DDA29

Medical Writing for Non-interventional and Database Studies

EMWA 48th CONFERENCE
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Pre-workshop assignment

Objective
To see if the participants can discriminate between clinical trials, observational studies and database research and to provoke some brainstorming about different objectives that might be addressed by observational and database studies vs. clinical trials.

Content
You will receive 6 short summaries of scientific projects which are commonly performed during the phase III/IV development phase of a pharmaceutical compound. For each of the 5 projects please judge whether it constitutes a clinical trial, an observational study and/or database study

Assessment criteria
Please send a word file detailing your choices, why interventional vs. non-interventional; could this be considered a database study?

Instructions
Please return your assignment (**last page only**) **by 30 October 2018 to** thomas.wagner@merckgroup.com. You will receive feedback on your assignments during the first 30 min of the workshop.

Resources and materials
Please read and complete the attached Word file. It may be also be of benefit to browse through the Internet to find some definitions and examples of non-interventional/ observational/database studies.

Time required
2 h

Summary 1

The French Multiple Sclerosis Registry (OFSEP)

Tracking Information	
First Submitted Date	August 22, 2016
First Posted Date	September 7, 2016
Last Update Posted Date	September 7, 2016
Study Start Date	January 2011
Estimated Primary Completion Date	December 2019 (Final data collection date for primary outcome measure)
Current Primary Outcome Measures (submitted: September 6, 2016)	• Number of cases of MS included [Time Frame: 6 months up to 8 years] • number of patients [Time Frame: 6 months up to 8 years] • demographic characteristics [Time Frame: 6 months up to 8 years] • geographical distribution [Time Frame: 6 months up to 8 years] • disease characteristics [Time Frame: 6 months up to 8 years] • simple disease-modifying treatment description [Time Frame: 6 months up to 8 years]
Original Primary Outcome Measures	*Same as current*
Change History	No Changes Posted
Descriptive Information	
Brief Title	The French Multiple Sclerosis Registry
Official Title	The French Multiple Sclerosis Registry
Brief Summary	OFSEP is an observational cohort of Multiple Sclerosis (MS) and related disorders set up in France. It aims to provide a major epidemiological tool on MS for the scientific community in France and abroad. This tool must help to answer a large number of questions concerning the causes and mechanisms of MS, the prognostic factors of disease progression, the effectiveness and safety of therapeutic drugs, the impact of the disease on patients and society, etc. In December 2015, it has already included more than 54.000 patients. To achieve this goal, OFSEP's objectives are To maintain and develop the French cohort of patients suffering from MS or related diseases and

	syndromes. This means collecting standardized socio-demographic and clinical data as part of the routine medical follow-up of patients already in the cohort and recruitment of new patients. To supplement the existing clinical data with standardized and quality biological samples and MRI scans. To improve the previous data with medical/administrative data from the health insurance fund databases in particular, in order to get more information on comorbidity, treatment protocols and the medico-economic aspects of this disease. To use OFSEP infrastructures to facilitate the implementation of specific studies requiring the collection of additional data or specific patient monitoring processes. To ensure the availability of these data and samples to researchers, health care authorities and industrial players to enable analysis and thus provide answers to research questions or public health issues. This availability is only possible after scientific and regulatory evaluation of the request. To provide regular descriptions of the patient population in the cohort to offer statistics, targets and up-to-date information on this disease and thus enable a better approach to the personal, professional and social impacts of the illness, the effects of basic treatments and the requirements related to the follow-up of this disease in France. To conduct specific studies on the entire population of patients in the cohort (parent cohort) or on patient sub-groups with specific characteristics (nested cohorts). Four nested cohorts have been defined: patients with radiologically isolated syndromes, patients with clinically isolated syndromes, patients with primary progressive courses of the disease and patients with neuromyelitis optica (Devic's syndrome) spectrum disorders.
Detailed Description	*Not Provided*
Study Type	XXXXXXXXXXXXXXXXXX
Study Design	XXXXXXXXX Model: Cohort Time Perspective: Prospective
Target Follow-Up Duration	*Not Provided*
Biospecimen	*Not Provided*
Sampling Method	Non-Probability Sample
Study Population	All MS and NMOSD patients domiciliated in France
Condition	• Multiple Sclerosis

	• Neuromyelitis Optica Spectrum Disorders
Intervention	*Not Provided*
Study Groups/Cohorts	• Radiologically Isolated Syndromes (RIS) • Clinically Isolated Syndromes (RIS) • Primary progressive MS (PPMS)
Publications *	*Not Provided*

Summary 2

A Retrospective Study of the Effectiveness and Safety of Nivolumab in Advanced/Metastatic Non-Small Cell Lung Cancer (NSCLC) Patients in Japan

Condition or disease	Intervention/treatment
Non-Small Cell Lung Cancer	

Study Design

Study Type :	XXXXXXXXXXXXXXXX
Estimated Enrollment :	1000 participants
Observational Model:	Cohort
Time Perspective:	Retrospective
Official Title:	Effectiveness and Safety of Nivolumab in Advanced/Metastatic Non-Small Cell Lung Cancer (NSCLC) Patients - Retrospective Study of Japanese Real-World Data Through Clinical Chart Review
Actual Study Start Date :	March 1, 2017
Estimated Primary Completion Date :	January 31, 2019
Estimated Study Completion Date :	January 31, 2019

Groups and Cohorts

Group/Cohort	Intervention/treatment
NSCLC patients Initiated Nivolumab treatment at least once from 01 Apr. 2016 through 31 Dec. 2016	Other: Non-interventional Non-interventional

Outcome Measures

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Primary Outcome Measures :

1. Description of clinical usage of nivolumab in previously treated NSCLC patients [Time Frame: Approximately 9 months]
2. Overall Survival (OS) [Time Frame: Approximately 9 months]

   Measured from time of initial diagnosis and treatment with nivolumab until date of death

3. Progression Free Survival (PFS) [Time Frame: Approximately 9 months]

Time since index date (initial diagnosis and treatment with nivolumab) to either the first disease progression date or last known tumor assessment date, or death due to any cause, whichever occurs first

Secondary Outcome Measures :

1. Percentage of patients receiving bi-weekly nivolumab
   [Time Frame: Approximately 9 months]
2. Percentage of patients receiving monotherapy or combination therapy
   [Time Frame: Approximately 9 months]
3. Percentage of patients receiving nivolumab as second or later line of therapy
   [Time Frame: Approximately 9 months]
4. Median treatment duration and range by line and histology
   [Time Frame: Approximately 9 months]
5. Rate of permanent and temporary discontinuations
   [Time Frame: Approximately 9 months]
6. Reasons for discontinuation of nivolumab [Time Frame: Approximately 9 months]
7. Reasons for re-challenge of nivolumab [Time Frame: Approximately 9 months]
8. Objective Response Rate (ORR) as assessed by investigator
   [Time Frame: Approximately 9 months]

   ORR is defined as the number of participants with best overall response (OR) of confirmed complete response (CR) or partial response (PR) divided by the total number of participants who received treatment

Eligibility Criteria

Ages Eligible for Study:	Child, Adult, Older Adult
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No
Sampling Method:	Non-Probability Sample

Study Population

Previously treated advanced/metastatic NSCLC patients treated with nivolumab in Japan.

Criteria

Inclusion Criteria:

- Previously treated advanced/metastatic NSCLC patients treated with nivolumab at least once from 01-Apr-2016 through 31-Dec-2016

Exclusion Criteria:

Patients who meets the inclusion criteria will be included in the analysis to describe real-world clinical usage of nivolumab. However, patients treated with nivolumab falling in following criteria will be excluded for analysis for the other primary endpoint; overall effectiveness:

- History of participation in any clinical trials prior- or post-nivolumab treatment
- Patients who are a part of a Post-marketing surveillance study

Other protocol defined inclusion/exclusion criteria could apply

Summary 3

1. Study identification

EU PAS Register Number EUPAS25655
Official title An Analysis of Real-World Data on the Safety of Etanercept in Elderly Patients with Rheumatoid Arthritis
Study title acronym
Study type Observational study
Brief description of the study Both rheumatoid arthritis (RA) and older age are associated with a higher risk of comorbidities, and the appropriate treatment approach for older patients is unclear. We evaluated real-world data (RWD) to determine whether there is an association between etanercept (ETN) and select adverse events (AEs) in patients with RA, stratified by age. We hypothesized that there is no difference in risk of AEs between younger (aged ≤65 yr) and older (aged >65 yr) patients.
Was this study requested by a regulator? No
Is the study required by a Risk Management Plan (RMP)? Not applicable
Other study registration identification numbers and URLs as applicable

Scope of the study

What is the scope of the study?

Risk assessment

Primary scope : Risk assessment

12. Main objective(s)

What is the main objective of the study?
Both RA and older age are associated with a higher risk of comorbidities, and the appropriate treatment approach for older patients is unclear. We evaluated RWD to determine whether there is an association between ETN and select AEs in patients with RA, stratified by age. We hypothesized that there is no difference in risk of AEs between younger (aged ≤65 yr) and older (aged >65 yr) patients.
Are there primary outcomes? Yes
The primary outcome is that we determine that our hypothesis is correct that there is no difference in risk of certain AEs between younger (aged ≤65 yr) and older (aged >65 yr) patients using Enbrel.
Are there secondary outcomes? Yes
Determine the risk of CHF, SI, NMSC, and ILD in patients using Enbrel

13. Study design

What is the design of the study?
Cohort study

14. Follow-up of patients

Will patients be followed up? Not applicable/no follow-up

15. Data analysis plan

Please provide a brief summary of the analysis method
Data from 2013 to 2018 were analyzed from the IBM Watson Health MarketScan Database which contains information on 104.5 million distinct patients, including 531,996 with RA.

Patients were required to be enrolled ≥1 yr prior to RA diagnosis; the first exposure to ETN was after RA diagnosis and before the AE of interest: congestive heart failure (CHF), serious infection (SI), non-melanoma skin cancer (NMSC), or interstitial lung disease (ILD). Proportion of patients experiencing each AE was determined for patients ≤65 yr and >65 yr receiving and not receiving ETN. Differences were evaluated using Fisher's Exact test. Logistic regression models assessed the interaction between ETN and age group. Propensity matching was performed, and logistic regression was applied using the propensity-score-matched cohort. Patients receiving and not receiving ETN were matched by age, age >65 yr, gender, and geographical region.

Summary 4

Tracking Information

First Submitted Date ICMJE	October 1, 2010
First Posted Date ICMJE	January 24, 2012
Last Update Posted Date	January 24, 2012
Study Start Date ICMJE	May 2009
Actual Primary Completion Date	June 2010 (Final data collection date for primary outcome measure)
Current Primary Outcome Measures ICMJE **(submitted: January 23, 2012)**	A concentration SPECT scan will be given to assess the changes in regional cerebral blood flow to the brain in our study participants. [Time Frame: The SPECT scan is one day imaging exam. A follow up scan will be performed following a 2-12 month supplement intervention.] For the concentration study the subject will start the Conner's Continuous Performance Task, a 15-minute computer-administered test of attention, subsequent to the accommodation period. Three minutes into task performance 20 milliCuries of Tc-99m-hexamethylpropylene amine oxime will be injected through the catheter with attention to minimal disruption of the subject's attention task. The subject will proceed to completion of the attention task. The concentration scans will then be compared to a healthy brain subject normative database.
Original Primary Outcome Measures ICMJE	*Same as current*
Change History	No Changes Posted
Current Secondary Outcome Measures ICMJE **(submitted: January 23, 2012)**	Quantitative electroencephalography (QEEG) will be used to assess the damage to neural networks in our study participants. [Time Frame: The QEEG testing is one day exam. A follow up test will be performed following a 2-12 month supplement intervention.] Subjects will undergo quantitative electroencephalography (QEEG) testing in both the eyes open and eyes closed condition to measure the electrical activity patterns of the brain. Brain maps will be generated and compared against a normative database.
Original Secondary Outcome Measures ICMJE	*Same as current*
Current Other Outcome Measures ICMJE	*Not Provided*
Original Other Outcome Measures ICMJE	*Not Provided*

Descriptive Information

Brief Title ICMJE	Single Photon Emission Computed Tomography (SPECT) Imaging Study of Professional American Football Players
Official Title ICMJE	Brain Single Photon Emission Computed Tomography and Quantitative Electroencephalography In Former NFL

Brief Summary	Players: A Single-Site Exploratory Pilot Study The investigators primary objective is to acquire preliminary data on one-hundred former NFL veterans with at least one full year of professional service using brain SPECT imaging in order to assess the degree to which NFL football puts players at risk for traumatic brain injury (TBI). TBI severity shall be gauged via visual inspection by a clinician trained in neuroanatomy, and also by a statistical comparison of subjects' brains to an in-house proprietary database comprised of the brains of healthy subjects. The investigators secondary objective is to acquire additional data on these players such that investigators may establish causative factors and risks associated with said TBI. The investigators tertiary objective is to acquire data on subjects using various mental health metrics in order to determine the effects of TBI.
Detailed Description	*Not Provided*
Study Type ICMJE	XXXXXXXXXXXXXX
Study Phase	Not Applicable
Study Design ICMJE	Intervention Model: Single Group Assignment Masking: None (Open Label) Primary Purpose: Treatment
Condition ICMJE	Traumatic Brain Injury
Intervention ICMJE	Dietary Supplement: Multivitamin Supplement intervention We recommend the following protocol: 1. 2 tablets of a high quality multivitamin BID 2. 2 capsules of omega 3 fish oil BID for a total of 3 grams daily 3. 3 capsules of a brain and memory formula BID which contains Acetyl-L-Carnitine (HCL) 1000 mg, Ginkgo Biloba Extract 120 mg, Alpha-Lipoic Acid (ALA) 300 mg, Huperzine A (Huperzia serrata)150 mcg, N-Acetyl-L-Cysteine (NAC) 600mg, Phosphatidyl Serine (soy) 100 mg, Vinpocetine 15mg 4. Weight loss Other Names: Omega 3 Fatty Acid Acetyl-L-Carnitine (HCL) Ginkgo Biloba Extract Alpha-Lipoic Acid (ALA) Huperzine A (Huperzia serrata) N-Acetyl-L-Cysteine Phosphatidyl Serine

	Vinpocetine
Study Arms	Experimental: Supplement intervention Dietary Supplement: Multivitamin, Omega 3 Supplement, Brain and Memory Formula Intervention: Dietary Supplement: Multivitamin Supplement intervention
Publications *	• Amen DG, Newberg A, Thatcher R, Jin Y, Wu J, Keator D, Willeumier K. Impact of playing American professional football on long-term brain function. J Neuropsychiatry Clin Neurosci. 2011 Winter;23(1):98-106. doi: 10.1176/appi.neuropsych.23.1.98. • Amen DG, Wu JC, Taylor D, Willeumier K. Reversing brain damage in former NFL players: implications for traumatic brain injury and substance abuse rehabilitation. J Psychoactive Drugs. 2011 Jan-Mar;43(1):1-5. doi: 10.1080/02791072.2011.566489.

Summary 5

Safety and Efficacy Comparison Of Two TAVI Systems in a Prospective Randomized Evaluation II (SCOPE II)

Tracking Information	
First Submitted Date	March 30, 2017
First Posted Date	June 20, 2017
Last Update Posted Date	February 12, 2018
Actual Study Start Date	April 20, 2017
Estimated Primary Completion Date	April 2019 (Final data collection date for primary outcome measure)
Current Primary Outcome Measures (submitted: June 16, 2017)	Composite of all-cause mortality or stroke rates [Time Frame: 1 year] The primary objective is to compare the composite of all-cause mortality or stroke rates at 1 year (powered for non-inferiority).
Original Primary Outcome Measures	*Same as current*
Change History	Complete list of historical versions of study NCT03192813 on ClinicalTrials.gov Archive Site
Current Secondary Outcome Measures (submitted: June 16, 2017)	• New permanent pacemaker rate [Time Frame: 30 days] The first secondary objective is to compare the new permanent pacemaker rate at 30 days (powered for superiority). • All cause mortality at 30 days [Time Frame: 30 days] All cause mortality • Stroke at 30 days [Time Frame: 30 days] Stroke
Descriptive Information	
Brief Title	Safety and Efficacy Comparison Of Two TAVI Systems in a Prospective Randomized Evaluation II
Official Title	Safety and Efficacy Comparison Of Two TAVI Systems in a Prospective Randomized Evaluation II: A Randomized, Controlled, Non-inferiority Trial Evaluating Safety and Clinical Efficacy of the Symetis ACURATE Neo Compared to the Medtronic Evolut R Bioprosthesis in Transfemoral Transcatheter Aortic Valve Implantation
Brief Summary	Current care randomized clinical trial comparing the CE marked Symetis ACURATE neo™ Aortic Bioprosthesis and ACURATE TF™ Transfemoral Delivery System with the CE marked Medtronic CoreValve Evolut R TAVI system (or any future CE-marked CoreValve versions).
Detailed Description	Transcatheter aortic valve implantation (TAVI) is an established and valuable treatment option for patients

	with severe symptomatic aortic stenosis and at high surgical risk for aortic valve replacement. The use of TAVI is rapidly expanding worldwide and its indications are widening into intermediate and lower risk populations. However, device comparisons by use of randomized trials are scarce in particular for newer generation transcatheter valves. The Symetis ACURATE neo™, a self-expanding transcatheter valve delivered via transfemoral access, is a second-generation device that gained CE mark approval in June 2014. The SCOPE-II trial will compare the safety and performance of the Symetis ACURATE neo™ with the self-expanding Medtronic Evolut R system, a widely used and well-established transcatheter heart valve, which obtained CE mark in 8NOV2006 and HAS approval on 13JAN2015.
Study Type	XXXXXXXXXXXXX
Study Design	xxxxxxxxxxxxxx Model: Case-Control Time Perspective: Prospective
Target Follow-Up Duration	*Not Provided*
Biospecimen	*Not Provided*
Sampling Method	Probability Sample
Study Population	764 patients presenting with severe symptomatic aortic stenosis with the indication for TAVI, as agreed by the Heart Team. If all eligibility criteria and none of the exclusion criteria are fulfilled, patients will be allocated in a 1:1 ratio to either the Symetis ACURATE neo™ or the Medtronic CoreValve Evolut R (or any future CE-marked CoreValve versions) by permuted block randomization.
Condition	Aortic Valve Stenosis
Intervention	• Device: Symetis ACURATE neo™ transfemoral TAVI system Symetis ACURATE neo™ transfemoral TAVI system: Support frame made of nitinol, supra-annular processed tri-leaflet porcine pericardial valve and an outer skirt to mitigate paravalvular regurgitation (manufactured by Symetis SA, Ecublens, Switzerland). • Device: Medtronic CoreValve Evolut R TAVI System Medtronic CoreValve Evolut R Transcatheter Aortic Valve Implantation (TAVI) System (or any future CE-marked Corevalve versions): The support frame is manufactured from nitinol, which has multilevel, self-expanding properties and is radiopaque. The bioprosthesis is manufactured by suturing valve leaflets and a skirt from porcine pericardium into a tri-leaflet configuration (manufactured by Medtronic

Study Groups/Cohorts	CoreValve LLC, Santa Ana, USA). • Symetis ACURATE neo™ transfemoral TAVI system Patient assigned to this group will be implanted with Symetis ACURATE neo™ transfemoral TAVI system. Intervention: Device: Symetis ACURATE neo™ transfemoral TAVI system • Medtronic CoreValve Evolut R TAVI System Patient assigned to this group will be implanted with Medtronic CoreValve Evolut R Transcatheter Aortic Valve Implantation (TAVI) System. Intervention: Device: Medtronic CoreValve Evolut R TAVI System

Name of Participant:

Please state here, which of the following categories you would give to the 5 examples and the main reason for you to decide it in this way:

Clinical Trial, Non-interventional study, Database study.

Summary 1

Summary 2

Summary 3

Summary 4

Summary 5