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Clinical characteristics and real-world outcomes in patients with mucopolysaccharidosis II over 18 years: final report of the Hunter Outcome Survey

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ABSTRACT

Background: Mucopolysaccharidosis II (MPS II) is a rare, progressive, X-linked lysosomal storage disease. Enzyme replacement therapy (ERT) with intravenous (IV) idursulfase has been approved for the treatment of patients with MPS II since 2005. The Hunter Outcome Survey (HOS; NCT03292887) was established as a condition of approval to monitor the long-term safety and effectiveness of idursulfase. Here, we report the final results from HOS.

Methods: HOS was a multicenter, long-term, observational registry that enrolled patients with a biochemically and/or genetically confirmed diagnosis of MPS II who were untreated or treated with idursulfase and/or bone marrow transplant. Patients were enrolled prospectively (alive at enrollment) and retrospectively (deceased at enrollment). For prospectively enrolled patients, it was requested that data from routine examinations were recorded after each follow-up visit and/or a minimum of every 6 months. The safety population (SP) included patients who received at least one dose of idursulfase and were alive at HOS entry. The treatment outcomes population (TOP) included patients who received at least one dose of idursulfase and were alive at HOS entry, excluding patients who received a bone marrow transplant, patients for whom an informed consent form could not be generated by the center, and patients with a missing date of birth. Safety and effectiveness endpoints were analyzed with descriptive statistics.

Results: In total, 1332 patients were enrolled in HOS. For patients in the SP ($N = 1014$), the median (10th percentile, 90th percentile) age at initiation of ERT with idursulfase was 5.7 (1.6, 18.1) years, ranging from 0.0 to 65.5 years. In the TOP ($N = 989$), a consistent and sustained decline in urinary glycosaminoglycan levels, trends of sustained improvements in walking capacity and left ventricular mass index, and reductions in liver and spleen size were observed. Treated patients also demonstrated a median increase in survival time of approximately 10

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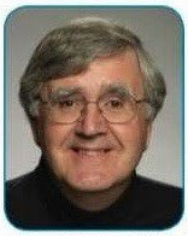
The HOS Steering Committee



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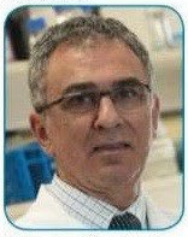

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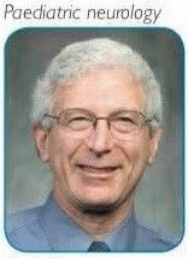

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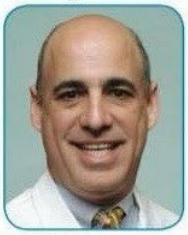

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hos news

HOS is registered at ClinicalTrials.gov (ID: NCT03292887) Issue 8 November 2018

Welcome to the HOS newsletter

Welcome to the 8th edition of **HOS news**, which we hope will provide a useful summary of recent developments relating to the Hunter Outcome Survey (HOS).

Highlights

- The registry continues to grow, with an increase of 30 patients between January and July 2018.
- The HOS Steering Committee (SC) met recently at the Society for the Study of Inborn Errors of Metabolism (SSIEM) Annual Symposium (4–7 September 2018, Athens, Greece), where two HOS posters were also presented. Discussions were focused mainly on ongoing analyses of HOS data for current and future publications, with topics of interest including early initiation of enzyme replacement therapy (ERT) and statistical modelling of predicted outcomes of long-term idursulfase treatment.
- Updates to streamline the HOS Case Report Form (CRF) have been agreed and will be implemented in the coming year, as discussed on page 2.

HOS in numbers

As of July 2018, the HOS registry contains data from:

33 countries **146** centres

1266 patients

84% of prospective patients have received treatment with idursulfase

We would like to take this opportunity to thank all Investigators, site staff, patients and their families for their participation in and ongoing commitment to the registry, and we hope that you enjoy this issue of **HOS news**.

The Shire HOS team

Snapshot of a centre

MacKay Memorial Hospital, Taipei, Taiwan

How long has your centre been involved with HOS, and how many patients with mucopolysaccharidosis type II (MPS II) do you care for?

We started working with HOS in 2007 and have cared for 40 patients with MPS II. Of these, five are still being actively followed within HOS.

You recently published an article reporting the clinical characteristics of 61 Taiwanese patients enrolled in HOS – please could you summarize the key findings?

The mean ages (± standard deviation) at symptom onset and diagnosis were 2.9 ± 3.2 (n = 55) and 5.3 ± 5.4 years (n = 56), respectively. The earliest signs and symptoms were hernia, facial features characteristic of MPS II and claw hands. More than 78% of patients had undergone a surgical procedure, most commonly a hernia repair, often at a young age and before diagnosis. Respiratory failure was the leading cause of death (11/25 patients), followed by cardiac arrest or failure (6/25 patients). Overall, our findings highlight the importance of medical and surgical histories in diagnosing MPS II in Taiwanese patients.

Left to right: Miss Fang-Ju Lin (Study Coordinator), Dr Shuan-Pei Lin (Principal Investigator), Dr Chih-Kuang Chuang (Technical Chief, Medical Research Department), Dr Hsiang-Yu Lin (Sub-Investigator)

What impact might this publication have on the care you are able to provide for your patients, either now or in the future?

The life expectancy of Taiwanese patients with MPS II has improved in recent decades, possibly owing to the establishment of efficient consultation systems that encourage timely referral of patients to specialists and promote multidisciplinary care. Our recent publication could help to further raise awareness of the common early clinical features and surgical procedures among patients with MPS II in Taiwan. These findings could also serve as baseline data for the analysis of the long-term effects of ERT and haematopoietic stem cell transplantation in patients with MPS II, and may aid the development of quality-of-care strategies.

What challenges have you encountered at your site and how have you overcome them?

In a few cases, patients' families have decided to let the disease follow its natural course instead of accepting treatment. Our staff members try very hard to empathize with their situations and encourage them to bring the patients back to our hospital for regular routine examinations. Although some families have withdrawn consent and refused follow-up contact from the HOS site team, we still show great solicitude about the patients' health and try to keep in contact with them via patient support group activities.

hos hunter outcome survey

Sponsored by Shire

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