

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Extended interval dosing of natalizumab: is efficacy preserved?

This is a pre print version of the following article:

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1757446> since 2020-10-01T15:16:20Z

Publisher:

SAGE PUBLICATIONS LTD

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

Abstract: P587

Type: Poster Sessions

Abstract Category: Therapy - Long-term treatment monitoring

Introduction: Some clinicians in Italy extended the dose of natalizumab infusions after 24 doses, with the hypothesis of reducing PML risk; this idea was supported by recent reports.

Objective: To make this strategy feasible, it is necessary to ascertain the therapeutic durability of the extended dosing strategy.

Aim: To evaluate the non-inferiority in controlling disease activity of an extended interval dosing (EID) of natalizumab.

Methods: Patients who received natalizumab for at least 24 weeks in 14 Italian centers were included in the analysis. Patients were grouped in 2 categories according to the mean number of weeks between doses (< =5.5 weeks, standard interval dosing (SID); >5.5 weeks, EID). Only the dose intervals before the first relapse was used to estimate the mean intervals between doses, to minimize the bias associated to a possible return to SID in patients under EID after they experienced a relapse. The non-inferiority of EID vs SID was a priori defined as satisfied if the upper limit of the 95%CI of the annualized relapse rate (ARR) in the EID group did not exceed the mean ARR of the SID group by 0.02 relapse/year. Baseline characteristics were compared between groups by a Mann Whitney U test. ARR during follow up was estimated and compared between groups by a multivariate Poisson regression model.

Results: 341 patients were included in this analysis. The median interval between doses was 4.9 weeks (range 3.7-8.4), with a clear bimodal distribution (modes at 4 and 6 weeks) associated with individual centers strategies (the median was 4.5 weeks in 220 patients from 12 centers and 6.2 in 121 patients from 2 centers). 221 patients were in the SID (median dose interval=4.5 weeks) and 120 in the EID group (median dose interval=6.3 weeks). The ARR during follow up adjusting for all the baseline variables (age, disease duration, relapses in 2 years pre-natalizumab start, EDSS, number of previous treatments) was 0.042 (95%CI=0.026-0.067) in the SID group, and it was 0.007 (95%CI=0.002-0.028) in the EID group. The non-inferiority of EID vs SID was satisfied.

Conclusions: In this cohort there is no evidence of a reduced efficacy of natalizumab by extending the intervals between doses from a median of 4.5 to a median of 6.3 weeks. This observation confirms previous results and together with the emerging evidence of a reduced risk of PML associated to an EID supports the need of a randomized study to change the standard of the natalizumab dosing schedule.

Disclosure: M. Clerico: received personal compensations for advisory boards, public speaking, editorial commitments or travel grants from Biogen Idec, Merck Serono, Fondazione Serono, Novartis, Pomona, Sanofi-Genzyme and Teva.

A. Signori: received teaching honoraria from Novartis

C. Cordioli: received advisory board and/or speaker honoraria from Novartis, TEVA, Biogen, Merck Serono, Genzyme

S. De Mercanti: nothing to disclose

E. Signoriello: received travel funding and speaker honoraria from Biogen, Novartis, Sanofi Genzyme, Bayer, Teva

G. Lus: received travel funding, research support, speaker honoraria from Biogen, Novartis, Sanofi Genzyme, Bayer, Teva, Almirall,

Allergan, Ipsen

G.T. Maniscalco: has served on advisory boards and/or received travel grants and speaker honoraria from Almirall, Biogen,

Merck Serono, Novartis and Teva

E. Curti: has served on scientific advisory boards for Merck Serono and has received funding for travel from Biogen, Merck

Serono, Novartis, Sanofi Genzyme, and Roche

L. Loreface: received speaker fee from Teva and serves on scientific advisory boards for Merck Serono

E. Cocco: have received honoraria for consultancy or speaking from Bayer, Biogen, Novartis, Sanofi, Genzyme, Serono

and Teva.

V. Nociti: has served on scientific advisory boards for Biogen, Teva, Sanofi-Genzyme and Merck Serono and has received

travel grants and/or speaker honoraria from Merck Serono, Teva, Biogen, Sanofi-Genzyme Roche and Novartis

M. Mirabella: received honoraria for scientific advisory board, consulting and/or speaking fees, research support or travel

grants from Almirall, Bayer Schering, Biogen, CSL Behring, Sanofi-Genzyme, Merck Serono, Novartis, Teva, Ultragenix;

principal investigator in clinical trials for Biogen, Merck Serono, Novartis, Roche, Sanofi Genzyme, Teva, Ultragenix

D. Baroncini: received travel grants from Genzyme, Merck and Biogen for participation at national and international

congresses; he received speaking honoraria from Sanofi and Novartis, and personal compensation from Almirall for

scientific publication

D. Landi: received travel funding from Biogen, Merck Serono, Sanofi-Genzyme, Teva, honoraria for speaking from Sanofi-

Genzyme, Teva, Biogen and consultation fees from Merck Serono, Teva, Roche. She is currently subinvestigator in clinical

trials being conducted for Biogen, Novartis, Roche, Celgene

G. Mataluni: nothing to disclose

M. Petruzzo: nothing to disclose

R. Lanzillo: received personal compensation from Merck Serono, Biogen, Novartis, Almirall, Genzyme, and TEVA for public

speaking, editorial work and advisory boards

I. Gandaglia: received funding for travel from Biogen, Novartis, Genzyme, Merck Serono and honoraria from Almirall and

Genzyme

A. Laroni: received consulting honoraria and/or speaker fees from Novartis, Genzyme, Biogen, Sanofi, Merck Serono, and

Teva and received research support from Biogen

R. Frangiamore: received travel funding from Biogen, Merck Serono, Sanofi-Genzyme, Teva to take part in conferences

and scientific events

A. Sartori: received funding for travel and/or speaker honoraria from Novartis, Teva, Merck, Genzyme, Almirall, Roche

P. Cavalla: has served on advisory boards and/or has received travel grants and/or speaker honoraria from Merck Serono, Teva, Italia, Biogen, Almirall, Novartis, Sanofi-Genzyme
G. Costantini: nothing to disclose
M.P. Sormani: received personal compensation for consulting services and for speaking activities from Merck Serono, Teva, Novartis, Roche, Genzyme and Biogen
R. Capra: received lecture fees and/or travel grants from Novartis, Biogen, Celgene, Novartis, TEVA, Genzyme and Sanofi-Aventis