

ISPOR LATAM

TECHNOLOGY ENABLED PATIENT ADHERENCE AS A SOURCE OF RWD

PANEL DISCUSSION

For distribution to ISPOR Latin America Participants

SEPTEMBER 16, 2017

CONFIDENCIAL

NEW YORK CITY SAN FRANCISCO LONDON SHANGHAI

Agenda

INTRODUCTION	CASE STUDIES	REAL WORLD APPLICATIONS	DISCUSSION
17:30-17:40	17:40-18:00	18:00-18:15	18:15-18:30
> Welcome and objectives	 Examples of successfully implemented 	 Discuss how adherence-tracking can be implemented in 	Questions for the audience
 Status Quo of non- adherence data- tracking 	adherence-based tracking studies: ECOS, SMART & STAR	LatAm to improve outcomes	



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Today, the session will be led by three speakers.

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The objective of this session is the discuss how patient adherence tracking can be leveraged as a source of real world evidence.

SESSION OBJECTIVES

- Provide an overview of the different mechanisms to track patient adherence
- Review three case studies of cloud-enabled data collection that have been implemented in real life
- Discuss how cloud-enabled data collection systems can be used in LatAm to track adherence and real world outcomes



Non-adherence is a major health cost, with numerous studies indicating that non-adherence rates lead to poor outcomes, high costs and lost productivity.

NON-ADHERENCE IMPACT ON HEALTHCARE

THE PROBLEM OF NON-ADHERENCE

- Non-response and poor adherence are critical issues, which can be costly for the healthcare system
- It is expected that 13 72% of patients are non-adherent to their prescription
- In EU, non-adherence is predicted to cause 194,500 deaths each year, costing up to EUR 1.25 billion

BENEFITS OF ADDRESSING NON-ADHERENCE

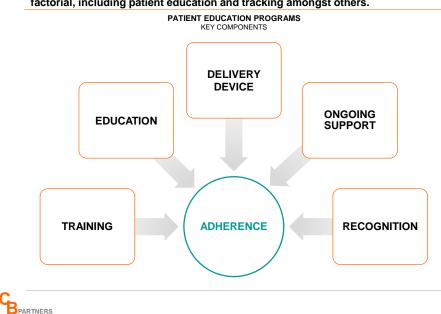
Improvement in patient adherence would **positively impact the** wider health economy by improving health population outcomes, enhancing quality of life and reducing per capita costs



Stiefel M NK., 2012.

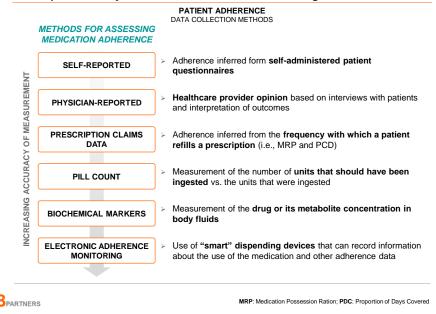
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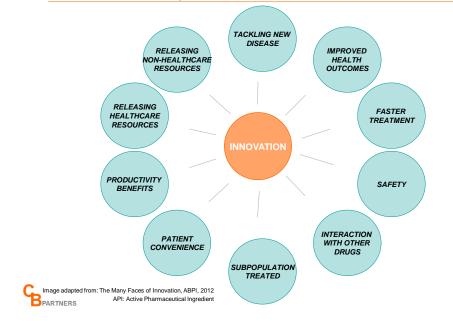


A successful patient adherence program has to be patient-centric and multifactorial, including patient education and tracking amongst others.

Data collection methods for monitoring patient adherence have evolved from self-reported surveys to cloud-based electronic monitoring.



Not all pharmaceutical innovations require a new API; electronic monitors are an innovation which can improve health outcomes and convenience.



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Two real-life case studies demonstrate the ability and impact of leveraging technology to track patient adherence.

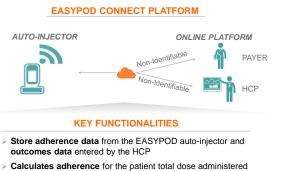




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EASYPOD connect is a secure online platform for monitoring adherence of patients who are prescribed SAIZEN and are using the EASYPOD auto-injector.

OVERVIEW



- Calculates adherence for the patient total dose administered and total number of injections
- > Generates data reports and graphics
- > Generates and sends injection and data upload reminders
- Monitors patient's treatment over time and with possibility to compare historical data



HCP: Healthcare Provider 10

ECOS is an observational study to evaluate the adherence and predictive factors in pediatric patients prescribed with SAIZEN.

ECOS OBSERVATIONAL STUDY METHODOLOGY

OBJECTIVE

- PRIMARY: Evaluate the level of adherence of pediatric patients receiving SAIZEN via EASYPOD
- SECONDARY: Assessment of the impact of adherence on clinical outcomes, the concentrations of insulin-like growth factors and identification of factors that may influence adherence to treatment

METHODOLOGY

- PATIENT POPULATION: 1,972 children with growth hormone deficiency (65.7%), small for gestational age (15.0%) and Turner Syndrome (7.7%)
- DESIGN: multi-center, observational, prospective study carried out in 23 countries with a follow-up duration of up to 5 years, with interim analysis every year
- > DATA COLLECTED:
 - · From EASYPOD: adherence data
 - From HCP Notes: demographic, anthropometric and diagnostic data
- DEFINITION OF ADHERENCE:

 # DAYS WITH INJECTION RECEIVED

 ADHERENCE (%) =

DAYS WITH PLANNED INJECTION



Davies et al. 2015

The ECOS study results indicated patients receiving the auto-injector have better adherence than previously reported in other retrospective studies.

ECOS OBSERVATIONAL STUDY RESULTS





SMART study assessed adherence to, and effectiveness and convenience of, treatment with REBISMART in patients with relapsing multiple sclerosis (RMS).

SMART OBSERVATIONAL STUDY METHODOLOGY

OBJECTIVE

- PRIMARY: Evaluate the level of adherence of RMS patients treated with REBISMART
- SECONDARY: Assess the impact of adherence on clinical outcomes and identification of factors that may influence adherence to treatment

METHODOLOGY

- PATIENT POPULATION: 912 RMS patients with Expanded Disability Status Scale score ≤ 6 that had received REBISMART for ≤ 6 weeks
- DESIGN: multi-center, observational, prospective study carried out in 14 EU countries with a follow-up duration of 1 year

> DATA COLLECTED:

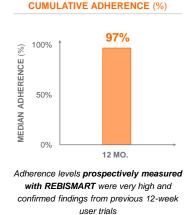
- · Primary Endpoint: cumulative adherence to treatment
- Secondary Endpoint: reasons for missed injections, proportion of patients who prematurely terminated treatment and reasons for ED, proportion of relapse-free patients, proportion of patients free of disease activity, mean number of relapses, serious AE and evaluation of the device
- > DEFINITION OF ADHERENCE:

•	ADHERENCE (%) =	# OF INJECTIONS ADMINISTERED	x 100		
BPARTNERS	ADHERENCE (%) =	# OF INJECTIONS EXPECTED	x 100	Bayas et al. 2015	14

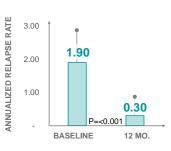


Patients with RMS self-injecting REBISMART had excellent adherence at 12 months, which was associated with good clinical outcomes.

SMART OBSERVATIONAL STUDY RESULTS



ANNUALIZED RELAPSE RATE



Treatment with REBISMART was efficacious: 80% of patients were relapsefree at 12 months, mean ARR was significantly lower at 12 months and EDSS did not increase during the study period



MO.: Months; ARR: Annualized Relapse Rate; EDSS: Expanded Disability Status Scale; RMS: Relapsing Multiple Sclerosis

Bavas et al. 2015



STAR assessed the local tolerability, safety, disease activity and adherence of SC REBIF in patients with RMS.

STAR OBSERVATIONAL STUDY METHODOLOGY

OBJECTIVE

- PRIMARY: Assess the local tolerability of SC REBISMART in patients with RMS
- SECONDARY: Assess the impact of adherence on clinical outcomes and identification of factors that may influence adherence to treatment

METHODOLOGY

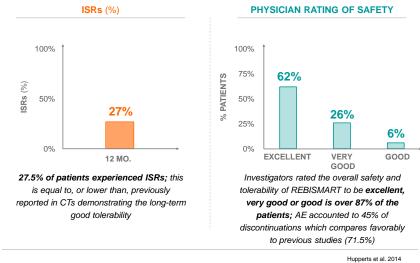
- PATIENT POPULATION: 251 RMS patients with Expanded Disability Status Scale score ≤ 6 that had received REBISMART for ≤ 6 weeks
- DESIGN: multi-center, observational, prospective study carried out in 6 EU countries with a follow-up duration of 1 year
- > DATA COLLECTED:
 - · Primary Endpoint: Proportion of patients with ISRs
 - Secondary Endpoint: general safety profile, adherence, effect of adherence on disease activity
- DEFINITION OF ADHERENCE:





STAR study confirmed the good local and general tolerability of REBISMART seen in CTs was also observed in the real world setting.

STAR OBSERVATIONAL STUDY RESULTS





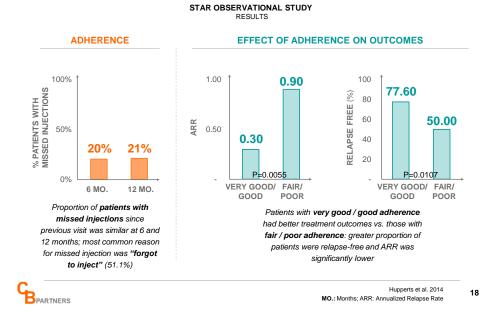
MO.: Months; ARR: Annualized Relapse Rate; EDSS: Expanded Disability Status Scale; RMS: Relapsing Multiple Sclerosis

Hupperts et al. 2014

ISR: Injection Site Reaction



Results from the STAR study revealed the association between good adherence and lower ARR, confirming the importance of good adherence.





Other Real World Evidence studies using REBISMART:

Patient adherence to subcutaneous (injections using the RebiSmart [®] inje [®] ; a retrospective real-world study are and German patients with multiple and German patients with multiple administration by electronic auto-injector is associated with high adherence in patients with relapsing remitting multiple sclerosis in a real-life study Eline Jervine, Sart Auda ¹ ^{Marcher} Finland Marcher Study and Patients with relapsing remitting multiple sclerosis in a real-life study Patient Preference Impact of adherence on subcutaneous beta-1 a effectiveness administered by in patients with multiple sclerosis	Prediment when Osing ReeDismatrix in Particulations with Relapsing-Remittin Sciences in Particulations in Partin in Particulation in Partin in Particulation in	Vasco Sagado. Bjom Sparing & Xiaojun You ** Long-term adherence of patients with relapsing- ** Long-term adherence of patients with relapsing- permitting multiple sclerosis to subcutaneous self injections of interferon β -1a using an electronic device: the RIVER study Alessanda Lugrasi, Francesca be Robertis, Marinella Clerico, Vincenzo Bressich Morza, Diego Centone, Stefano Borghesan, Giorgia Teresa Maniscato & no helari of the RIVER study 2. Exploratory analysis to Predictors of patient adherence to subcutaneous interferon beta-1a in multiple sclerosis: TRACER study Damiano Paolicelli, Benoma Cocc, Viannia Di Lecce, Vita Dinneo, Lucia Molas, Bober Lamib, Paola Poredictors of patient Alesana Caccinguerra, Maria Tojano & for the TRACER Group Patient adherence to and tolerability of self- administered interferon β -1a using an electronic autoinjection device: a multicente, open-label,
Maria Dolores Edo Solsona' Emilio Monte Boquet' Bonaventura Cannova "Organisment of Pianniag: Bonaventura Cannova "Organisment of Neurologi Hopeda Estruch? José Luis Poveda Andrés' "Wennes Types	the RebiSmart [®] injection device	administered interferon β -1a using an electronic



Case Studies illustrate the potential benefits of technology enabled patientadherence programs.

> CASE STUDY TAKEAWAYS OVERVIEW

TAKEAWAYS

- Electronic monitoring provides an objective measure of adherence, therefore not subject to patient reporting errors
- Patient adherence programs can be used to collect outcomes data, thus confirming the effect of therapy in real world setting
- > Program offers benefits to patients, payers and physicians:
 - · Helps patients engage in the management of their disease
 - Provides HCPS with easily accessible information to aid treatment management
 - Provides payers aggregate views on patient outcomes and can support the negotiation of outcomes-based agreements



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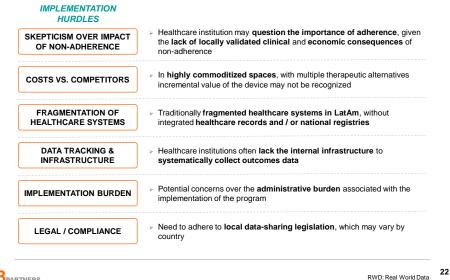
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implemented adherence-based tracking studies: ECOS, SMART & STAR	can be implemented in LatAm to improve outcomes	
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Adherence programs can provide benefits to patients, physicians and institutions; however, several hurdles have limited successful implementation.

ADHERENCE-BASED TRACKING





Combining the data-tracking with payer-specific applications that provide additional value may increase willingness to implement these schemes.

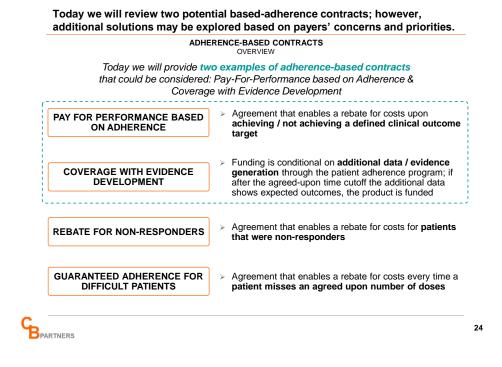
ADHERENCE-BASED TRACKING POTENTIAL APPLICATIONS

POTENTIAL APPLICATIONS FROM TECHNOLOGY ENABLED PATIENT ADHERENCE PROGRAMS

- > ADHERENCE-TRACKING: provides real-life aggregate views on institutional patient adherence, which traditionally could only be obtained through randomized or observational CTs
- > WASTAGE-TRACKING: electronic monitoring devices can calculate real-life wastage, which traditionally could only be measured through research programs
- INTERVENTION MONITORING: possibility to monitor the performance of clinics, and measure the impact of adherence on treatment outcomes (i.e., what is the success rate of the intervention?)
- **CONTRACT DESIGN:** data collected can be used to **support the design** of a tailored outcomes-based agreement

This discussion will focus on how adherence-based contracts can be leveraged to align incentives of all stakeholders and pockets of opportunity where these may be implemented in LATAM





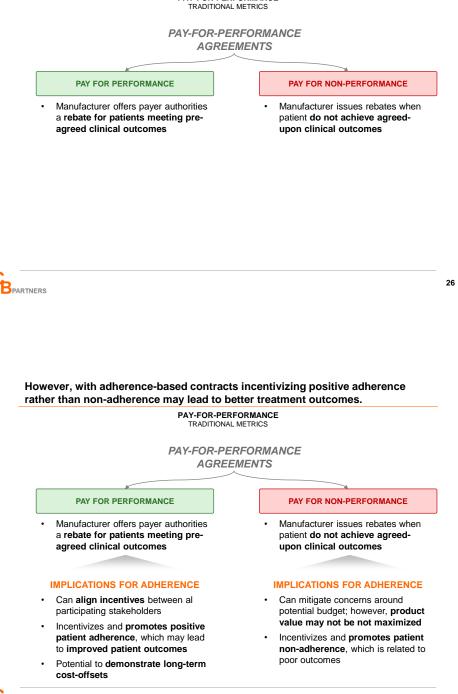
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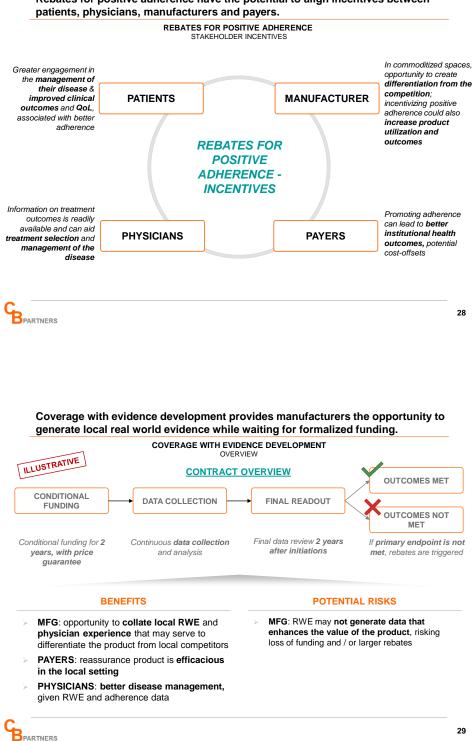
In a Pay-For-Performance agreement, when should a manufacturer issue an agreed-upon rebate?

- (A) Patient DOES NOT reach an agreed upon clinical outcome
- (B) Patient **DOES** reach an agreed upon clinical outcome

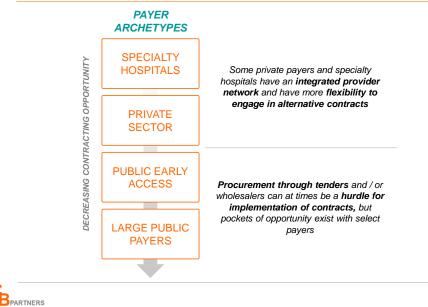


Traditionally, Pay-For-Performance agreements trigger a rebates when a preagreed outcomes is not met. PAY-FOR-PERFORMANCE





Rebates for positive adherence have the potential to align incentives between



Opportunity for implementation of adherence-based contracts will vary across different payer archetypes in LatAm.

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Specialty hospitals generally have a slightly higher WTP and better infrastructure vs. largest public institutions, therefore being an attractive pocket for ABC.

		SPECIALTY HOSPITALS POCKETS OF OPPORTUNITY	
_	MARKET SEGMENTS	OPPORTUNITIES	ISSUES & RISKS
* MEX	UMAEs	 Direct negotiations (i.e., may by-pass the tender) Opportunity for funding even if not in "Cuadro Basico" 	 Small number of patients may limit revenue potential General procurement through tenders
COL	IPS	 Direct negotiations or through wholesalers, often in collaboration with EPS Single institution with self network Serve as service providers for EPS 	 Need to align incentives between IPS, EPS and wholesalers
ARG	SPECIALTY HOSPITALS	Opportunity for direct negotiation Single institution with self network	 Small number of patients, may limit uptake May call for tenders in highly competitive Tas (e.g., RA., AS, MS)



	MARKET	POCKETS OF OPPORTUNITY	
	SEGMENTS	OPPORTUNITIES	ISSUES & RISKS
RA	HMOs	 Direct negotiations Integrated provider network Patient volumes (9.25% of BRA market; ~ 19.2 million) 	 Funding not mandated if not include in the Rol from ANS, need to gain access through individual providers
RA	UNIMED	 Direct negotiations Integrated provider network Patient volumes (9.00% of BRA market; ~ 18.6 million) 	 Funding not mandated if not include in the Rol from ANS, need to gain access through individual providers
RG	PREPAGAS	 Opportunity for direct negotiation Some PREPAGAS have an integrated provider networked 	 Fungding is not centrally regulated, and may vary between depending on inclusion in individual vademecums
EX	PRIVATE	 Opportunity for direct negotiation Some may have an integrated provider networked Physicians often have a public and private practice, therefore can be advocated in the public payers 	Small patient volume (5% of MEX population)

LatAm markets have a flourishing private sector that could be an early adopter of electronic monitoring.

Smaller public institutions may serve as early access routes given they provide more flexibility that larger public institutions.

		EARLY PUBLIC SEGMENTS POCKETS OF OPPORTUNITY	3
	MARKET SEGMENTS	OPPORTUNITIES	ISSUES & RISKS
BRA	STATE FUNDING	 Decisions may indirectly influence private and public providers Funding for non-CONITEC indications Patient volumes (28% of BRA market; ~ 75.5 million) 	Tender-based procurement
MEX	(e.g., SEDENA,SEMAR)	 Integrated provider network Opportunity exists to opt out of tender Higher WTP vs. other public institutions Prior experience with Pay-for- Performance 	 May opt for joining centralized negotiations (mesa negociadora) and tender
ARG	OS-PROVINCIAL	 Opportunity for direct negotiation Integrated provider network 	 Decentralized system of OS-P, would require a strong field team to engage with all ove

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Public and social security sector are the largest in volume, but traditionally costdriven with limited examples of implementation of alternative contracts.

PRIVATE SECTOR

FRIVATE SECTOR
POCKETS OF OPPORTUNITY

	MARKET SEGMENTS	OPPORTUNITIES	ISSUES & RISKS
BRA	SUS	 Highest patient volume opportunity in BRA 	 Price-driven single award tender procurement Limited experience with outcomes- based based agreements
(MEX	IMSS, ISSSTE, SP	 Highest patient volume opportunity in MEX 	 Competitive single-award tender system Price erosion through reverse action tenders Prescription limited to the tender brand
• ARG	OS: NACIONALES	 Provides coverage to the employed (majority of the population) High cost drugs founded through SUR 	 Fungding is not centrally regulated, and may vary between depending on inclusion in individual vademecums
COL	EPS	Opportunity for direct negotiation with IPS and wholesalers	 Need to align incentives between IPS, EPS and wholesalers
COL		IPS and wholesalers	IFS, EFS and Wholesalers

BPARTNERS

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