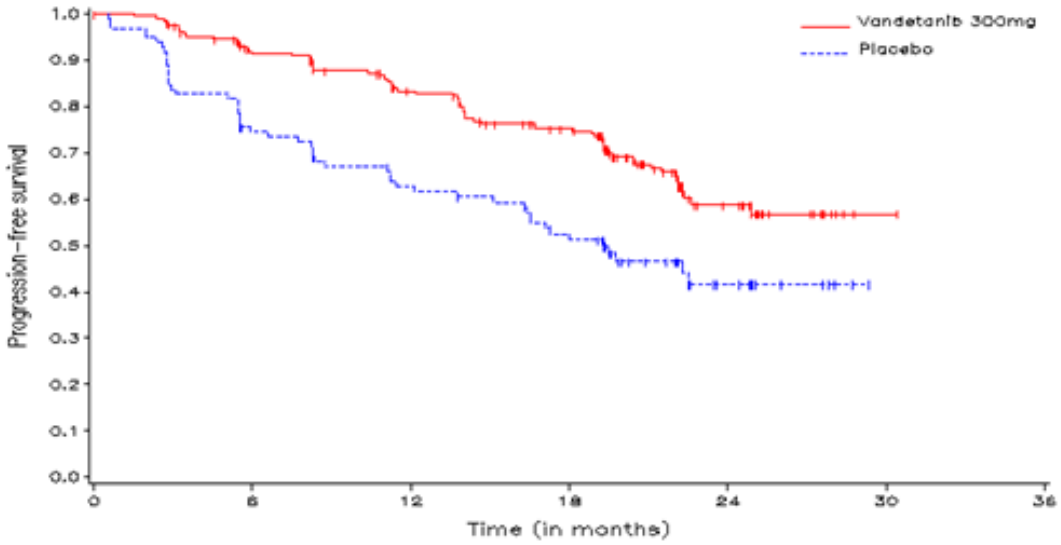
- Vandetanib in medullary thyroid cancer

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2014/04/WC500165803.pdf

Vandetanib in MTC: Efficacy

Note: Hypothetical example modified from Vandetanib EPAR; presented data are not necessarily accurate or complete.

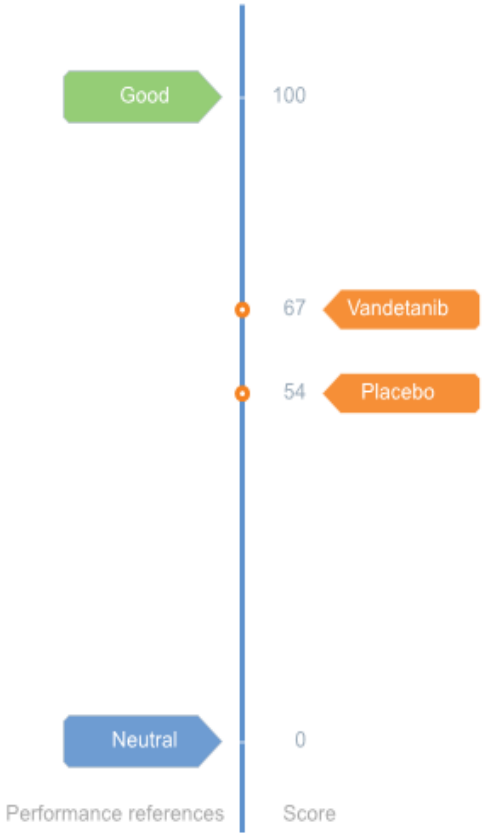
	Placebo	Vandetanib
Progression-free survival (median months)	19.3	30.5
Objective Response Rate	13%	45%



n at months	0	6	12	18	24	30	36
Vandetanib 300mg	231	196	169	140	40	1	0
Placebo	100	71	57	45	13	0	0

Patient Jury Results: Vandetanib

	Progression - free su	Objective Response R	Infections CTC3 Grad	Diarrhoea CTC3 Grade	QTC related events C	Total
Good	100	100	100	100	100	100
Vandetanib	51	39	77	100	90	67
Placebo	32	10	85	100	99	54
Neutral	0	0	0	0	0	0
Weigths	37%	21%	11%	32%	0%	



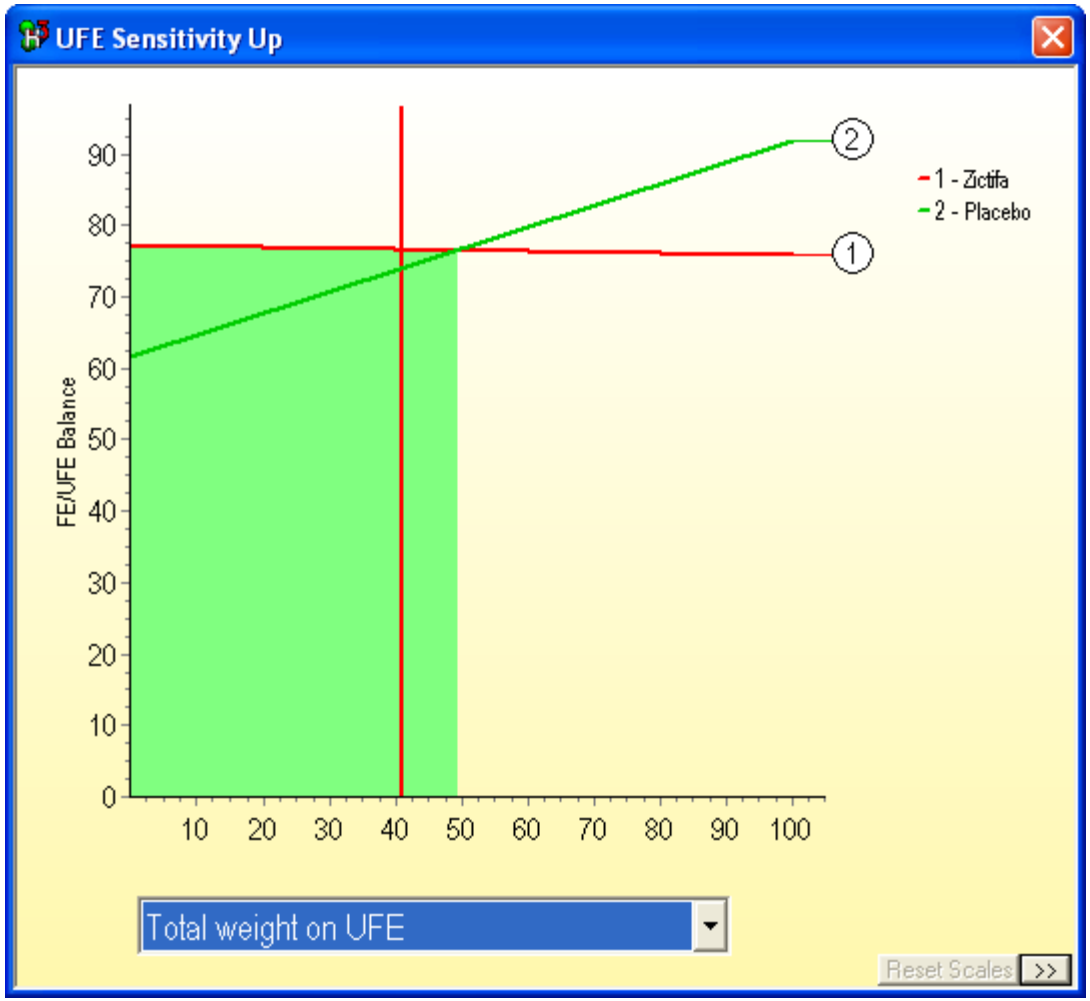
CHMP: improvement in PFS, ORR … are of importance … The management of the risk of QT prolongation … are particularly important. Benefits outweigh the important risks outlined

Decision Analysis Modelling (MCDA)

Hypothetical example

5. Sensitivity Analysis
6. Scenario Analysis…

(explore various scores/weights)



Conclusions

- SAGs: important tool for bringing patients' values and preferences into the system
  - Overall interactions with patients groups have proved useful;
  - They bring a crucial patient perspective to the discussions on medicinal products
  - Can help to provide valuable insights such as acceptable levels of associated risks
- Methods to elicit patient preferences are being piloted