AMED生物統計家育成支援事業シンポジウム
2021年3月11日

「リアルワールドデータの最前線」開催趣旨説明

東京大学大学院 医学系研究科
生物統計情報学講座
野村 尚吾

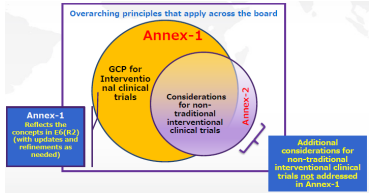
開発効率化に向けた動向

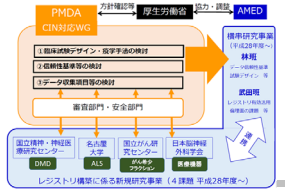
米国： 21st century cures act（2016～）
- 開発コスト削減・審査期間削減に向けた種々の取組み
  - **RWE**の利活用
  - マスタープロトコール/アダプティブデザイン
- 種々のドラフトガイダンスが公表済み

ICH： ICH-E6(R3) and E8(R1)
- **治験以外のデータソース**の利活用

日本： CIN構想やMID-NET
- 主に**NC所有の患者レジストリの利活用**について議論

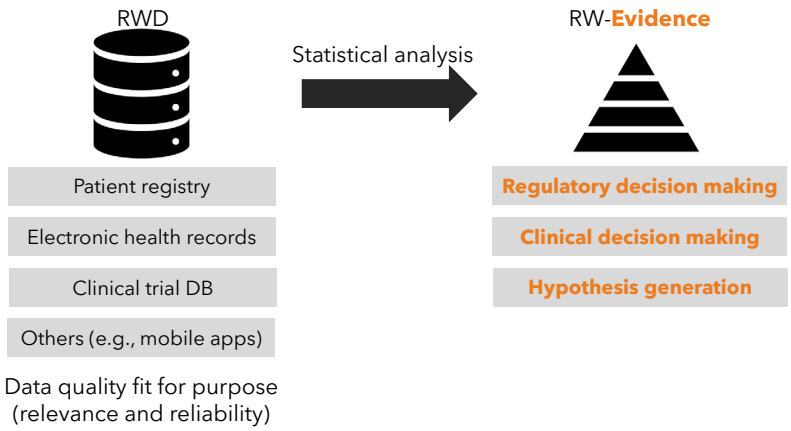
ICH Reflection on "GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6
January 2017



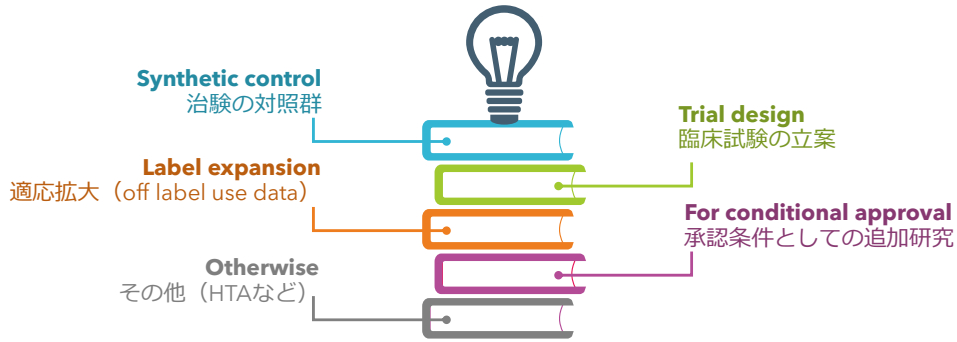


http://atdd-frm.umin.jp/2017/slide/2-3.pdf
https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/SignificantAmendmentstotheFDCAct/21stCenturyCuresAct/default.htm
https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

やりたいこと



医療RWDの活用： How and When



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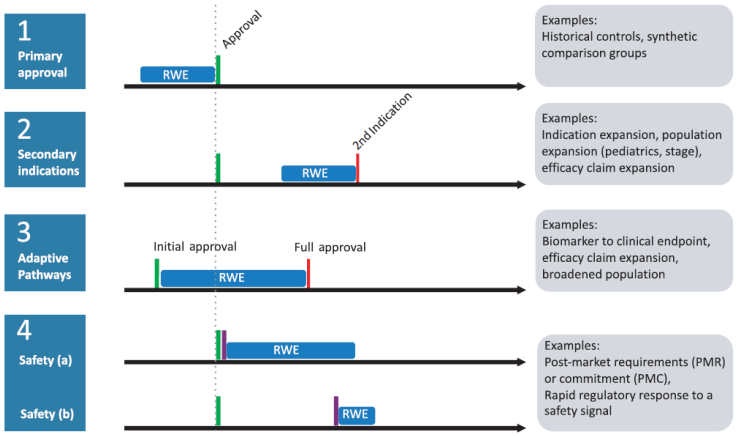
Franklin JM, Clin Pharmacol Ther 2019

医療RWDの活用： How and When



1 in 2

of 2019 approved FDA submissions for new drugs and biologics included a real-world evidence study.

In 2019, 49 percent of FDA-approved NDAs and BLAs included an RWE study. In 2020, that figure jumped to 75 percent.[1]

How RWE studies informed FDA decisions[2]

12% Substantial evidence

60% Supportive evidence

20% Inconclusive

8% Not addressed

AETION 2020, eBook: The role of real-world evidence in FDA approvals.
https://aetion.com/evidence-hub/ebook-the-role-of-real-world-evidence-in-fda-approvals/

商用利用可能なデータベース（米国）

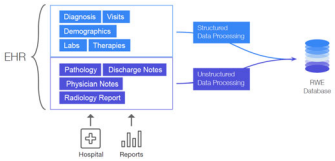
公的機関が構築/提供するもの

– SEER-Medicare DB, NCDB (National Cancer DB)、FDAの申請データ など

企業や団体が構築/提供するもの

medidata Synthetic Control Database™

flatiron



COTA

AETION

syapse

ClinicalStudy DataRequest.com

Project Data Sphere

適応拡大の例

CLINICAL CANCER RESEARCH | CCR DRUG UPDATES

FDA Approval Summary: Palbociclib for Male Patients with Metastatic Breast Cancer

Suparna Wedam[1], Lola Fashoyin-Aje[1], Erik Bloomquist[1], Shenghui Tang[1], Rajeshwari Sridhara[1], Kirsten B. Goldberg[2], Marc R. Theoret[1,2], Laleh Amiri-Kordestani[1], Richard Pazdur[1,2], and Julia A. Beaver[1]

palbociclibの適応拡大 (2019/4)： 男性乳がん

– GCP準拠でないRWDで確認された抗腫瘍効果（奏効割合）に基づき有効性を確認

Studies to Support Efficacy								
Real-World Analysis of Males Treated for Metastatic Breast Cancer in the US (Flatiron Health)	NA	Detailed retrospective male patient information from electronic health records (EHRs)	NA	Real world treatment response	NA	25 with palbociclib therapy and 34 with endocrine therapy alone	Males with HR-positive, HER2-negative metastatic breast cancer	NA
Other Study								
A5481097 (Study 1097, "IQVIA")	NA	Retrospective analysis of claims data	NA	NA	NA		Male patients with metastatic breast cancer	NA

Approval letter @FDA: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2019/207103Orig1s008ltr.pdf
Review summary @FDA: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/207103Orig1s008.pdf

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外部対照群の例

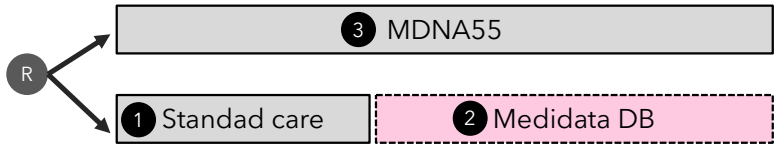
Manufacturer/ Product	RWE: Submitted in support of	RWE: Included in FDA-defined safety population	FDA'S DECISION ON THE RWE STUDY/STUDIES: Substantial evidence	Supportive evidence	Inconclusive	RWE: Submission type	RWE: Referenced in package insert
Janssen **BALVERSA™** (erdafitinib)	Effectiveness				●	Standard of care external control arm	
Daiichi Sankyo **ENHERTU®** (fam-trastuzumab deruxtecan-nxki)	Effectiveness				●	Natural history external control arm	
Genentech **ROZLYTREK®** (entrectinib)	Effectiveness				●	Standard of care external control arm	
Karyopharm Therapeutics **XPOVIO®** (selinexor)	Effectiveness				●	Natural history external control arm	
Global Alliance for TB Drug Development **PRETOMANID**	Effectiveness		●			External control arm Literature	●

				FDA: Approval	FDA: Label Expansion	EMA: Conditional Approval	EMA: Approval	NMPA: Label Expansion
Pragmatic	Janssen	Invega sustenna	Schizophrenia		✓ (2018)			
External Comparators	Merck Serono/ Pfizer	Bavencio	Metastatic merkel cell carcinoma	✓ (2017) Accelerated*		✓ (2017)		
	Biomarin	Brineura	Infantile batten disease	✓ (2017)			✓ (2017)	
	Gilead/Kite	Yescarta	Diffuse large B-cell lymphoma	✓ (2017)			✓ (2018)	
	Novartis	Kymriah	Diffuse large B-cell lymphoma				✓ (2018)	
	Fresenius	Omegaven	Parenteral nutrition-associated cholestasis	✓ (2018)				
	Amgen	Blincyto	B-cell precursor acute lymphoblastic leukemia in 1st / 2nd complete remission with MRD ≥ 0.1%		✓ (2018)		✓ (2019)	

AETION 2020, eBook: The role of real-world evidence in FDA approvals.
https://aetion.com/evidence-hub/ebook-the-role-of-real-world-evidence-in-fda-approvals/

Hybrid controlの例

再発脳腫瘍に対する治験（第3相試験）@U.S.



Primary endpoint: OS (1:1 comparison)

The 'End-of-Phase 2' meeting outcome is **very encouraging** for the company and shows that the ***FDA is open to utilizing innovative trial designs*** to expedite results for conditions where patients have few if any treatment options.

Reference:
https://ir.medicenna.com/news-releases/news-release-details/medicenna-provides-mdna55-rgbm-clinical-program-update-following
https://www.oaoa.com/news/business/medidata-synthetic-control-arm-supported-by-the-us-food-and-drug-administration-fda-for-use/article_0b3af804-560e-51d4-8f63-e27361da014d.html
https://scr.zacks.com/News/Press-Releases/Press-Release-Details/2020/MDNA-Planning-for-Innovative-Hybrid-Registration-Trial-for-MDNA55-article/default.aspx

観察研究から推定した治療効果はRCTと一致するか？

10.1161/CIRCULATIONAHA.120.051718

Emulating Randomized Clinical Trials with Nonrandomized Real-World Evidence Studies: First Results from the RCT DUPLICATE Initiative

Running Title: *Franklin et al.; Emulating RCTs with Nonrandomized RWE*

Jessica M. Franklin, PhD[1]; Elisabetta Patorno, MD, DrPH[1]; Rishi J. Desai, MS, PhD[1];

https://www.rctduplicate.org/
Duke-Margolis center: Evaluating RWE from Observational Studies in Regulatory Decision-Making: Lessons Learned from Trial Replication Analyses
https://healthpolicy.duke.edu/events/evaluating-rwe-observational-studies-regulatory-decision-making-lessons-learned-trial

斬新な方法論の活用を後押しする制度 @FDA

Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products

Draft Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
September 2019

https://www.fda.gov/drugs/development-resources/complex-innovative-trial-designs-pilot-program
https://www.fda.gov/media/130897/download
https://www.youtube.com/watch?v=zLuvSQkG6TU

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シンポジウムの目的と構成

目的

- 日本の現状（法規制や産学の取り組み）を理解したい
- 特に、学術目的以外で何が課題になるのか理解したい

構成

演者	演題
一般社団法人医療データ活用基盤整備機構 岡田 美保子 先生	リアルワールドデータの概要について
国立がん研究センター 中田 はる佳 先生	医療データ活用に関する規制と市民意識

構成（つづき）

演者	演題
中外製薬株式会社 葛西 隆 様	Regulatory-grade RWDの医薬品開発への活用
京都大学大学院 武藤 学 先生	CyberOncologyを基軸としたリアルワールドデータの収集と利活用
厚生労働省安全対策課長 中井清人 先生	官の立場からRWDの活用に向けて
国立がん研究センター 柴田 大朗 先生	AMED「患者レジストリデータを活用した、臨床開発の効率化に係る レギュラトリーサイエンス研究」班の取り組み
医薬品医療機器総合機構 安藤 友紀先生	AMED安藤班・PMDAの取り組み

その他

質疑応答について

- Zoomから参加されている方： Zoomウェビナーの質問ボタン
- YouTube視聴の皆さま： YouTubeのコメント欄

発表資料は後日公開予定です

それでは、リラックスして聴講下さい

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