**Comparative effectiveness of Cladribine tablets vs other drugs in relapsing-remitting multiple sclerosis: an approach merging randomized controlled trial with real life data**

**Abstract: P981**

**Type:** Poster Sessions

**Abstract Category:** Therapy - Immunomodulation/Immunosuppression

A. Signori[1], F. Saccà[2], R. Lanzillo[2], G.T. Maniscalco[3], E. Signoriello[4], A. Repice[5], P. Annovazzi[6], D. Baroncini[6], M. Clerico[7], E. Binello[8], R. Cerqua[9], G. Mataluni[10], P. Perini[11], S. Bonavita[4], L. Lavorgna[4], I.R. Zarbo[12], A. Laroni[13,14], L.P. Gutierrez[15], S. La Gioia[16], B. Frigeni[16], V. Barcella[16], J. Frau[17], E. Cocco[17], G. Fenu[17], V. Torri Clerici[15], A. Sartori[18], S. Rasia[19], C. Cordioli[19], M.L. Stromillo[20], A. Di Sapio[21], S. Pontecorvo[22], R. Grasso[23], S. Barone[24], C. Barrilà[25], C.V. Russo[2], S. Esposito[4], D. Ippolito[4], D. Landi[10], A. Visconti[26], M.P. Sormani[1,27]

[1]Department of Health Sciences - Section of Biostatistics, University of Genoa, Genoa, [2]Department of Neurosciences, Reproductive Sciences and Odontostomatology, Multiple Sclerosis Center, Federico II University, [3]Neurological Clinic and Multiple Sclerosis Center, AORN A.Cardarelli, [4]University of Campania 'Luigi Vanvitelli', Naples, [5]University of Florence, Firenze, [6]ASST Valle Olona, Gallarate, [7]University of Torino, San Luigi Gonzaga Hospital, Torino Orbassano, [8]Ospedale Universitario Città della Salute e della Scienza di Torino, Torino, [9]University Polytechnic Marche, Ancona, [10]Policlinic Tor Vergata, Rome, [11]University of Padua, Padua, [12]University of Sassari, Sassari, [13]University of Genoa, [14]IRCCS San Martino-IST, Genoa, [15]IRCCS Foundation Carlo Besta Neurological Institute, Milan, [16]ASST Papa Giovanni XXIII, Bergamo, [17]University of Cagliari, Cagliari, [18]University of Trieste, Trieste, [19]ASST Spedali Civili, Brescia, [20]University of Siena, Siena, [21]Regina Montis Regalis Hospital, Mondovì, [22]Sapienza University, Rome, [23]Neurologia Universitaria OORR, Foggia, [24]University Magna Graecia of Catanzaro, Catanzaro, [25]Valduce Hospital, Como, [26]Medical Department, Merck Serono, Rome, [27]IRCCS Ospedale Policlinico San Martino, Genoa, Italy

**Introduction:** Cladribine tablets was tested against placebo in randomized controlled trials (RCT).
**Objective**: To compare the effectiveness of Cladiribine tablets vs other approved drugs in relapsing-remitting multiple sclerosis (RRMS) naïve patients, by matching RCT to observational data.
**Methods:** Naïve patients from the pivotal trial assessing Cladribine tablets vs placebo (CLARITY) were propensity-score matched to data from the Italian multicenter database i-MuST. This database included 3006 naïve patients diagnosed 2010-2018 in 24 Italian MS centers who started a disease-modifying therapy. The annualized relapse-rate (ARR) over 2 years from treatment start was compared between patients treated with Cladribine tablets and other approved drugs (Interferon, Glatiramer-Acetate, Fingolimod, Natalizumab, Dymethil-fumarate), having the comparisons with placebo as a reference. Treatment effects were estimated by an inverse-probability weighted (IPW) negative-binomial regression model. The treatment effect has been also evaluated according to disease activity (HDA: high disease activity defined as $\geqslant$2 relapses during the year prior to study entry).
**Results:** From the i-MuST database a total of 1168 patients were treated with Interferon, 402 with Glatiramer-acetate, 113 with Fingolimod, 149 with Natalizumab and 295 with Dymethil-fumarate. Patients' weighted characteristics resulted well balanced between groups. All the tested drugs had an effect vs placebo close to those detected in RCT. Patients treated with Cladribine tablets had a significantly lower ARR as compared with Interferon (RR=0.48;p< 0.001), Glatiramer-Acetate (RR=0.49;p< 0.001) and Dymethil-fumarate (RR=0.6;p=0.011), a comparable ARR with Fingolimod (RR=0.74;p=0.24) and a significantly higher ARR than Natalizumab (RR=2.13;p=0.014). The effect of Cladribine tablets low dose was amplified in HDA patients across all treatments except Fingolimod.
**Conclusions:** In RRMS patients, Cladribine tablets showed lower ARR compared with matched patients who started another DMT, similar with fingolimod, behind natalizumab. The effect was amplified in the subgroup of HDA patients.
**Disclosure:**
AS received teaching honoraria from Novartis
FS received personal compensation from Novartis, Almirall, Genzyme, Biogen, Merck Serono Forward Pharma, and TEVA
RL received personal compensation from Merck Serono, Biogen, Novartis, Almirall, Genzyme and TEVA
GTM received personal compensation from Serono, Biogen, and TEVA
ES received personal compensation from Almirall, Biogen, Genzyme, Novartis and Teva
AR received personal compensation from Biogen Idec, Genzyme, Novartis, and Merck Serono
PA received personal compensation from Novartis, Merck Serono, Genzyme, Biogen, and Teva Italia
DB received personal compensation from Almirall, Genzyme and TEVA.
MC received personal compensation by Merck Serono, Biogen, Novartis, and Genzyme.
EB has nothing to disclose
RC has nothing to disclose
GM has nothing to disclose
PP received personal compensation from Merck Serono, Biogen Idec, Genzyme Sanofi, Bayer Schering Pharma, Novartis and Teva.
SB received personal compensation from Merck Serono, Novartis, Teva, Biogen and Genzyme
LL received funding for travel and/or speaker honoraria from Novartis, Genzyme, Teva, Merck, Almirall and Bayer.
IRZ received personal compensation or funding from Biogen Idec, Genzyme,Teva, Merck and Novartis.
AL has received personal compensation from Novartis, Genzyme, Biogen and TEVA for public speaking and advisory boards.
LPG has nothing to disclose
SLG has nothing to disclose
BF has nothing to disclose

VB has nothing to disclose
JF received personal compensation for Biogen, Merck Serono, Teva.
EC received personal compensation from Almirall, Bayer, Biogen, Genzyme, Novartis, Serono and TEVA for public speaking, editorial work and advisory boards.
GF recieved personal compensation from Novartis, Merck Serono, Biogen and Teva.
Valentina Torri Clerici received personal compensation from Novartis, Almirall, Genzyme, and Teva
AS has received speaker honoraria from Novartis, Teva, Merck-Serono and Genzyme.
SR has nothing to disclose
CC received personal compensations for consultanting from MerkSerono and Novartis.
MLS has nothing to disclose
ADS received personal compensation froom Novartis, Biogen, Merck Serono, Teva, Genzyme, Allergan
SP received personal compensation from Almirall, Biogen, Genzyme and Teva
RG has nothing to disclose
SB has nothing to disclose
CB has nothing to disclose
CVR has nothing to disclose
SE has nothing to disclose
DI has nothing to disclose
DL has nothing to disclose
AV is a full time employee at Merck Serono
MPS received personal compensation for consulting services and for speaking activities from Merck Serono, Teva, Novartis, Roche, Genzyme and Biogen.