Impact of the clinical trial design strategy on product market uptake and overall commercial success

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Introduction

Recent breakthroughs in the space of cardiovascular diseases, oncology and some rare diseases have revolutionised the treatment paradigm and improved outcomes for many patients. Bringing this into the context of regulatory approval and health technology assessments (HTA) across Europe has meant that proving a significant level of efficacy against existing comparators rather than placebo is increasingly hard. Thus, pharmaceutical companies increasingly face difficulties designing their clinical trials in a way that corresponds to the needs of regulators, whilst at the same time optimising the overall commercial success of products and minimising costs associated with their clinical trial programmes. There is therefore a growing need for pharmaceutical companies to re-evaluate their trial design strategies. In light of these considerations, the study aims to assess if a broad, investment-heavy clinical trial strategy results in broader market access and improved commercial success, and to provide a set of recommendations on possible winning trial design strategies.

Methodology

The selected therapy areas and products included familial hypercholesterolaemia (FH) – Praluent and Repatha, stroke prevention in atrial fibrillation (SPAF) – Xarelto, Pradaxa, Eliquis and Savaysa, and pulmonary arterial hypertension (PAH) – all seven orphan drugs indicated for PAH.

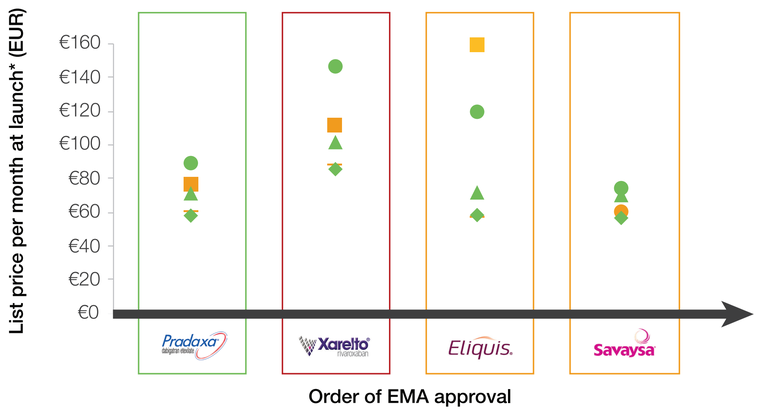
Information was collected on pivotal phase II and III clinical trials in the EMA submission from clinicaltrial.gov. Clinical trial programmes were classified as broad or targeted based on exclusion and inclusion criteria, targeted population and therapeutic positioning.

Each pivotal trial was quantitatively assessed using sets of criteria tailored to the specificities per indication. These included the targeted patient population, the exclusion criteria, the targeted line of treatment, and comorbidities and risk factors. A cumulative score was given to each clinical trial, and subsequently to the overall clinical trial programme strategy which allowed designation of each trial into one of three categories “Broad”, “Less Targeted”, or “Targeted”.

HTA outcomes per product including any restrictions, in addition to launch price, were collected from the EU5 HTA websites.

Finally, commercial success was interpreted based on sales data and the product’s uptake curve, using information collected from GlobalData.com. To ensure analysis was exhaustive, the possible impact of other factors, including the patient population, disease characteristics, level of competition and price comparators, were also evaluated in each indication after the initial three-phase analysis. However, these additional factors did not significantly impact our conclusion.

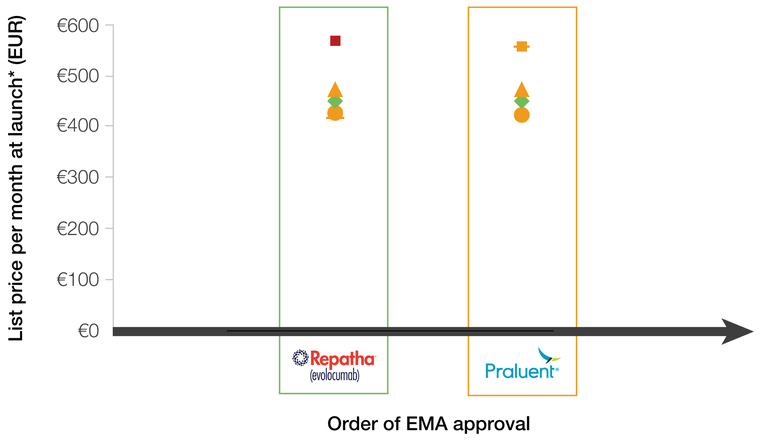
Results



SPAF Although Pradaxa was the first to market with a broad trial design strategy, it has not managed to capitalise on this. Xarelto, in comparison, entered the market second but used a more targeted trial design. This approach paid off, with Xarelto, obtaining on average the highest price (at launch) across the EU5. Conversely, Eliquis adopted a mixed broad and narrow approach across its two pivotal SPAF trials. In terms of commercial success, it seems as though Xarelto has not performed as well as Eliquis, however this could in part be driven by confounding factors including adverse events.

PAH PAH is a highly competitive orphan indication with multiple products entering the market. Over time, in contrast to SPAF, the trial designs have become less restricted with a broader clinical trial population included. Interestingly, over time, despite a broader population, HTA outcomes have been slowly getting more negative, while the price across the EU5 has been increasing.

Sales in orphan indications seem less impacted by broad vs targeted strategies. First to market product has a much better chance to establish its position, even without a price premium. This can be observed from the sales data where Tracleer, the first to enter the market in 2002 with a targeted trial design, still achieved highest sales in 2016 among PAH drugs.



FH In terms of clinical trial design, Praluent had an overall broader strategy focusing on primary FH and mixed dyslipidaemia with six pivotal studies. Repatha on the other hand was investigated for the same patient populations but in only one study and leveraged a more targeted approach by instead focused on patients with familial homozygous FH.

The results are ambiguous as to whether this strategy paid off for Repatha in terms of HTA outcomes. Although Repatha achieved faster market access with a marginally better price than Praluent, both products gained similar HTA restrictions.

Where the targeted approach seemed to make a difference is in the level of commercial success post launch. Whilst the first year sales for both products are similar, Repatha managed to achieve nearly double the sales of Praluent in the subsequent year.

Key

Trial strategy	HTA outcome	Market
Broad	Positive HTA, a few restrictions	UK, Spain
Slightly targeted	Less positive HTA, some restrictions	France, Italy
Narrow	Negative HTA, restrictions imposed	Germany

Discussion and conclusions

This study finds that a clinical trial strategy that is more targeted generally yields a better market success in terms of price, HTA outcomes and commercial success, than broader, bigger and less selective clinical trials do. In each case investigated, the most successful product in each therapy area was the one with the more targeted approach. Furthermore, when this is put in the context of therapy areas increasingly more crowded and commoditised, having a broad strategy is unlikely to pay off.

Payers appear to prefer clinical trials that are more selective in their exclusion and inclusion criteria, allowing them to identify the precise patient population that will truly benefit from the new treatment. An additional benefit is that by rightly identifying the patients most likely to respond to the drug, the trial can successfully show a significant improvement and added benefit compared to existing comparators.

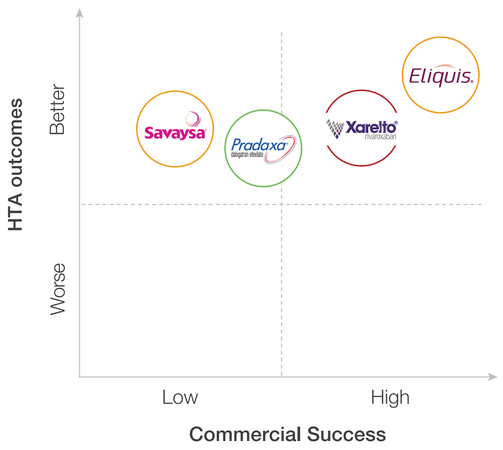
In a broader clinical trial this effect would be diluted due to the larger patient sample with limited potential to deliver a positive HTA recommendation. These results must be considered also in the context of other contributing factors to the commercial success of a product such as the time to market (i.e., 1st, 2nd or a me-too product). However, from a clinical trial design perspective our analysis showed maximal return on initial investment can be achieved with a more targeted clinical programme.

HTA outcomes factors

- Recommendation
- Any restrictions in access
- Reimbursement
- Time to access

Commercial success factors

- First year sales
- Recent sales
- How fast it picks up sale after launch



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