safety analyses: The cinderella of Biostatistics?

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This session is a reflection and advertisement on the safety statistics in our day-to-day work.



What comes into your mind if you think about Statistics in Pharma

Efficacy?

it's all about benefit / risk!







How present is Safety in our thinking? **ICH E9 (R1)**

Let's take the new ICH E9 (R1) Addendum on Estimands and Sensitivity analysis in clinical trials as an example

Is this an Efficacy or an Safety Guideline, or both?

Hits when searching for effect, efficacy, safety, and risk[#]

✓ 😤 C:\U\ICH_E9_R1_Addendum on estimands_2019.pdf	✓ ☆ C:\U\ICH_E9_R1_Addendum on estimands_2019.pdf
🔯 treatment effect" will be misunderstood. This addendur	
the treatment effect(s) of interest that a clinical trial sho	 C:\U\ICH_E9_R1_Addendum on estimands_2019.pdf and risks of a treatment (medicine) for a given medical cond
treatment effect of interest is facilitated by constructin	$\overline{\mathbb{W}}$ the $\operatorname{\mathbf{risk}}$ of an adverse drug reaction while the patient is expo
the treatment effect of greatest relevance to regulatory a	
ifferent treatment effects ITT principle is the basis/ corr	> 3 * safety/risk
these treatment effects that are reliable for decision mak	> 4 * efficacy
is about treatment effects and the practical benefits of bal	
the treatment effect of interest in a way that determines	> 46 * treatment effect
that treatment effect and the observations from each su	
🔯 a treatment effect is estimated, or a hypothesis related to	
treatment effect is tested, whether related to efficacy o	
of treatment effects: how the outcome of treatment con	to efficacy or safety. While the main focus is on randomised clinical t
of treatment effects. Now the outcome of treatment con	🤯 of efficacy; the event might require to be of certain magnitude or de <u>c</u>
the treatment effect reflecting the clinical question pose	by of efficacy. An estimand can be constructed to target a treatment effe
targeted treatment effect. The description of an estiman European Stat Leader Meeting 2020-07-25	of efficacy". Where that has been defined as an intercurrent event, th

ty/risk acy tment effect

=> Efficacy only? What came into your mind?

be made available"

isn't it?

I must admit, my first association was efficacy, but treatment effect is both,

By the way the first sentence reads: "To properly

inform decision making by ... clear descriptions

(medicine) for a given medical condition should

of the benefits and risks of a treatment

[#] adjusted for 2 findings not related to safety



How present is Safety in our thinking **EMA Benefit-Risk project**

Who knows about the EMA Benefit-Risk project?



Research projects

Benefit-risk methodology

Benefit-risk methodology

The European Medicines Agency's opinions are based on balancing the desired effects or 'benefits' of a medicine against its undesired effects or 'risks'. The Agency can recommend

the authorisation of a medicine whose benefits are judged to be greater than its risks. In

contrast, a medicine whose risks outweigh its benefits cannot be recommend.

marketing.

Weighing up the benefits and risks of a medicine is a complex process, since it involves a large amount of data. In addition, there is always some uncertainty around the actuar risks of a medicine, because they can only be determined by looking at the information at a given point in time.

	Work package	Status
/es	 Describing the benefit-risk assessment models already being used in the European Union's regulatory network 	Completed March 2010
ua or	Assessing the suitability of the current tools and processes used in benefit-risk assessments	Completed August 2010
	Field-testing the most appropriate models in five European medicine regulatory agencies	Completed June 2011
	Refining the most suitable models for use in medicines regulation to create a new benefit-risk tool	Completed February 2012
	5. Training European assessors to use the final tool	Started March 2012



Focus we give Safety Example Visualisation - ASCO

> 42,500 attendees in 2019 to the Annual Meeting

> I would guess

99.9% of all presentations display efficacy using graphics for visualisation &

83.4% of all presentations display safety as tables only (and sometimes related AEs only)





Focus we give Safety **Recognition**

- > During a submission who is the star
 - the efficacy stats?
 - the safety stats?
- Moving to safety statistics how might this be perceived
 - climbing up the job ladder?
 - put on the sideline?
- > Do we recognise that for safety statistics a special skill set is needed?
- > When do we start to think about safety in drug development
 - when writing the ISS SAP?
 - just after first patient in, e.g. we support the risk management plan early?
- > What do we do when a new safety finding is recognised
 - throw the messenger into the dungeon?
 - congratulate the messenger that we have identify the risk early?



For reflection

- > What is the value of safety analysis in your company?
- > What is the value you give safety when communicating with your team?
- > What is the resourcing provided on safety (stats & programming)?
- > What is your view on the need of a special skill set?
- > What is the complexity of safety analyses (prg & stats) compared to efficacy analyses?
- > What is the data source your team is using for safety assessment?

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Discussion



