

Luncheon Symposium 2

FOSTER NEXThaler: An innovative dry powder inhaler delivering an extrafine fixed combination of beclometasone and formoterol to treat

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Massimo Corradi

Topics

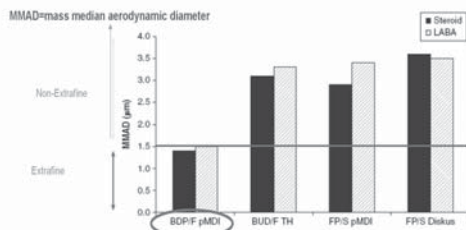
- Main characteristics of Foster®
- Foster® in pivotal studies in asthma and COPD
- Foster® DPI

Foster: the first extra-fine BDP/FF*fixed combination in a metered-dose inhaler



*BDP = beclometasone dipropionate; FF = formoterol fumarate dihydrate

BDP/FF* particles in Foster are extra-fine with a diameter of $\sim 1\mu\text{m}$

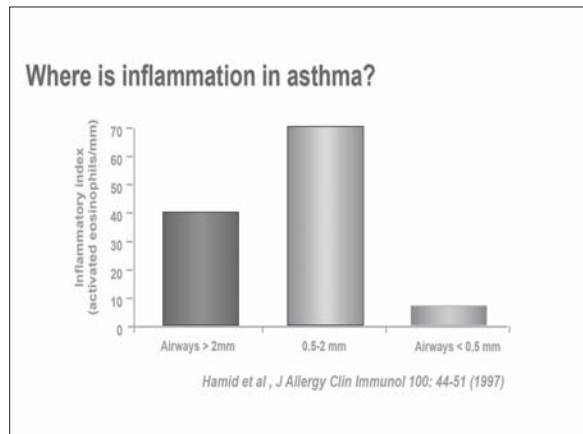
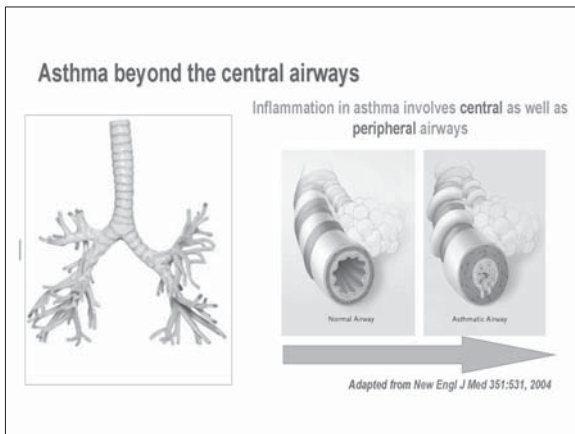
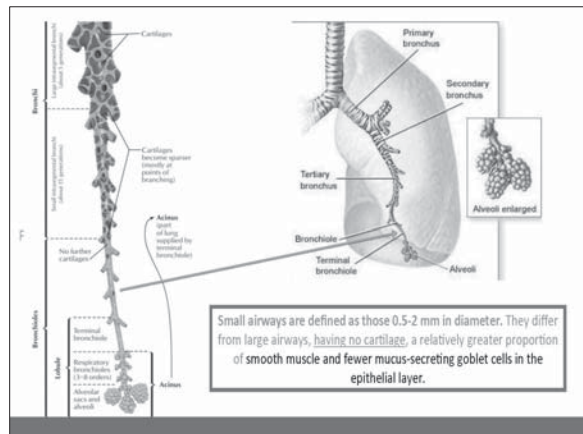
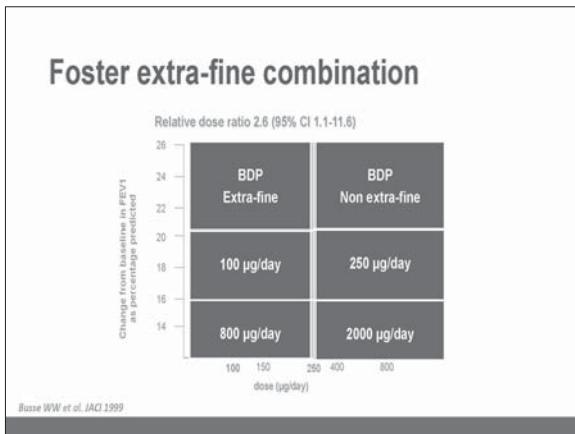
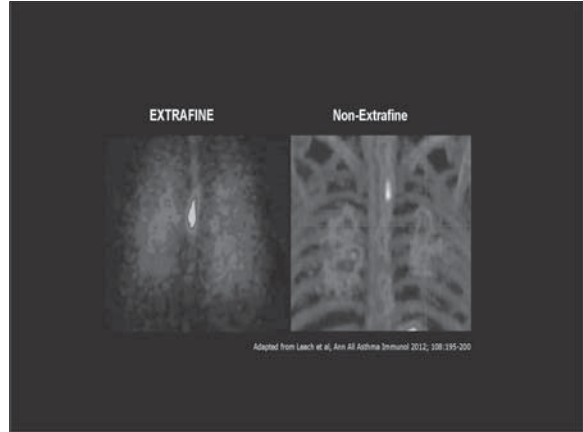
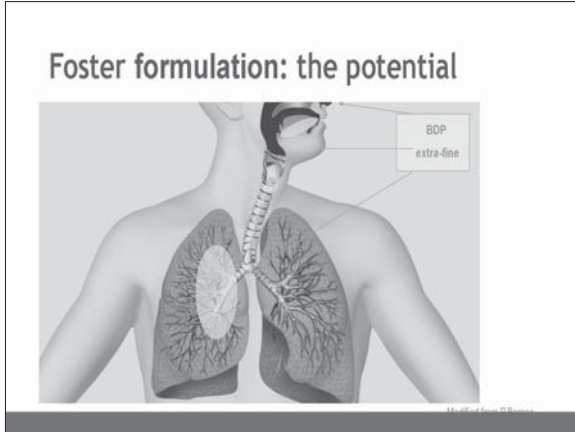


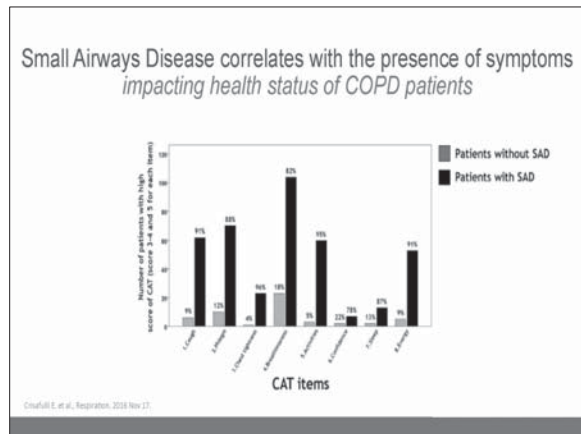
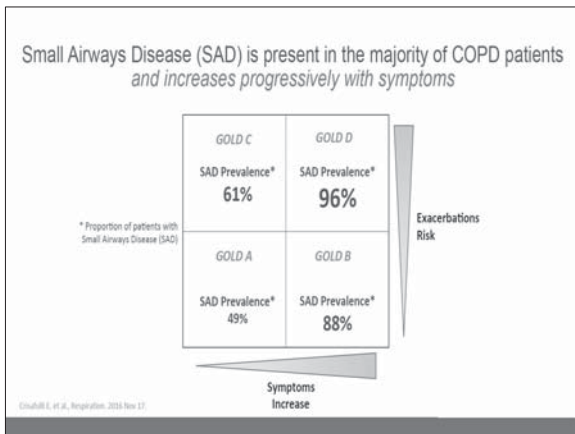
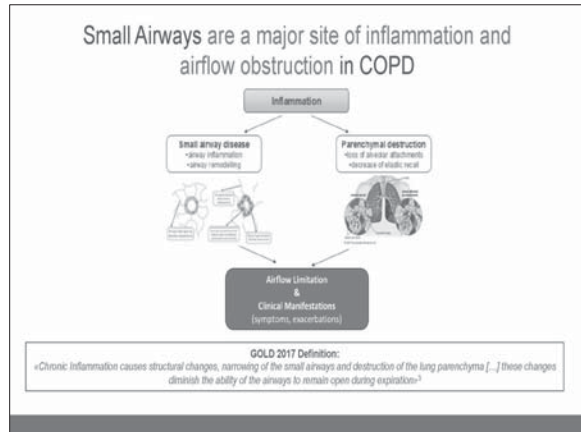
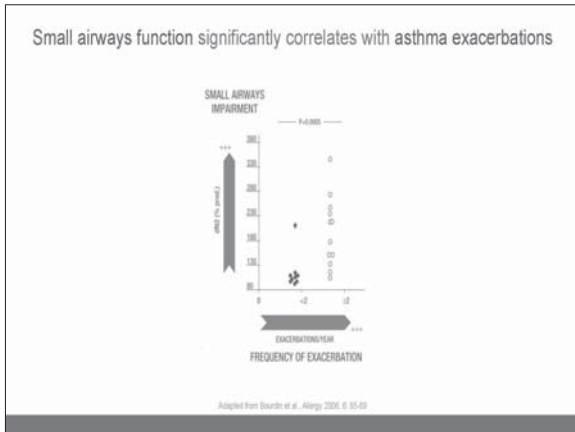
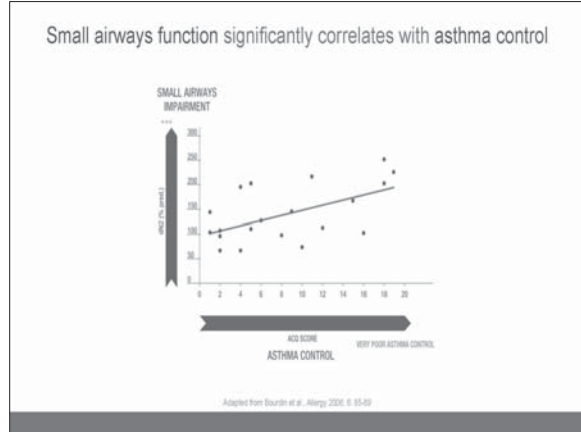
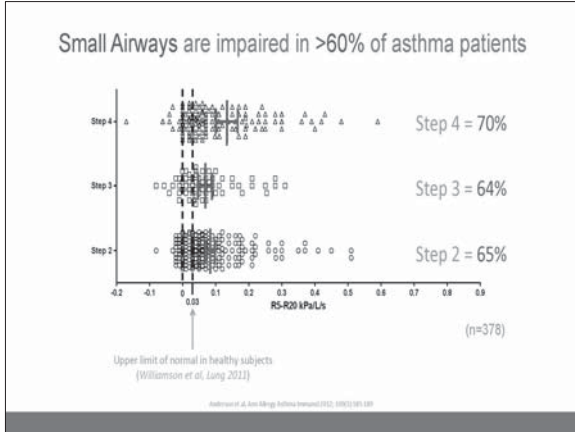
Fabbri et al. Expert Opin. Pharmacother. (2008) 9(3):473-490

*BDP = beclometasone dipropionate; FF = formoterol fumarate dihydrate

Foster formulation: the potential



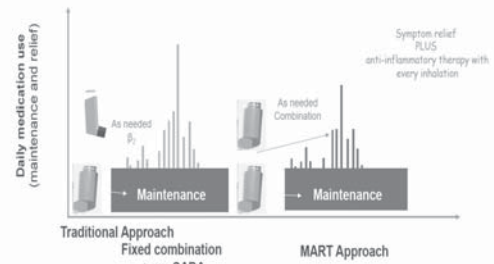




Topics

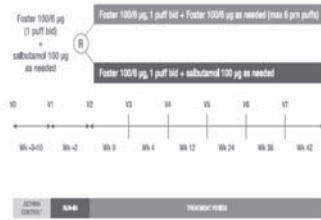
- Main characteristics of Foster®
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The traditional and MART approach in asthma

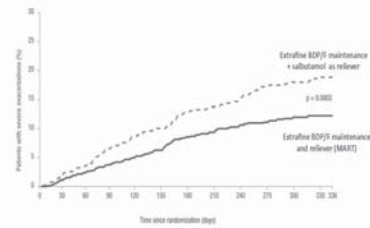


48-WEEK RANDOMIZED CONTROLLED TRIAL WITH 1,701 ADULT ASTHMATIC PATIENTS TO COMPARE EFFICACY OF FOSTER® FOR MAINTENANCE AND RELIEVER THERAPY VERSUS FOSTER® FOR MAINTENANCE + SALBUTAMOL AS RELIEVER*

STUDY DESIGN

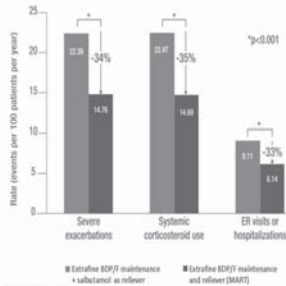


FOSTER MART provides significantly prolonged time to first severe exacerbation



Papi et al. Lancet Respir Med. 2013

FOSTER MART provides significant reduction in yearly rate of severe exacerbations



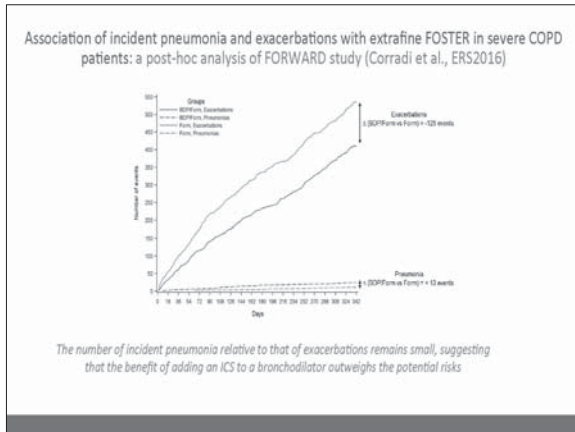
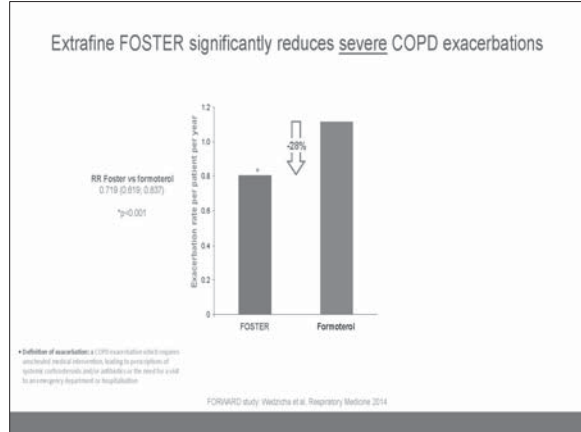
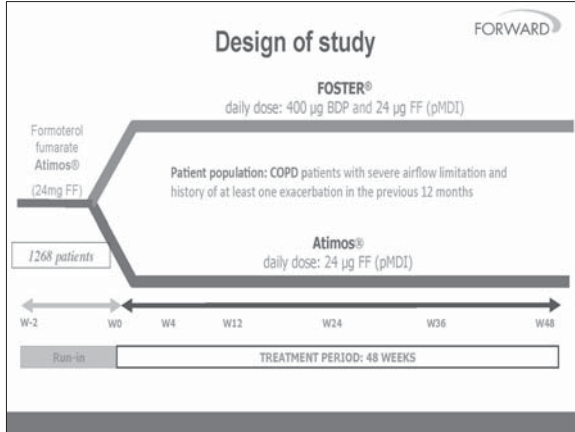
Papi et al. Lancet Respir Med. 2013

FOSTER MART: The right idea in the right device

Beclometasone-formoterol as maintenance and reliever treatment in patients with asthma: a double-blind, randomised controlled trial



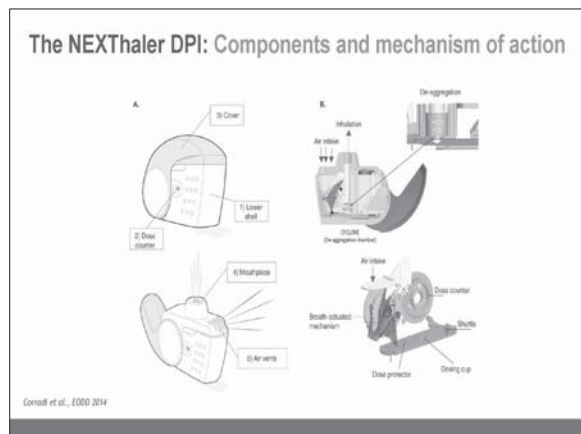
- MART approach should especially be considered for patients with :
- not fully controlled asthma and in need of reliever medication
 - asthma exacerbations in the past requiring medical intervention



- ### Topics
- Main characteristics of Foster®
 - Foster® in pivotal studies in asthma and COPD
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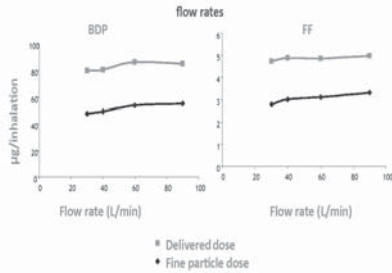
FOSTER NEXThaler

Device	Medium resistance, breath-actuated, multidose reservoir	
Active Ingredients	Extraxfine beclomethasone dipropionate (BDP) and formoterol fumarate (FF)	
Strength	BDP/FF 100/6 µg	
Doses	120	
Indication	ASTHMA and COPD (please refer to your local SmPC)	
Posology	1 or 2 inhalations twice daily	
Shelf-life	18 months + 6 months out of the pouch (24 month total)	
Storage	25°C	



Device characteristics: Flow-independency

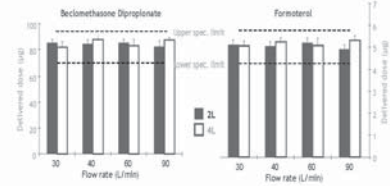
RESULTS: Delivered dose, as well as Fine particle dose, of Foster NEXThaler are **NOT** affected by different flow rates



Pozzuffi et al., EDD 2013

Device characteristics: Volume-independency

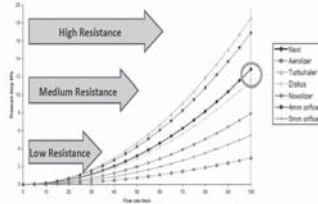
RESULTS: Delivered dose of Foster NEXThaler was **NOT** affected by different inhalation volumes at all tested flow rates



Pozzuffi et al., EDD 2013

Device characteristics: Medium-resistance

NEXThaler is a medium resistance powder inhaler



Source: data on file

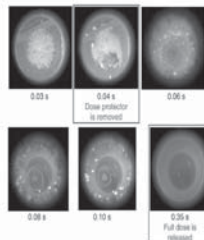
Device characteristics: Extrafine delivery

NEXThaler is the first dry powder inhaler delivering extrafine particles

This unique characteristic mainly depends on two factors:

- the use of a specific extrafine formulation powder
- the highly innovative release and de-aggregation system

Device characteristics: Fast de-aggregation and release



During inhalation, full dose is released in about 0.35 s after hearing a click.

Therefore, the click is a feedback of full dose release.

This effect is seen at all flow rates tested (40-60-100 L/min)

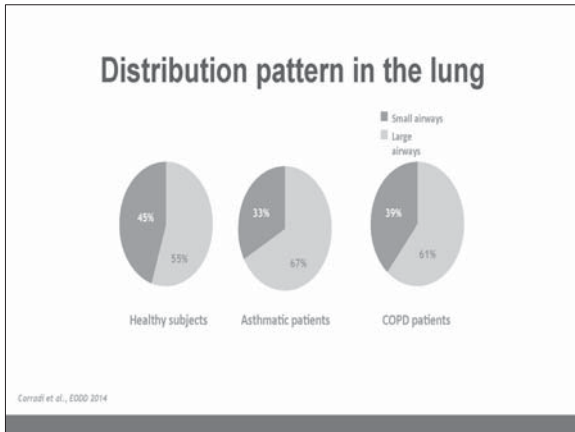
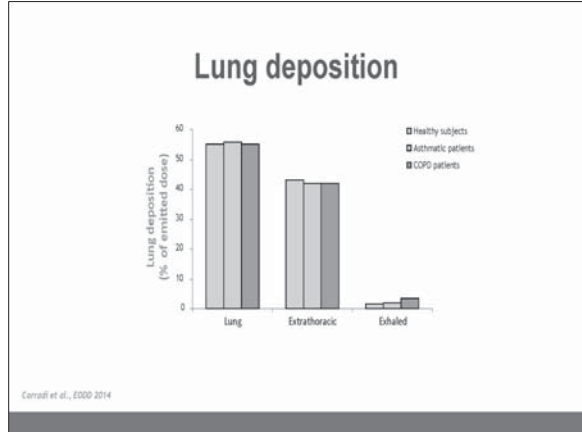
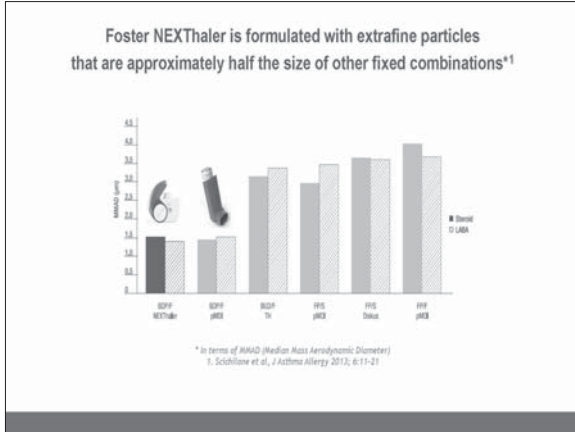
Corradi et al., EDDO 2014

Device characteristics: Extrafine delivery

- This system is set-up by the patient's inhalation. The powder is released only when the airflow inside the device grants for perfect de-aggregation.
- Once the formulation enters the cyclone, the air movements optimize the impact of the powder on the internal walls and make possible the release of the extrafine active principles



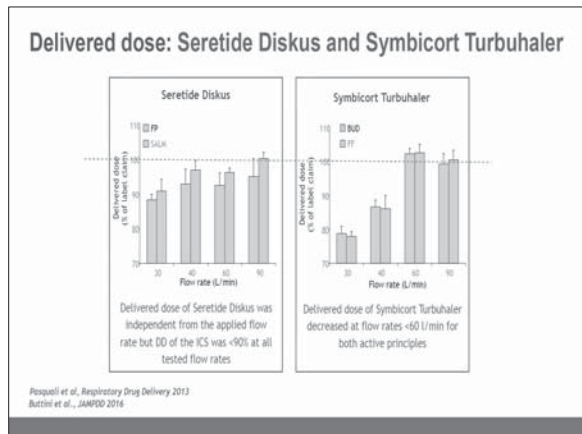
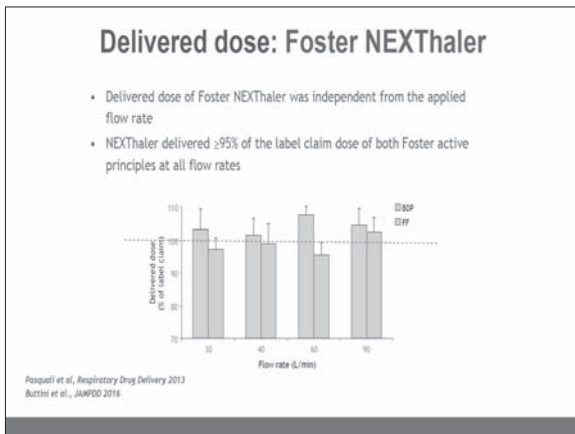
Extrafine particles are already present inside the formulation. The de-aggregation step is necessary to de-aggregate drug powder and then release extrafine active principles from carrier molecules.



Comparative in vitro study

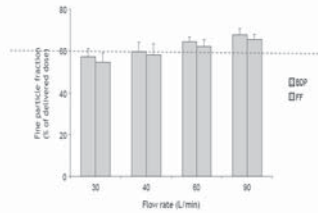
- To compare in vitro performance parameters of Foster NEXThaler vs Seretide Diskus and Symbicort Turbuhaler at different flow rates
- Measurements were performed using a next generation impactor (NGI)
- Each analysis was carried out in triplicate at 4 different flow rates (30, 40, 60, 90 L/min)

Pasquili et al., Respiratory Drug Delivery 2013
Buttini et al., JAMPDD 2016



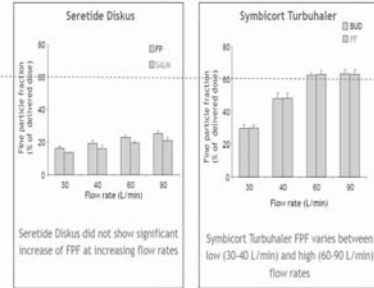
Fine particle dose: Foster NEXThaler

Fine particle dose delivery of Foster NEXThaler was consistent across different flow rates



Pasquall et al., Respiratory Drug Delivery 2013
Buttini et al., JAMPDD 2016

Fine particle dose: Seretide Diskus and Symbicort Turbuhaler



Pasquall et al., Respiratory Drug Delivery 2013
Buttini et al., JAMPDD 2016

Peak Inspiratory Flow (PIF) study

NEXThaler has been designed as a breath-actuated DPI to guarantee optimal drug delivery and lung deposition

As the internal design of each inhaler is different and methods of producing an aerosol are not identical, the resistance the patient encounters when inhaling - and the speed of inhalation at which the optimum performance occurs - will differ from device to device

This study was aimed at verifying that NEXThaler can be actuated by patients of any age and disease severity

Corradi et al., E000 2014

Baseline patients' characteristics

- 89 patients (68 asthmatics and 21 COPD)
- Mean age: 34 ± 28 years (range 5-84 yrs)
- 39% female

	FEV ₁ (L)
OVERALL (N=89)	1.91 ± 0.80
ASTHMATIC CHILDREN (N=27)	1.67 ± 0.44
MODERATE ASTHMATIC ADOLESCENT (N=20)	2.94 ± 0.73
MODERATE ASTHMATIC ADULTS (N=11)	2.14 ± 0.57
SEVERE ASTHMATIC ADULTS (N=10)	1.49 ± 0.38
MODERATE COPD (N=10)	1.64 ± 0.50
SEVERE COPD (N=11)	1.04 ± 0.16

Corradi et al., E000 2014

Results: PIF values

- All patients with asthma and COPD, irrespective of disease severity, were able to trigger the BAM both at visit 1 (primary outcome) and visit 2
- Mean PIF values measured with the In-Check Dial were greater than the threshold set for the BAM activation (35-45 l/min) and not influenced by age and disease severity

Mean ± SD PIF values measured with In-Check Dial device in patients at Visit 1

	PIF (l/min)
OVERALL (N=89)	102.9 ± 20.3
ASTHMATICS - OVERALL (N=68)	104.4 ± 20.6
ASTHMATIC CHILDREN (N=27)	94.4 ± 22.5
ASTHMATIC ADOLESCENTS (N=20)	114.2 ± 12.8
MODERATE ASTHMATIC ADULTS (N=11)	110.3 ± 18.2
SEVERE ASTHMATIC ADULTS (N=10)	105.7 ± 20.9
COPD - OVERALL (N=21)	97.9 ± 18.6
MODERATE COPD (N=10)	91.6 ± 21.1
SEVERE COPD (N=11)	103.6 ± 15.2

Corradi et al., E000 2014

Results: Preferability questionnaire

According to usability evaluation questionnaire, the vast majority of patients did not find any problems in being trained and use NEXThaler correctly

QUESTION	OVERALL	
	YES	NO
Are 5 minutes enough for being trained successfully on how to use the device?	83 (98.8)	1 (1.2)
Is verbal description alone enough to successfully use the device?	83 (98.8)	1 (1.2)
Is the dose counter appearance clear?	82 (97.6)	2 (2.4)
Did you hear a click when opening the inhaler?	83 (98.8)	1 (1.2)
Did you hear a click soon after drug inhalation?	81 (96.4)	3 (3.6)
Is the mouthpiece sized appropriately for users?	75 (85.3)	9 (10.7)

Corradi et al., E000 2014

Device characteristics: Comparative Table

Features	NEXThaler	Diskus	Turbuhaler
Resistance	Medium	Medium	High
Dose counter	Yes, 1 count decrement	Yes, 1 count decrement	No, dose indicator only changing every 10 doses
Dosage release	Breath Activated Mechanism (BAM) ~40 L/min	No BAM Optimal flow 30-90 L/min	No BAM Optimal flow 60-90 L/min
Extrafine delivery	Yes	No	No
Number of operating manoeuvres	3 OPEN-INHALE-CLOSE (The cover is linked to the dose charging system)	6*	6*
Flow-independent delivery of full doses	Yes	Flow-independent but not full dose delivery	No flow-independent delivery and no full dose delivery
Feedback systems	3 a. full dose feedback system (click) b. dose counter c. distinctive taste	2 a. dose counter b. distinctive taste	1 a. dose indicator (only changing every 10 doses)

* Berger W, Curr Drug Deliv 2009; 4:38-49

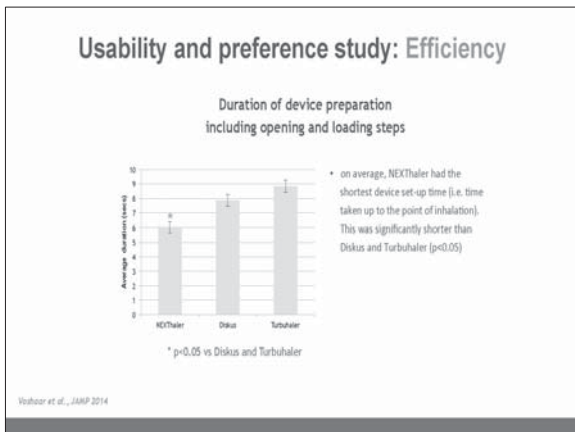
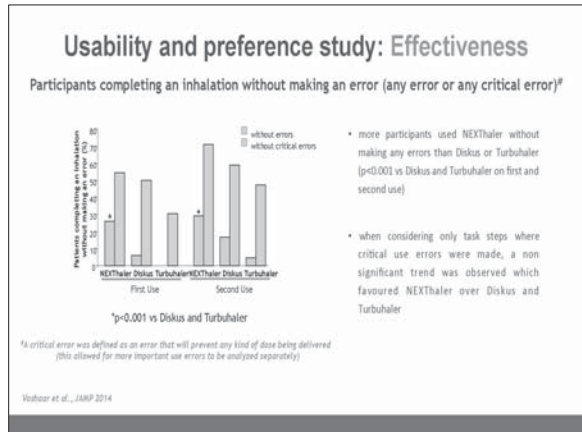
Usability and preference study: Study design

- 66 asthmatics with at least 3 months of diagnosis. All patients were current users of pMDIs, none had previous experience of using DPIs
- A pilot study was conducted to test the protocol prior to the main study
- One-on-one interview, where the assessors observed patients using each of the three devices in turn (empty inhalers)
- After reading the patient information leaflet, patients were asked to use the inhaler while errors were logged through video recording
- A set of questions was asked to determine patients' preference

Usability and preference study: Main goal

To compare usability and preference of NEXThaler vs Diskus and Turbuhaler

- 3 key components of usability:
 - Effectiveness:** accuracy and completeness with which users achieve specified goals
 - Efficiency:** resources expended in relation to the accuracy and completeness with which users achieve goals
 - Satisfaction:** freedom from discomfort, positive attitude towards the use of the product



Usability and preference study: Satisfaction

Usability Measures	NEXThaler	Diskus	Turbuhaler	p values
OVERALL, Easiest to use	74.2%	16.7%	9.1%	p<0.001 for NEXThaler vs Diskus and Turbuhaler
OVERALL, Prefer to own	75.4%	16.9%	7.7%	p<0.001 for NEXThaler vs Diskus and Turbuhaler

Voisard et al., JAMP 2014

Conclusions

- NEXThaler outperformed Diskus and Turbuhaler in effectiveness, efficiency and satisfaction measures

- Key reasons as to why NEXThaler performed best:

- fewer task steps; more efficient use, simpler to use, reduced scope for error
- full dose feedback system (BAM and dose counter) provided greater confidence in full dose administration
- ease of operation, loads automatically, clear counter, good device feedback

- Videoclip