Maximising returns

Maximising returns: combining newborn screening with gene therapy for spinal muscular atrophy

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Summary sentence: Newborn screening has clinical and economic benefits when combined with gene therapies treating SMA.

Few would argue that the recent series of breakthroughs successfully delivering effective SMN protein-restoring gene therapy to patients with Spinal Muscular Atrophy (SMA) represents a milestone achievement in the field of neuromuscular diseases. The approval of nusinersen (Spinraza), onasemnogene abeparvovec (Zolgensma) and risdiplam (Evrysdi) by regulatory agencies has, for the first time, provided genuine disease-modifying therapeutic options[1,2]. Whilst these therapies fall short of a cure, the benefits delivered far exceed what was realistically predicted and hoped for, both in terms of patient survival and achievement of major motor milestones[2-4].

Understandably, significant efforts have been made by SMA patient organisations and charities to ensure rapid access to SMN-restoring therapies for as many patients as possible. However, access to these therapies has become a highly-charged societal and political debate, largely due to high list prices: onasemnogene abeparvovec has a list price of $2.1 million per single dose, and nusinersen costs $750,000 for the first year of treatment alone[2]. Whilst there have been notable successes with negotiating discounted prices by many health care providers, it is clear that cost remains a considerable issue with regards to providing access. Therefore, strategies that can either reduce costs, and/or maximise therapeutic benefits, are urgently being sought.

Extensive pre-clinical work, alongside emerging data from clinical trials, indicate that early treatment delivery has a significant impact on the efficacy of SMN-restoring therapies[2,4]. Thus, implementation of newborn screening (NBS), facilitating pre-symptomatic treatment, could have a major impact on the effectiveness and economic viability of SMA therapies. In this

issue, Shih et al.[5] report important new real-world data suggesting that NBS coupled with gene therapy improves the quality and length of life for SMA patients, whilst also delivering significant cost savings.

Shih and colleagues[5] took advantage of an Australian state-wide NBS programme for SMA, allowing them to estimate financial costs and also quality-adjusted life-years (QALYs). By accessing this unique and important dataset, Shih and colleagues demonstrated that the cost of combined NBS and early gene therapy would be less than $50,000 per QALY. This represents a cost per QALY that falls well within the willingness-to-pay thresholds (of between $50,000 per QALY to $500,000 per QALY) suggested by the Institute for Clinical and Economic Review[1], providing strong evidence to support clinical- and cost-effectiveness for NBS.

However, it should be noted that these findings[5] are geographically-restricted, and may not reflect the situation outside of Australia. Given the widespread introduction of NBS programmes for SMA in the USA over the last few years, comparable data from a different geographical and healthcare setting will likely soon be forthcoming. Moreover, the clinical landscape for SMA is already shifting towards a second generation of therapies, where SMN+ approaches are being developed[2,4]. Resulting competition in the SMA 'marketplace' will hopefully serve to reduce list prices and increase access for the wider patient population. The findings of Shih and colleagues[5] suggest that NBS, and therefore early pre-symptomatic treatment of SMA patients, has a key role to play in this future landscape, from both clinical and financial perspectives.

CONFLICT OF INTEREST STATEMENT

The author has served on SMA advisory boards for Roche.

REFERENCES

1. Darrow JJ, Sharma M, Shroff M, Wagner AK. (2020) Efficacy and costs of spinal muscular atrophy drugs. *Sci Transl Med.* 12:eaay9648.

2. Chaytow H, Faller KME, Huang Y-T, Gillingwater TH. (2021) Spinal muscular atrophy (SMA): from approved therapies to future therapeutic targets for personalized medicine. *Cell Rep Med.* 2:100346.

3. van der Ploeg AT. (2017) The Dilemma of Two Innovative Therapies for Spinal Muscular Atrophy. *N Engl J Med.* 377:1786-1787.

4. Groen EJN, Talbot K, Gillingwater TH. (2018) Advances in therapy for spinal muscular atrophy: promises and challenges. *Nat Rev Neurol.* 14:214-224.

5. Shih STF, Farrar M, Wiley V, Chambers G. (2021) Newborn screening for spinal muscular atrophy with disease-modifying therapies: a cost effectiveness analysis. *J Neurol Neurosurg Psychiatry* XXX:XXX