

# INIBITORI DELLE ESTERASI E DANNO NERVOSO PERIFERICO: DALLA CLINICA AI MODELLI SPERIMENTALI

Moretto Angelo

*Dip. Medicina del Lavoro, ICPS Ospedale "Luigi Sacco" – Università di Milano*

In seguito all' "epidemia" di polineuropatie periferiche (Ginger Jack) osservata negli Stati Uniti durante il proibizionismo negli anni '30 del secolo scorso e associata all'uso di reagenti contaminati da tri-orto-cresilfosfato (TOCP) per la produzione illegale di bevande alcoliche, è iniziata la ricerca del modello sperimentale per lo studio e la comprensione del meccanismo di questa neuropatia periferica. Inizialmente gli studi, focalizzati sulla descrizione morfologica, avevano portato alla definizione della neuropatia come demielinizzante perché le osservazioni venivano fatte quando la malattia era conclamata. Solo negli anni '60-'70 è stato definitivamente chiarito che la lesione è assonale con demielinizzazione secondaria. Intanto, alla fine degli anni '50 due tecnici di laboratorio in Inghilterra, che stavano studiando un estere organofosforico come potenziale insetticida anticolinesterasico, svilupparono una polineuropatia simile alla Ginger Jack. Successivamente altri esteri organofosforici si dimostrarono in grado di causare la polineuropatia, anche dopo una singola dose. La gallina fu identificata come il modello sperimentale adeguato, nella quale la neuropatia si sviluppava dopo 10-15 giorni dalla singola dose. Di qui l'aggettivo "ritardata" applicato alla neuropatia da esteri organofosforici. Nell'ipotesi che il bersaglio della neuropatia fosse una esterasi, dopo l'esclusione dell'acetilcolinesterasi e della pseudocolinesterasi, fu identificata una proteina con attività esterasica (neuropathy target esterase, NTE). Questa fu inizialmente definita come un sito legante specificamente esteri organofosforici neuropatici che si dimostrò in grado di idrolizzare esteri artificiali, fra quali fu poi utilizzato il fenil valerato. Si dimostrò poi che il meccanismo della neuropatia veniva innescato se l'attività NTE era inibita per almeno il 70% e andava successivamente incontro ad un riarrangiamento non enzimatico ("aging"). Infatti, gli inibitori della NTE che non causavano "aging" (ad esempio carbammati, sulfonil fluoruri e fosfinati) non inducevano la neuropatia. Inoltre, se somministrati prima dell'organofosforico neuropatico, proteggevano dalla neuropatia se inibivano almeno il 30% della NTE. Quindi l'attività enzimatica della NTE non è rilevante per l'assone ed il suo ruolo fisiologico non è noto. Topi knock-out per NTE non sopravvivono lo stadio embrionale per mancato sviluppo della placenta e vasculogenesi difettosa. Altri inibitori non neuropatici delle esterasi, compresa la NTE, si sono dimostrati in grado di causare un aggravamento della neuropatia da organofosforici e di altre neuropatie periferiche tossiche e della lesione traumatica negli animali da esperimento. Sulla base di dati sperimentali è stata fatta l'ipotesi che il meccanismo della promozione coinvolgesse i processi di compenso e riparazione delle lesioni assonali. Ricerche sono in corso sulla base dell'ipotesi che il bersaglio sia una esterasi. L'ipotesi, più volte sostenute, che esposizioni croniche a basse dosi di organofosforici si associno ad alterazioni elettrofisiologiche del nervo periferico non sono supportate da dati epidemiologici convincenti e da dati sperimentali. Alcune esterasi sono coinvolte nella idrolisi/inattivazione degli esteri organofosforici. In particolare, la paraoxonasi (PON1, PON2, PON3), che sembra avere un ruolo nel metabolismo dei lipidi e che idrolizza anche altri organofosforici oltre al paraoxon, presenta un polimorfismo genetico. E' stata avanzata l'ipotesi che soggetti con alcune varianti genetiche dell'enzima siano a maggiore rischio di sviluppare sclerosi laterale amiotrofica. Non è ancora chiaro quale sia il ruolo di queste varianti nell'aumento di rischio, né esiste un modello sperimentale per poter studiare questo fenomeno.

# CHARCOT-MARIE-TOOTH TYPE 1A DISEASE AND THERAPY WITH ASCORBIC ACID: THE CMT-TRIAAL

Pareyson D\*, Schenone A\*\*, Rizzuto N\*\*\*, Fabrizi G\*\*\*, Santoro L\*\*\*\*, Vita G\*\*\*\*\*, Quattrone A\*\*\*\*\*, Padua L\*\*\*\*\*, Gemignani F\*\*\*\*\*, Visioli F\*\*\*\*\*, Solari A\*\*\*\*\*

*\*Fond. IRCCS, Ist. Neurologico "C. Besta", Divisione di Biomichimica e Genetica – Milano, \*\*Dip. Neurologia, Oftalmologia e Genetica - Università di Genova, \*\*\*Dip. Scienze Neurologiche e della Visione, Sez. Neurologia Clinica - Università di Verona, \*\*\*\*Dip. Scienze Neurologiche - Università "Federico II" di Napoli, \*\*\*\*\*Clinica Neurologica - Università di Messina, \*\*\*\*\*Clinica Neurologica - Università di Catanzaro, \*\*\*\*\*Dip. Neuroscienze, Università Cattolica e Fond. "Don Gnocchi" – Roma, \*\*\*\*\* Clinica Neurologica - Università di Parma, \*\*\*\*\*Dip. Scienze Farmacologiche, Farmacia - Università di Milano, \*\*\*\*\* Fond. IRCCS, Ist. Neurologico "C. Besta", Unità di Neuroepidemiologia – Milano*

There are no pharmacological treatments for Charcot-Marie-Tooth disease type 1A (CMT1A), associated with the peripheral myelin protein 22 (PMP22) gene duplication. Ascorbic acid (AA) has been shown to be effective in transgenic mice overexpressing PMP22. We designed a randomized controlled trial of AA in CMT1A, named CMT-TRIAAL (CMT-Trial Italian with Ascorbic Acid Long term). The CMT-TRIAAL is a phase III randomized, double blind, placebo-controlled study, involving 222 CMT1A adults from 8 Italian centers. Aims of the trial are: to assess the clinical efficacy and safety of a long-term AA treatment in CMT1A; to devise and validate an evaluation protocol suitable for future CMT trials; to prospectively assess the disease course using valid and reliable scales. Eligible for the study are symptomatic adults with genetically confirmed CMT1A. Treatment consists of two-year oral AA (1500 mg/day) or placebo. Primary trial endpoint is a change in CMT Neuropathy Score. Secondary efficacy endpoints are changes in distal maximum voluntary isometric contraction; 10-meter timed walking; 9-hole-peg test; Overall Neuropathy Limitations Scale; pain and fatigue VAS; health-related quality of life (SF-36); electrophysiology. Assessments are performed at baseline and every six months thereafter. PMP22 expression in skin nerves will be evaluated in consenting patients from three centres.

Results/Conclusion. The planned one-year enrolment started on March 2006. Between March and December 2006, a total of 265 patients had been screened (female 156 [59%], mean age 42.6 year [SD 13.3; range 18-70]), and 194 of them (87 % of target) had been randomized to receive AA or placebo (female 117 [60%], mean age 41.9 [SD 13.0; range 18-70]). Main reasons for exclusion were lacking or different genetic diagnosis (n=18), other causes of neuropathy (n=17), other major diseases (n=6), renal stones (n=5), recent or planned limb surgery (n=5). Analysis of the baseline assessment is under way.

Presented on behalf of the CMT-TRIAAL Study Group.

Supported by Telethon Italy Grants GUP04002-GUP05007, and partially by the Italian Drug Agency-AIFA.

# REHABILITATION TREATMENT AND BAROPODOMETRIC ANALYSIS IN PATIENTS AFFECTED BY CHARCOT-MARIE-TOOTH (CMT) INHERITED NEUROPATHY

Grosso M\*, Schenone A\*, Zuccarino R\*\*, Monti Bragadin M\*, Coatti E\*\*\*, Reni L\*, Narciso E\*, Grandis M\*, Bellone E\*, Mantero M\*\*\*

*\*Dip. Neuroscienze, Oftalmologia e Genetica - Università di Genova, \*\*Fides - Genova, \*\*\* Unità Riabilitazione, Osp. S. Martino - Genova*

CMT disease is the most frequent hereditary neuropathy. As specific drugs are not available for CMT, only a rehabilitation treatment is possible. CMT patients show poor standing and gait abnormalities, due to plantar flexor failure, foot drop, cavovarus foot deformity and poor proprioception. By clinical scales (MRC, Tinetti test, the short battery of lower limbs performance scale), we evaluated 15 patients (10 females and 5 males) undergoing a personalized rehabilitation treatment characterized by respiratory, proprioceptive and stance reeducation, and by a deambulation training. Moreover, Foot Analysis System (FAS) and Computerized Baropodometric Analysis (CPA) were used to evaluate all the patients, wearing or not personalized orthosis. By FAS and CPA, isobaric areas, plantar foot loading surface, areas of the different pressure zones, tridimensional images and stabilometric measurements were calculated. FAS and CPA were also performed before and after rehabilitation treatment in 6 patients.

After treatment all the patients improved in every impairment scale: mean Tinetti test increased from 13 to 15/16, ankle dorsiflexion increased of 10°, mean MRC on lower limbs distal muscles changed from 3.5 to 4.0/5 and the lower limb performance scale increased from 9 to 11/12.

With FAS and CPA all the patients showed, at baseline, higher barycenter ellipsis with bare feet ( $5.76 \pm 1.2 \text{ cm}^2$ ) than wearing shoes with orthosis ( $2.6 \pm 0.9 \text{ cm}^2$ ). Interestingly, wearing shoes without orthosis induced a further increase of barycenter ellipsis ( $7.2 \pm 1.9 \text{ cm}^2$ ). In 6 patients FAS and CPA were also evaluated after rehabilitation treatment. A decrease in mean barycenter ellipsis with bare feet was found ( $6.75 \pm 1.5 \text{ cm}^2$  vs  $3.73 \pm 0.9 \text{ cm}^2$ ).

In conclusion, rehabilitation treatment is effective in improving stability and gait abnormalities in CMT patients. Moreover, FAS and CPA show that orthosis and correct shoes significantly ameliorate the areas of feet pressure thus improving stability and balance.

# POOR ACCEPTANCE OF ANKLE-FOOT ORTHOSES IN PATIENTS WITH CHARCOT-MARIE-TOOTH DISEASE

Vinci P\*, Gargiulo P\*\*

*\*Ass. Italiana "Charcot – Marie–Tooth" - Roma, \*\*Facoltà di Psicologia 2 - Università di Roma " La Sapienza"*

Charcot-Marie-Tooth disease (CMT) is a genetic neuropathy that weakens the foot and leg muscles: footdrop, alone or associated with foot rotation and plantarflexor failure, may result. Severe footdrop impairs the swing phase of gait, obliges to tiring compensations and causes stumblings and falls: therefore ankle-foot orthoses (AFOs) are prescribed.

Objective: to evaluate the acceptance of AFOs in a sample of CMT patients previously prescribed with them.

Materials: 25 Italian patients (8 males 17 females; mean age: 41.6 range 16-54 years) fitting in the stages 3 (n=7), 4 (n=14) and 5 (n=4) of functional classification proposed by Vinci et al.

Methods: clinical examination by a physiatrist with measurement of the leg-sole angle (°) in swing with their footwear; brief interview by a psychologist.

Results: only 5 patients (20%) used AFOs (3 wore prefabricated leaf-spring polypropylene AFOs in ready-made shoes and 2 used high-top boots incorporating a custom-made "aesthetic in-shoe device for footdrop") with good functional results (°= 90 -94 ). Two patients wore laced boots padded in the back by rubber-foam with quite good results (°= 93 -98 ). The remaining subjects either used high-top boots (n= 9) with partial correction of footdrop (°= 100 -106 ) or normal low shoes (n= 9) with the same severe footdrop as barefoot.

The interview revealed that almost all patients had frequent feelings of discomfort when looking at their own feet and legs, and sorrow for not being able to use trendy footwear. The 3 subjects using traditional AFOs said that they hated them and one of them complained of pain. Patients not using AFOs justified their decision with statements such as: "I am not yet ready to accept them" or "I can still do without them for a while" or "I cannot find an acceptable shoe to put them inside". Twelve patients had not even gone to the orthotist to try them on.

Discussion and conclusions. Acceptance of AFOs is objectively poor. This seems to be related to physical and psychological discomfort associated to AFOs. We suggest that prescription of AFOs be accompanied with psychological support and that research of more comfortable and cosmetically acceptable solutions for the problem of footdrop be stimulated.

## LONG-TERM EFFICACY OF RITUXIMAB IN ANTI-MAG POLYNEUROPATHY

Benedetti L\*, Briani C\*\*, Carpo M\*\*\*, Cocito D\*\*\*\*, Beronio A\*\*\*\*\*, Zara G\*\*, Zambello R\*\*, Sormani MP\*\*\*\*\*, Mancardi GL\*, Nobile-Orazio E\*\*\*\*\*, Schenone A\*

*\*Dept. of Neurosciences, Ophthalmology and Genetics - University of Genova, \*\*Dept. of Neurosciences, Clinical and Experimental Medicine - University of Padova, \*\*\*Dept. Neurological Sciences, Fond. IRCCS, Osp. Maggiore Policlinico, "Mangiagalli-Regina Elena" – Milano, \*\*\*\* Neurologia I, Dept. of Neuroscience, ASO "San Giovanni Battista" – Torino, \*\*\*\*\*Dept. of Neurology, Osp. "S. Andrea" - La Spezia, \*\*\*\*\*DISSAL, Unit of Biostatistics - University of Genova, \*\*\*\*\*Dept. Neurological Sciences, IRCCS Humanitas Clinical Institute, Rozzano – University of Milan*

**Objective:** In a previous study on 13 patients treated with Rituximab for polyneuropathy associated with antibodies to Myelin-Associated Glycoprotein (MAG), 8 patients (62%) improved in both the Inflammatory Neuropathy Cause and Treatment (INCAT) Sensory Sumscore and the MRC sumscore, and 7 of them also in the INCAT disability score. The improvement in the mean INCAT Sensory Sumscore was significant at 12 month and correlated with lower anti-MAG antibody titres. Our aim was to extend the study to a larger number of patients, and to assess the safety and efficacy of Rituximab after a long term follow-up (36-48 months), and the need for retreatment.

**Materials and methods:** 27 patients with anti-MAG polyneuropathy treated with Rituximab were prospectively followed for up to 48 months (13 patients had a 12 months, 12 patients a 36 months and 2 patients a 48 months follow-up after therapy). We studied the long term clinical response and the biologic effects using the MRC sumscore, the INCAT arm and leg disability scores, the INCAT Sensory Sumscore, the dosage of CD19+ B-cells, IgM, and anti-MAG antibodies. Nerve conduction studies were performed in each patient.

**Results:** In all patients CD19+ B-cells were suppressed for 9-12 months, while median serum IgM levels were still reduced after 36 months. Anti-MAG antibody titres raised again after 24 months. At 36 months 75% of responder patients still showed a clinical stabilization, whereas 25% started worsening after 24-48 months. Eight patients underwent a second treatment with Rituximab, with clinical improvement present only in those patients who were responsive to the first course.

**Conclusions:** The results of this preliminary open label study indicate that in responder patients Rituximab has a long-lasting efficacy, and that a second treatment is effective and safe.

# VEGF LEVELS PREDICT RESPONSE TO THERAPY IN PATIENTS WITH POEMS

Terenghi F, Giannotta C, Casellato C, Nobile-Orazio E

*Dept. Neurological Sciences, "Dino Ferrari" Center, IRCCS Humanitas Clinical Institute, Rozzano – University of Milan*

POEMS syndrome is a rare cause of neuropathy with multiorgan involvement. The pathogenesis is not well understood but overproduction of vascular endothelial growth factor (VEGF) is considered responsible for the characteristic symptoms. In previous studies, VEGF level decreased in parallel with clinical improvement and the effect was more pronounced after high-dose melphalan followed by autologous peripheral blood stem cell transplantation (auto-PBSCT) than after low-dose oral melphalan. In some patients VEGF levels were also found to predict clinical recurrence.

We correlated serum VEGF levels with the clinical course and response to therapy in 4 men with POEMS causing a severe motor sensory polyneuropathy predominantly affecting the lower limbs. Two patients were treated with high-dose melphalan and auto-PBSCT and two with 6 to 9 courses of oral melphalan (0.24 mg/Kg/day for 4 days every 6 weeks) and steroids. Clinical response was assessed by the MRC scale for muscle strength on 40 muscles. Serum VEGF levels were measured by ELISA (R&D systems, Minneapolis).

Both patients undergoing auto-PBSCT rapidly improved starting one month after therapy with a parallel marked decrease of VEGF levels; in one (No. 1) the MRC score raised in 6 months from 188 to 193 and VEGF decreased from 6500 to 1200 pg/ml; in the other (No. 2) the MRC score raised from 113 to 127 after 3 months and VEGF decreased from 11000 to 3600 pg/ml. In this patients the MRC decreased after 6 months to 117 and VEGF raised to 8900 pg/ml. The two patients treated with low dose oral melphalan started to improved after two and seven months respectively after an initial worsening; in one (No. 3) the MRC initially decreased from 144 to 100 after one month then progressively increased up to 132 after 18 months, while VEGF levels immediately decreased from 7000 to 820 pg/ml and remained stable after 18 months (880 pg/ml). In the other (No. 4), the MRC initially decreased from 170 to 140 at 4 month then raised to 152 after 9 months while VEGF progressively decreased from 3600 to 382 pg/ml. At 14 month VEGF increased to 1100 pg/ml and the MRC worsened to 145.

In all our patients VEGF levels not only correlated with the clinical response but also often anticipated the clinical effect confirming that measuring VEGF levels can help predicting response to therapy in patients with POEMS.

# RANDOMIZED, OPEN LABEL TRIAL ON THE EFFICACY AND TOLERABILITY OF OXCARBAZEPINA VERSUS GABAPENTIN IN THE TREATMENT OF NEUROPATHIC PAIN

Jann S\*, Muscia F\*\*, Sterzi R\*

*\*Dip. Neuroscienze, Osp. "Niguarda" – Milano, \*\* Divisione Neurologia, Osp. Valduce – Como*

This was a multicentric, randomized, open-label, parallel group, comparative trial, consisting of a 6-week prospective Screening Phase followed by 1-3 week Titration Phase, and 6-week Treatment Phase. Our objective was to evaluate the efficacy of oxcarbazepine versus gabapentin in the treatment of painful neuropathies testing the hypothesis that oxcarbazepine has a faster onset of action in comparison with gabapentin. The primary efficacy variable was the change in the weekly pain rating assessed on the VAS of the short-form McGill Pain Questionnaire between the Screening Phase and the end of the First week of Treatment -Treatment Phase. Thirty-nine patients were enrolled in the trial 20 (51.28%) on oxcarbazepine, and 19 (48.72%) on gabapentin. Twenty-nine patients completed the study, 10 patients (25, 64%) discontinued the trial: 9 for adverse events (5 on oxcarbazepine; and 4 on gabapentin) and 1 patient on oxcarbazepine discontinued for withdrawal of consent. After one week of study treatment VAS decrease  $\geq 50\%$  was observed in 6 patients (37.50%) in the oxcarbazepina group, and 1 patient (7,69%) on the gabapentin group, VAS decrease  $\geq 40\%$  was observed in 12 patients (75.00%) in the oxcarbazepina group, and 1 patient (7,69%) on the gabapentin group ( $p < 0.0003$ ), and VAS decrease  $\geq 30\%$  was observed in 12 patients (75.00%) in the oxcarbazepina group, and 1 patient (7,69%) on the gabapentin group ( $p < 0.0003$ ). The mean VAS score dropped from 73.3 at Baseline to 46.0 at the end of the first seven treatment days in the oxcarbazepina group, and from 72.7 at Baseline to 62.4 at the end of the first seven treatment days in the gabapentin group; for a mean reduction of - 27.3 in the oxcarbazepina group, and -10.3 in the gabapentin group ( $p < 0.005$ ). The mean VAS score dropped from 73.3 at Baseline to 31.7 at the end of study in the oxcarbazepina group, and from 72.7 at Baseline to 38.5 at the end of study in the gabapentin group; for a mean reduction of - 41.7 in the oxcarbazepina group, and -33.6 in the gabapentin group. Both treatments were well tolerated with the most common adverse events consisting of nervous system disorders for both treatment groups. The results suggest that oxcarbazepine administered as monotherapy has a faster onset of action than gabapentin, achieving a meaningful reduction in VAS score already after the first seven days of treatment.

# EVALUATION OF THE ANALGESIC ACTIVITY OF PREGABALIN IN BURNING MOUTH SYNDROME

Penza P\*, Camozzi F\*, Lombardi R\*, Martini A\*, Bonadeo S\*\*, Majorana A\*\*, Sapelli P\*\*, Lauria G\*

*\*Neuromuscular Diseases Unit, National Neurological Institute "Carlo Besta" – Milan, \*\*Dental Clinic, School of Dentistry - University of Brescia*

Burning Mouth Syndrome (BMS) is a chronic disorder recently recognized as a form of painful neuropathy affecting small nerve fibers of the tongue. An effective treatment for BMS is still lacking. Pregabalin is an antiepileptic drug commonly used for treatment of neuropathic pain from postherpetic neuralgia and diabetic peripheral neuropathy. The effectiveness of pregabalin in BMS has not been assessed. The aim of this prospective open-label study was to evaluate the efficacy of pregabalin in controlling pain in BMS. Patients with a clinical and histopathological diagnosis of BMS and with a VAS > 4 were recruited. Primary endpoint was a reduction of 50% in pain severity at VAS analysis. Secondary efficacy variables were number of responders, patient global impression of change (PGIC), and short sleep quality questionnaire (SQNRS). Pregabalin was given twice a day starting at 150 mg daily and could be increased up to 600 mg daily if a satisfactory pain control was not achieved at 15-day follow-up visits. When pain control was achieved, the dose of pregabalin was maintained for 30 days. Preliminary data on twelve patients are presented. In all the patients, biopsies demonstrated a diffuse denervation of epithelium and fungiform papillae. Five patients dropped out because of side effects (dizziness and daily sleepiness) in the first two weeks. In seven responder patients, pregabalin induced an improvement of 63% in pain severity that was stable at 42-day visit (baseline mean VAS = 6.5, 42-day visit mean VAS = 2.4). Five patients needed to increase the starting dosage from 150 mg up to 300 mg daily to achieve satisfactory pain control, without increment of side effects. PGIC and SQNRS were slightly improved in all responders. Pregabalin appears to be an effective treatment in patients with BMS.

Pfizer independent research grant.

# BOTULINUM TOXIN TREATMENT FOR OROPHARYNGEAL DYSPHAGIA ASSOCIATED WITH DIABETIC NEUROPATHY

Restivo DA\*, Marchese Ragona R\*\*, Lauria G\*\*\*, Squatrito S\*\*\*\*, Gullo D\*\*\*\*

*\*Division of Neurology, Garibaldi Hosp. – Catania, \*\* ENT Dept. - University of Padua, \*\*\* Neuromuscular Diseases Unit, National Neurological Inst. “Carlo Besta” – Milan, \*\*\*\*Endocrinology, Dept. of Internal and Specialistic Medicine, Garibaldi Hosp - University of Catania*

Objectives: No specific treatment for oro-pharyngeal dysphagia related to diabetic neuropathy has been described to date. Chemical myotomy of the cricopharyngeus (CP) muscle by botulinum neurotoxin type A (BoNT/A) has been shown effective in reducing or abolishing dysphagia associated with upper esophageal sphincter (UES) hyperactivity of different etiologies. In the present study, we evaluated the efficacy of BoNT/A injections into the CP muscle in diabetic patients with severe oro-pharyngeal dysphagia associated with diabetic autonomic and/or somatic peripheral neuropathy.

Research design and methods: Fourteen type 2 diabetic patients with severe dysphagia for both solid and liquid foods associated with autonomic and/or peripheral somatic neuropathy were investigated. Swallowing function was evaluated by clinical examination, videofluoroscopy and simultaneous needle electromyography (EMG) of CP and pharyngeal inferior constrictor (IC) muscles. Clinical evaluation, using a four-level dysphagia severity score, was performed every other day for the first week and thereafter every other week until week 24. Videofluoroscopy and EMG follow-up were carried out at week 1, 4, 12, 16, 18, and 24 after BoNT/A injection. BoNT/A was injected percutaneously into the CP muscle under EMG control. Results: BoNT/A induced the complete recovery of dysphagia in 11 patients and a significant ( $p = 0.0001$ ; ANOVA) improvement in 3 patients within  $4 \pm 1.2$  days (range 3-7 days). The clinical improvement was confirmed by videofluoroscopy and electromyography. Conclusion: Our findings suggest a potential benefit from BoNT/A treatment in dysphagia associated with diabetic neuropathy. Randomized controlled trials are needed to confirm this observation.

# REGISTER OF CIDP PATIENTS NON RESPONDERS TO TRADITIONAL THERAPY

Cocito D\*, Nobile – Orazio E\*\*

*\*Dept. of Neurosciences - University of Turin, \*\* Dept. Neurological Sciences "Dino Ferrari" Center, 2nd Neurology, IRCCS Ist. Clinical Humanitas – University of Milan*

The Study will be retrospective and will include all the never responders CIDP patients or those became non responders to conventional therapies (corticosteroids, immunoglobulins, plasmapheresis), that since at least three months are in therapy with non conventional drugs (all those drugs for which signalings of efficacy can be found actually in literature). The CIDP diagnosis shall satisfy the task force's criteria of the European Federation of Neurological Societies and the Peripheral Nerve Society. To know the percentage of non responders to traditional therapies in comparison with the total, all the patients, even the responders to traditional therapies, will be included in the database.

For each patient data will be collected inherent in: 1) Age, sex, duration of the disease at the beginning of non conventional therapy. 2) Clinical Scale (a functional scale as the Rankin is proposed in consideration of the retrospective characteristics of the Study) for the patient's evaluation before the beginning of the non conventional therapy and at the moment of the data collection. 3) Type of non conventional therapy adopted (and previous conventional therapy). "Responder" will be defined a patient that, after the therapy, shows an increasing of one point at the Rankin scale. The data will be collected by each single centre participating to the Study, using ad hoc data base; data analysis will be centralized (Neuroscience Department, University of Turin), that reserves the opportunity of require external advices for the epidemiologic and statistic evaluation. The estimated duration of the study is about one year.