

**April 2017 Nancy Morgan** 





## Advanced Literature Search and Screening

## Overall goal:

- Use DOC Library platform and library services to answer research questions
- Understand Doctor Evidence methodologies and processes



## Objectives

- Understand the methodologies and technologies that power DOC Library
- Search, sort and filter relevant publications quickly and efficiently
- View, rate and annotate, share, and download abstracts and full-text articles
- Conduct advanced research in an Evidence Project by study title, abstract or text
- Request a specific Evidence Project



### What does DRE do?

- Identify relevant published literature to answer scientific questions and extract data from these sources using proprietary software technologies
  - Create curated and searchable libraries
  - Create relational databases suitable for analyses
- Consult with our clients to provide meaningful insights that inform decisions and guide tactics
  - Structured consulting process
  - Frequent and regular touchpoints with our clients
  - Deliverables include written reports, slide decks and publications



# DRE - Sanofi Library Services

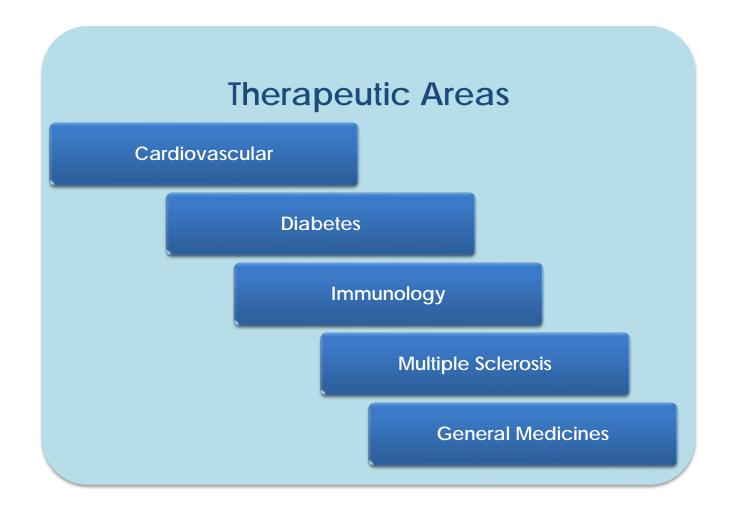
Access studies in DOC Library Request a targeted literature package Share literature enterprise-wide across teams and projects



## **DOC Library**

- ✓ 69 Master Libraries
- ✓ 136,140 References

Access DOC Library through <a href="https://sanofi.doctorevidence.com">https://sanofi.doctorevidence.com</a>. Please note that Chrome is the recommended browser.





### Literature Surveillance, Monthly Updates and Summaries

### Early development through launch

- Provide inputs for protocol development and safety / risk management planning
- Provide information for evidence development planning
- Make the most of current research while identifying evidence gaps
- •Inform planning for **primary research**, e.g., choice of endpoints and comparators
- Determine which adverse events might be associated with a product
- Perform burden-of-illness **research** for communicating value
- •Identify the most used methods and data sources within a therapeutic area
- Identify and synthesis inputs for economic modeling
- Estimate **comparative safety and efficacy** of comparators and/orother products
- Track competitor products and stay abreast of new data and coverage decisions
- Produce materials for inclusion in value dossiers and HTA submissions

### Post launch and lifecycle management

- Understand **new indications** in the context of specific commercial, medical and regulatory strategy
- Understand real-world effectiveness and surveillance
- Communicate value based on ongoing research and new evidence



# DOC™ Library: Features and Processes



## Search and Screening Process

Development of a PICO question to define the Patients, Interventions, Comparators, and Outcomes of interest

Consultations with DRE medical librarians, clinical team and methodologists

A Rapid Intelligence assessment of the available literature to determine project feasibility

The development of a search protocol, which is converted into a unique broad search strategy



## Search Strategy

- The search strategy includes keywords, synonyms, and MeSH terms for each of the concepts represented in the PICO.
- The lead Doctor Evidence Librarian then conducts a broad search of published literature in PubMed, Embase, Cochrane and other pertinent databases.
- Citations are categorized based on client needs and full-text articles are retrieved.
- All full-texts are re-evaluated for eligibility by the Methodology Lead.
- Reliability of the screening is confirmed by both technological and quality assurance processes within the DOC Library environment, overseen by Doctor Evidence's CMO.



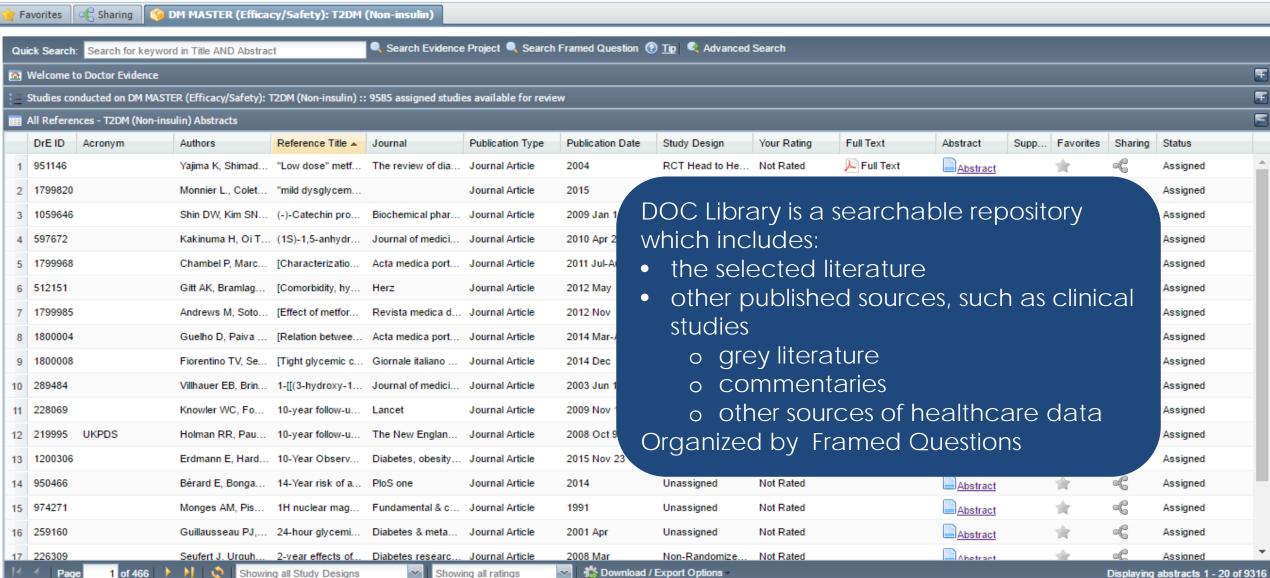
### Advanced Technologies to Ensure Retrieval of Relevant Articles

- ✓ Pattern recognition (i.e., color coding, bolding, etc.) for ability to quickly confirm study design and/or parameters.
- ✓ Keyword recognition: ability to quickly identify the relevant studies by using tools to find relevant terms/phrases in titles, abstracts and full text.
- ✓ Correction and/or re-categorization of studies due to inaccuracies found in MeSH descriptors and PubMed filters.
- ✓ NLP/Machine learning: increasing reliance on technologies that help automate the correct identification and categorization of references.
- ✓ Quality control program to efficiently audit included and excluded references to ensure that search results have maximized retrieval of relevant references and minimized retrieval of any irrelevant references (maximize accuracy).





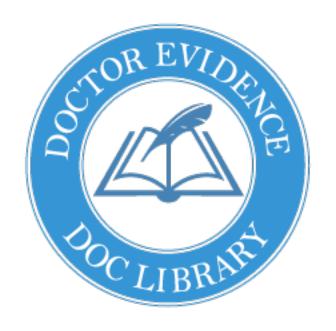
#### Welcome to Doctor Evidence





# Navigating DOC Library





# **Navigating DOC Library**



## Demonstration and Activities



### **Activities**

- 1. Open the Evidence Projects menu and reorder the libraries by dragging your most relevant library to the top of the list
- 2. Navigate to the Evidence Package "MS MASTER (Efficacy/Safety): Alzheimer's Disease" to view the broad master library that contains all Alzheimer's-related literature
- 3. Download the PICO specification document to view the search and screening protocol that defined this library
- 4. Open the "Competitor Agents RCT" Framed Question to view the reference list of Randomized Controlled Trials

Log in to DOC Library through signing on at <a href="https://sanofi.doctorevidence.com">https://sanofi.doctorevidence.com</a>



### **Activities**

- 5. Use the 'Advanced Search' feature to find the references published after 2010 that report: MCI OR "mild cognitive impairment"
- 6. Export the reference list to either Reference Manager (RIS), Excel, or Word document format
- 7. View an abstract and rate it as Relevant
- 8. Open the Notes tab of the abstract view and add a new note
- 9. Share the abstract with <a href="mailto:nmorgan@doctorevidence.com">nmorgan@doctorevidence.com</a>



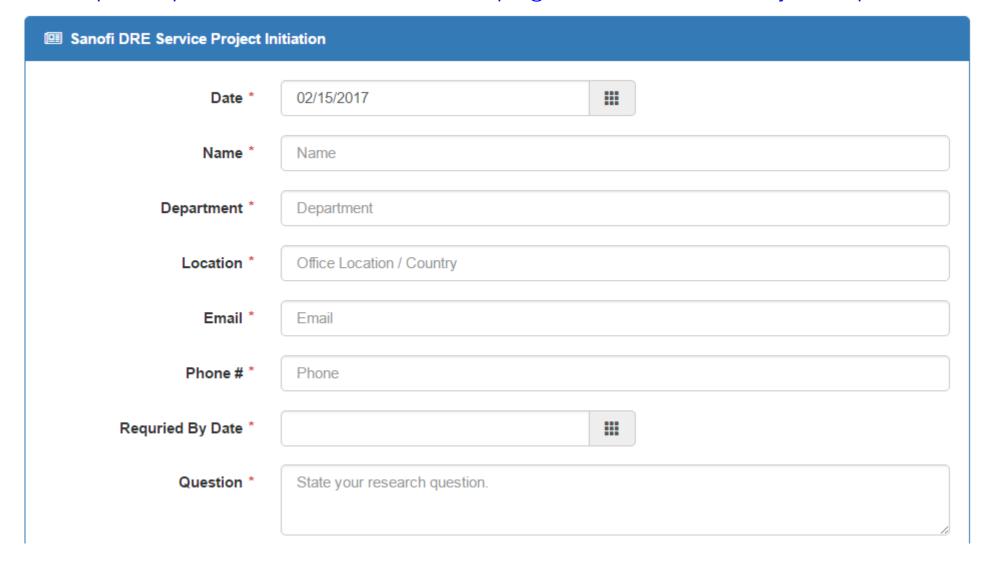
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# Initiating a Project



## Requesting a Customized Library Package

https://reports.doctorevidence.com/pages/Client/ServiceProject.aspx





### Initiating a Project - Additional Contact Info

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### Pertinent assets from DOC Library are extracted and available in DOC Data for analyses

### **Published Monday**

**Articles** 

Atezolizumab versus docetaxel for patients with previously  $\Re M$ treated non-small-cell lung cancer (POPLAR): a multicentre, open-label, phase 2 randomised controlled trial



Louis Fehrenbacher, Alexander Spira, Marcus Ballinger, Marcin Kowanetz, Johan Vansteenkiste, Julien Mazieres, Keunchil Park, David Smith, Angel Artal-Cortes, Conrad Lewanski, Fadi Braiteh, Daniel Waterkamp, Pei He, Wei Zou, Daniel S Chen, Jing Yi, Alan Sandler, Achim Rittmeyer, for the POPLAR Study Group\*

Background Outcomes are poor for patients with previously treated, advanced or metastatic non-small-cell lung cancer Lancet 2016; 387: 1837-46 (NSCLC). The anti-programmed death ligand 1 (PD-L1) antibody atezolizumab is clinically active against cancer, Published Online including NSCLC, especially cancers expressing PD-L1 on tumour cells, tumour-infiltrating immune cells, or both. March 9,2016 We assessed efficacy and safety of atezolizumab versus docetaxel in previously treated NSCLC, analysed by PD-L1 http://dx.doi.org/10.1016 expression levels on tumour cells and tumour infiltrating immune cells and in the intention to-treat population.

Methods In this open-label, phase 2 randomised controlled trial, patients with NSCLC who progressed on post-platinum chemotherapy were recruited in 61 academic medical centres and community oncology practices across 13 countries in Europe and North America. Key inclusion criteria were Eastern Cooperative Oncology Group performance status 0 or 1, measurable disease by Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1), and adequate (LEGIRENDALOF MD); US haematological and end-organ function. Patients were stratified by PD-L1 tumour-infiltrating immune cell status, Oncology Research, The histology, and previous lines of therapy, and randomly assigned (1:1) by permuted block randomisation (with a block Woodands, TX, USA size of four) using an interactive voice or web system to receive intravenous atezolizumab 1200 mg or docetaxel 75 mg/m² once every 3 weeks. Baseline PD-L1 expression was scored by immunohistochemistry in tumour cells (as Fairfax, VA, USA (A Spira): percentage of PD-L1-expressing tumour cells TC3≥50%, TC2≥5% and <50%, TC1≥1% and <5%, and TC0<1%) and tumour-infiltrating immune cells (as percentage of tumour area: IC3≥10%, IC2≥5% and <10%, IC1≥1% and <5%, and ICO<1%). The primary endpoint was overall survival in the intention-to-treat population and PD-L1 subgroups at 173 deaths. Biomarkers were assessed in an exploratory analysis. We assessed safety in all patients who received at least WZou PhD, D S Chen MD, one dose of study drug. This study is registered with ClinicalTrials.gov, number NCT01903993.

Findings Patients were enrolled between Aug 5, 2013, and March 31, 2014. 144 patients were randomly allocated to the atezolizumab group, and 143 to the docetaxel group. 142 patients received at least one dose of atezolizumab and 135 received docetaxel. Overall survival in the intention-to-treat population was 12 · 6 months (95% CI 9 · 7 – 16 · 4) for atezolizumab versus 9.7 month

overall sur HR 0-54 ( p=0.871]). l

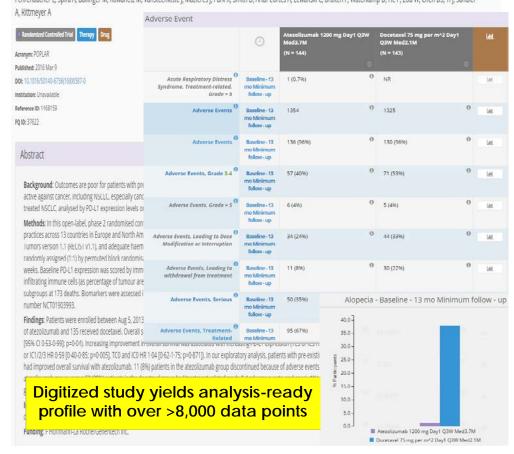
gene expression, had improved overall survival with atezolizumab, 11 (8%) patients in the atezolizumab group discontinued because of adverse events versus 30 (22%) patients in the docetaxel group. 16 (11%) patients in the atezolizumab group

USA(D) smith (D): Compass versus 52 (39%) patients in the docetaxel group had treatment-related grade 3-4 adverse events, and one (<1%) patient in the Oncology, Vancouver, WA, USA atezolizumab group versus three (2%) patients in the docetaxel group died from a treatment-related adverse event.

# Atezolizumab versus docetaxel for patients with previously treated non-small-cell lung cancer (POPLAR): a

multicentre, open-label, phase 2 randomised controlled trial. Fehrenbacher L, Spira A, Ballinger M, Kowanetz M, Vansteenkiste I, Mazieres I, Park K, Smith D, Artal-Cortes A, Lewanski C, Braiteh F, Waterkamp D, He P, Zou W, Chen DS, Yi I, Sandler

**Available for Analysis Tuesday** 





# DOC Data Training to follow....



# Appendix



### Types of PICO Questions

# Efficacy and Safety

- Efficacy/safety of an intervention
- Often in comparison to other interventions

### Prognostic

- Likelihood of an outcome based on patient characteristics
- Identify which patients may be at risk for an intervention
- Identify patient populations who may respond favorably to an intervention

### Economic

- Economic impact of a disease or of a health intervention in comparison to other health interventions
- Budget impact or cost-effectiveness

### Epidemiological

- Distribution of health related events
- Incidence
- Prevalence
- Patient characteristics or comorbidities within a certain population



### Examples of Research Questions: Efficacy/Safety

Is it possible for increased platelet aggregation without increased risk of bleeding in patients at risk of secondary stroke who are treated with aspirin and other antiplatelet therapy compared to aspirin alone?

#### Patient

- Patients who have had a recent\* transient ischemic attack/ischemic stroke, and are
- contraindicated for anticoagulation therapy\*\*
- \*defined as those randomized within 1 month of event.
- \*\*defined as history of major bleed while on anticoagulation therapy

#### Intervention

Combination of acetylsalicylic acid (ASPIRIN) with another antiplatelet drug:

- Clopidogrel (PLAVIX)
- Prasugrel (e.g. EFFIENT)
- Ticagrelor (e.g. BRILINTA)
- Vorapaxar (e.g. ZONTIVITY)

#### Comparator

 Acetylsalicylic acid (ASPIRIN) monotherapy

#### Outcome

Efficacy/effectiveness:

- Atherothrombotic stroke
   Adverse Events:
- Any
- Any Severe
- Any Serious
- Totals
- Withdrawals due to AE
- Specific AEs/Other
   Major bleeding
  - oMajor adverse cardiac event
  - Mortality



### Examples of Research Questions: Prognostic

What are the predictors of (re)/hospitalization or mortality in inpatients and outpatients with HF, including biomarkers for prediction of these outcomes?

#### Patient

 Patients with heart failure

#### Intervention

N/A

#### Comparator

• N/A

#### Outcome

- Predictors for (re)/hospitalization or mortality
- Symptoms and signs
- •Swelling or edema
- Dyspnea/orthopnea
- Worsening of both as reported by patients
- Signs
- •Edema/signs of fluid retention
- Increase in body weight > 1kg/day
- Pulmonary rales
- •Biomarkers: BNP and NT proBNP
- Change in NYHA Class
- •Renal function, creatinine/eGFR
- Previous events
- Previous hospitalization
- •Rate of hospitalization
- •ER visits without hospitalization



### Examples of Research Questions: Economic

What is the effectiveness and value of dupilumab for the treatment of mild-to-moderate atopic dermatitis.

#### Patient

 Adults (>= 18 years) with moderate-to-severe atopic dermatitis inadequately controlled with topical therapy

#### Intervention

•Dupilumab

#### Comparator

- Emollient therapy
- •Topical corticosteroids (Including but not limited to):
  Betamethasone valerate,
  Betamethasone dipropionat
  Desoximetasone, Fluocinolone
  acetonide, Fluticasone
  propionate, Hydrocortisone,
  Mometasone furoate,
  Triamcinolone acetonide,
  Clobetasone butyrate,
  Methylprednisolone aceponate,
  Diflucortolone valerate
- Topical calcineurin inhibitors: tacrolimus, pimecrolimus
- Placebo
- Phototherapy (Including but not limited to): narrowband ultraviolet B (UVB or UV-B or NBUVB – 311–313 nm), Broadband UVB phototherapy, PUVA (Psoralen and UVA), UV-A, UVA1, high-dose UVA1 (340–400 nm),
- Cyclosporin
- Combinations of any of the above

#### Outcome

- •Efficacy/effectiveness:
  olnvestigator's Static Global
  Assessment (ISGA)
  olnvestigator's Global
  Assessment (IGA)
  oEczema Area and Severity
  Index (EASI): 50, 75, 90
  oScoring Atopic Dermatitis
  (SCORAD) score
- oAny oAny Severe
- oAny Serious oTotals

Adverse Events:

- oWithdrawals due to AE
- oSpecific AEs/Other



### Examples of Research Questions: Epidemiologic

What is the published literature explicitly examining the prevalence and/or incidence of MS?

#### Patient

 Any population based on geography, socioeconomic status, etc.

#### Intervention

N/A

#### Comparator

N/A

#### Outcome

 Incidence/prevale nce of MS

