Who and why; How do we allocate screening slots for highly competitive trials?
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The rapidly changing cystic fibrosis (CF) trial landscape brings exciting opportunities and new challenges. Securing screening slots into recent late phase trials of CFTR modulators can be fiercely competitive with the number of eligible patients far exceeding the available slots.

Reviewing the literature suggests the extent of the situation is unprecedented within CF and other disease groups. It is difficult to explain the phenomenon; and could simply be a case of underreporting. However, there are some distinctive features of the current CF trial paradigm and disease characteristics that may plausibly contribute to the unusual circumstances, such as the interest modulators have received in the CF community and the large pool of relatively stable patients who may be eligible to participate.

With several competitive trials on the horizon, our site developed a Standard Operating Procedure (SOP) to efficiently allocate slots whilst helping patients to understand the selection process. Here, we share some illustrative experiences of developing the SOP and invite comment on how other sites have approached similar problems. Although each site has its own nuances in trial delivery, we suggest the general principles of our model have potential widespread application across centres where patient interest exceeds screening slot availability.

Deciding how to prioritise enrolment in trials is complex. Offering opportunities to those who have previously participated in trials or who proactively contact the trial team may represent pragmatic strategies, as does choosing patients who engage well with clinical care. However, there is increasing evidence that factors such as education level and socioeconomic status influence patient opportunities within the clinical trials space. We propose that targeted selection may drive this phenomenon, contributing to inequality of opportunity and resulting in a less representative sample of patients entering trials. As such, the overarching principle of our SOP was to offer equal opportunities to all patients meeting
the trial’s inclusion/exclusion criteria and minimise conscious or unconscious selection bias by healthcare professionals.

An initial challenge was how to approach inclusion/exclusion criteria which introduce elements of subjectivity. To maintain patient safety, trial integrity and the core values of good clinical practice, inclusion/exclusion criteria specify that patients must be able to give consent and comply with student requirements. It was decided patients should only be excluded on these criteria with multidisciplinary team agreement to minimise potential bias from individual judgement calls. In actuality this group represented a negligible proportion of our clinic population.

The approach to patients who had participated in early phase trials was one of the more controversial discussions within our team, and highlights some of the complexities of defining prioritisation strategies. Some team members advocated giving special consideration to those who had committed the time and accepted the higher risk of early phase trials. They feared removing the incentive of easier passage into later phase trials may slow recruitment to early phase trials. Others reasoned that patients who have taken part in early phase trials have already demonstrated that they tolerate the compound, thus preferential selection of these patients narrows the available safety data. Early phase trial selection criteria are tighter than phase three trials, so reselecting these patients may favour a healthier population. As such, to meet our primary goals of equal opportunity and reduce selection bias, participation in an early phase trial did not change the way in which patients were considered for a screening slot.

Overall the SOP has ensured a transparent approach to allocating screening slots; minimising selection bias, improving equity of opportunity, mitigating potential challenges and complaints and opening recruitment to patients who may otherwise not have been considered. The first time it was used, the entire group selected to screen had not participated in a commercial trial previously and included a teenager with autistic-spectrum disorder, who has proved to be an excellent trial candidate. His parents said “No-one picked our son to have CF and no-one picked him for the trial. Both were acts of random selection.”
We’re incredibly grateful that he has had the opportunity to trial this drug, and he is doing really well.”

A patient who was not selected to screen shares their views on the SOP: “To not be selected is definitely upsetting. When an opportunity arises that could provide access to a potentially life-changing medication it’s unsurprising that so many people want to be a part of the trial. However, to me, this SOP is a great initiative. If you’re not selected you can take comfort in the knowledge that somebody else is getting a chance, and you can understand why they got that chance.” An emergent challenge is how to manage the disappointment of those who do not get places on trials; and ensure that their disappointment does not impact on their downstream relationships with their clinical teams. We hope that the transparency of our system goes someway to assist this process.
Declaration of interest

RD and SS have no declarations of interest. NJS has consulted for Vertex Pharmaceuticals, Chiesi, Roche, Pulmocide, PTC Therapeutics and Gilead. JCD has served on advisory boards and participated in clinical trial leadership, educational activities and grant review board activities for a number of pharma companies active in CF clinical trials: Vertex, PTI, Galapagos, AbbVie, AlgiPharma, Chiesi, Enterprise, Teva, Ionis, Eloxx, Roche, Gilead.


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