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HBD Think Tank East 2023

Achievements of HBD Activities and Future Expectations (HBDの成果と期待)

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I have no COI related to this presentation.

The Beginning of HBD

- HBD has started in 2003. HBDは2003年から始まった。
- At the time, Device Lag was a major issue between Japan and the U.S. (also raised in MOSS(Market-oriented sector-selective talk)).
It is Caused by gradual development from Europe to the U.S. and to Japan.
当時は、日米間ではデバイスラグが大きな問題（MOSS協議でも提起）
原因は「欧州→米国→日本」と段階的な開発によるもの
- At the time, we were hesitant to conduct clinical trials for medical device in Japan, therefore promoting global clinical trials was much more difficult.
当時は、医療機器で国際共同治験を進めるところか、日本で臨床試験を行なうことにも躊躇していた状況



HBD Concept

Let's explore ways to tear down (harmonize) the development barriers between Japan and the U.S. not through table discussions, but through actual actions.

机上での議論ではなく、実際に行動を起こしながら、日米間にある開発の壁を取り壊す（ハーモナイズ）方策を探ろう。

Let's try it By Doing !

HBD Activities

WG1: Implementation of Global Clinical Trials with a single protocol, educational activities (ongoing)

単一プロトコルによる国際共同治験の実施、教育活動（継続中）

WG2: Post-Market Registry 市販後レジストリー

➤ Establishment of Post-Marketing Registries such as INTERMACS, J-MACS, etc. (Activities have been suspended since the registries were established.)

INTERMACS, J-MACSなどの市販後レジストリーの構築（レジストリーを構築したため活動休止）

WG3: Resolving Clinical Trial Infrastructure Issues 治験インフラの課題解決

➤ Although there are variations among facilities in Japan and the U.S., it was confirmed that Japanese facilities are not at a low level. (The Issues was confirmed through global clinical trials and completed.)

日米とも施設によるばらつきはあるが、日本の施設がレベルが低い訳ではないことを確認
（国際共同治験により確認し活動終了）

WG4: Regulatory Harmonization 規制調和

➤ Comparative study of GCPs in Japan, the U.S., and Europe GCPの日米欧の比較検討

➤ Japan-U.S. Comparative Evaluation of STED STEDに関する日米比較評価

（The WG will close by publishing the results in a paper.）（結果を論文化、公表してWGは終了）

HBD WG1 Activities (current status)

- International Clinical Trials: Many cardiovascular POC are currently being conducted, including two drug-eluting stents.

国際共同治験：薬剤溶出ステント2品目をはじめ、現在、多くの循環器領域でのPOCが実施されている

(POC)

Combo Stent

CSI (atherectomy device, approved)

TVA

- HBD for Children activity since CRT2017: International harmonization on cardiovascular devices for children with incurable diseases

HBD for ChildrenがCRT2017より活動：難病の小児用の循環器デバイスについて、国際調和を目指す

Pediatric devices tend to be developed late because the market is small and business is difficult, so this is a good model case for international cooperative development.

小児デバイスはマーケットが小さく、ビジネスが難しいことから開発が遅れがちであり、国際共同開発におけるよいモデルケースになる。

HBD WG1 Activities (current status)

- Scientific Sessions: Discussions on hot topics at conferences, etc., to publicize HBD activities and find out new POC.

サイエンティフィックセッション：学会等でHotなトピックについて議論をすることでHBD活動を周知するとともに、新たなPOCを掘り起こす。

- SWG activities: Development of guidance, etc. (e.g., Concept of Clinical Trials regarding CLI)

SWG活動：ガイダンス等の作成など（CLIに関する臨床試験の考え方等）

- Publication of results (in the form of papers)

成果の公表（論文化）

Achievements of HBD Activities

Major vascular stents approved in US & Japan (2007-15)

Prod uct	Cate gory	Applica tion in JP	Approv al in JP	Applica tion in US	Approval in US	Device Lag (Mo.)	Application Lag (Mo.)	Clinical data submitted to PMDA**
A	CA, DES	2005.12 .22	2007.03. 30	2003.06. 19	2004.03.04	36	30	US study + small Japanese study
B	CA, BMS	2007.03 .29	2008.07. 04	2004.04. 12	2004.09.10	46	35	Foreign*** study
C	CA, DES	2008.03 .31	2009.01. 28	2006.03. 08	2008.10.10	3	24	Foreign study
D	CA, DES	2007.05 .09	2009.03. 24	2006.11. 20	2008.02.01	13	6	Foreign study + small Japanese study
E	CA, DES	2008.05 .29	2010.01. 08	2007.06. 01	2008.07.02	18	11	US study + Japanese study
F	CA, DES	2010.07 .14	2011.09. 05	2010.06. 17	2011.04.22	5	1	Foreign study
G	SFA, DES	2010.07 .30	2012.01. 24	2010.06. 04	2012.11.14	-10	1	MRCT (US, Japan, Germany)
H	CA, DES	2011.03 .15	2012.02. 08	2011.03. 28	2011.11.22	3	0	MRCT
I	CA, DES	2011.08 .18	2012.09. 06	2011.12. 05	2012.06.01	3	-4	MRCT +Japanese study
J	SFA, BMS	2013.12 .06	2015.01. 14	2014.03. 11	2015.05.22	-4	-3	MRCT (US, Japan) + Japanese study

※HBD related product

Actual Status of Device Lag without Global Clinical Trials (FY2019～2022)

【 Objective 】 To investigate the status of device lag in recent years.
近年のデバイスラグの状況を調査する

【 Methods 】

1. 2019-2022 (FY) for 4 years
2. All new medical devices approved by PMDA and also approved by FDA from PMDA's Web site (except for partial changes without assessment reports)
PMDAのWeb Siteより、PMDAで承認された新医療機器でFDAでも承認された全品目（審査報告書なしの一変は除く）
3. Calculate the difference of approval dates (U.S. approval date – Japan approval date) 承認日の差（米国承認日－日本承認日）を算出

【 Result 】

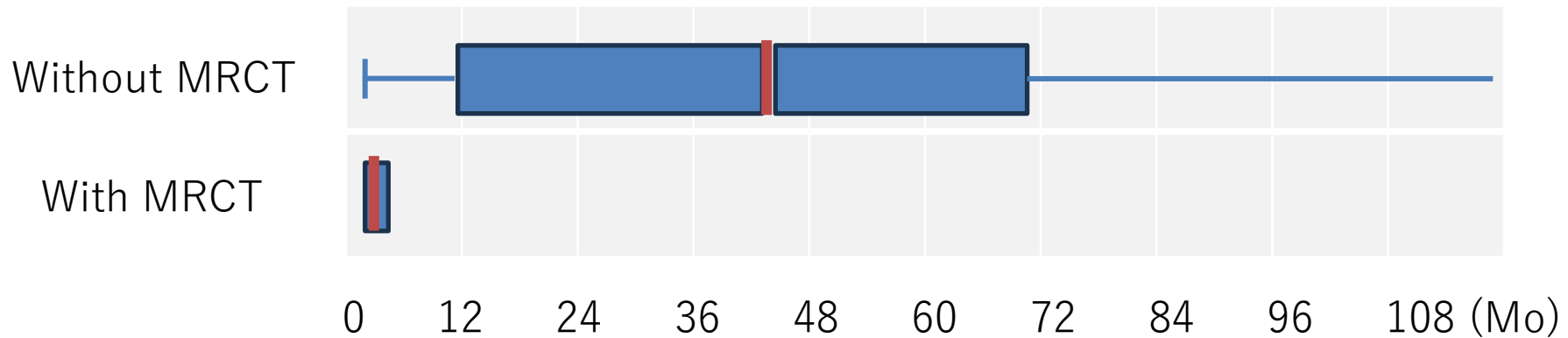
Number of items evaluated 評価品目数

FY	2019	2020	2021	2022
Without MRCT	8	6	9	8
With MRCT*	0	1	1	0

*All MRCTs are in the cardiovascular area
MRCTはすべて循環器領域

Actual Status of Device Lag without Global Clinical Trials

【 Result 】



- With MRCT, device lag was reduced. MRCT実施した品目については、明らかにデバイスラグが短縮
- Greater variability in not conducted MRCT. MRCT非実施品目においては、ばらつきが大きい
- In without MRCT, there are products with short lags, it is believed that the PMDA consultations were conducted before the application on what data to use and how to construct the logic.
ラグが短い品目については、申請前からどのようなデータでどのように論理構築をするかについてPMDAと相談していたと考えられる
- While it is preferable to conduct MRCTs, even if it is difficult to conduct MRCTs, it would be useful to consult with the regulatory authorities before proceeding.
MRCT実施が望ましいが、MRCT実施が困難な場合でも、早めに規制当局と相談して進めることが有用と考える

Achievements (成果のまとめ)

- Proof that global clinical trials can be conducted in the cardiovascular field (successful case)
循環器領域において、国際共同治験が実施できることを証明（成功事例）
- Global Clinical Trials Ensure Reduced Device Lag.
国際共同治験によりデバイスラグが確実に減少
- Noteworthy: Not only companies that participated in HBD activities experienced a decrease in application lag.
注目ポイント：HBD活動に参加した企業だけが申請ラグが減ったわけではない

In other words, HBD has made a significant contribution to the generalization of global clinical trials in Japan's development.

すなわち、HBDが、日本国内の開発において、国際共同治験実施を一般化することに大きく貢献した

Important Point: To generalize, it is necessary to show best practices; HBD is making a big difference in society by showing best practices and sharing the information.

大事なポイント：一般化するには、成功事例を示すことが必要。HBDは成功事例を示すとともに、その情報を共有することで、社会に大きな変革をもたらした

Issues (課題)

- Subject Matter 対象の課題
 - Cardiovascular Field 循環器領域
 - Mainly PMA products PMA製品が中心
 - Lack of interest from Small and Medium Enterprises 中小企業の関心が低い
 - What is the impact on all areas? 全領域への影響は？
- Global Clinical Trials decrease and Device Lag is not resolved. 国際共同治験は減少、デバイスラグは解消されていない

Expansion into other field

The fundamental concept of HBD's activities HBDの活動の根本の考え方

All stakeholders from Japan and the U.S., industry, government, and academia gather to identify and discuss frankly issues.

Set and execute a POC for the issue. PDCA cycle and make improvements.

日米、産官学のすべてのステークホルダーが集い、率直に課題を抽出し、議論する。

課題に対して、POCを設定して実行する。PDCAサイクルを回し、改善する。

(Response Measures)

1. Need to provide information on the concept and achievements of HBD activities to other field.

HBD活動の考え方、成果について、他領域にも情報提供することが必要

2. Consider POC if there are field of interest. (but may not need to be concerned with incorporating into the current HBD)

関心がある領域があれば、POCを検討する。（ただし、今のHBDに取り込むことにこだわる必要はないかもしれない）

This concept is not limited to the cardiovascular field.

However, individual consideration should be given since there might be different points depending on the medical department.

この考え方は、循環器領域に限ったことではない。

ただし、診療科により、異なる点もあることを踏まえ、個別に検討が必要

Impact on non-PMA

This fundamental concept is also not limited to PMA products.

Isn't there room for consideration of harmonization that includes other than clinical trials as well?

HBDの基本的な考え方は、PMA製品に限ったことではない。

臨床試験以外も含めたハーモナイズについても、検討の余地はあるのではないか？

Consideration of the need for harmonization other than clinical trials.

Is there any possibility that product evaluation could be considered?

(e.g., To what extent is it necessary to evaluate safety in non-clinical studies before conducting FIH, and if there are no model animals, is a simulation model (e.g., a simulation model that can evaluate long-term results) necessary?)

臨床試験以外のハーモナイズについての必要性の検討

製品評価についても検討できる可能性はないか？

（たとえば、FIH実施前に、非臨床試験でどこまで安全性を評価する必要があるか、モデル動物がない場合はシミュレーションモデル（長期成績を評価できるシミュレーションモデルなど）の必要性）

Utilize RWD and Conduct Clinical Trials Efficiently

JAPAN

Although the PMDA's review period has been significantly shortened, reimbursement prices are low. It makes difficult for the company to do business.

The brakes are being applied to the introduction of foreign products. Medical device development tends to proceed behind, especially for pediatric and intractable diseases.

Necessity of development in Japan → to HBD

PMDAの審査期間は大幅に短縮したものの、保険償還価格が低く、ビジネスとして難しい状況

海外製品の導入にブレーキがかかりつつある

特に小児・難病等を対象として医療機器開発は遅れがち
日本で開発する必要性→HBDへ

US

Although the U.S. market is large, efficiency of development is an issue.

FDA Promotes Utilization of RWDs.

米国は市場規模が大きいものの、開発の効率化は課題としてある

FDAはRWDの利活用を推進



Future medical device development is a development strategy with a perspective of global expansion

今後の医療機器開発は、国際展開を見据えた開発戦略

Promoting the Medical Device Development in Japan 日本の医療機器開発の促進

Efficient Development (efficient clinical trials) 開発の効率化（臨床試験の効率化）

Infrastructure to maximize the use of RWD and other resources for development

RWDなどを最大限開発に利用できる仕組み

There are many things that can be done with HBD.

Avoiding Japan Passing, Device Loss

HBD has contributed to eliminating device lag through all stakeholders' efforts for almost 20 years.

Currently, Japan Passing and Device Loss are issues that need to be resolved.

We expect that we will get through these issues with HBD as well.

HBDは、約20年間の関係者の努力により、デバイスラグの解消に貢献してきた。

現在、Japan Passing、Device Lossという解決すべき課題が生じている。

本課題においても、HBDで乗り切れることはできると期待する。



Harmonization by Doing

Harmonization by Data

Harmonization by Drinking