a flavour of patients' organisations views on ICH E6 guidelines GOOD CLINICAL PRACTICES

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ICH E6(R3) Good Clinical Practice workshop with PCWP and HCPWP, 3 June 2020

An excellent opportunity to revise or even set standards about

Scope: clinical trials for the regulation of medicines, or more?

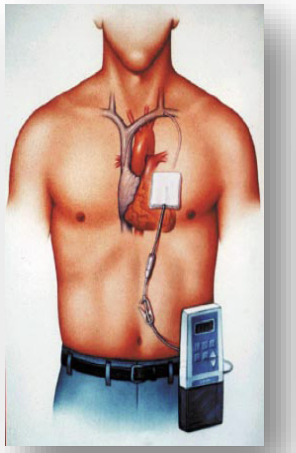
Beyond "pivotal" trials

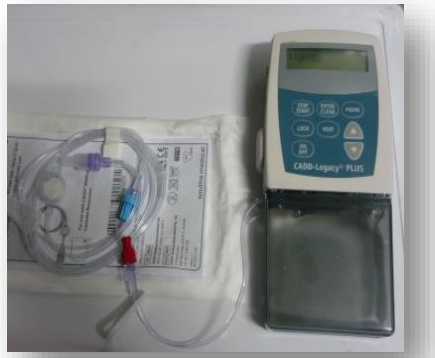
- Treatment strategy trials with authorised products
- To answer questions
  - Which products work best when first line treatment fails?
  - Combination therapy?
- Observational study with an off-label use: not a CT?
- Annex 1 - Interventional clinical trials

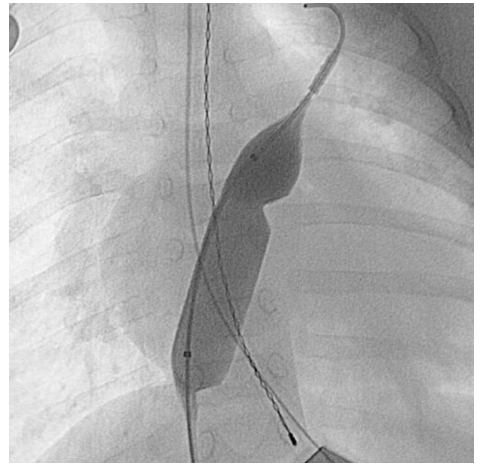
Medicines/medical devices

- Active substances combined with a medical device
- Testing medical devices alone
- Do we need different standards for trials to test medical devices than for medicines?

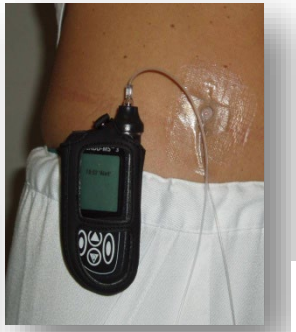
Compared to SOC: but what is SOC? Pulmonary hypertension

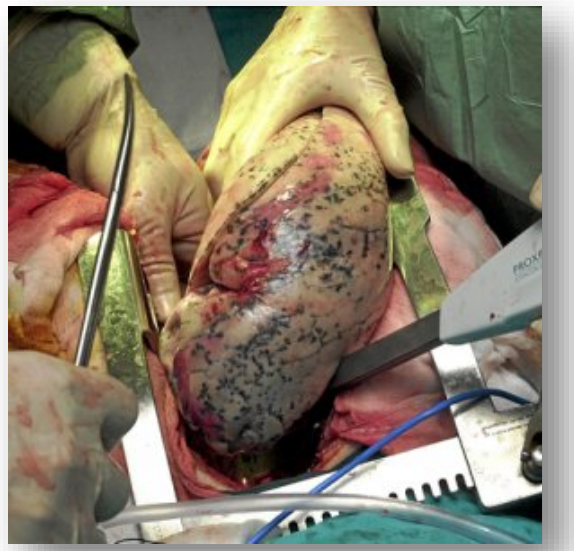






Atrial septostomy





Lung transplantation

An excellent opportunity to revise or even set standards about

The conduct of clinical trials is evolving

Virtual and mixed trials

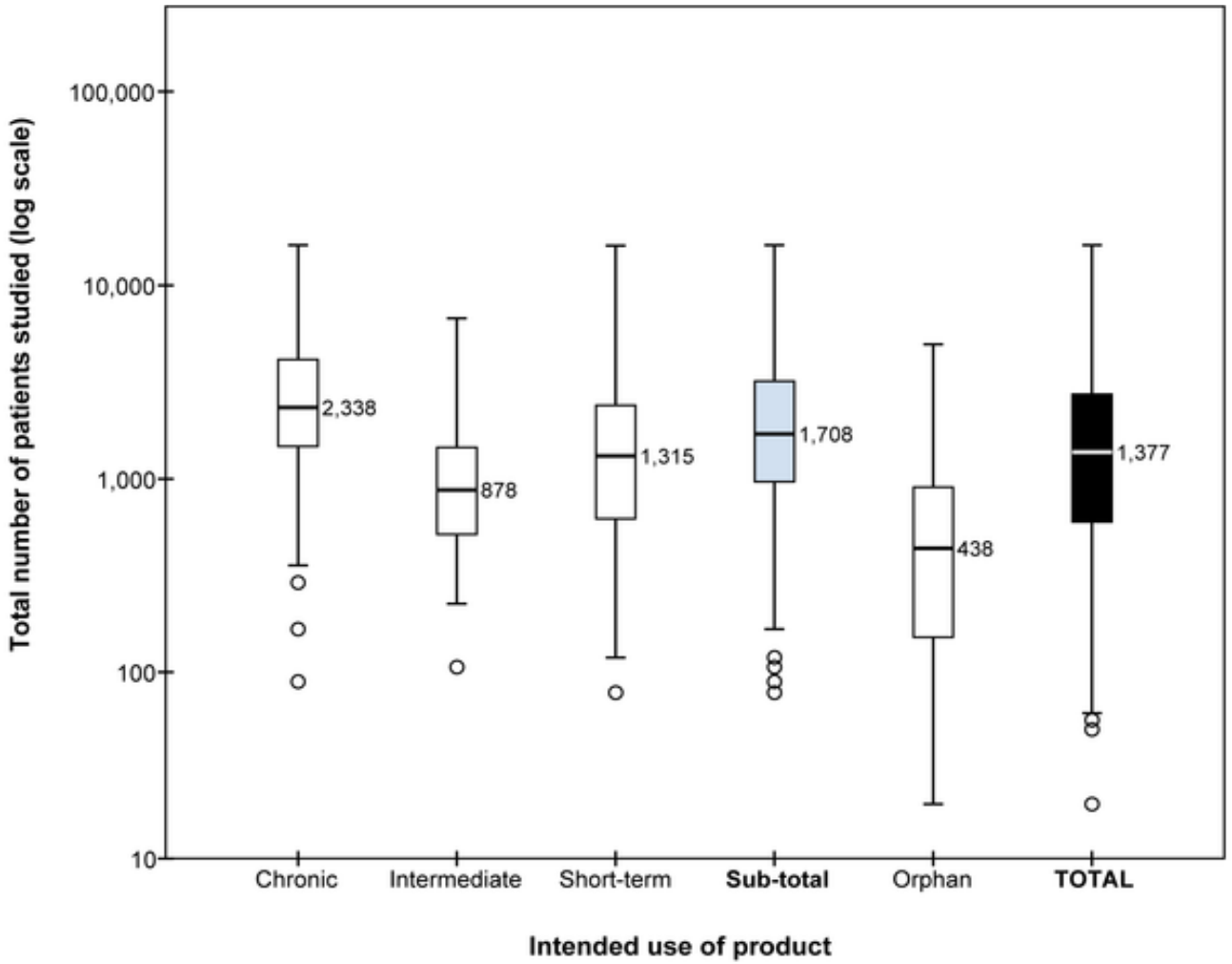
- Telemedicine with clinical investigator / research nurse
- Connected devices to measure patient outcomes
- IMP shipped to participant's address
- e-consent

Patient populations

- Large populations of 3,000 or more trial participants in a dossier and precision medicine or rare diseases?
- New approaches to generate more data

Trial population of 3,000 per dossier?

Figure 1. Boxplots with medians of the number of patients studied before approval.



Duijnhoven RG, Straus SMJM, Raine JM, de Boer A, et al. (2013) Number of Patients Studied Prior to Approval of New Medicines: A Database Analysis. PLoS Med 10(3): e1001407. doi:10.1371/journal.pmed.1001407
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001407

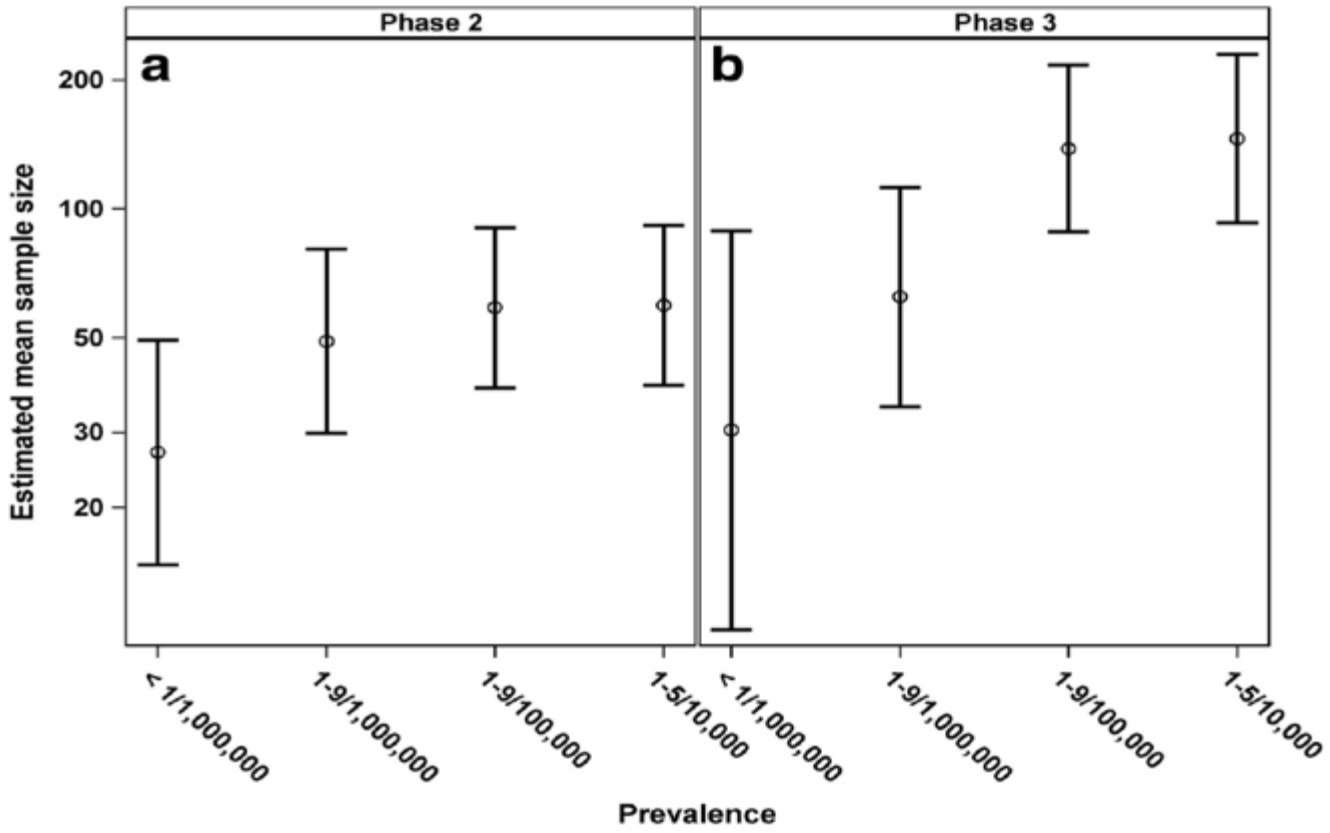
RESEARCH Open Access

Does the low prevalence affect the sample size of interventional clinical trials of rare diseases? An analysis of data from the aggregate analysis of clinicaltrials.gov

Siew Wan Hee[1*], Adrian Willis[2], Catrin Tudur Smith[3], Simon Day[4], Frank Miller[5], Jason Madan[6], Sarah Zohar[7] and Nigel Stallard[1]

Presented by Olivier Collignon, PhD, on 16 April 2018
EMA, National expert seconded from the Luxembourg Institute of Health

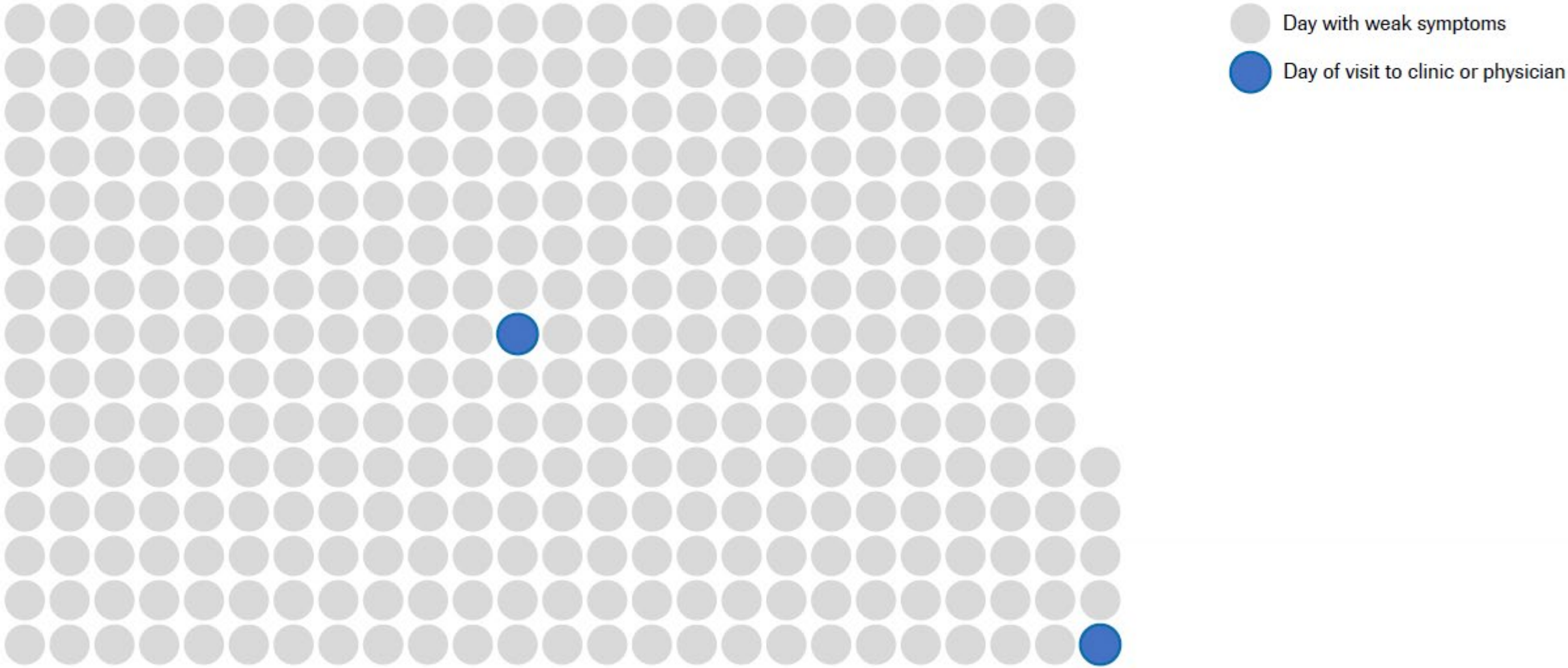
"We found that t here were very few multi-nation trials suggesting that the opportunities to conduct larger or 'adequately' size trials were underused."



How is the patient doing outside of the clinic?

Credit: Tom Metcalfe
PHC Center of Excellence,
Roche Pharma Product Dev.
DIA Value, Access, and Regulatory Strategy Conference
8-9 October 2018, London

A year in the life of a patient with e.g. Parkinson's



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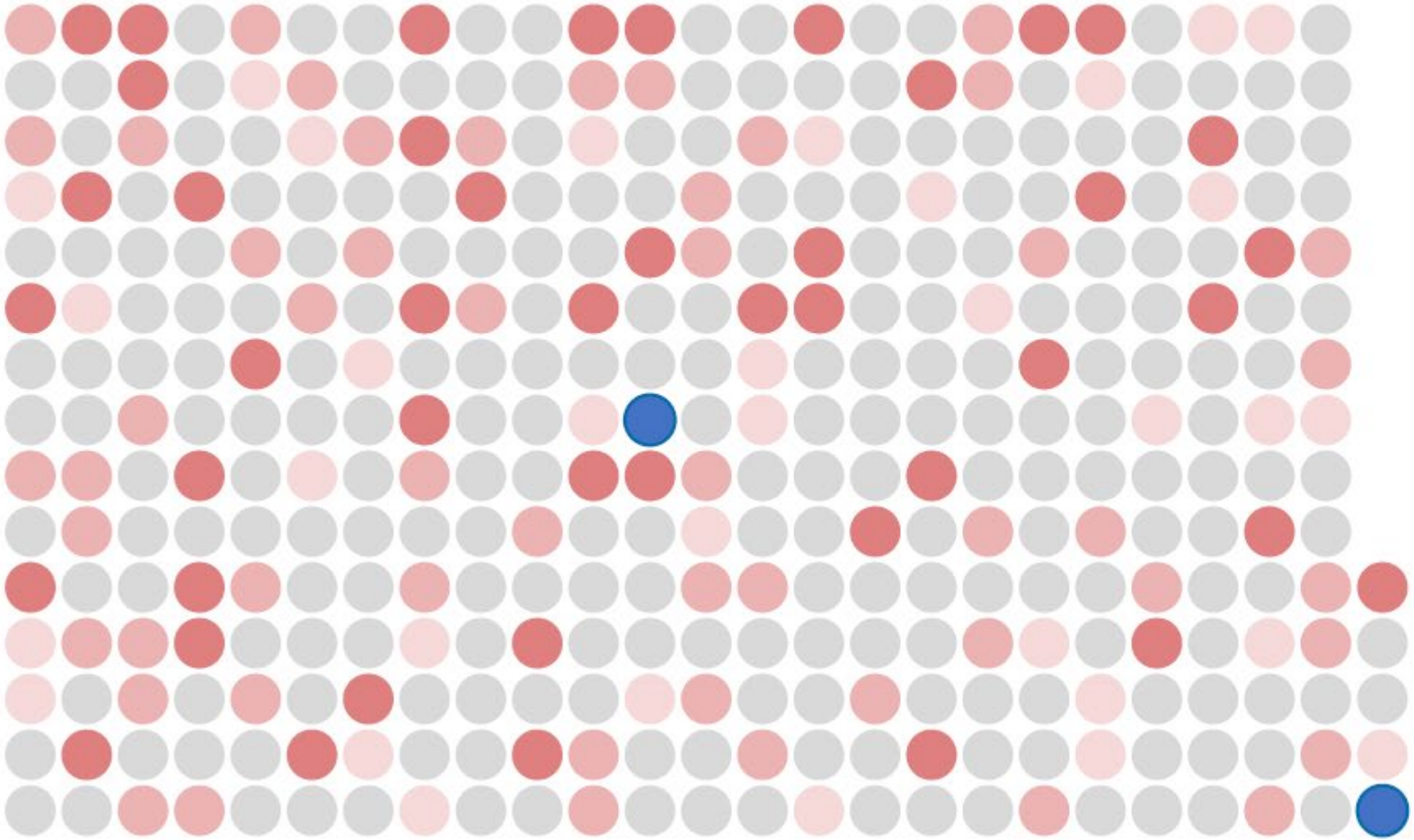
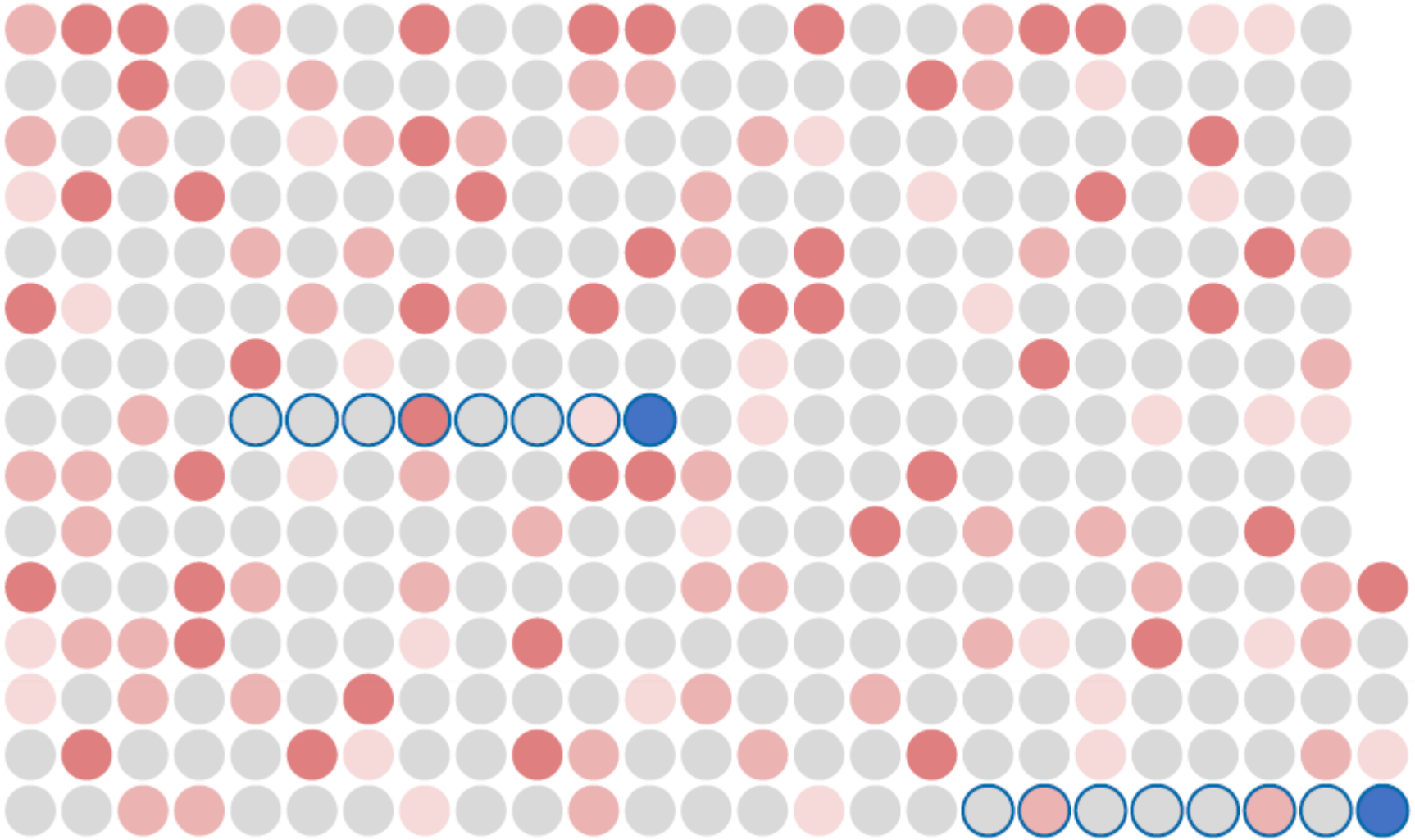


Day with weak symptoms

Day of visit to clinic or physician

Day with stronger symptoms

A year in the life of a patient with e.g. Parkinson's



Day with weak symptoms

Day of visit to clinic or physician

Day with stronger symptoms

Patient's recall period

And also

- *Adaptive trials, single arm trials with large effect size…*

• Anti-PD-L1 products (e.g. Keytruda)

Phase I trial, single arm, evolving into phase III (more participants recruited)

With important effect size that could be attributed to the treatment (otherwise high mortality condition)

Use of placebo difficult as no more equipoise?

• Multi-factorial trial design testing different IMPs

Head-to-head comparison of several investigational products in same trial

Lowering the risk to be randomised to the placebo arm

E.g. several antibodies tested for asthma

• And important other issues

Such as access to the experimental product at the end of the trial

Roll-over studies – on-treatment studies - longer-term registries

Or data collection in compassionate use

In short

- Third revision of ICH E6 guidelines are very welcome
- Patient organisations could certainly contribute
- Starting with *Interventional clinical trials* and *Additional considerations for non-traditional interventional clinical trials*
- As we need to explain all these changes to our members and patients in general

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Thank you.

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