Patients' Involvement,

What Does that Mean?
Variability between diseases and patients

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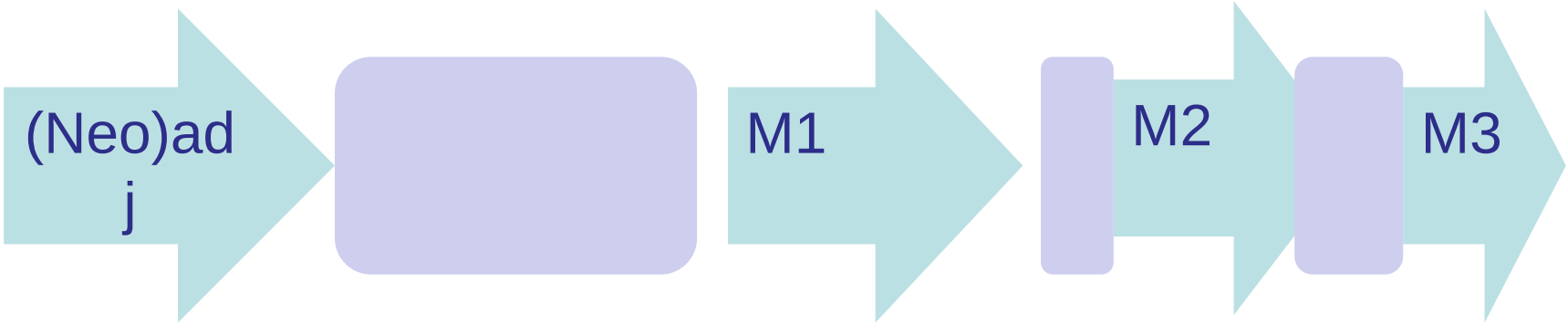
Disclaimer

No CoIs

Personal views only, don’t blame EMA or ANSM

Specifics of Oncology
Polyphasic Disease



Specifics of Oncology
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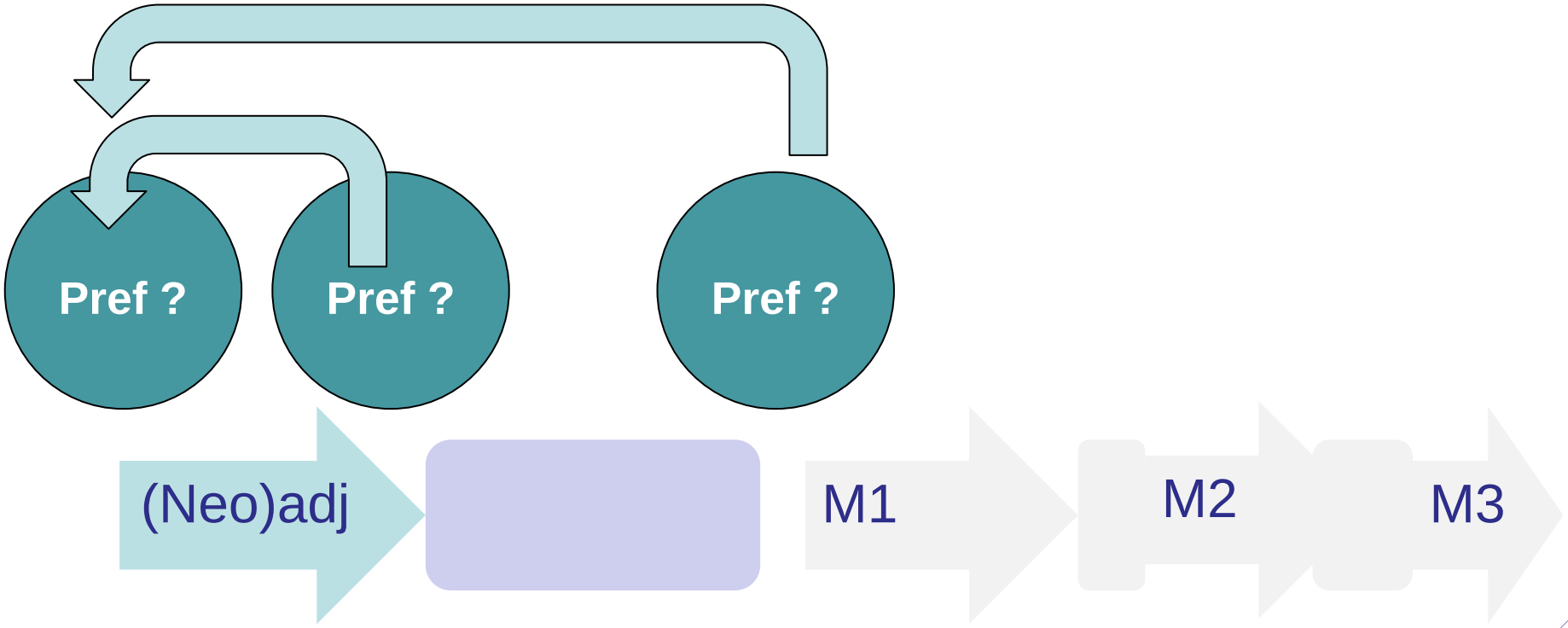
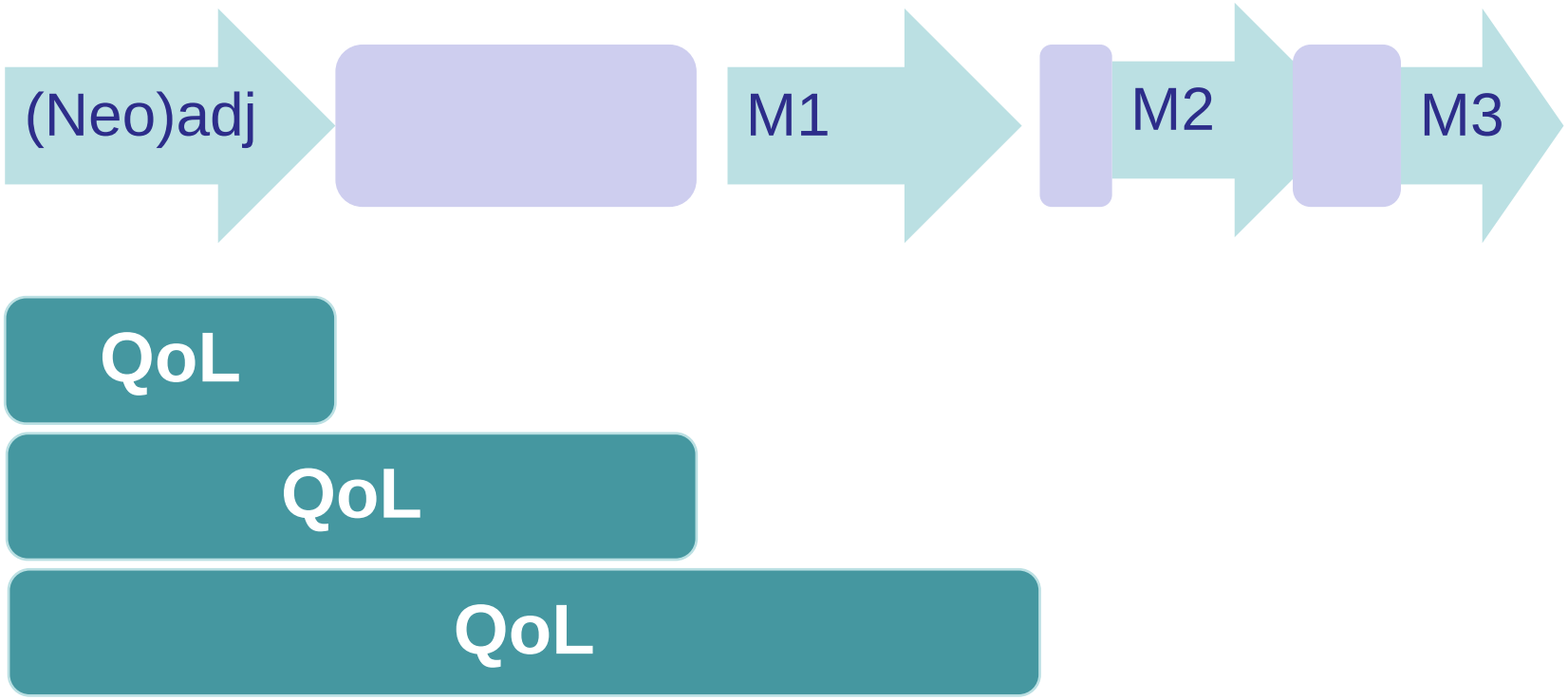
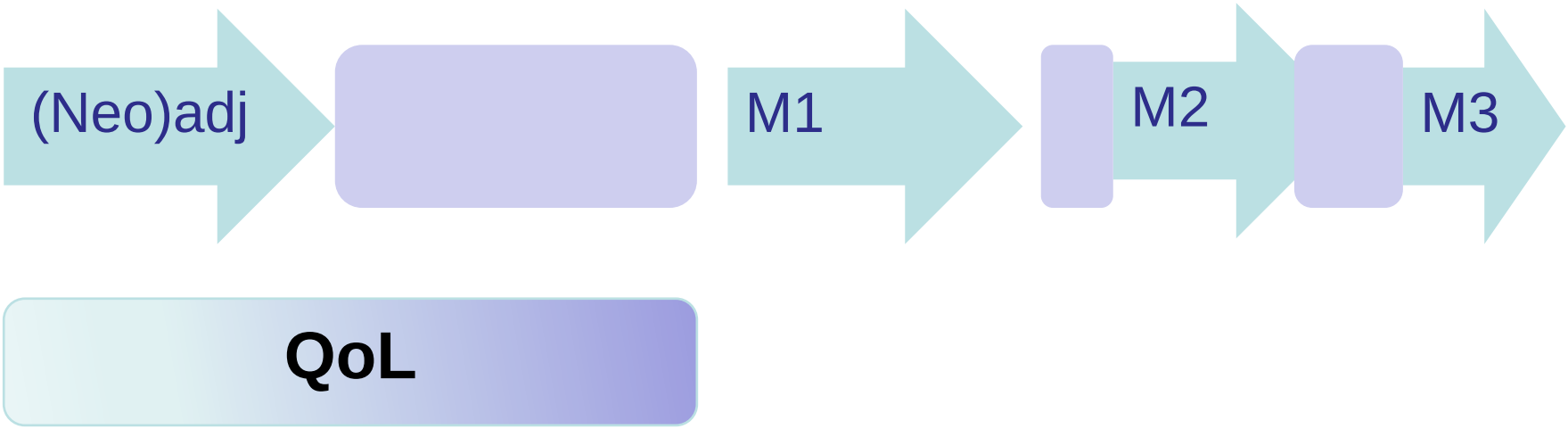


Specifics of Oncology
Polyphasic Disease



Specifics of Oncology
Both Disease and Treatments affect QoL
Simultaneously? Sequentially? Overlaps?



Some Questions

Is a 3-month increase in treatment-free period worth it?

PFS, B/R

Is a maintenance delaying the next painful chemo by 3 months worth it?

EFS, B/R

Is an adjuvant increasing cure hope from 80% to 90% worth it?

Cure, B/R

Do you accept a last painful chemo that may bring a few more weeks to your life expectancy?

Individual trade-off

Important to inform some (regulatory) decisions

Should it go to PI?

Robustness, Relevance, Utility.

EORTC
European Organisation for Research and Treatment of Cancer

Evaluating cancer treatments based on overall survival and quality of life

Why improving patient's HRQoL is part of EORTC's core mission?

Winette van der Graaf, medical oncologist, Netherlands Cancer Institute Amsterdam
President of the EORTC

Conflict of interest

- Springworks advisory board
- Agenus advisory board
- PTC Therapeutics advisory board
- Eli Lilly research project

- All fees to the institute

Mission EORTC

To increase cancer patients' survival and improve their quality of life

Do this through:

- **Generating robust medical evidence**: design, coordinate and conduct multidisciplinary, clinical and translational trials, leading to therapeutic progress and new standard of treatment in care

- **Setting Standards**: being a reference for methodological research and an authority in establishing the standards of treatment in care

EORTC
European Organisation for Research and Treatment of Cancer

Multidisciplinary approach

- EORTC aims ultimately to increase people's survival and quality of life by testing new therapeutic strategies based on existing drugs, surgery, and radiotherapy.

- EORTC also helps develop new drugs and approaches in partnership with the pharmaceutical industry and in **patients' best interests.**

What are patients' best interests and how to study patients' best interest?

- Activity of a treatment
- The balance of safety versus toxicity

➡ The impact of a treatment on patients' daily life, including health-related quality of life, depends on much more than the treatment alone

There is a notorious mismatch..

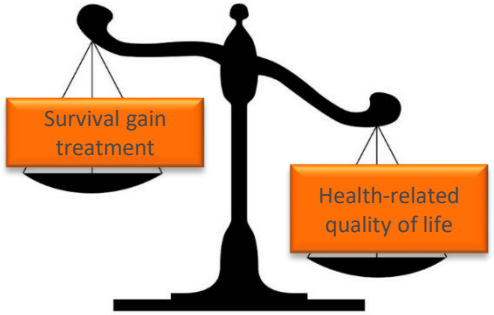
Doctors, despite their extended ears

don’t listen well or know very well what the impact of cancer and its treatment on patient’s daily life and the impact on HRQol really is…

We need the patient’s voice

EORTC already long ago realised the relevance of the voice of patients and patients reported outcomes

Evaluation of clinical trials traditionally focus on objective outcomes such as disease-free, progression-free survival, overall survival, response rate, adverse events.



However, to get a more holistic overview we need to asses the patients' perspectives, which can provide important additional information to evaluate benefits and risks of interventions in cancer clinical trials.

Patient-reported outcomes (PROs)

"Refer to a host of outcomes coming directly from patients about how they feel or function in relation to a health condition and its therapy without interpretation by healthcare professionals or anyone else"[1]

- Symptoms (e.g. pain, fatigue)
- Perception of daily functioning (e.g. physically, socially)
- Health-related quality of life

We need instruments (mostly questionnaires and survey's) to capture information about PROs: patient reported outcome measures (PROMs)

[1] U.S. Department of Health and Human Services, Food and Drug Administration. Guidance for industry: Patient- reported outcomes measures: Use in medical product development to support labeling claims.

Is talking about HRQoL new?

No…

Already in 1986, the EORTC Quality of Life Group realised that a research program was necessary to develop a Quality-of-Life Instrument for Use in International Clinical Trials in Oncology.

At that time only a very few studies (in breast and lung cancer and sarcoma) had incorporated quality of life aspects.

The instrument to-be-developed should have core questions and an option for a modular approach.

The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology

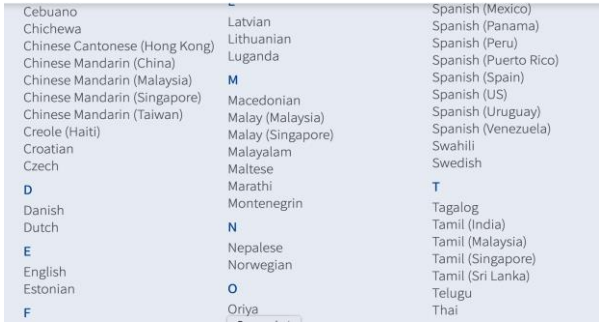
N K Aaronson, S Ahmedzai, B Bergman, M Bullinger, A Cull, N J Duez, A Filiberti, H Flechtner, S B Fleishman, J C de Haes, et al.

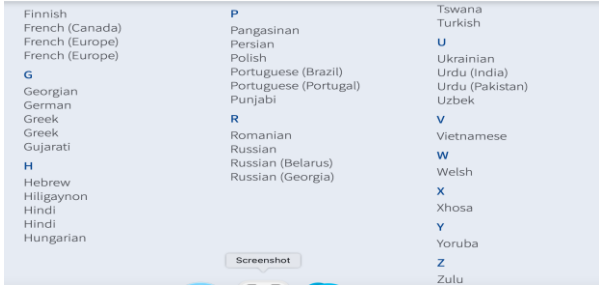
PMID: 8433390 DOI: 10.1093/jnci/85.5.365

Abstract

Background: In 1986, the European Organization for Research and Treatment of Cancer (EORTC) initiated a research program to develop an integrated, modular approach for evaluating the quality of life of patients participating in international clinical trials.

Purpose: We report here the results of an international field study of the practicality, reliability, and validity of the EORTC QLQ-C30, the current core questionnaire. The QLQ-C30 incorporates nine multi-item scales: five functional scales (physical, role, cognitive, emotional, and social); three symptom scales (fatigue, pain, and nausea and vomiting); and a global health and quality-of-life scale. Several single-item symptom measures are also included.





	2018	2019	2020	2021	2022	Average per year	Total
Total	2,959	3,280	3,886	4,128	2,632	1,297.17	45,401
THE EUROPEAN-ORGANIZATION-FOR-RESEARCH-AND-TREATMENT-OF-CANCER QLQ-C30 - A QUALITY-OF-LIFE INSTRUMENT FOR USE IN INTERNATIONAL CLINICAL-TRIALS IN ONCOLOGY AARONSON, NK; AHMEDZAI, S; (...); TAKEDA, F Mar 3 1993 | JOURNAL OF THE NATIONAL CANCER INSTITUTE 85 (5) , pp.365-376	651	648	754	867	551	326.47	9,794

Chest. 1996 May;109(5 Suppl):110S-112S. doi: 10.1378/chest.109.5_supplement.110s.

Quality of life as a new end point

P Kosmidis [1]

Affiliations — collapse

Affiliation

1 Department of Medical Oncology, Metaxa Cancer Hospital, Piraeus, Greece.

PMID: 8635386 DOI: 10.1378/chest.109.5_supplement.110s

Abstract

Quality of life (QOL) is a relatively new clinical end point that is particularly relevant to the typically palliative therapy for non-small cell lung cancer. Patients' assessments of their QOL are shown to differ from their physicians', emphasizing the subjective nature of QOL. A number of relevant instruments and assessment techniques are employed. Results from a study using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 instrument before and during chemotherapy are presented. Some parameters improved while others did not, preventing a simple interpretation. There are arguments for compiling indexes of QOL while retaining measures for individual parameters and a desire for the consistent international use of an instrument such as the EORTC questionnaire.

Next to the EORTC QLQ C30

2 other core instruments have been developed

- The EORTC-QLQ-C15-PAL for palliative care patients and
- The EORTC QLQ-F17 which includes only the functional scales and the global Health Status/Quality of Life scale of the EORTC C30

- Modules
- Validated questions (>1000) in the EORTC item library
- Translations in 120 languages

Back to the nineties

RECIST 2000 Patrick Therasse

- The response evaluation criteria in solid tumours **(RECIST)** was developed in the **late 1990s** to replace the WHO criteria for response evaluation. The new criteria included important changes such as unidimensional tumour measurement, selection of target lesions with a minimum size, details concerning imaging modalities and a new threshold for assignment of objective progression.

- **RECIST was published in February 2000 and very quickly came into operation first in clinical trials performed under the auspices of EORTC, US NCI or NCI Canada Clinical Trials Group but was adopted quickly thereafter by the entire cancer clinical research community.**

Therasse, et al, JNCI 2000: 205-16

Since RECIST 1.1 in 2009

Learning by doing…the place of ..

- (New) functional imaging?
- Immunotherapy assessment iRECIST
- Radiomics?
- The meaning of mixed responses?

- Still, the main question remains: How best to evaluate the benefit of clinical trials for patients?

Eisenhauer et al. Eur J Cancer 2009; 45: 228-47

Example of the complexity of endpoints (I)

Objectives:

1) To study if cancer drug trials that show improvement in OS or PFS also improve global QOL of patients with cancer compared with the control treatment,

2) to assess how unchanged or decreased QOL outcomes are reported in trial publications.

Methods:

Retrospective study

Patients with advanced stage of cancer - phase 3 RCTs which reported also QoL, published (in English) in 2019.

.

Samuel JN, JAMA Oncol. 2022;8:879-886.

QoL in clinical trials, review RCTs 2019 (II)

Results:

45 phase 3 RCTs: enrolled 24 806 participants (13 368 in the experimental arm and 11 438 in the control arm)

1) Improvement in global QOL with the experimental agent was reported in 11 (24%) RCTs.

The RCTs with improved QOL were more likely to also show improved OS vs trials with unimproved QOL : 7 of 11(64%) trials vs 10 of 34 (29%) ($p<0.04$).

Six trials (13%) reported a decrease in QOL, 3 of them were trials with targeted drugs,

11 trials reported an increase in QOL – 6/11 (55%) were trials with immunotherapy drugs.

2) Of the 34 trials in which QOL was not improved compared with controls, 16 (47%) reported these results in a positive frame.

Conclusion: Only a small proportion of RCTs of cancer drugs showed benefit in global QOL with the experimental agent, which had an association with OS (not with PFS).

There is a tendency to report negative trials regarding QoL more favourable.

The vision of Common sense Oncology (started 2023) ‘Outcomes that matter to patients’

EORTC: ‘outcomes that are in patients best interest’

Panel: Common Sense Oncology: outcomes that matter

Mission

To ensure that cancer care focuses on outcomes that matter to patients

Vision

Patients have access to cancer treatments that provide meaningful improvements in outcomes that matter, irrespective of where they live or their health system. To realise this vision, we aspire that:

- Patient outcomes that matter must be at the centre of every drug registration trial; and patient outcomes that matter should be the standard for every drug regulatory decision
- Reporting of trials is transparent and uses language that can be understood clearly by oncologists and patients
- Patients receive clear communication regarding treatment options that enables them to make informed decisions that are aligned with their personal goals and values
- The only treatments that are registered, reimbursed, and recommended are ones that meaningfully improve patients’ lives
- Common Sense Oncology that is grounded in evidence-based medicine and critical appraisal becomes a core curricular component for oncology training programmes
- Health systems invest in both developing new treatments and ensuring that patients have access to and benefit from proven effective treatments

Booth et al. Lancet Oncol. 2023 ;24:833-835.

To conclude

- We should collect data in clinical trials and make objective relevant assessments of patients' HRQoL next to imaging and survival endpoints to serve our patients and regulators.

- The long history of clinical trials, data collection and input from our patients' panel and experts in the Disease Oriented Groups and Taskforces and from HQ at EORTC enable a better insight into optimal trial design and analysis.

EORTC
European Organisation for Research and Treatment of Cancer

Thank you for your attention

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The tale of two trials: improving the use of PROs and HRQoL in cancer clinical research

Jaap Reijneveld, MD, PhD, neurologist

Brain Tumor Center, Amsterdam UMC

Epilepsy Center SEIN, Heemstede

Chair of EORTC Quality of Life Group

Conflicts of interest

None to declare

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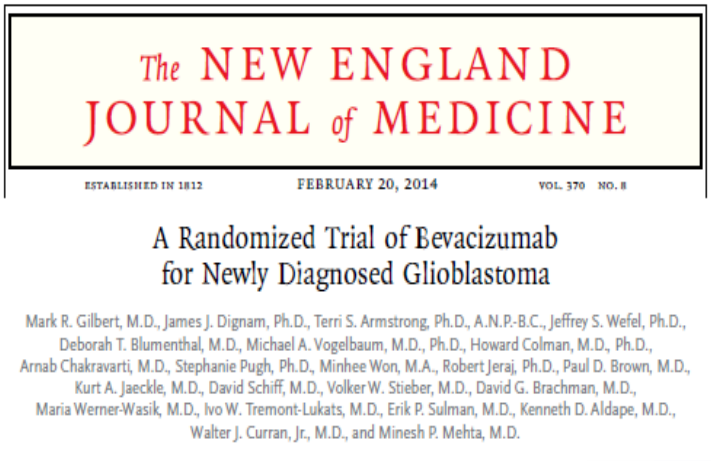
The tale of two trials: improving the use of PROs and HRQoL in cancer clinical research

The tale of two tumor trials…..

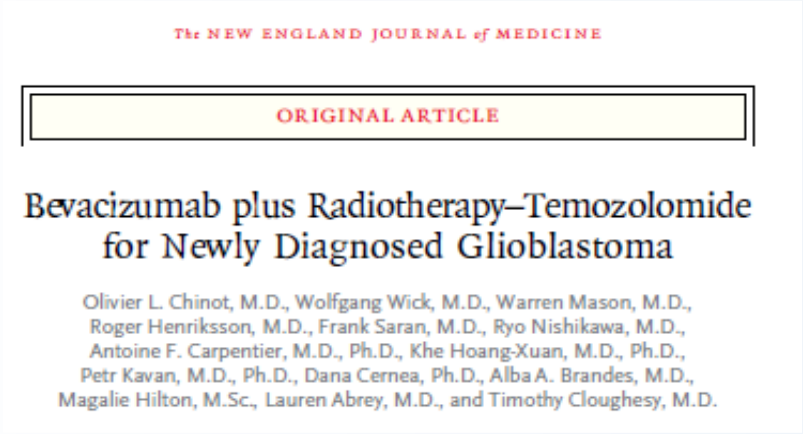


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 20, 2014 VOL. 370 NO. 8

A Randomized Trial of Bevacizumab for Newly Diagnosed Glioblastoma

Mark R. Gilbert, M.D., James J. Dignam, Ph.D., Terri S. Armstrong, Ph.D., A.N.P.-B.C., Jeffrey S. Wefel, Ph.D., Deborah T. Blumenthal, M.D., Michael A. Vogelbaum, M.D., Ph.D., Howard Colman, M.D., Ph.D., Arnab Chakravarti, M.D., Stephanie Pugh, Ph.D., Minhee Won, M.A., Robert Jeraj, Ph.D., Paul D. Brown, M.D., Kurt A. Jaeckle, M.D., David Schiff, M.D., Volker W. Stieber, M.D., David G. Brachman, M.D., Maria Werner-Wasik, M.D., Ivo W. Tremont-Lukats, M.D., Erik P. Sulman, M.D., Kenneth D. Aldape, M.D., Walter J. Curran, Jr., M.D., and Minesh P. Mehta, M.D.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bevacizumab plus Radiotherapy–Temozolomide for Newly Diagnosed Glioblastoma

Olivier L. Chinot, M.D., Wolfgang Wick, M.D., Warren Mason, M.D., Roger Henriksson, M.D., Frank Saran, M.D., Ryo Nishikawa, M.D., Antoine F. Carpentier, M.D., Ph.D., Khe Hoang-Xuan, M.D., Ph.D., Petr Kavan, M.D., Ph.D., Dana Cernea, Ph.D., Alba A. Brandes, M.D., Magalie Hilton, M.Sc., Lauren Abrey, M.D., and Timothy Cloughesy, M.D.

Gilbert *et al* N Engl J Med 2014; Chinot *et al* N Engl J Med 2014

The tale of two tumor trials…..

	NEJM, 2014a (Gilbert et al)	NEJM, 2014b (Chinot et al)
Population	Newly diagnosed glioblastoma with central histological confirmation	
Treatment	Placebo vs new treatment	
Sample size	309 vs 312	463 vs 458
Overall survival (OS)	No benefit in OS 16.1 vs 15.7 months (HR=1.13 [0.93-1.37]; p=0.11)	No benefit in OS 16.7 vs 16.8 months (HR=0.88 [0.76-1.02]; p=0.10)
Progression Free Survival (PFS)	Benefit in PFS 7.3 vs 10.7 mths (HR=0.79 [0.66-0.94]; p=0.004)	Benefit in PFS 6.2 vs 10.6 mths (HR=0.64 [0.55-0.74]; p<0.001)
Health-related quality of life (HRQOL)	**Worsening in HRQOL** "Longitudinal evaluation also revealed *greater deterioration* in the [new treatment]…"	**Benefit in HRQOL** "…*deterioration-free survival was significantly longer among patients* in the [new treatment] than among those in the placebo group …"

Courtesy of Madeline Pe

What went wrong?

EORTC
European Organisation for Research and Treatment of Cancer

What went wrong?

Where they assessing the same **patient population**?

Were they assessing the same **HRQOL areas** at the **same time points**?

Were they assessing the same **endpoints?**

Were the same **populations of patients** included in the analysis?

Courtesy of Madeline Pe

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Courtesy of Madeline Pe

The tale of two tumor trials…..

	NEJM, 2014a	NEJM, 2014b
Patient population	Adult newly-diagnosed histologically confirmed GBM, KPS ≥ 70	Adult newly-diagnosed histologically confirmed supratentorial GBM, WHO ≤ 2, no prior therapy

Courtesy of Madeline Pe

Patient population – selection bias

METHODS

PATIENTS

Patients 18 to 70 years of age with newly diagnosed and histologically confirmed glioblastoma (World Health Organization [WHO] grade IV astrocytoma) were eligible for the study. Eligible patients had a WHO performance status of 2 or less and adequate hematologic, renal, and hepatic function (absolute neutrophil count, ≥1500 per cubic millimeter; platelet count, ≥100,000 per cubic millimeter; serum creatinine level, ≤1.5 times the upper limit of normal in the laboratory where it was measured; total serum bilirubin level, ≤1.5 times the upper limit of normal; and liver-function values, <3 times the upper limit of normal for the laboratory). Patients who were receiving corticosteroids had to receive a stable or decreasing dose for at least 14 days before randomization. All patients provided written informed consent, and the study was approved by the ethics committees of the participating centers.

Stupp *et al.* N Engl J Med 2005

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Patient population – cultural differences

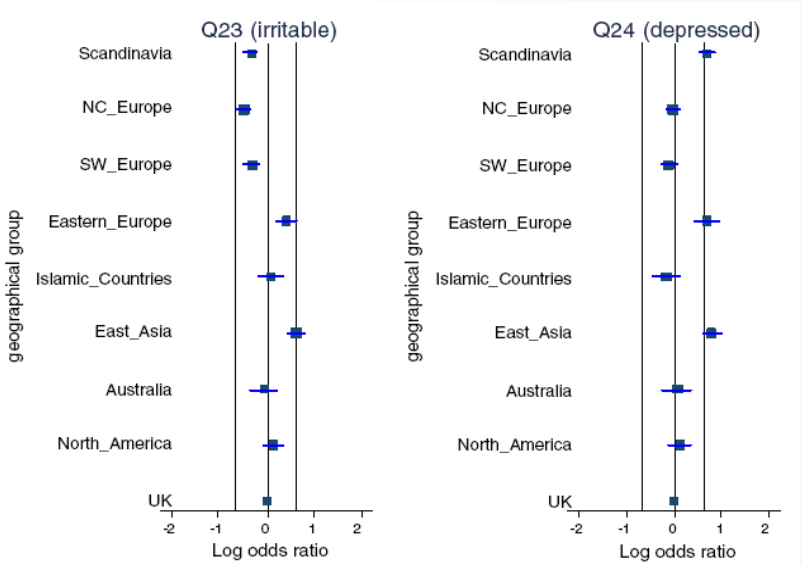

Figure 2. Emotional functioning (EF).

Scott *et al.* Qual Life Res 2007

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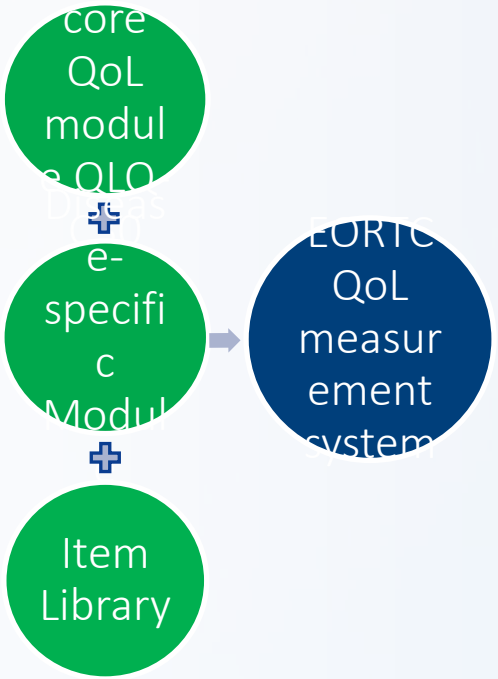
Courtesy of Madeline Pe

EORTC QLG measurement vision

Free-of-charge for academic users

Royalties for commercial users



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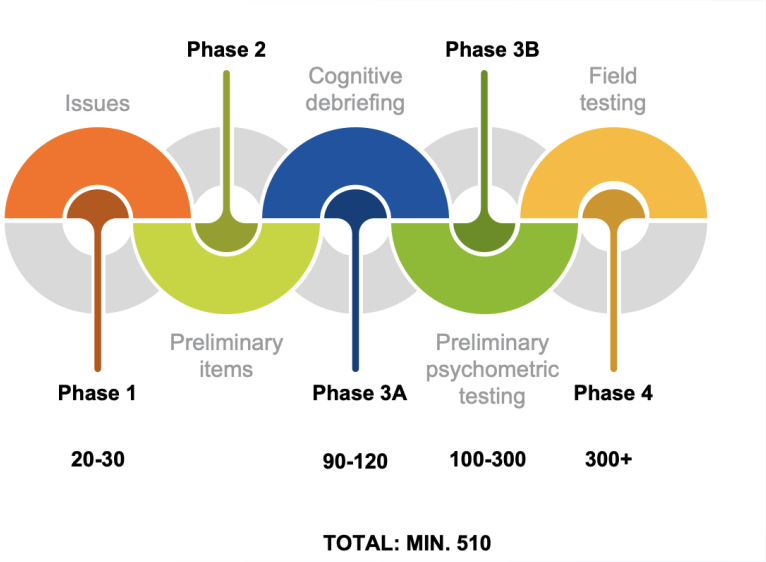
The patients' voice …



Courtesy of Dagmara Kulis; EORTC Module Development Guidelines. 5th Edition. Brussels: 2021.

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The tale of two tumor trials…..

	NEJM, 2014a	NEJM, 2014b
HRQOL measure	EORTC QLQ-C30 & QLQ-BN20	
HRQOL areas	Cognitive functioning, motor dysfunction, communication deficit	Global health status, physical functioning, social functioning, motor dysfunction, and communication deficit

Conclusions about HRQOL were not necessarily based on the same HRQOL areas.

Courtesy of Madeline Pe

EORTC
European Organisation for Research and Treatment of Cancer

Timing of PRO assessments…..

Health-related quality of life in patients with high-risk low-grade glioma (EORTC 22033-26033): a randomised, open-label, phase 3 intergroup study

Jaap C Reijneveld, Martin J B Taphoorn, Corneel Coens, Jacoline E C Bromberg, Warren P Mason, Khê Hoang-Xuan, Gail Ryan, Mohamed Ben Hassel, Roelien H Enting, Alba A Brandes, Antje Wick, Olivier Chinot, Michele Reni, Guy Kantor, Brian Thiessen, Martin Klein, Eugenie Verger, Christian Borchers, Peter Hau, Michael Back, Anja Smits, Vassilis Golfinopoulos, Thierry Gorlia, Andrew Bottomley, Roger Stupp, Brigitta G Baumert

Summary

Background Temozolomide chemotherapy versus radiotherapy in patients with a high-risk low-grade glioma has been shown to have no significant effect on progression-free survival. If these treatments have a different effect on health-related quality of life (HRQOL), it might affect the choice of therapy. We postulated that temozolomide compromises HRQOL and global cognitive functioning to a lesser extent than does radiotherapy.

Methods We did a prospective, phase 3, randomised controlled trial at 78 medical centres and large hospitals in 19 countries. We enrolled adult patients (aged ≥18 years) with histologically confirmed diffuse (WHO grade II) astrocytoma, oligodendroglioma, or mixed oligoastrocytoma, with a WHO performance status of 2 or lower, without previous chemotherapy or radiotherapy, who needed active treatment other than surgery. We randomly assigned eligible patients (1:1) using a minimisation technique, stratified by WHO performance status (0–1 *vs* 2), age (<40 years *vs* ≥40 years), presence of contrast enhancement on MRI, chromosome 1p status (deleted *vs* non-deleted *vs* indeterminate), and the treating medical centre, to receive either radiotherapy (50·4 Gy in 28 fractions of 1·8 Gy for 5 days per week up to 6·5 weeks) or temozolomide chemotherapy (75 mg/m² daily, for 21 of 28 days [one cycle] for 12 cycles). The primary endpoint was progression-free survival (results published separately); here, we report the results for two key secondary endpoints: HRQOL (assessed using the European Organisation for Research and Treatment of Cancer's [EORTC] QLQ-C30 [version 3] and the EORTC Brain Cancer Module [QLQ-BN20]) and global cognitive functioning (assessed using the Mini-Mental State Examination [MMSE]). We did analyses on the intention-to-treat population. This study is closed and is registered at EudraCT, number 2004-002714-11, and at ClinicalTrials.gov, number NCT00182819.

Findings Between Dec 6, 2005, and Dec 21, 2012, we randomly assigned 477 eligible patients to either radiotherapy (n=240) or temozolomide chemotherapy (n=237). The difference in HRQOL between the two treatment groups was not significant during the 36 months' follow-up (mean between group difference [averaged over all timepoints] 0·06, 95% CI −4·64 to 4·75, p=0·98). At baseline, 32 (13%) of 239 patients who received radiotherapy and 32 (14%) of 236 patients who received temozolomide chemotherapy had impaired cognitive function, according to the MMSE scores. After randomisation, five (8%) of 63 patients who received radiotherapy and three (6%) of 54 patients who received temozolomide chemotherapy and who could be followed up for 36 months had impaired cognitive function, according to the MMSE scores. No significant difference was recorded between the groups for the change in MMSE scores during the 36 months of follow-up.

Interpretation The effect of temozolomide chemotherapy or radiotherapy on HRQOL or global cognitive functioning did not differ in patients with low-grade glioma. These results do not support the choice of temozolomide alone over radiotherapy alone in patients with high-risk low-grade glioma.

Funding Merck Sharp & Dohme-Merck & Co, National Cancer Institute, Swiss Cancer League, National Institute for Health Research, Cancer Research UK, Canadian Cancer Society Research Institute, National Health and Medical Research Council, European Organisation for Research and Treatment of Cancer Cancer Research Fund.

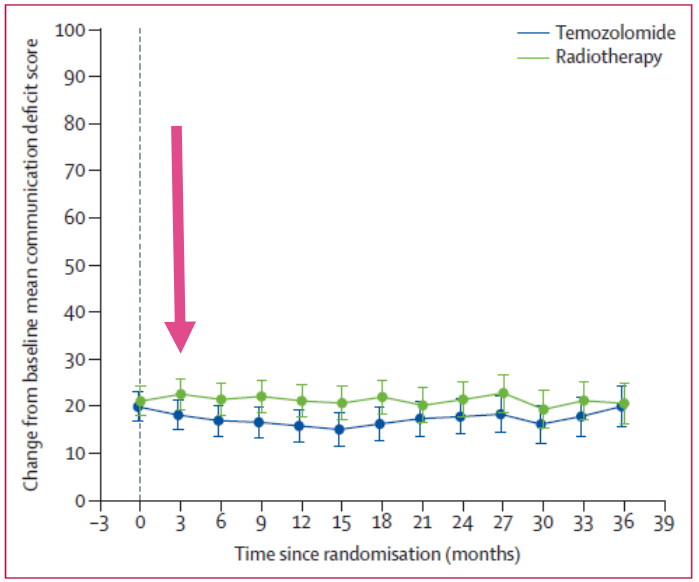


Figure 2: **Changes from baseline in communication deficit scores**
Error bars are SDs. 0 months is the baseline. A higher communication deficit score means more symptoms.

Reijneveld *et al.* Lancet Oncol 2016

EORTC
European Organisation for Research and Treatment of Cancer

What went wrong?

Where they assessing the same **patient population**?

Were they assessing the same **HRQOL areas** at the **same time points**?

Were they assessing the same endpoints?

Were the same **populations of patients** included in the analysis?

Courtesy of Madeline Pe

The tale of two tumor trials…..

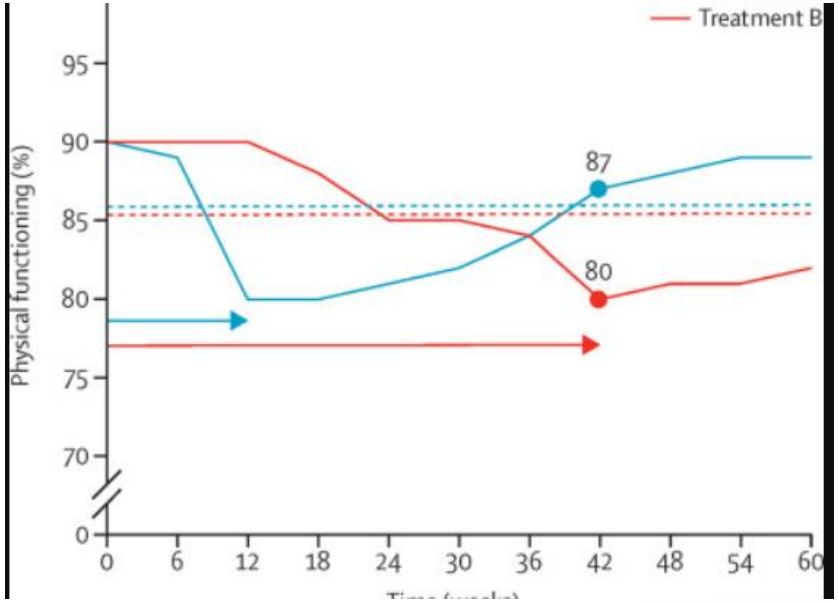
	NEJM, 2014a	NEJM, 2014b
Endpoints	Change in HRQOL scores at 46 weeks *(~10 months)*	Time to >/10 point worsening from pre-treatment scores without improvement OR disease progression OR death *(Result: ~4 months to ~8 months)*

Conclusions about HRQOL were not based on the same endpoint.

The two trials were responding to different aspects of the data.

Courtesy of Madeline Pe & Mees Egeler

Assessing the same endpoints?



Based on the chosen analysis, the results would show that:

1. The time to deterioration analysis would favor treatment B (12 weeks vs 42 weeks)
2. The overall analysis would not favor either treatment
3. Examining differences at the end of treatment would favor treatment A.

Courtesy of Madeline Pe & Mees Egeler

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The tale of two tumor trials…..

	NEJM, 2014a	NEJM, 2014b
Endpoints	Change in HRQOL scores at 46 weeks *(~10 months)*	Time to >/10 point worsening from pre-treatment scores without improvement OR disease progression OR death *(Result: ~4 months to ~8 months)*
	What if a patient's **disease progresses** and the patient does not respond to the questionnaire at week 46?	What if a patient's **disease progresses** and the patient dropped out of treatment before a >/10 point worsening is recorded? **Missing data**
	Ignored = not included in the analyses*	disease progression = >/10 point worsening of HRQOL scores **Handling of missing data**

Courtesy of Madeline Pe

What went wrong?

Where they assessing the same **patient population**?

Were they assessing the same **HRQOL areas** at the **same time points**?

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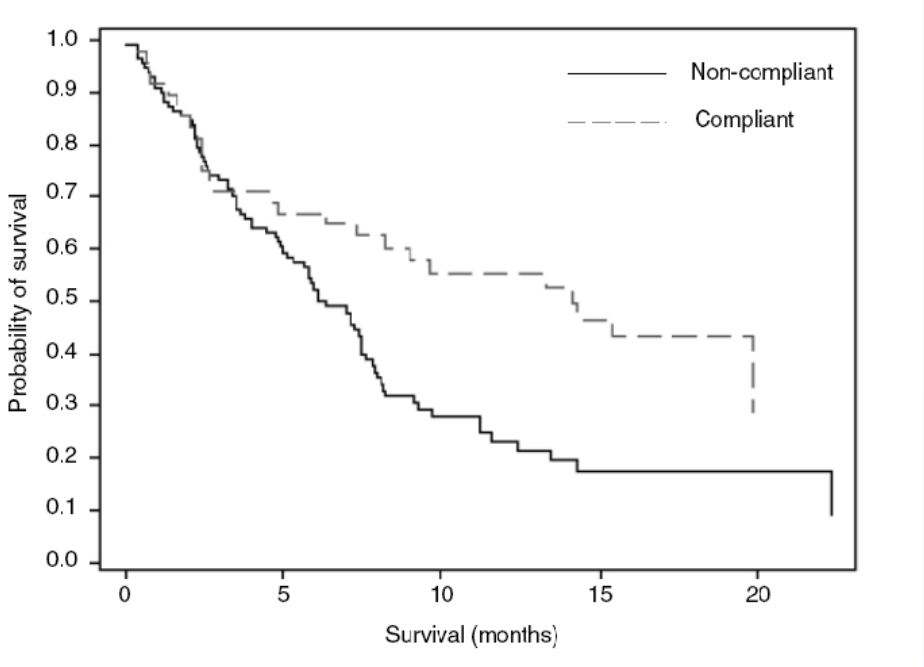
Courtesy of Madeline Pe

Compliance – patient level



Taphoorn *et al.* Lancet Oncol 2005; Walker *et al.* J Neuro Oncol 2005

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European Organisation for Research and Treatment of Cancer

Compliance – institutional level

Institutions with good QOL compliance have better survival outcomes.

HRQOL compliance is not independent from clinical care of HRQOL

Greimel *et al.* Gynecol Oncol 2013

The tale of two tumor trials…..

	NEJM, 2014a	NEJM, 2014b
Analysis population	Only patients alive and free of disease at 46 weeks	All patients included in the trial

The patient population included in the analyses differed between the two trials.

Courtesy of Madeline Pe

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The HRQOL results of the two trials are not directly comparable…

but they looked like they were…

Courtesy of Madeline Pe

Solutions

How can we make things better?

Where they assessing the same **patient population**?

Were they assessing the same **HRQOL areas** at the **same time points**?

Were they assessing the same **endpoints?**

Were the same **populations of patients** included in the analysis?

Courtesy of Madeline Pe

What went wrong?

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Courtesy of Madeline Pe

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Courtesy of Madeline Pe

EORTC Quality of Life Group

EORTC
European Organisation for Research and Treatment of Cancer

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Courtesy of Madeline Pe

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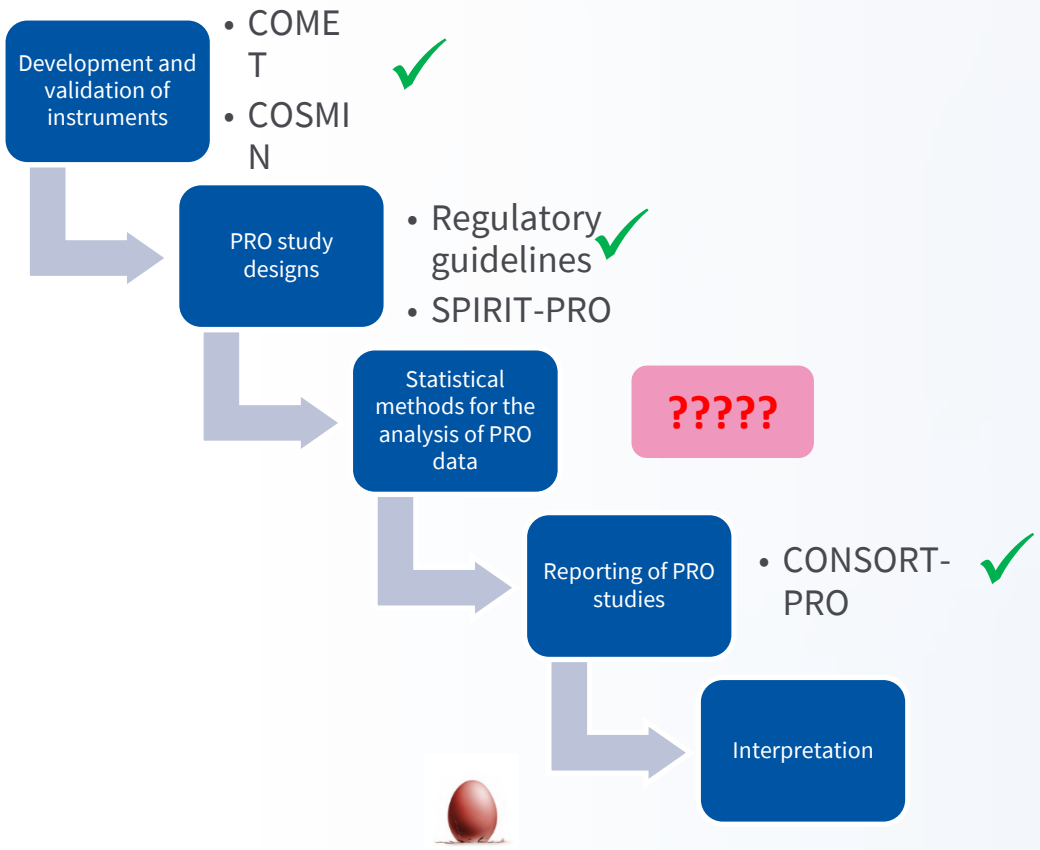
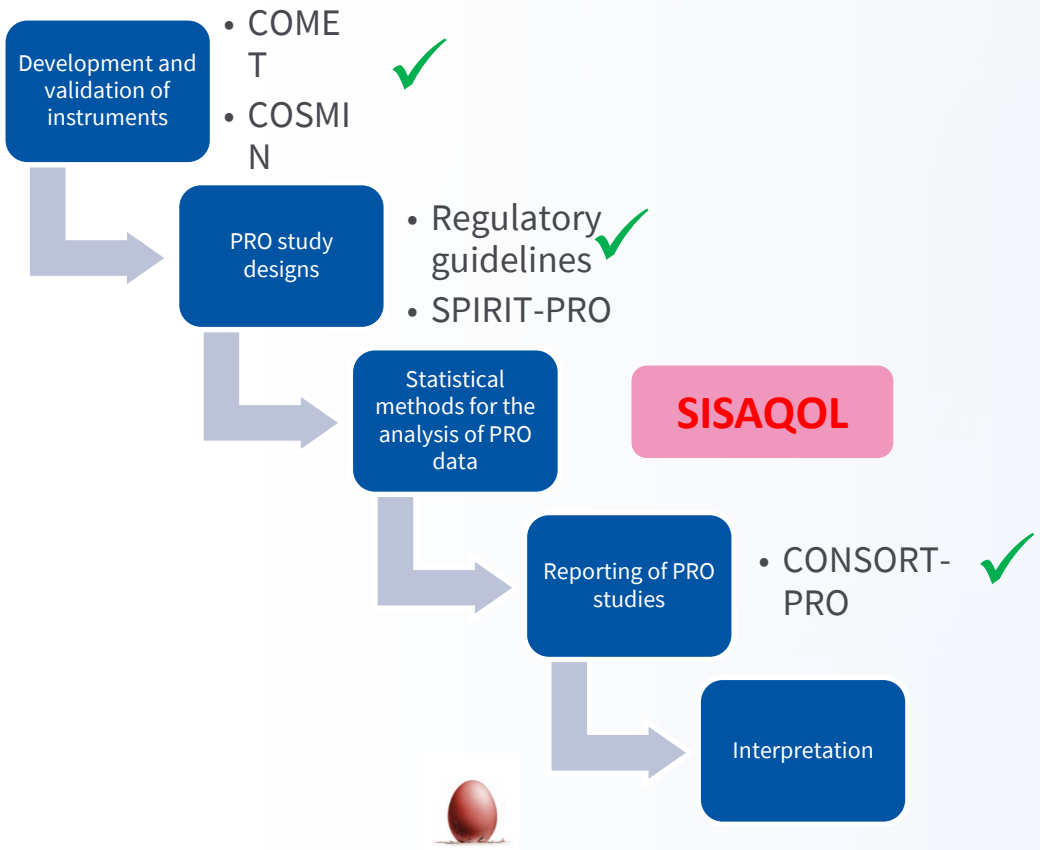
Something was missing..



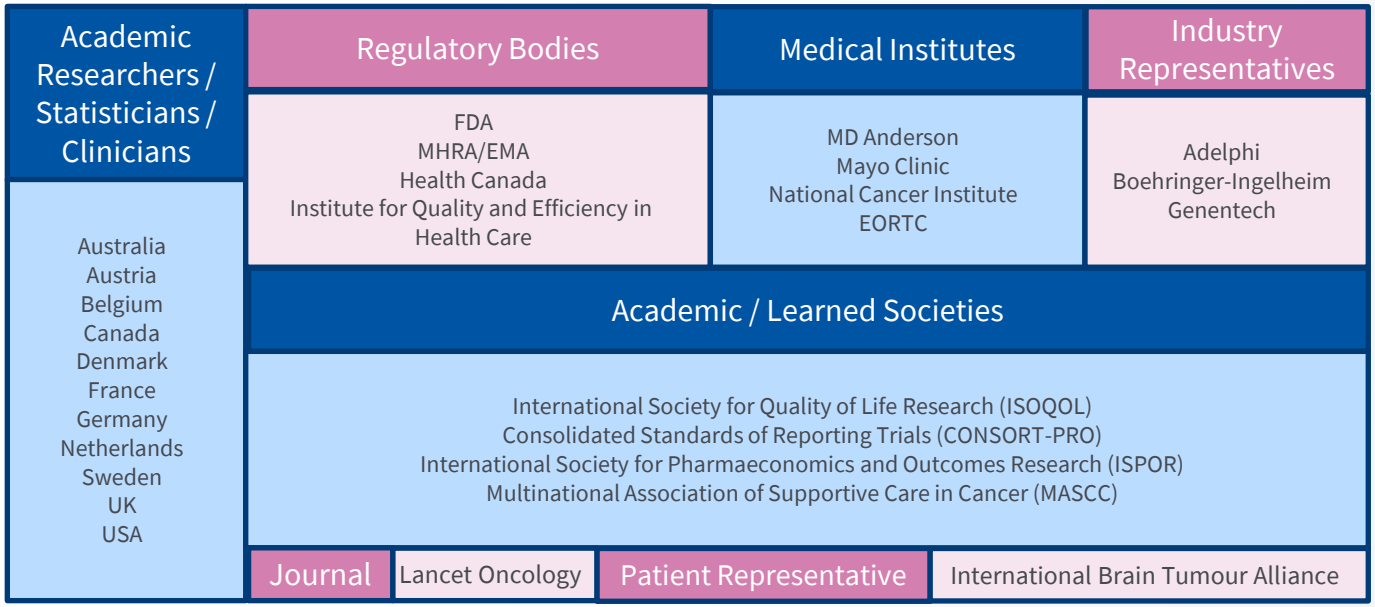
Courtesy of Madeline Pe

Something was missing..



Courtesy of Madeline Pe

Setting International StandArds in QOL Research (SISAQOL) Consortium



Courtesy of Madeline Pe

EORTC
European Organisation for Research and Treatment of Cancer

Take home messages

The EORTC QOL Group has an extensive portfolio of QOL measures (and continuously updates and further improves them)

We do not only build ‘planes’, but also teach how to fly with them

The next challenge will be to assess how our patient-reported outcomes (PRO) and health-related quality of life (HRQoL) data inform regulatory decisions

EORTC
European Organisation for Research and Treatment of Cancer

THANK YOU

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA current and future activities on Patient Experience Data (PED), including PROs and HRQoL in medicines' development and evaluation

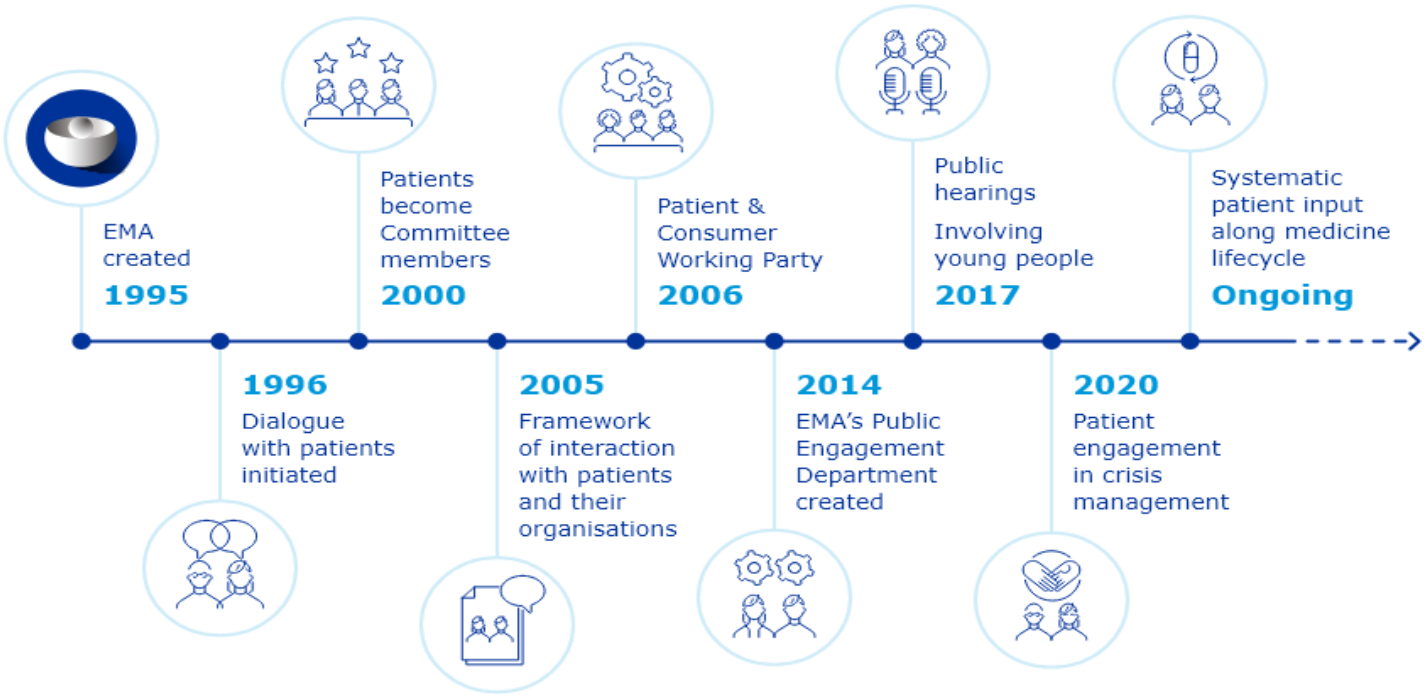
EMA and EORTC workshop: How can PRO and HRQoL data inform regulatory decisions

Presented by Juan Garcia Burgos on 29 February 2024
Head of Public and Stakeholders Engagement Department

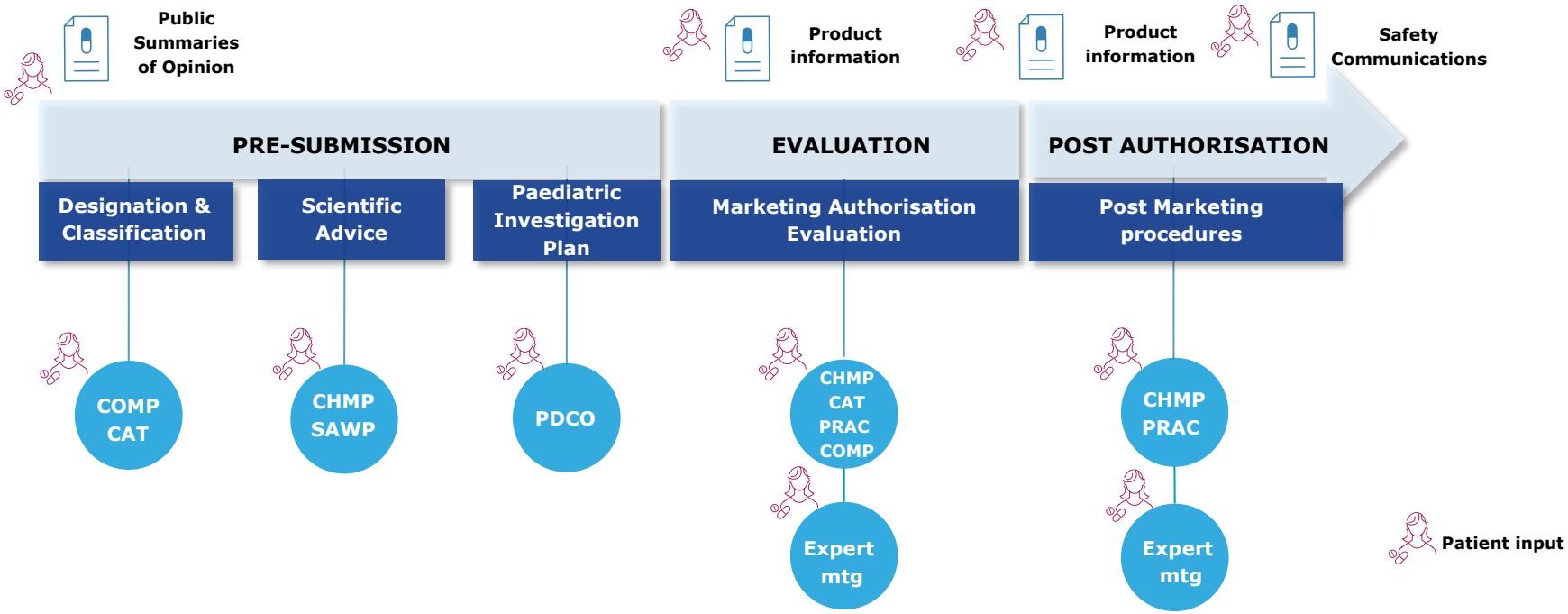
Outline

- EMA's journey of patient involvement
- How patients participate in EMA regulatory activities
- Definitions of Patient Experience Data (PED)
- Why is Patient Experience Data important?
- Status of Patient Experience Data in the EU
- Reflection Paper on Patient Experience Data
- Scientific advice and qualification of novel methodologies
- Conclusions

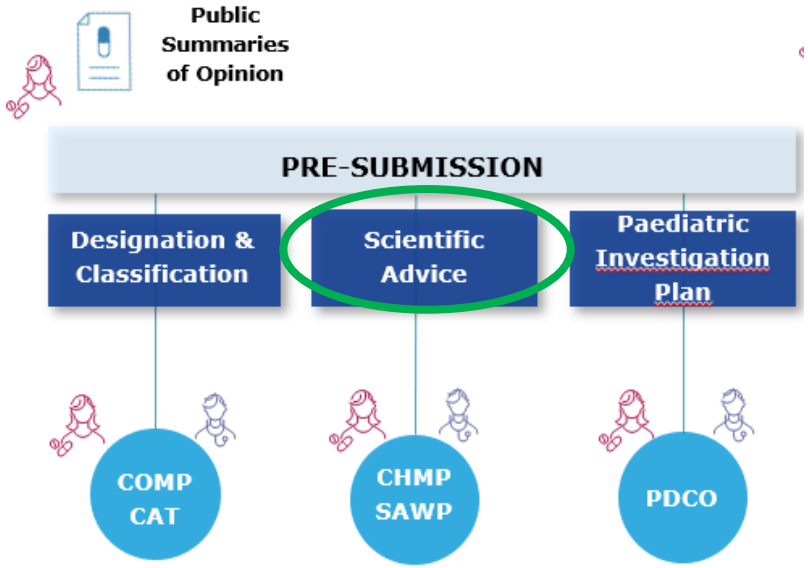
EMA's journey of patient involvement

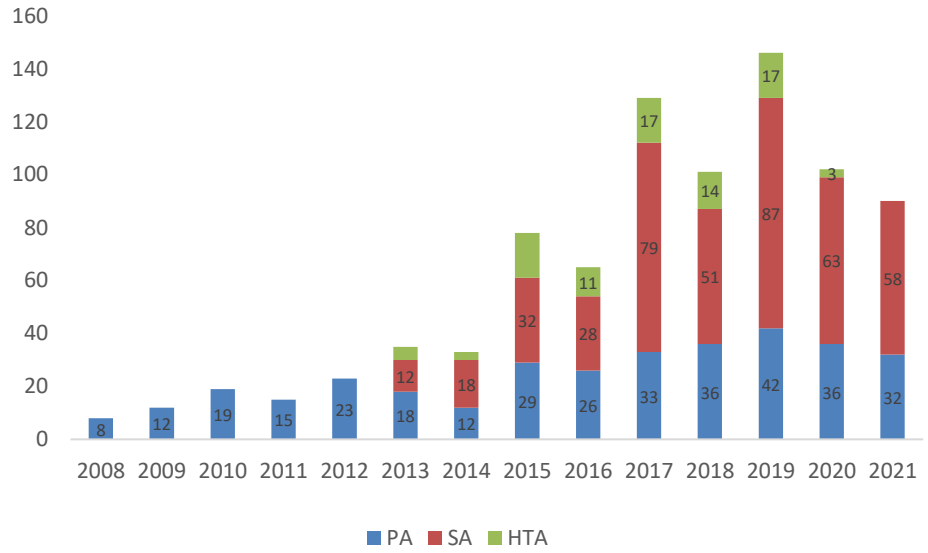


How patients participate in EMA regulatory activities



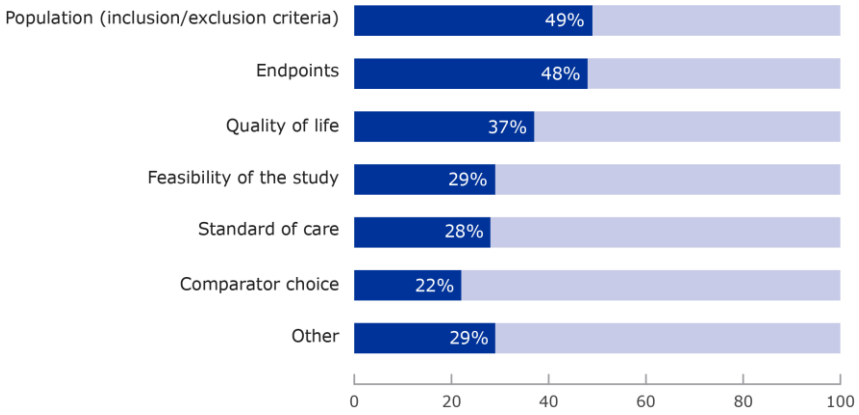
Patient Engagement in pre-submission phase: Scientific Advice



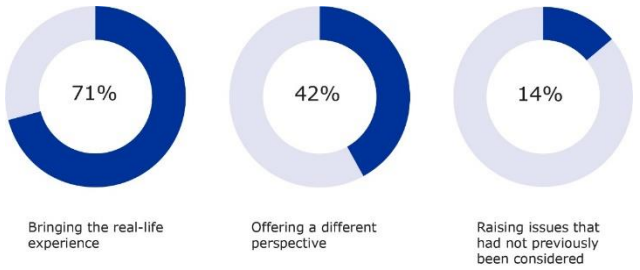


Published in [Frontiers in Medicine]

Where patients gave input



Added value of patient input and involvement

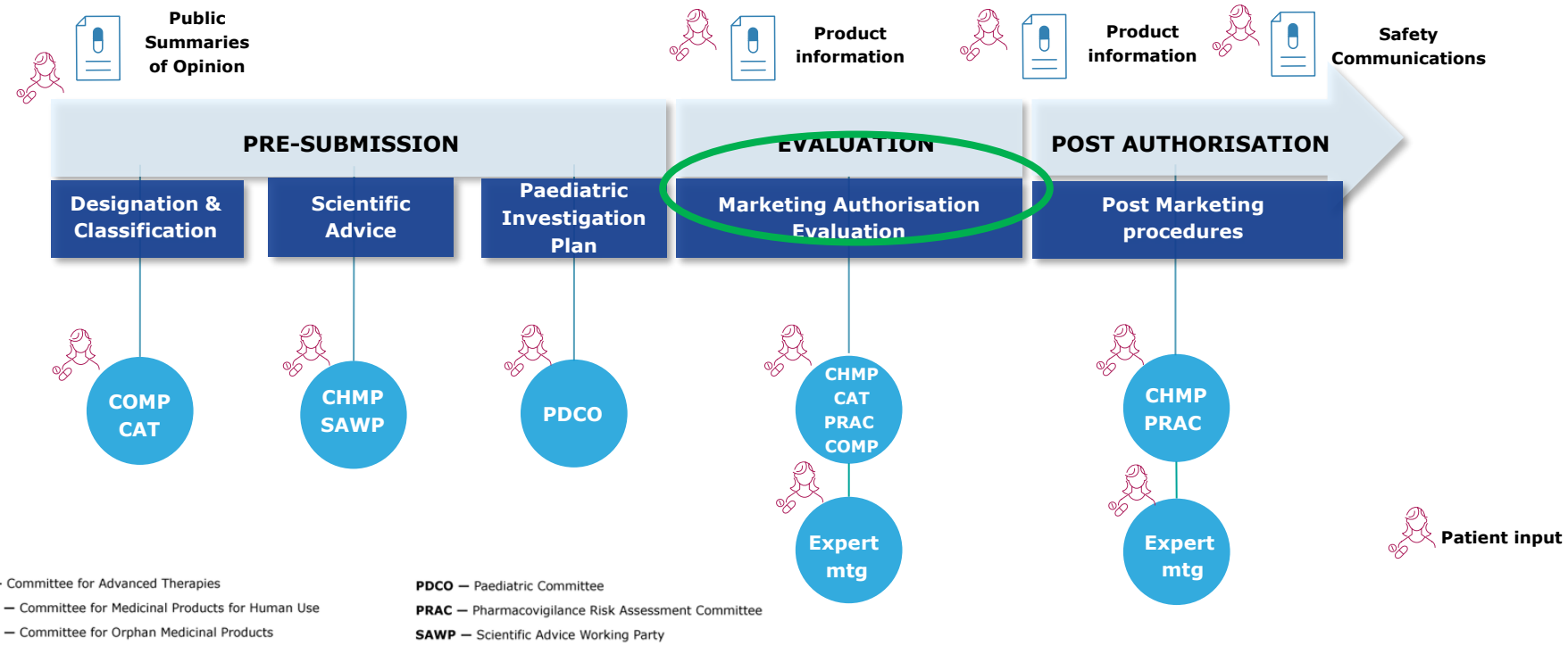


Patient input resulted in further reflection in **52%** of cases.

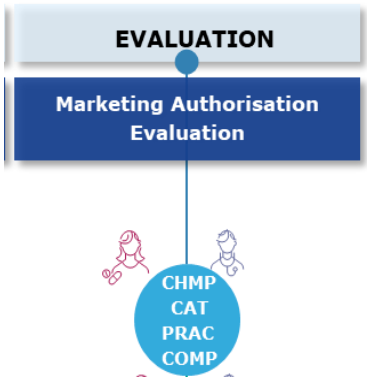
20% of cases - recommendations made to the developer were modified based on patient contributions.

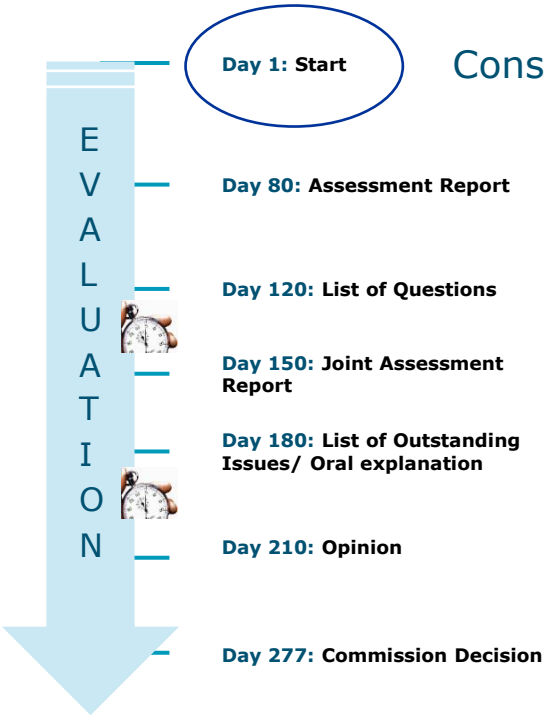
>85% cases: patient **agreement** with the proposed development plan.

Patient involvement in the medicines regulatory lifecycle



Patient Engagement in evaluation phase: CHMP





Consultation of ORGANISATIONS

Scientific Advisory/ad hoc expert Groups

Oral explanations

Consultation of INDIVIDUALS

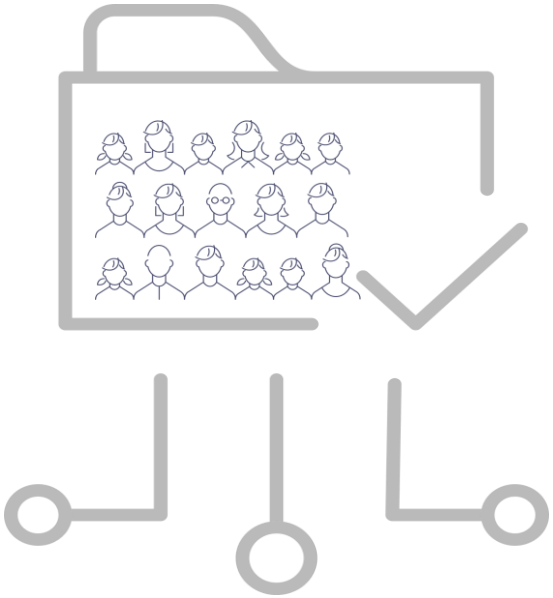
Information from patients during early contact with CHMP

- daily impacts,
- treatment options,
- perspectives and perceptions of adverse effects,
- what constitutes important improvements and
- desired benefits for new treatments

Can include information on PROs and HRQoL

PATIENT / CARER EXPERIENCE OF: **<condition>**
Please include below any aspects that are of particular importance to patients/carers, such as quality of life, standard treatments and how acceptable they are, therapeutic/unmet medical needs, what benefits they would hope for in new medicines as well as what level of side effects they would consider acceptable. • Highlight if there are large differences between groups of patients/carers about these aspects or if these views are generally similar across the condition. • Please also mention any aspects about the condition or its treatments that you feel are not well-understood or not sufficiently considered. • Please include anything else you feel is important for EMA to know. Try to keep your main points to 1-2 pages, if necessary, include more details in an appendix. Please do not include any individual patients contact details or health data. ☐ Tick here to confirm you give consent for EMA to share your views anonymously with third parties, as applicable.

Definition of Patient Experience Data in the EU



- **Data reported directly by patients or their carers**, without interpretation by clinician

Proposed EU definition as part of the EMA 2022 workshop:

Data collected via a variety of patient engagement activities and methodologies *to collect patients' experience of their health status, symptoms, disease course, treatment preferences, quality of life and impact of health care*

- **Reflects patient experience and preferences** of medicines and their views on their conditions

Definition **to be agreed with stakeholders**

Types of Patient Experience Data

- **Patient Reported Outcomes (PROs)** refer to a health/treatment outcome reported directly by the patient without the interpretation of a clinician or another person.
- **Patient Preferences (PPs)** refer to how desirable or acceptable is to patients a given alternative or choice among all the outcomes of a given medicine.
- **Patient Engagement (PE)** refers to all activities involving interaction with patients to gather their experience on disease, preferences, outcomes and treatments.

- not only **quantitative sources** of evidence (e.g., PROs, PREMs) **but also qualitative sources** (i.e., information obtained as part of patient engagement activities reflecting broader patient perspective e.g., outcome of focus groups)

- **Patient Experience Evidence (PEE)** is patient experience data **qualified as valid scientific evidence following a scientific assessment**

**Defined and agreed during the Multi-stakeholder workshop (Sept 2022)*

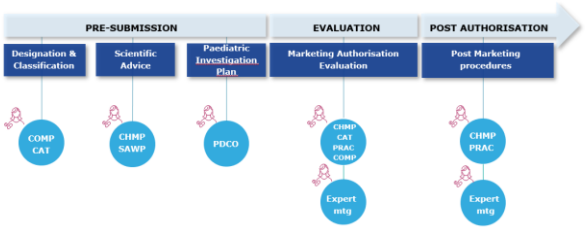
Why is Patient Experience Data important?

- Patients are **users of medicines**
- Patients are experts **in their disease and treatment**
- PED helps ensure **more patient-relevant outcomes**
- Patients are instrumental in helping to **optimise medicines development and regulatory decision-making**

Multi-stakeholder workshop (Sept 2022)

Patient experience data is relevant at different stages:

- During **clinical trial design**
  - Selection of endpoints (which matters more to patients)
- During **benefit-risk assessment**
  - Patient preferences (trade-offs)
- Post-marketing for **Pharmacovigilance and Risk Minimisation**
  - Adverse Drug Reaction reporting



Status of PED in the EU

- Reinforcing patient relevance in evidence generation is **key priority for the EU Network Strategy** and in EMA's **Regulatory Science Strategy**
- **Need for systematic inclusion of PED** in medicines development and regulation
- **PED is a new scientific discipline** – balance difficult methodological discussions with stakeholder engagement
  - Collaboration of multi-disciplinary experts cross-Agency and within EU Network
- **Opportunities for patient-generated digital data** thanks to novel technologies
- The **EU Network Strategy's delivery plan** and **CHMP's 2023 workplan** incorporate two key deliverables:
  - **Reflection paper** on the best EU approach to generate, collect and analyse PED
  - Explore how to **improve transparency in the Assessment Report**

Update on progress

√ 2022

EMA workshop on PED

√ 2023

PED cross-Agency group & Action Plan

√ 2023

PED Expert group

2024

Reflection Paper & Public Consultation

Update of Assessment Report

Upcoming reflection paper on EU approach to PED

- **Reflection paper:** framework for discussion or clarification particularly **in areas where scientific knowledge is fast evolving or regulatory experience is limited**
- **General EU framework or principles** – not a methodological guidance
- **Key action** derived from the 2022 PED workshop - requested by stakeholders
- Reflection paper is in the **Work Programmes of both CHMP and PRAC**
- **Publication for public consultation expected Q3 2024**

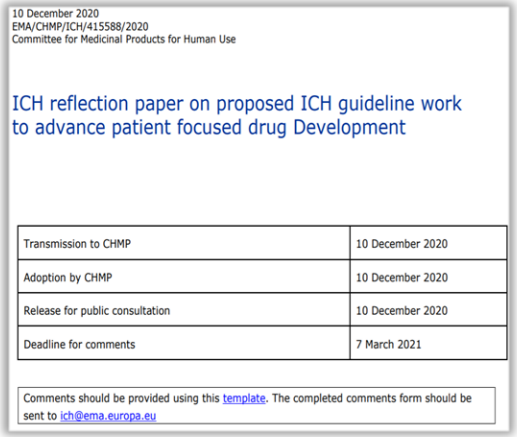
EU reflection paper to complement ICH Guidelines on PED

- Proposal for **new ICH guidelines** will provide **globally harmonized approach** to inclusion of **patient's perspective in a methodologically sound** way, to improve quality, relevance, safety and efficiency of drug development and to inform regulatory decision making.

  1) Focus on informing the drug development process, patient-reported outcomes

  2) Focus on patient preferences regarding benefits and risks

- Scope of Reflection Paper will differ from that of ICH guidance
  - Reflection paper will not cover specific methodological guidance



10 December 2020
EMA/CHMP/ICH/415588/2020
Committee for Medicinal Products for Human Use

ICH reflection paper on proposed ICH guideline work to advance patient focused drug Development

Transmission to CHMP	10 December 2020
Adoption by CHMP	10 December 2020
Release for public consultation	10 December 2020
Deadline for comments	7 March 2021

Comments should be provided using this template. The completed comments form should be sent to ich@ema.europa.eu

Scientific advice & qualification of novel methodologies

The EU approach is to encourage companies to liaise early with regulators during Scientific Advice or Qualification, to discuss best way to generate and collect PED, and have a case-by-case discussion on their specific development plans

Scientific Advice

- **The developer of a medicine presents plans to develop a medicine** and identifies questions and possible solutions.
- **EMA gives advice** on the developer's proposals
- Scientific Advice can be provided on **any PED scientific question** (e.g., clinical trials)

Qualification of novel methodologies

- **Opinion on the acceptability of a specific use of a PED method**, such as the use of a novel PROs
- **Advice on protocols and methods** intended to develop a novel method with the aim of moving towards qualification

Conclusions

- **Engaging with patients in medicines evaluation**
  - Very positive experience to date
  - Brings relevant outcomes for patients, such as PROs and HRQoL, **into scientific discussions**
- **PED is a new scientific discipline**
  - **Collaboration of multi-disciplinary experts** and stakeholders is needed

- **EMA is working to progress on key PED deliverables**:
  - **Reflection paper** on the best EU approach to generate, collect and analyse PED
  - **Increase transparency** - Update of Assessment Report

Thank you
Any questions?

Further information

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