Evaluating long-term real-world data (RWD) from patients with Leber’s hereditary optic neuropathy (LHON) in light of the recommendations of the International Consensus statement

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Background

- LHON is a rare mitochondrial genetic disorder that results in severe, bilateral central vision loss in both eyes. Idiobene, the only approved treatment for LHON in Europe, has been shown to be efficacious in treating LHON regardless of genetic mutation.
- An International Consensus on the disease management and treatment of LHON with idiobene recommends:
  1. A minimum treatment duration of 12 months before evaluating efficacy
  2. That efficacy should be evaluated as improvement of two lines of visual acuity (VA) in one Early Treatment Diabetic Retinopathy Study (ETDRS) charts (or from off-chart to on-chart)
  3. Idiobene should be discontinued in non-responding patients
  4. Idiobene treatment should be maintained for 12 months after VA improvement has stabilized
  5. Idiobene treatment is currently not recommended in patients in the chronic stages of the disease.

Objectives

- To compare the practical clinical application of the International Consensus statement based on long-term real-world data (RWD) obtained from a Expanded Access Program (EAP)

Methods

- A retrospective evaluation of LHON patients treated with idiobene* (900 mg/day) in 18 international sites under routine clinical practice was conducted in order to assess the VA response to idiobene in real-world clinical practice, in two cohorts: a subacute/dynamic cohort (SD Cohort) and a chronic* cohort (C Cohort).
- Male or female patients treated with idiobene under the EAP were included. Patients were eligible if their most recent eye onset was <12 months (SD Cohort) or >12 months (C Cohort), and there was confirmation of one primary mutation and available post-baseline data.
- Efficacy was evaluated as clinically relevant recovery (CRR), best-corrected VA (BCVA) improvement from off-chart to reading 5 ETDRS letters, or 10 ETDRS letters on chart improvement, time to initial response and response magnitude over time (Table 1).

Results

- Response to treatment in subacute/dynamic patients (SD Cohort)
  - 41 of 87 patients (47%) experienced a CRR from nadir.
    - 44% CRRs occurred up to 6 months
    - 22% CRRs occurred between 6 and 12 months
    - 34% CRRs occurred after 12 months
  - Of the 46 non-responders, 41.3% discontinued before 12 months
  - Estimated 64% patients with a CRR up to 26.5 months (Figure 1)
  - Estimated 50% patients with a CRR by 22.8 months (Figure 1)
  - The maximum final gain in VA achieved by a patient in was 90 ETDRS letters (Table 3)
- In patients with CRR, the average magnitude of response increased from 22 letters at time of 1st CRR to 16 letters at the last visit (Figure 1)

Safety

- Safety signals were consistent with previously observed results.

Conclusions

- In general, our Real World Data support the guidance of the International Consensus statement.
- However, our data suggest that early discontinuation may prevent a patient achieving a response and also may limit the magnitude of benefit that can be achieved.
- Early discontinuation before VA improvement has reached a plateau may limit the potential magnitude of improvement achieved.
- The C Cohort consisted of patients whose most recent eye onset was beyond 12 months since onset, corresponding to the chronic phase in the International Consensus.
- Of the patients in C Cohort, showed a CRR, of which in 66% could be first observed as early as 7 months after therapy initiation.

References


★ LogMAR-Snellen equivalents

- R* (idiobene 150 mg tablets), Santhera Pharmaceuticals (Switzerland) Ltd
- K* (idiobene 150 mg capsules), Santhera Pharmaceuticals (German) Ltd

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Kaplan-Meier estimates of CRR from nadir in the SD cohort

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