ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

INTERPRETATION OF CLINICAL TRIALS

Alberto Sobrero

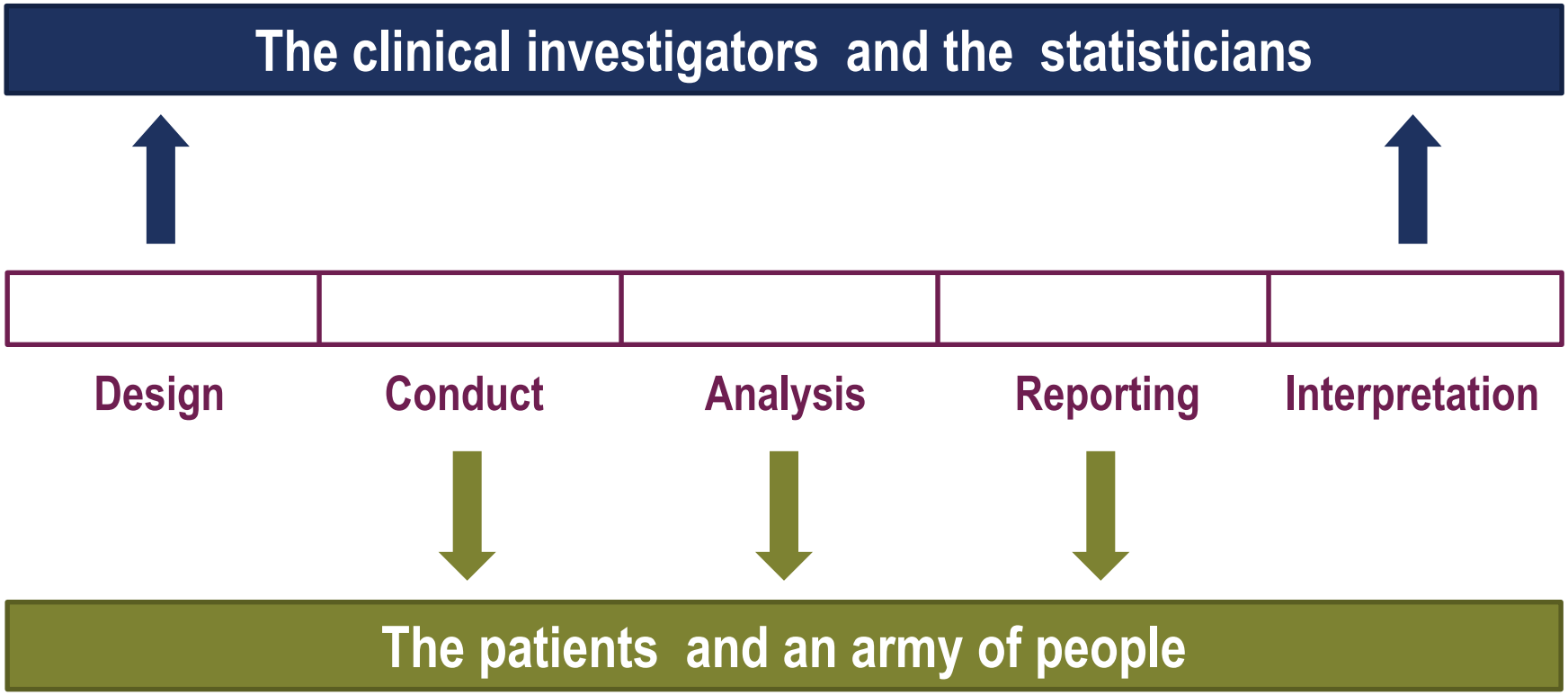
IRCCS San Martino IST, Genova Italy

oncology PRO
Educational Portal for Oncologists

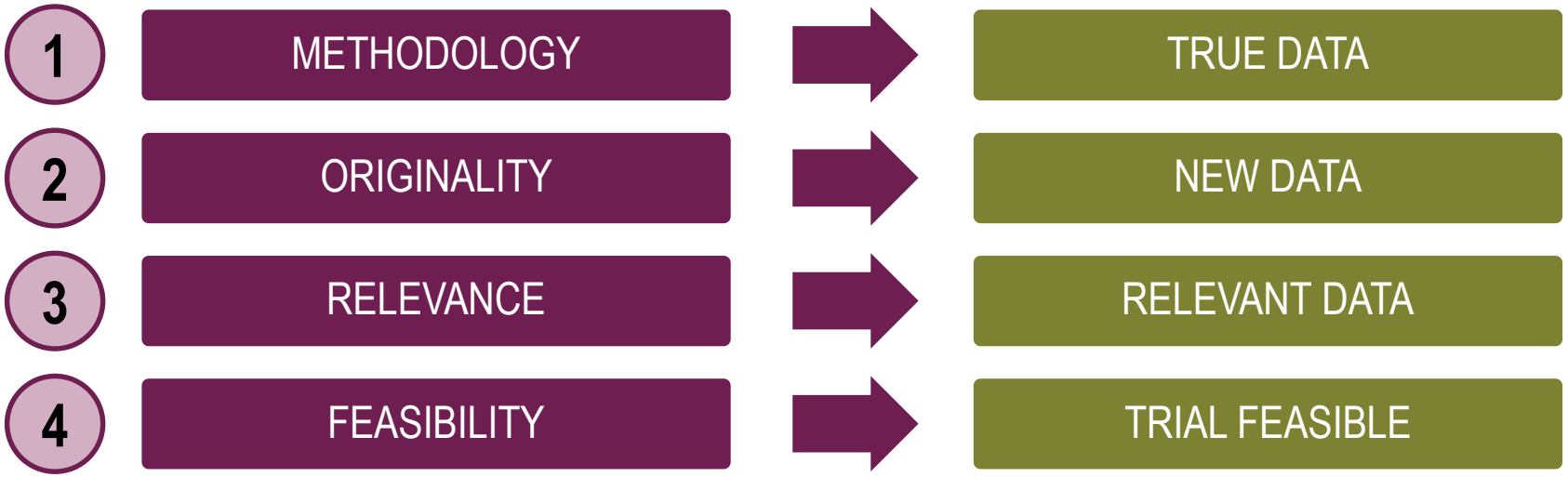
DISCLOSURES

Prof Sobrero is member of the Speakers Bureau and of the Advisory Board for:
Roche, Merck, Bristol-Myers Squibb, Celgene, Amgen, Servier, Sanofi, Lilly and Bayer.

CLINICAL TRIALS:
THE 5 PHASES AND THEIR ACTORS



DESIGN


1
METHODOLOGY
TRUE DATA
2
ORIGINALITY
NEW DATA
3
RELEVANCE
RELEVANT DATA
4
FEASIBILITY
TRIAL FEASIBLE

INTERPRETATION

SO WHAT ?

INTERPRETATION

1. How true ?
2. How generalizable ?
3. How relevant ?

1 How true ?

INTERNAL VALIDITY

+

INTERNAL and EXTERNAL CONSISTENCY

+

BIOLOGICAL AND CLINICAL PLAUSIBILITY

2 How generalizable ?

EXTERNAL VALIDITY

- Pt characteristics
- Therapeutic regimen
- Compliance
- Comparator arm

3 How relevant ?

Clinical relevance vs statistical significance

3 How relevant ?

1. Size of benefit?
2. Which endpoints? OS PFS RFS RR QOL
3. How were these expressed? Median , HR, % at….
4. Under which condition
5. How generalizable? → external validity
6. Which toxicity?

(Which cost?)

CLINICAL BENEFIT

EFFICACY

TOXICITY

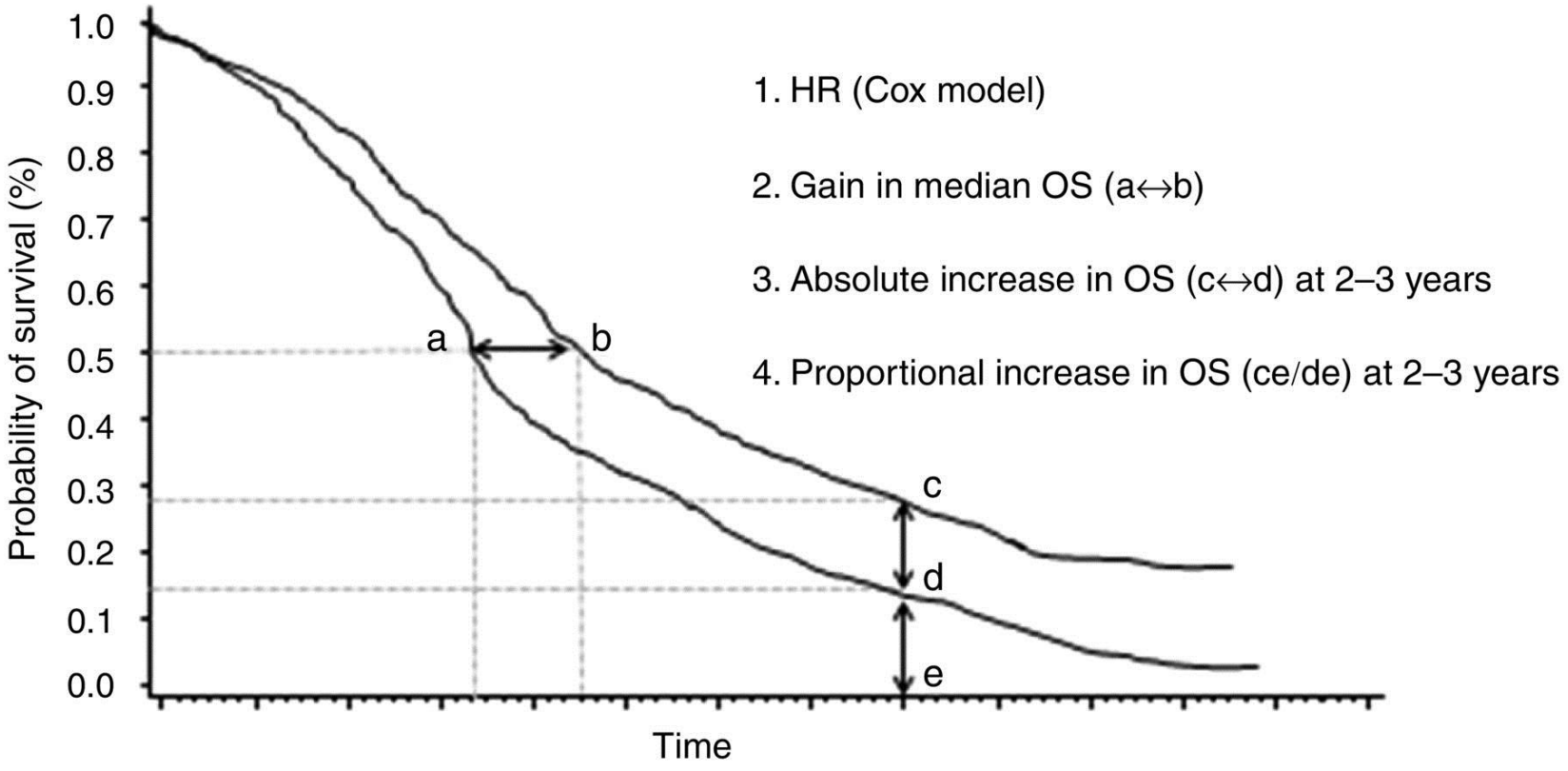
CONVENIENCE

Setting - curative vs palliative
- prognosis within palliative

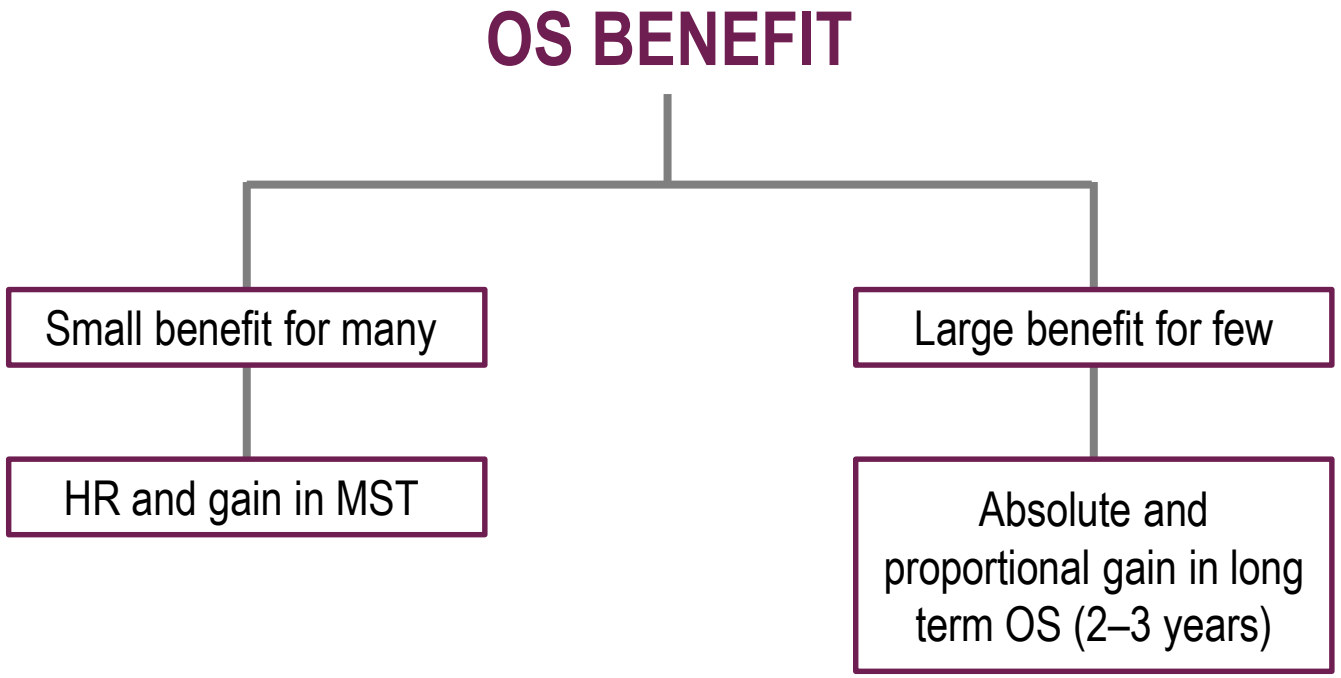
Endpoint - type
- ways to summarize the efficacy endpoint

Size - delta

A “model” of Kaplan–Meier figure showing the four OS-related parameters.



THE FOUR WAYS TO ASSESS OS BENEFIT



HR, hazard ratio; MST, median survival time; OS, overall survival.

Sobrero, Bruzzi, Clin Ca Res 2015.

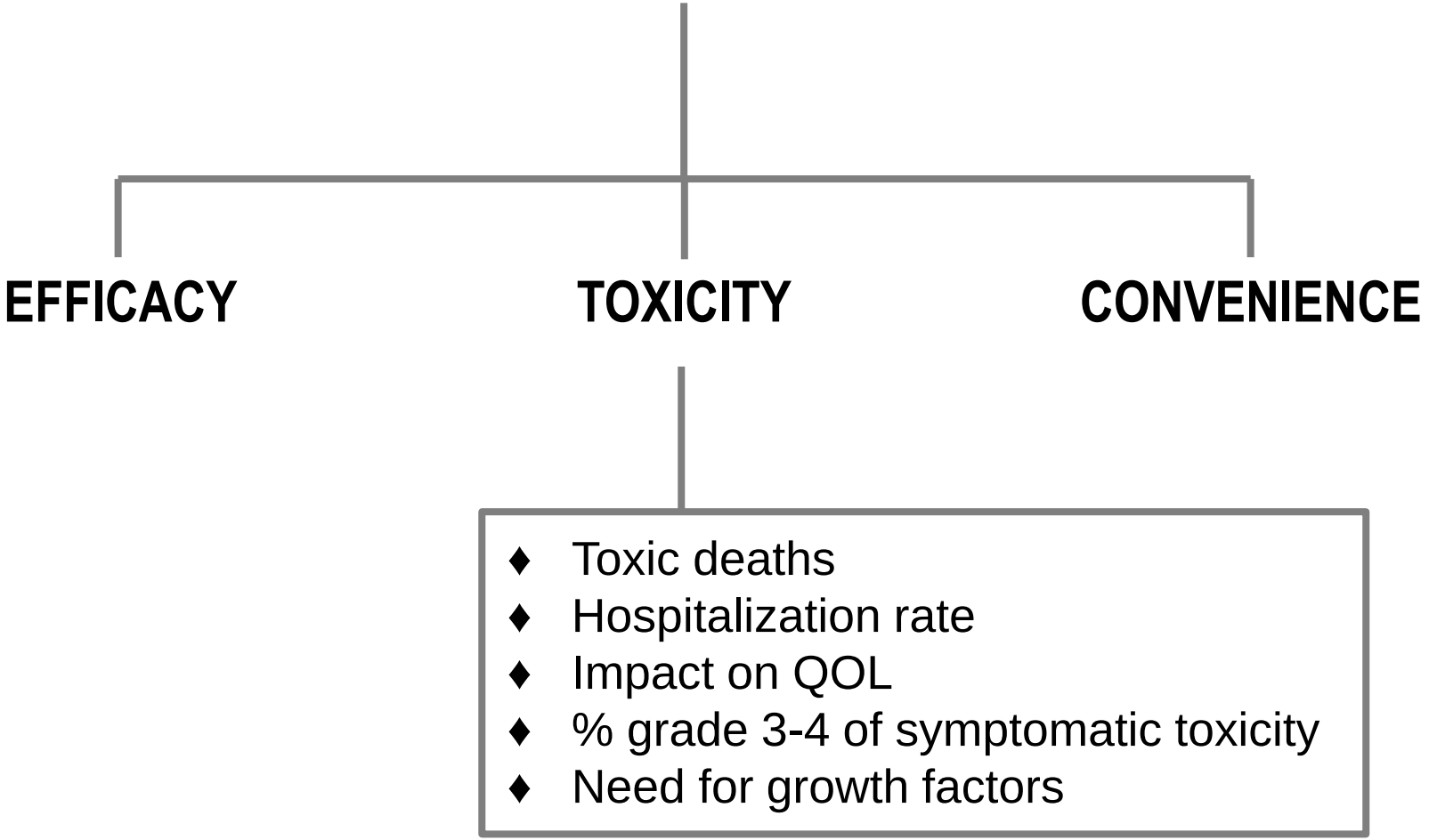
INCREASE IN MEDIAN PFS / OS FOR DIFFERENT HR AS A FUNCTION OF THE SEVERITY OF PROGNOSIS

MST / PFS in control (months)	Increase in median values (months) as a function of HR					
	HR 0.9	HR 0.8	HR 0.7	HR 0.6	HR 0.5	HR 0.4
3	0.3	0.7	1.3	2	3	4.5
6	0.6	1.5	2	4	6	9
12	1.4	2	5	8	12	18
24	2.6	6	10	16	24	36

Clinically worthless | **Unrealistic**

HR, hazard ratio; OS, overall survival; MST, median survival time; PFS, progression-free survival

CLINICAL BENEFIT



INTERPRETATION

SO WHAT ?

1. SUPERSTARS
2. INCREMENTALISTS
3. TRADE-OFFS
4. OUTCASTS

INTERPRETATION OF NEW DATA

Are these data true?

- Internal validity
- Internal consistency
- Plausibility
- External consistency

Are they relevant?

- External validity
- Clinical benefit

Are they practice-changing?

- ‘Relevant enough’

INTERPRETATION OF NEW DATA

Are these data true?

- Internal validity — stat. design, randomization endpoint , ITT
- Internal consistency — concordance among RR,PFS,OS
- Plausibility — philosophycal issue
- External consistency — results in other trials

Are they relevant?

- External validity — pt charact, schedule,compliance, comparator
- Clinical benefit — efficacy, toxicity, convenience

Are they practice-changing?

- 'Relevant enough' — clinical benefit, clinical value

CONCLUSIONS

- Never be dogmatic
- Consider internal validity
- Consider external validity
- Consider all aspects of efficacy
- Consider the entire story, when available

Thank you!