



Why do we have endpoints in clinical trials?

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Estimands

Matching Endpoints and Objectives in Clinical Trials

Armin Schöler, CDDF Webinar, Dec 1, 2020, www.cddf.org



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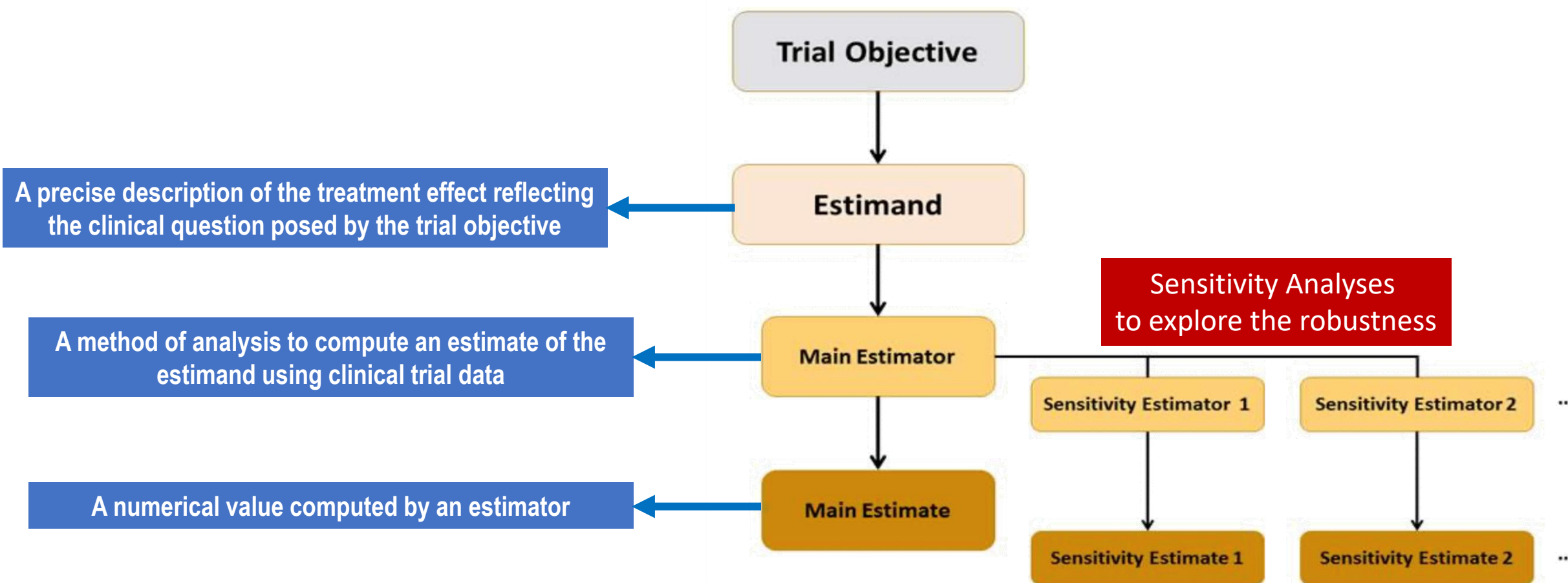
17 February 2020
EMA/CHMP/ICH/436221/2017
Committee for Medicinal Products for Human Use

ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials

Step 5



Endpoints: Clear Description of Benefits and Risks of a Treatment



Registration is open!
www.cddf.org



**CDDF SPRING
CONFERENCE 2021**

08 - 10 February 2021
Virtual Conference

Current and future challenges
of innovative oncology drug
development



Endpoints in Cancer Drug Development

Online multi-stakeholder workshop

- **April 26, 2021**
 - **When Overall Survival cannot be the Primary Endpoint**
- **April 27, 2021**
 - **Endpoints in Expedited Approval Pathways**
- **April 28, 2021**
 - **Patient Reported Outcomes – A Review of Strategies**

Program Committee:
Chitkala Kalidas (Bayer)
Claudia Hey (Merck KGaA)
Denis Lacombe (EORTC)
Ralf Herold (EMA)
Axel Glasmacher (CDDF)



The workshop will be a very interactive meeting with polling of critical questions, Q&A, discussions in break-out groups and panels in addition to presentations

Chat with the rest of the participants in 1:1 chats or group chats. Video calls are also available

Access the live sessions

Check out the Spring Conference welcome video

Networking



Live Sessions



Scientific Programme



Helpdesk



Live Sessions



Take a look at the Scientific Programme and speakers line-up

Need help to navigate the Virtual Platform? Click on this button

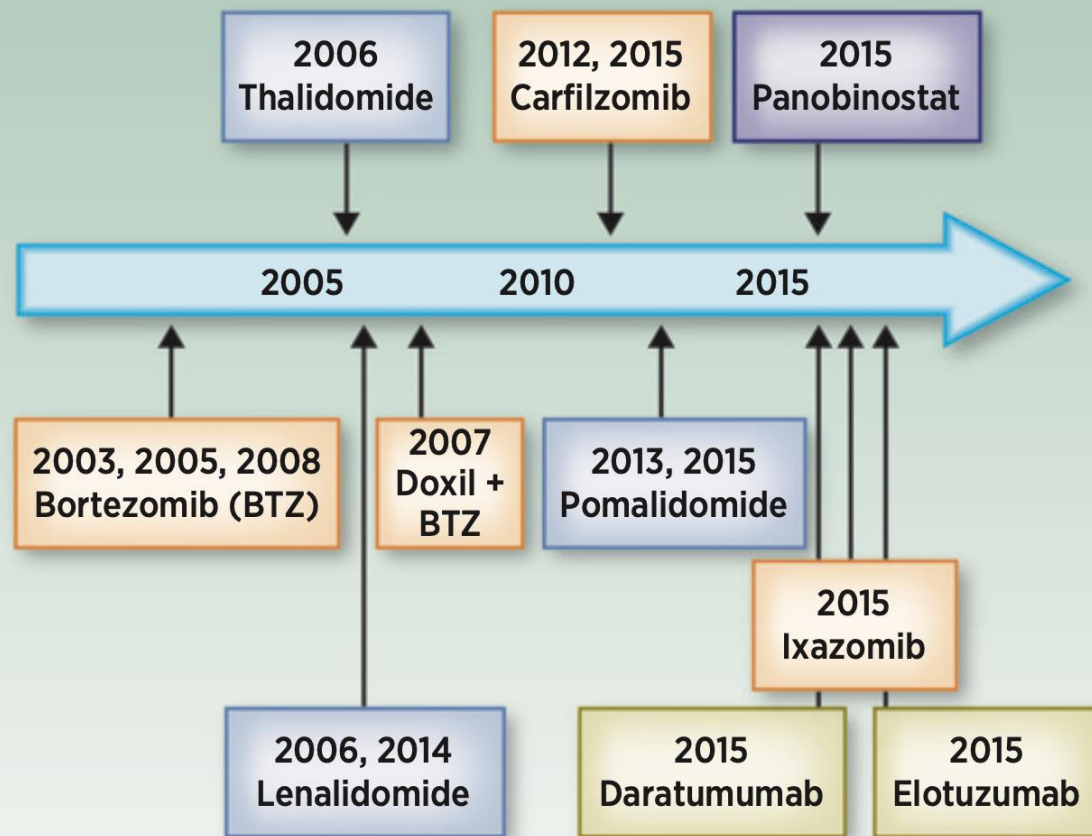
Follow the Cancer Drug Development Forum LinkedIn page

CDDF
Cancer Drug Development Forum



Should overall survival always be the primary endpoint?

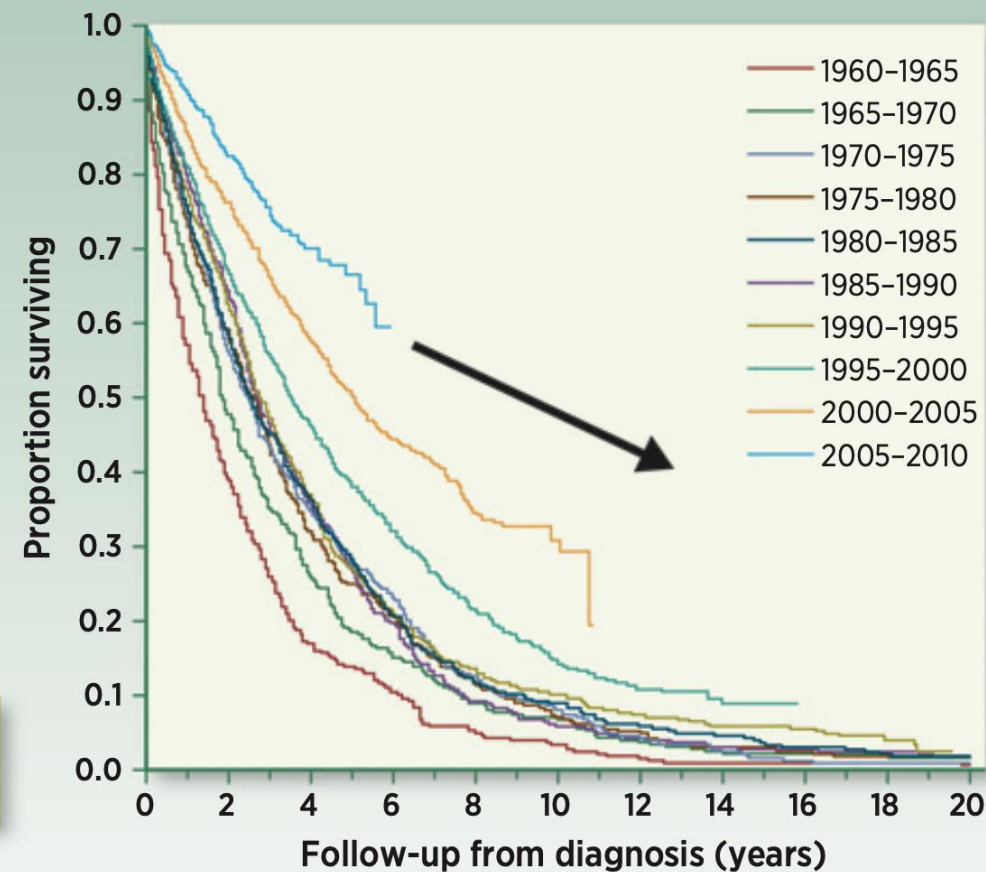
Preclinical and clinical studies leading to FDA approvals in MM



Immunomodulatory agent
Monoclonal antibody

Proteasome inhibitor
HDAC inhibitor

Improvement in overall survival from median of 3 to 8-10 years





In favour of alternative endpoints (e.g. PFS, MRD)

- Overly long study duration delays introduction of effective treatments
- Availability of effective subsequent therapy can mask treatment effects
- Unintended switch-over of control arm to treatment or other therapies
- Includes non-cancer deaths

In favour of OS only

- OS is the most important outcome for patients
- Alternate endpoints are not necessarily correlated with overall survival or clinical benefit
- Potentially subject to assessment or timing bias



When OS cannot be the primary endpoint

Virtual CDDF Multi-Stakeholder Workshop, April 26, 2021

- Introduction by the chairs Denis Lacombe (EORTC), Ralf Herold (EMA)
- Reflection on the challenge Axel Glasmacher (CDDF)
- Pathway towards solutions
 - Pharmaceutical Industry Chitkala Kalidas (Bayer) Elmar Schmitt (Merck KGaA)
 - Regulatory Agency Filip Josephson (EMA)
- Breakout groups: Discussion, questions for the panel
- Panel & Audience Discussion



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Endpoints in Expedited Approval Pathways



A balance between risk tolerance and avoidance

Eichler et al., Nat Rev Drug Discov 2013; 12: 907-16



Expedited Approval Pathways

FDA

- Fast track program
- Breakthrough therapy
- Priority review
- Accelerated approval

EMA

- Accelerated Assessment
- Conditional Approval
- PRIME: Priority Medicines

Accelerated approval based on response rates

- Often single-arm studies with > 100 pts. usually a last-line setting with no available approved therapy
- “Endpoint reasonably likely to predict clinical benefit over available therapies” (FDA)
- Assessment routinely includes response rates, duration of response, safety and other endpoints
- Critical comments: only modest response rates, lack of randomized trials in follow-up, may not correlate with survival
- Lack of control groups – risk of bias



Endpoints in Expedited Approval Pathways

Virtual CDDF Multi-Stakeholder Workshop, April 27, 2021

- Introduction by the chairs Serban Ghiorghiu (AstraZeneca), Axel Glasmacher (CDDF)
- Patient Perspective (NN)
- Regulatory Agency Perspective Vishal Bhatnagar (FDA)
- HTA Perspective (NN)
- Breakout groups: Discussion, questions for the panel
- Panel & Audience Discussion



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Patient-Reported Outcomes: Review of Strategies



Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma

Measuring QoL in interventional trials

If the intervention is more effective than the control:

- more control patients discontinue the study
- this creates an imbalance in the HR QoL assessment
- while the main benefit for QoL would be between those progressing and those not progressing

Patient in the centre

Use of mobile and wearable devices to assess PRO



Patient-Reported Outcomes – A Review of Strategies

Virtual CDDF Multi-Stakeholder Workshop, April 27, 2021

- Introduction by the chairs Anne Sophie Darlington (EORTC), Michael Zaiac (Novartis)
- Patient Perspective Jayne Galinsky (MPE)
- Regulatory Agency Perspective Vishal Bhatnagar (FDA)
- Industry Perspective Paul Kamudoni (Merck KGaA)
- HTA Perspective (NN)
- Breakout groups: Discussion, questions for the panel
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CDDF MULTI-STAKEHOLDER WORKSHOP

Endpoints in Cancer Drug Development

26 - 28 April 2021

ONLINE WORKSHOP

Possible further topics:
MRD Estimands

