Evaluating Biologics and their Biosimilars Using a Distributed Research Network to Demonstrate Real-World Outcomes

Pamala A. Pawloski,PharmD[1] Kevin Haynes PharmD,[2] Daniel Kent PharmD,[3] Cheryl N. McMahill-Walraven MSW PhD,[4] Catherine A. Panozzo MPH PhD,[5] Vanita Pindolia PharmD,[6] Catherine M. Lockhart PharmD, PhD,[7] Jeffrey Brown PhD,[5] Aaron Mendelsohn PhD MPH,[5] Charles E. Barr MD,[7] Bernadette Eichelberger PharmD[7]

[1]HealthPartners; [2]HealthCore Inc.; [3] Group Health-Kaiser Permanente Washington; [4]Aetna Inc; [5] Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute; [6]Henry Ford Health System; [7]Academy of Managed Care Pharmacy (AMCP)

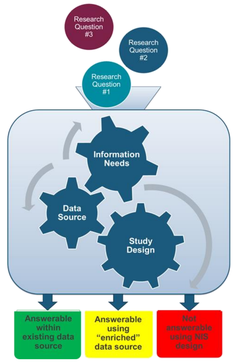
BBCIC Biologics & Biosimilars Collective Intelligence Consortium
AMCP BBCIC, LLC

INTRODUCTION

- The Academy of Managed Care Pharmacy's Biologics and Biosimilars Collective Intelligence Consortium (BBCIC) was convened in 2015.
- BBCIC is dedicated to monitoring biosimilar safety and effectiveness utilizing large datasets (~150 million lives) with de-identified medical and pharmacy data.
- Data are extracted using cutting-edge distributed research network (DRN) and surveillance methods.[1]
- Descriptive and comparative analyses were undertaken of different originator compounds in the same class as well as originators and their corresponding biosimilars. The descriptive analyses are being undertaken to demonstrate technical feasibility and if so, comparative analyses will use the DRN to compare different originators with each other as well as originator and biosimilar products.[2,3]
- BBCIC leverages the FDA's Sentinel Initiative DRN, an active surveillance collaboration of 18 member organizations from managed care integrated delivery networks, pharmacy benefit managers, and the coordinating center (Harvard Pilgrim Health Care), to collaborate with industry sponsors.
- Participating BBCIC organizations include: AbbVie, Aetna, Amgen, AMCP, Anthem Healthcore, Apobiologix, Boehringer Ingelheim Pharmaceuticals Inc , Express Scripts Inc., HealthPartners, Henry Ford Health System, Kaiser Permanente Washington Health Research Institute, Optum, Sandoz, and Harvard Pilgrim Health Care.
- Public representation on the BBCIC Planning Board include the American Society of Clinical Oncology, American College of Rheumatology, and the National Health Council.

METHODS

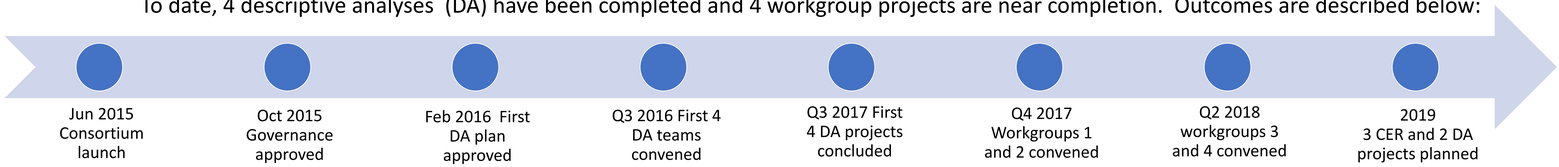
- Proposed studies are reviewed by the BBCIC Science Committee tasked with guidance over research plans, review of study applications, protocols, reports, and manuscripts.



- Descriptive analyses (DA) were conducted to understand patients, diseases, treatments, and outcomes.
- Comparative analyses are planned to asses originator biologic and biosimilar safety and effectiveness. [4]

RESULTS

To date, 4 descriptive analyses (DA) have been completed and 4 workgroup projects are near completion. Outcomes are described below:



Descriptive Analysis Project	Disease Indications	Drugs	Primary Outcome	Findings	Status
Insulins[5]	Diabetes	Insulin	Major adverse cardiac and hypoglycemia events following long-acting (LAI) and NPH insulin use in Types 1 and 2 diabetes.	Major adverse cardiac and hypoglycemia events associated with LAIs are comparable to other observational trials.	Two manuscripts are in development.
Colony Stimulating Factors (G-CSF)	Febrile Neutropenia risk reduction in non-myeloid malignancies treated with myelosuppressive anti-cancer drugs associated with febrile neutropenia	filgrastim (Neupogen), pegfilgrastim (Neulasta), tbo-filgrastim (Granix)	Febrile neutropenia hospitalizations among first cycle granulocyte-colony stimulating factor (G-CSF) prophylaxis for breast and lung cancer.	G-CSF prophylaxis can be discerned from treatment and rare safety events were identified.	A manuscript is in development.
Anti-inflammatories	•Rheumatoid Arthritis •Psoriasis •Psoriatic Arthritis •Ankylosing Spondylosis •Ulcerative Colitis •Crohn's Disease	adalimumab (Humira), infliximab (Remicade), rituximab (Rituxan), tocilizumab (Actemra), abatacept (Orencia), etanercept (Enbrel), certolizumab (Cimzia), golimumab (Simponi), ustekinumab (Stelara), vedolizumab (Entyvio), tofacitinib (Xeljanz), natalizumab (Tysabri)	Hospitalizations for serious infections following anti-inflammatory (AI) use for rheumatoid arthritis, psoriatic and gastrointestinal conditions.	Serious infection outcomes are comparable to other AI observational trials.	A manuscript has been approved by the science committee, has been submitted, and is under review for publication.
Erythropoeitin-Stimulating Agents (ESA)	Anemia (CKD, Hemodialysis)	epoetin alfa (Epogen, Procrit) darbepoetin alfa (Aranesp), methoxy polyethylene glycol-epoetin beta (Mircera)	Adverse events following erythropoietin stimulating agent (ESA) use in hemodialysis.	DRN ESA data lack granularity for CER outcomes. Future studies evaluating ESAs will be conducted using the Medicare ESRD data set.	A final report will be posted on www.BBCIC.org.

Workgroups Convened to address the following objectives and underway and expected to be completed by the end of 2018:

1) Treatment of switching/sequencing as a covariate/ confounder in BBCIC CER studies.
2) Investigate the extent to which NDCs are being supplied on physician-office claims.
3) In preparation for CER, ensuring all International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)codes are converted to ICD-10 codes.
4) Develop best-practices based on current methodology for conducting observational comparative effectiveness research.

ACKNOWLEDGEMENTS

This research was supported by the Biologics and Biosimilars Collective Intelligence Consortium. We wish to acknowledge the oversight and input from the BBCIC Governance and Science Committees during the development and conduct of the analyses and workgroup activities and for their review of this poster.

REFERENCES

1. Mendelsohn A, Barr C, Brown J, Cziraky M, King K, Lockhart C, Pawloski PA, Eichelberger B . Development and Management of a Distributed Research Network for Evaluating Real-World Outcomes for Biologics and their Biosimilars poster presentation, NEXUS 2018.
2. Shrank et al. Ann Pharmacotherapy. 2011;45(1):31-8.
3. http://www.gastro.org/press_releases/2015/7/29/national-survey-reveals-gastroenterologists-views-on-biosimilar-drugs
4. Lin ND. Research challenges in biosimilar safety and surveillance. Presented in C.E. Barr (Chair), *Biologics and biosimilars: payers, industry, and academia collaborating on post-marketing surveillance* symposium at DIA Global Annual Meeting; 2018 June 24-28; Boston, MA.
5. McMahill-Walraven C, Kent D, Panozzo C, Pawloski P, Haynes K, Lockhart C, Marshall, J, Eichelberger B. Descriptive analysis of the use of long- and intermediate-acting insulin, and key safety outcomes in adults with diabetes mellitus poster presentation, NEXUS 2018.

CONCLUSIONS

- Outcomes comparable to those in the published literature were demonstrated for 3 of 4 descriptive analyses: G-CSFs, long-acting insulins, and anti-inflammatories.
- ESA data do not contain needed granularity and future research will employ alternative data sources.
- Descriptive analysis projects have uncovered gaps in data availability, structure, or other needs that led to the convening of workgroups.
- In preparation for the planned CER studies, convened workgroups are identifying best practices that will be implemented.
- Following sufficient descriptive analyses, efficacy analyses, and biosimilar exposures, CER studies will be initiated to assess the safety and effectiveness of biosimilars compared with their originator compounds.

Next Steps

- Identification of sources to enrich and fill data gaps identified by DA will continue.
- CER studies are planned for G-CSFs, insulins, and anti-inflammatories in 2019.
- A descriptive analysis of trastuzumab is scheduled to begin in 2019.

Presented At: Academy of Managed Care Pharmacy Nexus Meeting. Orlando, FL. October 2018