

SUPPLEMENTARY MATERIALS

Table S1. WHO Trial Registration Data Set

Data Category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT06705608
Date of registration in primary registry	25 November 2024
Secondary identifying numbers	N/A
Source(s) of monetary or materials support	Canadian Institutes of Health Research
Primary Sponsor	Collaboration for Outcomes Research and Evaluation (CORE)
Secondary sponsor(s)	N/A
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Contact for scientific queries	Jacquelyn J. Cragg, PhD jacquelyn.cragg@icord.org Faculty of Pharmaceutical Sciences University of British Columbia 2405 Wesbrook Mall Vancouver, BC V6T 1Z3
Public title	Fingolimod and risk of skin cancer among individuals with multiple sclerosis: a population-based cohort study protocol
Scientific title	Fingolimod and risk of skin cancer among individuals with multiple sclerosis: a population-based cohort study protocol
Countries of recruitment	Canada
Health condition(s) or problem(s) studied	Skin cancer
Intervention(s)	Fingolimod Active comparators: natalizumab, alemtuzumab, dimethyl fumarate, teriflunomide
Key inclusion and exclusion criteria	Inclusion criteria: Multiple sclerosis; age > 18 years; no documented prior receipt of interventions; no skin cancer-related encounters in last 3 years, disease-modifying therapy indication for relapse-remitting multiple sclerosis.
Study type	Observational Method of allocation: Randomized assignment is emulated by adjustment for confounding factors to ensure exchangeability of study groups Masking: N/A Assignment: Parallel Purpose: Prevention
Date of first enrolment	1 January 2003
Target sample size	Population based
Recruitment status	N/A – Administrative health data sources
Primary outcome(s)	Skin cancer Method of measurement: ICD codes Timepoints: Months from treatment initiation
Key secondary outcomes	N/A

Table S2. Drug identification number for disease-modifying-therapies

DMT Agent	Approved DINs ^a	Off Label DINs
Azathioprine		02242907, 00004596, 02236819
Cladribine	02470179	02319918, 02494574
Cyclophosphamide		02241797, 02241798, 02241799, 02241800, 02241795, 02241796
Methotrexate		02509067, 02182963, 02524023, 02327236, 02464365, 02474735, 02474891, 02182777, 02182947, 02182955, 02182971, 02422166, 02422174, 02422182, 02422190, 02422204, 02099705, 02491311, 02491338, 02491346, 02491354, 02491362, 02182750, 02454750, 02454769, 02454777, 02454831, 02454858, 02454866, 02454874, 02170698
Mitoxantrone		02286300
Teriflunomide	02416328, 02502933, 02500639, 02504170, 02523833, 02500469, 02500310, 02500434, 02505843, 02501090	
Dimethyl Fumarate	02404508, 02420201, 02513803, 02513781, 02497034, 02497026, 02502704, 02502690, 02516055, 02516047, 02494817, 02494809, 02505770, 02505762, 02495368, 02495341	
Glatiramer Acetate	02245619, 02456915, 02460661	
Interferon Beta	02169649, 02237319, 02237320, 02269201, 02318253, 02318261, 02444399, 02444402	
Fingolimod	02365480, 02469561, 02469618, 02482606, 02469782, 02469715, 02487772, 02482533, 02469936, 02475669	
Natalizumab	02286386	
Alemtuzumab	02418320	2290960
Ocrelizumab	02467224	
Rituximab		02513447, 02241927, 02457350, 02473976, 02498316, 02495724, 02478382, 02478390
Minocycline		02278219, 02084090, 02084104

DINs were obtained from the Health Canada Drug Product Database Online Query (<https://health-products.canada.ca/dpd-bdpp/index-eng.jsp> accessed August 4, 2023).

^aDrugs approved by Health Canada for the treatment of MS.

Table S3. Covariates for emulating a target trial of DMT and skin cancer

Covariate	Categories/Values
Time-fixed	
Age at drug initiation	18–99 years old
Age at MS diagnosis	18–99 years old
Year of drug initiation	2003–2020
Sex	Female; Male
Time-varying	
Month of follow-up	0–204 months
Charlson Comorbidity Index	0–37 points
MS severity (proxy)	EDSS<6; EDSS≥6
Smoking status (proxy)	Never smoked; Ever smoked
Rheumatoid arthritis	Yes; No
Neighborhood income quintile-based residence	0–20%
	20–40%
	40–60%
	60–80%
	80–100%