SOM Innovation Biotech S.A.
Parc Científic de Barcelona
Baldiri Reixac, 4
08028 Barcelona
info@sombiotech.com ☏ +34 934 020 150

EudraCT study: **2014-001586-27**

Study title: **Study of SOM0226 in familial amyloid polyneuropathy (FAP) patients and asymptomatic carriers to evaluate protein stabilization activity**

STUDY SUMMARY

Objective: TTR stabilization in TTR healthy volunteers and TTR amyloidosis patients and carriers

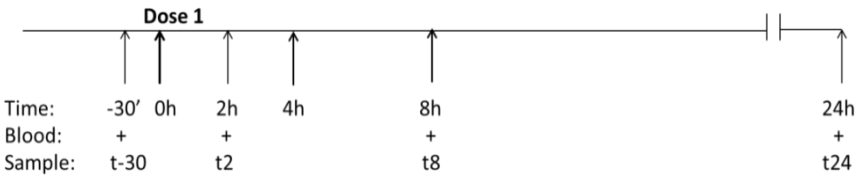
Subjects: Healthy volunteers, patients and carriers of TTR amyloidosis
20 subjects: 2 cohorts defined by genotype TTR variant:
- Wild type TTR (healthy volunteers): 5 subjects
- V30M TTR (FAP patients + asymptomatic carriers): 15 subjects

Dose: Interventional study in two phases:
Phase A: single dose (200mg)
Phase B: multiple doses (100mg every 4 h; 3 doses)

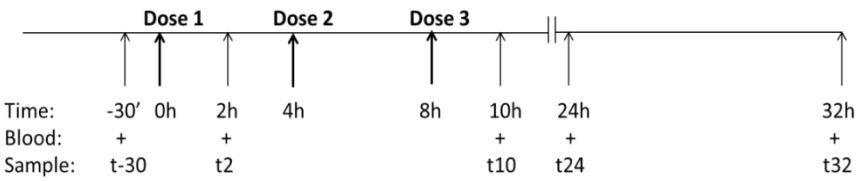
Endpoints: 1- TTR stabilization (plasma)
2- Pharmacodynamics assessment: dose max effect

Study type: Phase IIa proof of concept study

Phase A:



Phase B:



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SUMMARY OF RESULTS

The trial was ended prematurely because significant results were reached.

Results were published at https://doi.org/10.1080/13506129.2019.1597702.

AMYLOID
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ARTICLE

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Transthyretin stabilization activity of the catechol-*O*-methyltransferase inhibitor tolcapone (SOM0226) in hereditary ATTR amyloidosis patients and asymptomatic carriers: proof-of-concept study[#]

Josep Gamez[a], María Salvadó[a], Núria Reig[b], Pilar Suñé[c], Carles Casasnovas[d], Ricard Rojas-Garcia[e] and Raúl Insa[b]

[a]Neuromuscular Disorders Clinic, Department of Neurology, Vall d'Hebron University Hospital, VHIR, European Reference Network on Rare, Neuromuscular Disorders (ERN EURO-NMD), UAB, Barcelona, Spain; [b]Research and Development Department, SOM Biotech, S.L, Barcelona, Spain; [c]Pharmacy Department, Vall d'Hebron Research Institute (VHIR), Hospital Universitari Vall d'Hebron, Barcelona, Spain; [d]Neuromuscular Disorders Unit, Neurology Department, Bellvitge University Hospital – IDIBELL, Barcelona, Spain; [e]Department of Neurology, Neuromuscular Diseases Unit Hospital de la Santa Creu i Sant Pau, Center for Networked Biomedical Research into Rare Diseases (CIBERER), UAB, Barcelona, Spain

ABSTRACT

Objective: To assess the transthyretin (TTR) stabilization activity of tolcapone (SOM0226) in patients with hereditary ATTR amyloidosis, asymptomatic carriers and healthy volunteers.
Methods: A phase IIa proof-of-concept trial included two phases separated by a 6-week washout period. Phase A: single 200 mg dose of tolcapone; phase B: three 100 mg doses taken at 4 h intervals. The primary efficacy variable was TTR stabilization.
Results: Seventeen subjects were included (wild type, $n = 6$; mutation TTR Val30Met, $n = 11$). TTR stabilization was observed in all participants. Two hours after dosing, 82% of participants in phase A and 93% of those in phase B reached a TTR stabilization value of at least 20%. In phase A, there was an increase of 52% in TTR stabilization vs baseline values 2 h after dosing, which decreased to 22.9% at 8 h. In phase B, there was a significant increase of 38.8% in TTR stabilization 2 h after the first 100 mg dose. This difference was maintained after 10 h and decreased after 24 h. No serious adverse events were observed.
Conclusions: The ability of tolcapone for stabilizing TTR supports further development and repositioning of the drug for the treatment of ATTR amyloidosis.

EudraCT trial number: 2014-001586-27
ClinicalTrials.gov Identifier: NCT02191826

Abbreviations: AE: adverse event; ATTR: amyloid TTR; BMI: body mass index; CI: confidence interval; FAP: hereditary ATTR amyloidosis; INCAT: Inflammatory Neuropathy Cause and Treatment Score; MAO: monoamine oxidase inhibitor; MRC: Medical Research Council; NIS: Neuropathy Impairment Score; NSAID: non-steroidal anti-inflammatory drug; OLT: orthotopic liver transplantation; SD: standard deviation; TTR: transthyretin

ARTICLE HISTORY
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KEYWORDS
Amyloidogenesis inhibitor; tolcapone; catechol O-methyltransferase inhibitors; drug repositioning; drug repurposing; hereditary ATTR amyloidosis; proof-of-concept; transthyretin; TTR aggregation; TTR stabilization