TRIAL WATCH

Transition probabilities for clinical trials: investigating individual diseases

Clinical trial transition probabilities, the probability that a drug product moves from one clinical phase to the next, are used to assess the efficiency of drug development and in the valuation of investigational drug projects. These rates are typically calculated at the level of therapeutic areas, but it is unclear whether the transition probabilities for therapeutic areas accurately predict the transition probabilities for individual diseases within those areas.

To investigate this key question, we have analysed individual disease-level cumulative phase success probabilities for eight diseases: amyotrophic lateral sclerosis (ALS), Crohn's disease, cystic fibrosis, hepatitis C, multiple sclerosis (MS), rheumatoid arthritis (RA), schizophrenia and sepsis. These diseases were also classified as rare or not rare, and based on whether the level of understanding of their efficacy biomarkers was high/medium or low/none. Citeline's Pharmaprojects database was used to determine the number of drug development programme starts for each disease from 2000–2017, as well as the success of those programmes, encompassing ~1,800 programmes overall (see Supplementary Box 1 for details). The individual success probabilities were then compared with those of their therapeutic areas, as reported in two published studies by Hay et al. (*Nat. Biotechnol.* **32**, 40–51; 2014) and Thomas et al. (see Related links).

For five of the diseases that we studied, there are phases in the development process where the success probability of the individual disease deviates more than ten percentage points from the therapeutic area success probability, which we interpret as meaningful deviations (FIG. 1). For example, compared with drugs in the neurological therapeutic area overall, ALS drugs appeared to fail less frequently between phase I and phase II (cumulative phase success probability of 62% for neurology versus 75% for ALS) and between phase II and phase III (success probability of 19% for neurology versus 27% for ALS), but had greater rates of failure between phase III and launch (success probability of 9–15% for neurology versus 4% for ALS).

However, all three autoimmune disorders, Crohn's disease, RA and MS, appear to follow very similar success probability trajectories at each development stage, and almost precisely matched that of the therapeutic area (Supplementary Box 1). This finding does not appear to be driven by any single disease, and, given the number of drugs in development for the individual diseases, it also does not appear that this trend is driven by a single drug class (such as TNF blockers). It is also notable given the differences in the availability of efficacy biomarkers for these diseases, with MS and RA having biomarkers classified as 'high/medium', whereas Crohn's disease does not. Overall, the trends for the diseases analysed suggest that while having such biomarkers is important for success in phase III, there are other factors involved (see Supplementary Box 1). No clear trends were apparent with regard to success probabilities and whether a disease was rare or not.

In conclusion, it appears that the success probabilities for therapeutic areas are not precise predictors of the success probabilities for individual diseases in the area, albeit with some exceptions. This could have important implications for drug developers, investors and policymakers. Further study of additional individual diseases is needed to ascertain the magnitude of these differences across other diseases and within therapeutic areas.

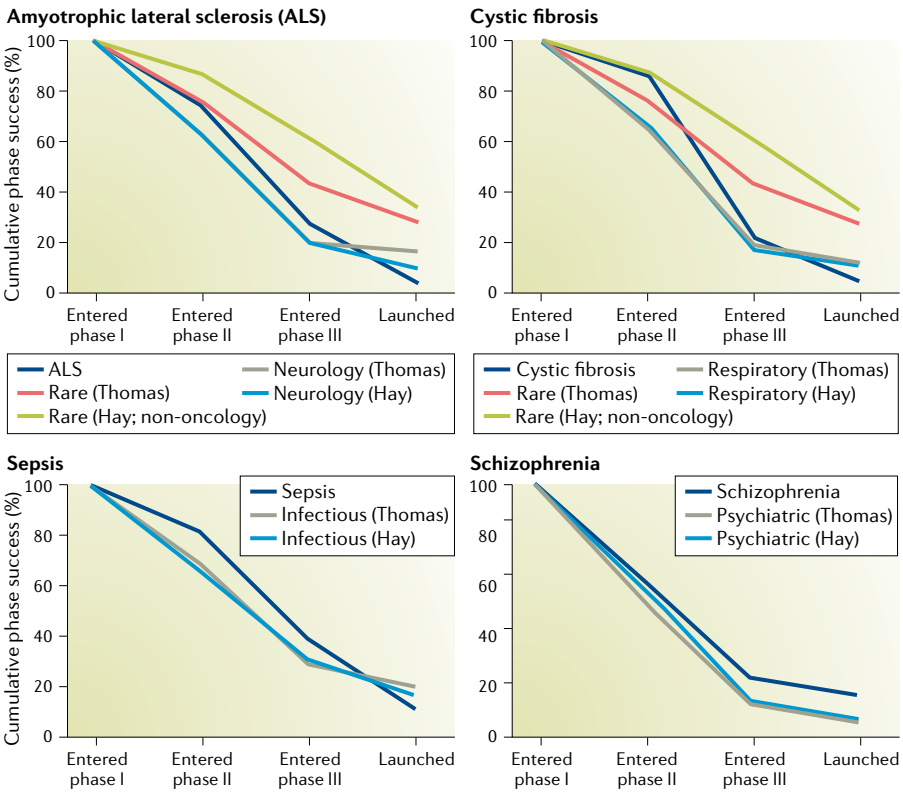

Fig. 1 | **Cumulative phase success probabilities for selected diseases in comparison to probabilities in the relevant therapeutic area.** Two published studies, Hay et al. and Thomas et al., were used for the therapeutic area comparisons. See Supplementary Box 1 for details.

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Competing interests
The authors declare no competing interests.

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Supplementary information
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