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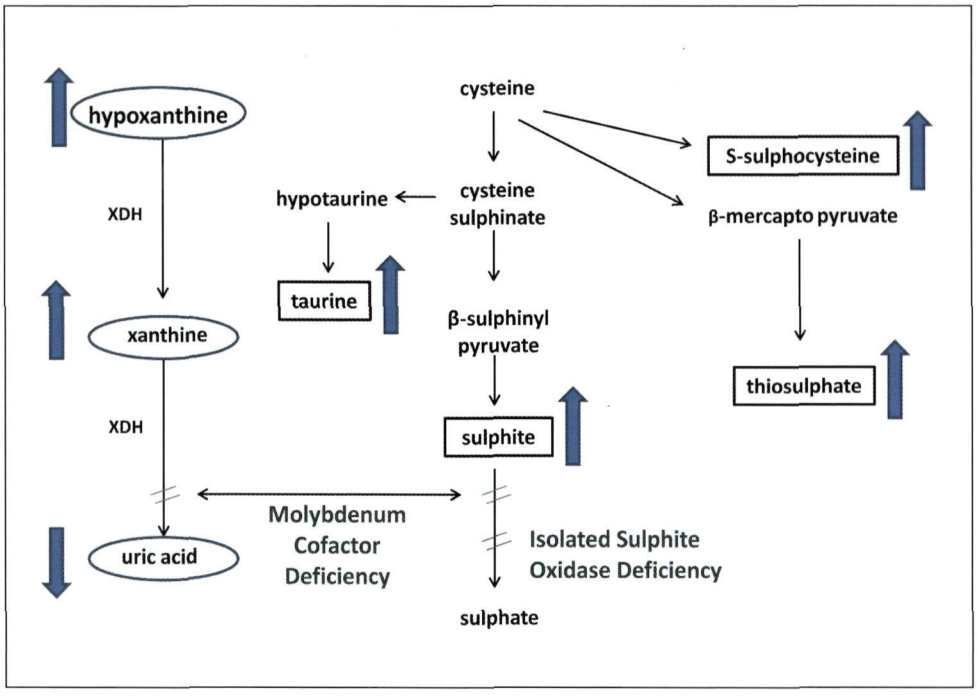

Preimplantation Genetic Diagnosis in Isolated Sulfite Oxidase Deficiency

Mustafa A. Salih, Thomas M. Bosley, Ibrahim A. Alorainy, Mohamed A. Sabry, Mohamed S. Rashed, Eiman A. Al-Yamani, Siham El-Akoum, Sarar H. Mohamed, Khaled K. Abu-Amero, Ali M. Hellani

Brief Communications - Can J Neurol Sci. 2013; 40: 109-112

Figure: *ISOD and MOCOD biochemistry. Diagram outlining biochemical compounds related to sulfate metabolism. Isolated sulfite oxidase deficiency (ISOD) and Molybdenum Cofactor Deficiency (MOCOD) both interfere with the metabolism of sulfite to sulfate by sulfite oxidase. This results in elevated serum and urinary levels of sulfite, S-sulfocysteine, thiosulfate, and taurine as indicated. Molybdenum Cofactor Deficiency also interferes with the metabolism of xanthine to uric acid through xanthine dehydrogenase, resulting in increased levels of xanthine and hypoxanthine and decreased levels of uric acid in this disorder.*

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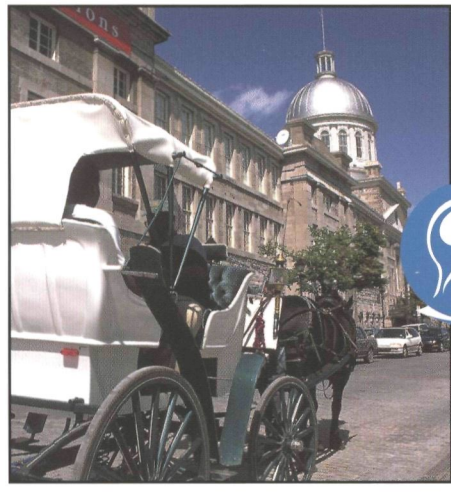
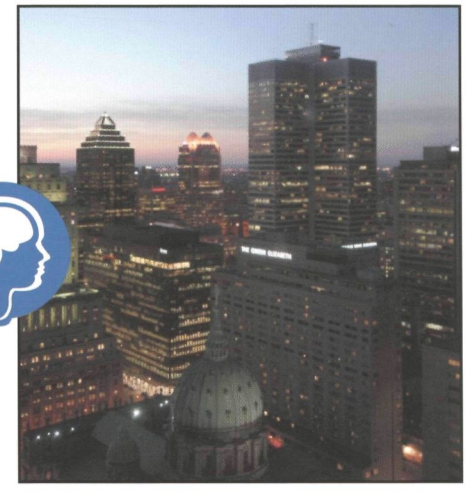
The CNSF Congress is a uniquely Canadian Neurosciences meeting, planned by volunteer representatives from the four CNSF member societies.

We thank our Members and the greater neurological community for their ongoing attendance and support of the CNSF Congress.

We look forward to seeing you at the Fairmont Queen Elizabeth Hotel in Montreal, June 11th to 14th !

More information available at: http://congress.cnsfederation.org/





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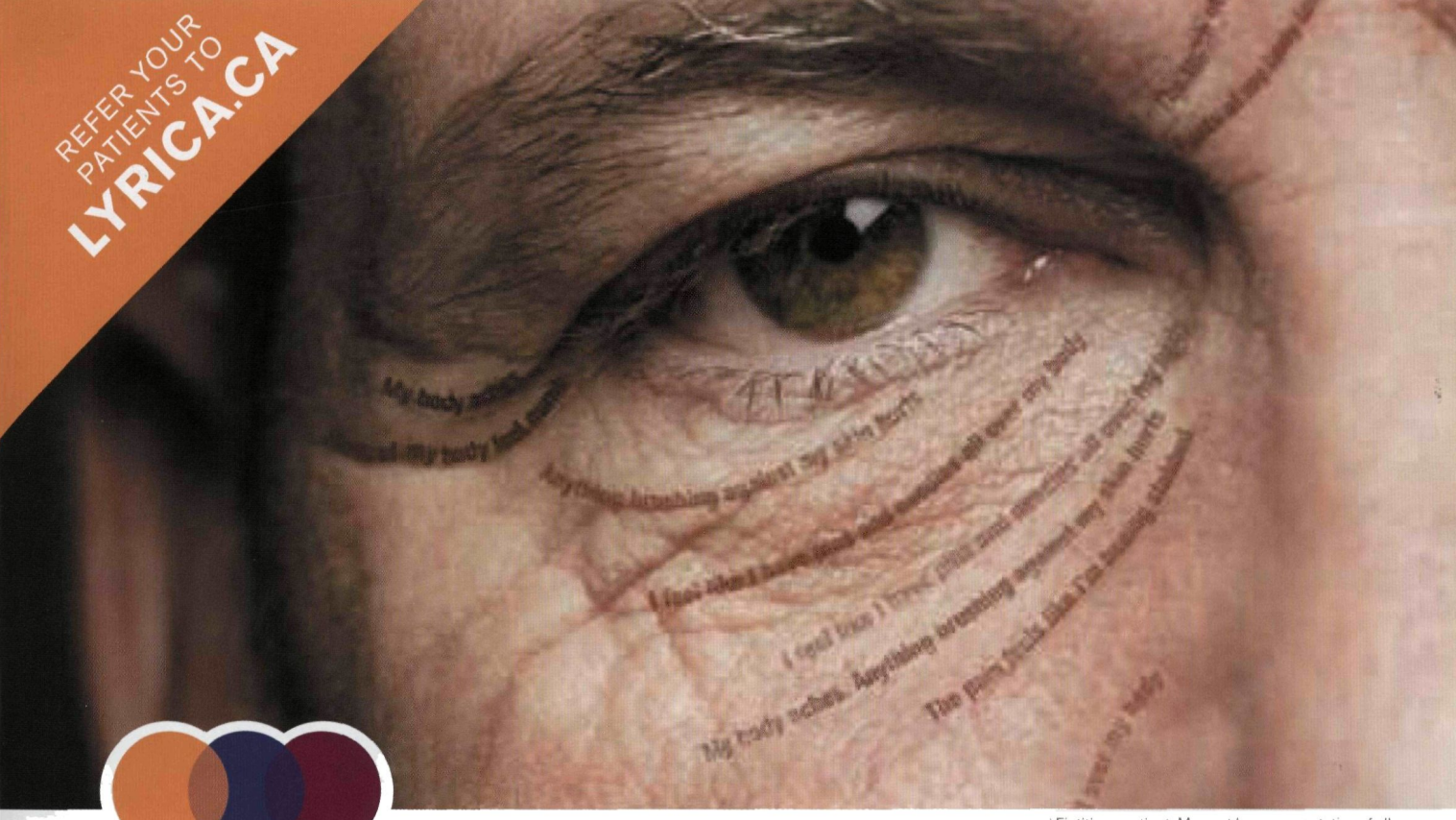
NEUROIMAGING HIGHLIGHTS

BRIEF COMMUNICATIONS

CANP MEETING ABSTRACTS

LETTERS TO THE EDITOR



*Fictitious patient. May not be representative of all cases.

FACED WITH PAIN[1,2*]

IN HIS STRUGGLE WITH NEUROPATHIC PAIN

Pregabalin: first-line treatment for chronic **neuropathic pain**[4]

First treatment indicated in Canada for adults for the management of pain associated with **fibromyalgia**[3]

Demonstrated powerful, rapid and sustained pain relief[3,5]

In neuropathic pain (NeP): Rapid and sustained pain relief (starting at week 2 for LYRICA 150-600 mg/day, n=141; $p<0.05$ vs. placebo, n=65) was demonstrated throughout a 12-week study in patients with DPN or PHN[5].

Demonstrated effective in relieving pain-related sleep difficulties[3]

In NeP: LYRICA reduced sleep disturbances across several studies in DPN and PHN, of 8-12 weeks duration[3].

Flexible dosing across all indications[3‡]

LYRICA (pregabalin) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia and spinal cord injury in adults. LYRICA is indicated for the management of pain associated with fibromyalgia in adults. The efficacy of LYRICA in the management of pain associated with fibromyalgia for up to 6 months was demonstrated in a placebo-controlled trial in patients who had initially responded to LYRICA during a 6-week open-label phase.

LYRICA is contraindicated in patients who are hypersensitive to pregabalin or to any ingredient in the formulation or component of the container.

The most commonly observed adverse events (≥5% and twice the rate as that seen with placebo) in the recommended dose range of 150 mg/day to 600 mg/day in PHN and DPN patients were: dizziness (9.0-37.0%), somnolence (6.1-24.7%), peripheral edema (6.1-16.2%), and dry mouth (1.9-14.9%) and were dose related; in SCI patients: somnolence (41.4%), dizziness (24.3%), asthenia (15.7%), dry mouth (15.7%), edema (12.9%), constipation (12.9%), amnesia (10.0%), myasthenia (8.6%), amblyopia (8.6%), and thinking abnormal (8.6%); in fibromyalgia patients: dizziness (37.5%), somnolence (18.6%), weight gain (10.6%), dry mouth (7.9%), blurred vision (6.7%), and peripheral edema (6.1%). In LYRICA-treated fibromyalgia patients, the most commonly observed dose-related adverse events were: dizziness (22.7-46.5%), somnolence (12.9-20.7%), weight gain (7.6-13.7%), peripheral edema (5.3-10.8%). The most commonly observed adverse events in the PHN, DPN, SCI and fibromyalgia patients were usually mild to moderate in intensity. Discontinuation rates due to adverse events for LYRICA and placebo, respectively, were 9% and 4% in DPN, 14% and 7% in PHN, 21% and 13% in SCI, and 20% and 11% in fibromyalgia. There was a dose-dependent increase in rate of discontinuation due to adverse events in DPN, PHN and fibromyalgia patients.

There have been post-marketing reports of angioedema in patients, some without reported previous history/episodes, including life-threatening angioedema with respiratory compromise. Caution should be exercised in patients with previous history/episodes of angioedema and in patients who are taking other drugs associated with angioedema.

In clinical trials and in post-marketing experience, there have been reports of patients, with or without previous history, experiencing renal failure alone or in combination with other medications. Caution is advised when prescribing to the elderly or those with any degree of renal impairment.

There have been post-marketing reports of events related to reduced lower gastrointestinal tract function (e.g., intestinal obstruction, paralytic ileus, and constipation) in patients, some without reported previous history/episode(s), during initial/acute and chronic treatment with LYRICA, primarily in combination with other medications that have the potential to produce constipation. Some of these events were considered serious and required hospitalization. In a number of instances, patients were taking opioid analgesics including tramadol. Caution should be exercised when LYRICA and opioid analgesics are used in combination, and measures to prevent constipation may be considered, especially in female patients and elderly as they may be at increased risk of experiencing lower gastrointestinal-related events.

Dosage reduction is required in patients with renal impairment (creatinine clearance <60 mL/min) and in some elderly patients as LYRICA is primarily eliminated by renal excretion.

Please see Prescribing Information for complete Warnings and Precautions, Adverse Reactions, Dosage and Administration and patient selection criteria.

‡Please consult Prescribing Information for complete Dosage and Administration instructions.

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PrLYRICA® PREGABALIN

See prescribing information and study parameters on page A-14, A-15

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VIMPAT® (lacosamide) is indicated as adjunctive therapy in the management of partial-onset seizures in adult patients with epilepsy (≥18 years of age) who are not satisfactorily controlled with conventional therapy. The clinical experience with VIMPAT® in elderly patients with epilepsy (≥65 years of age) is limited. Caution should be exercised during dose titration and age-associated decreased renal clearance should be considered in elderly patients. The safety and efficacy of VIMPAT® in pediatric patients (<18 years of age) have not been established and its use in this patient population is not indicated.

VIMPAT® is contraindicated in patients who are hypersensitive to the active substance or to any of the excipients and in patients with a history of, or presence of, second- or third-degree atrioventricular (AV) block.

Second degree or higher AV block has been reported in post-marketing experience. Patients should be made aware of the symptoms of second-degree or higher AV block (e.g. slow or irregular pulse, feeling of lightheadedness and fainting), and told to contact their physician should any of these symptoms occur. VIMPAT® should be used with caution in patients with known conduction problems (e.g. marked first-degree AV block, sick sinus syndrome without pacemaker), or with a history of severe cardiac disease such as myocardial ischemia or heart failure. In such patients, obtaining an ECG before beginning VIMPAT®, and after VIMPAT® is titrated to steady-state, is recommended. Caution should especially be exerted when treating elderly patients as they may be at increased risk of cardiac disorder or when VIMPAT® is given with other drugs that prolong the PR interval (e.g. carbamazepine, pregabalin, lamotrigine, beta-blockers, and class I antiarrhythmic drugs), as further PR prolongation is possible. In clinical trials of healthy subjects and patients with epilepsy, VIMPAT® treatment was associated with PR interval prolongation in a dose-dependent manner. VIMPAT® administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with diabetic neuropathy and/or cardiovascular disease. Patients should be made aware of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid or irregular pulse, shortness of breath) and told to contact their physician should any of these symptoms occur. Atrial fibrillation and flutter have been reported in open-label epilepsy trials and in postmarketing experience.

Multiorgan hypersensitivity reactions (also known as Drug Rash with Eosinophilia and Systemic Symptoms, or DRESS), Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported with anticonvulsants. If any of these hypersensitivity reactions are suspected, VIMPAT® should be discontinued and alternative treatment started.

Treatment with VIMPAT® has been associated with dizziness and ataxia, which could increase the occurrence of accidental injury or falls. Accordingly, patients should be advised not to drive a car or to operate other complex machinery or perform hazardous tasks until they are familiar with the effects of VIMPAT® on their ability to perform such activities.

In controlled trials in patients with partial-onset seizures, VIMPAT® treatment was associated with vision-related adverse events such as blurred vision and diplopia. Patients should be informed

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When seizure control is still an issue for your patient

Bring VIMPAT® into the picture

Efficacy in patients inadequately controlled on 1 to 3 AEDs*†[1]

- Significant median **36-39% reduction in seizure frequency** per 28 days from baseline to maintenance phase*[1]
  - VIMPAT® 400 mg/day vs. placebo: Ben-menachem, *et al.* (39% vs. 10%, $p \leq 0.01$); Chung, *et al.* (37.3% vs. 20.8%, $p \leq 0.01$); Halász, *et al.* (36.4% vs. 20.5%, $p \leq 0.05$)*[1]

Generally well tolerated when added to common concomitant therapy

- Some of the most frequently reported **adverse reactions** with VIMPAT® 400 mg/day were dizziness (30%), nausea (11%), and vision-related events, including diplopia (10%) and blurred vision (9%)

The recommended starting dose for VIMPAT® is 50 mg twice a day which should be increased to an initial therapeutic dose of 100 mg twice a day after one week. Depending on patient response and tolerability, the maintenance dose of VIMPAT® can be increased by 50 mg twice daily every week, to a **maximum recommended dose of 400 mg/day**.[1]

Please consult product monograph for complete dosing and administration instructions.

POWER for added control.

that if visual disturbances occur, they should notify their physician promptly. If visual disturbance persists, further assessment, including dose reduction and possible discontinuation of VIMPAT®, should be considered.

More frequent assessments should be considered for patients with known vision-related issues or those who are already routinely monitored for ocular conditions.

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. All patients treated with antiepileptic drugs, irrespective of indication, should be monitored for signs of suicidal ideation and behaviour and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

There are no studies with VIMPAT® in pregnant women. Since the potential risk for humans is unknown, VIMPAT® should not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the foetus. It is unknown whether VIMPAT® is excreted in human breast milk. Because many drugs are excreted into human milk, a decision should be made whether to discontinue nursing or to discontinue VIMPAT®, taking into account the importance of the drug to the mother.

As with all antiepileptic drugs, VIMPAT® should be withdrawn gradually (over a minimum of 1 week) to minimize the potential of increased seizure frequency.

In controlled clinical trials in patients with partial-onset seizures, some of the most frequently reported adverse reactions with VIMPAT® treatment were dizziness (16% and 30% for 200 mg and 400 mg treatment groups, respectively, vs. 8% placebo), nausea (7% and 11% vs. 4%), and vision related events [diplopia (6% and 10% vs. 2%) and blurred vision (2% and 9% vs. 3%)]. They were dose-related and usually mild to moderate in intensity. The adverse events most commonly leading to discontinuation were dizziness, coordination abnormal, vomiting, diplopia, nausea, vertigo, and vision blurred.

Please see the VIMPAT® Product Monograph for full prescribing information.

* 3 randomized, double-blind, placebo-controlled, multicentre trials studying VIMPAT® (lacosamide) as adjunctive therapy in adult patients with POS with or without secondary generalization. In the studies, patients were to have been taking a stable dosage regimen of one to three AEDs, with or without vagal nerve stimulation in the 4 weeks before enrollment and during the baseline period. Following the 8-week baseline phase, subjects were randomized and up-titrated by initiating treatment at 100 mg/day, and increased in weekly increments of 100 mg/day to the target dose. The titration phase lasted 4-6 weeks. Patients then entered a 12-week maintenance phase period. [2,3,4]

† AED=anti-epileptic drug

References: 1. VIMPAT® Product Monograph, UCB Canada Inc., October 6, 2011. 2. Ben-Menachem E, Biton V, Jatuzis D, *et al.* Efficacy and safety of oral lacosamide as adjunctive therapy in adults with partial-onset seizures. *Epilepsia* 2007; 48(7):1308-1317. 3. Chung S, Sperling MR, Biton V *et al.* Lacosamide as adjunctive therapy for partial onset seizures: A randomized controlled trial. *Epilepsia* 2010; 51(6):958-967. 4. Halász P, Kalviainen R, Mazurkiewicz-Beldzińska M, *et al.* Adjunctive lacosamide for partial-onset seizures: Efficacy and safety results from a randomized controlled trial. *Epilepsia* 2009; 50(3):443-453.

P VIMPAT™
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See prescribing summary on pages A-10 to A-13

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