Maximising returns

combining newborn screening with gene therapy for spinal muscular atrophy

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.

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