

EUGOGO STUDY C

A multicentre randomized controlled double blind clinical trial comparing the effectiveness and tolerability of different doses of intravenous glucocorticoid (IVGC) for the treatment of moderately severe Graves' Ophthalmopathy (GO)

Chief Investigator	Prof Wilmar Wiersinga
Design	Prospective, randomized placebo-controlled double blind clinical trial with two arms
Aims	<ul style="list-style-type: none"> To identify the lowest effective dose of IVGC in patients with moderately severe GO
Patients	159 patients with moderately severe GO
Eligibility	<ul style="list-style-type: none"> euthyroidism for at least 2 months with antithyroid drugs or following surgery, or 6 months following radiodine administration Active GO: Clinical Activity Score ≥ 3 out of 7 items Moderate to severe GO defined as having at least one of the following eye signs: <ul style="list-style-type: none"> Moderate to severe soft tissue involvement (class 2b-c NOSPECS) Eye muscle involvement Diplopia according to Gorman score of grades a-c no previous treatment for GO age 18-75 years
Main outcome	<p>Primary outcome:</p> <p>1. Efficacy:</p> <p>Objective assessment: improvement in at least one eye in two of the following outcome measures (without deterioration in any of these measures in both eyes)</p> <ul style="list-style-type: none"> improvement in lid aperture of at least 3 mm improvement of soft tissue involvement (change in at least 2 degrees of Class) improvement in proptosis by at least 2 mm using the same Hertel exophthalmometer improvement in extra-ocular muscle involvement <p>Subjective primary outcome: improvement in 6 or more points on either (or both) the GO-quality of life scales (GO-QoL)</p> <p>2. Safety: safety score: assign 2 point to each the major side effect e 1 point to each of the other</p> <ul style="list-style-type: none"> Development of diabetes mellitus requiring therapy Development of major depression or psychosis Severe infections requiring hospitalization Any side effect necessitating withdrawal Increase of body-weight (increase of >4 in BMI) Cushingoid features Gastric symptoms not improving on omeprazole Development or worsening of abnormal liver enzymes Development or worsening of hypertension Skin flushes after iv injection
Assessment	At baseline, after 6 weeks, 12 weeks and 24 weeks: <ul style="list-style-type: none"> Assessment of thyroid function and thyroid autoantibodies Glycaemia, liver enzymes Ophthalmologist evaluation GO-QoL
Intervention	<ul style="list-style-type: none"> One infusion per week for 6 weeks of 250 mg (2x125) of methylprednisolone acetate (MPA, Solumedrol) followed 6 weekly infusions of 125 mg MPAS. Total dose 1490

	<ul style="list-style-type: none"> mg • One infusion per week for 6 weeks of 540 mg (500+40) of MPA followed 6 weekly infusions of 290 mg MPA (125+125+40). Total dose 4980 mg • One infusion per week for 6 weeks of 830 mg (500+125+125+40+40) of MPA followed 6 weekly infusions of 415 mg MPA (125+125+125+40). Total dose 7470 mg
Duration of intervention	12 weeks
Trial duration	24 weeks
Open to	Eugogo centers
Participating Centers	Amsterdam, Pisa, Varese, Mainz, Thessaloniky, Brussels, Milano, Olten, Cardiff
Trial Co-ordinator	Prof Claudio Marocci, Azienda Ospedaliera Universitaria Pisana, Pisa (Italy)