Come scegliere la terapia:
Focus sull'associazione Fluticasone furoato/Vilanterolo

Fulvio Braido

Allergy and Respiratory Diseases Department
University of Genoa

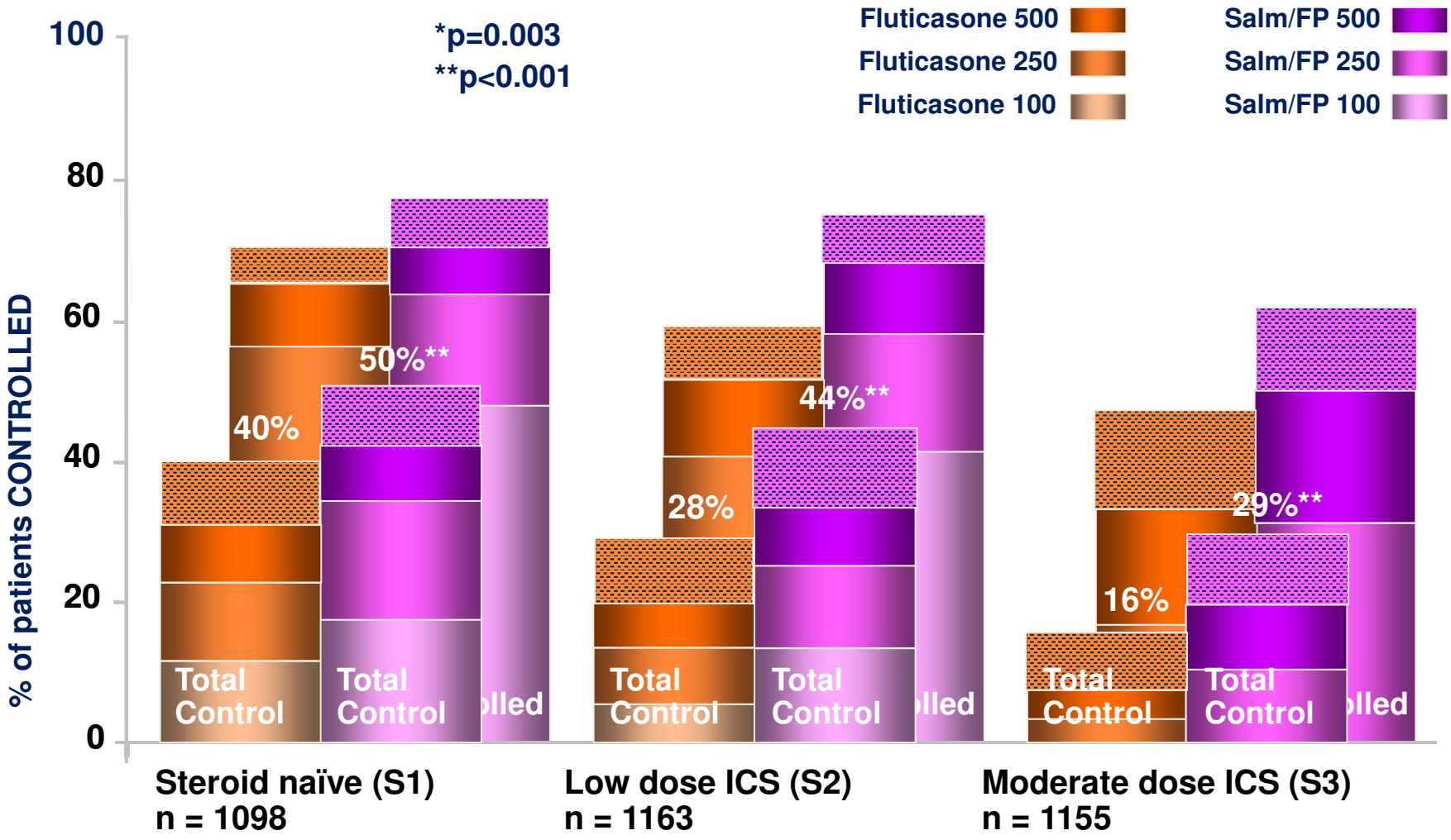
Come scegliere la terapia:

Farmaco o associazione di farmaci in grado di garantire il miglior controllo possibile

Farmaco o associazione di farmaci in grado di garantire da incontrare le esigenze dei pazienti

NKT1

Levels of control in the studio GOAL



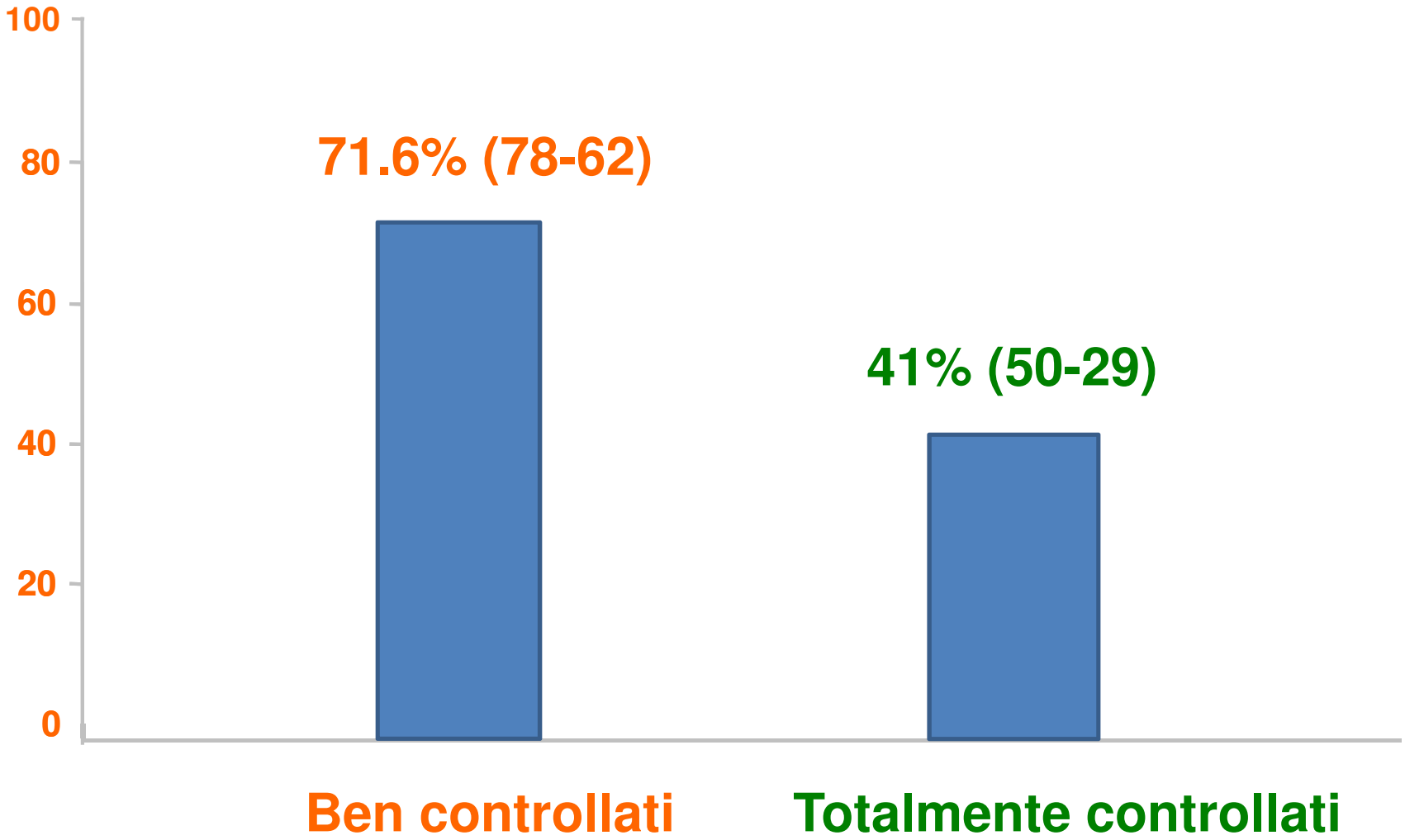
Bateman et al, ARJCCM 2004

Diapositiva 3

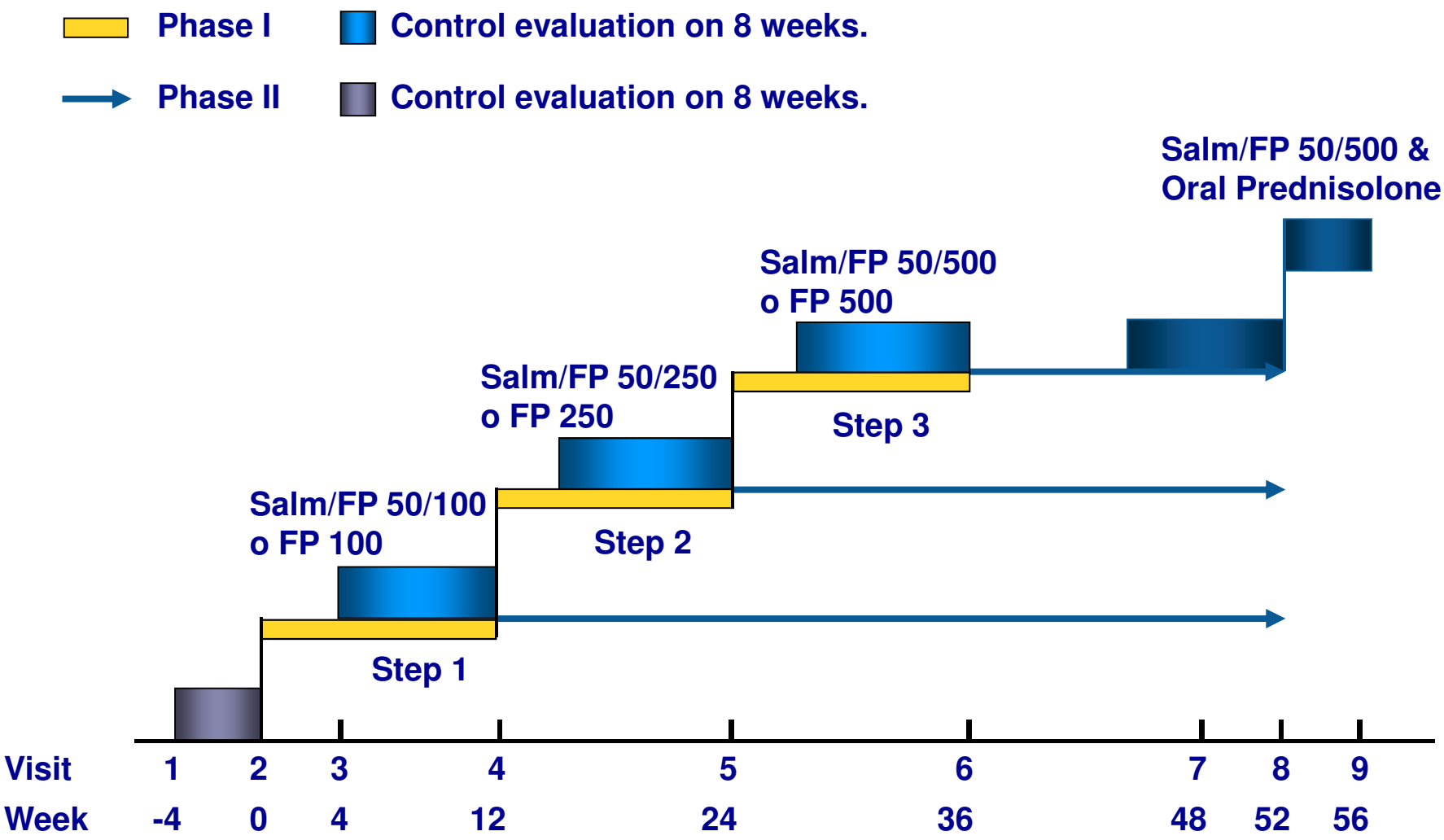
NKT1 Edit with total numbers

Namrata K Taak; 31/10/2006

Percentuale media di pazienti “controllati” alla fine dello studio GOAL



Asthma control approach



Bateman 2004

Svedsater *et al. Asthma Research and Practice* (2016) 2:4
DOI 10.1186/s40733-015-0016-0

Asthma Research and Practice

RESEARCH Open Access

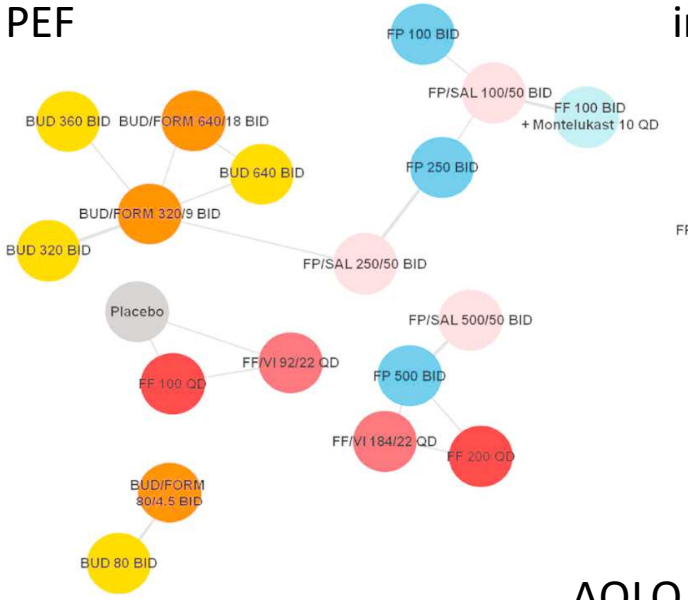
Once-daily fluticasone furoate/vilanterol versus twice daily combination therapies in asthma–mixed treatment comparisons of clinical efficacy

Henrik Svedsater[1*], Gillian Stynes[1], Jaro Wex[1], Lucy Frith[2], David Leather[2], Emanuela Castelnuovo[3], Michelle Detry[4] and Scott Berry[4]

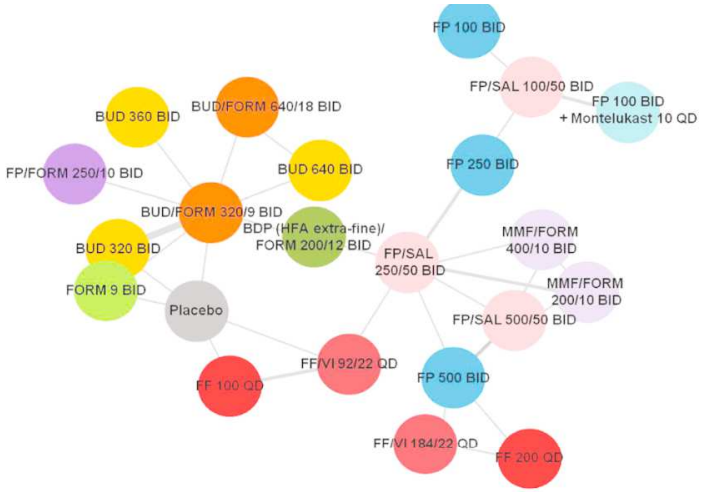
Data from **31 parallel-group randomised controlled trials** (RCTs) of ICS/LABA, of ≥8 weeks' duration in patients aged ≥12 years with asthma, identified by systematic review, were analysed using covariate-adjusted Bayesian hierarchical models for four efficacy outcomes (primary analysis)

Networks of study treatments, by outcome of interest

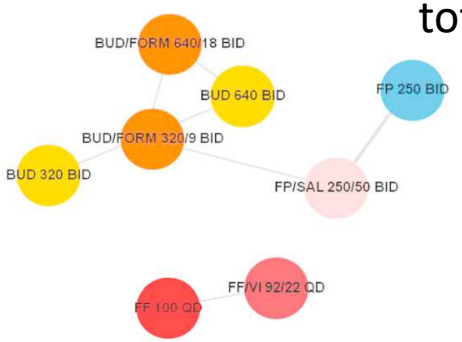
Change from baseline in morning PEF



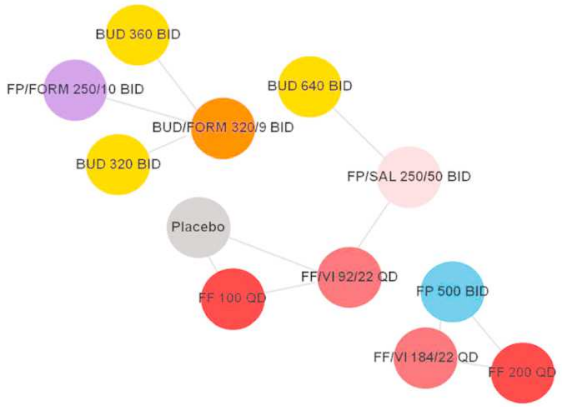
Change from baseline in FEV_1.



Annual rate of moderate/severe exacerbations



AQLQ total score



Posterior <u>probability of non-inferiority</u> for FF/VI versus other relevant ICS/LABA combination therapies

PEF

FEV1

Exac

QoL

A					
Treatment (mcg)	Comparator (mcg)	Mean difference, l (95 % CrI)	Probability of non-inferiority Margin (l/min)		
			12		15
FF/VI 92/22	FP/SAL 250/50	2.832 (−12.867–18.531)	97 %		99 %
FF/VI 92/22	BUD/FORM 320/9	0.579 (−15.155–16.312)	94 %		98 %
FF/VI 184/22	FP/SAL 500/50	11.323 (0.289–22.357)	>99 %		>99 %
FF/VI 184/22	BUD/FORM 640/18	15.136 (−0.943–31.215)	>99 %		>99 %
B					
Treatment	Comparator	Mean difference, ml (95 % CrI)	Probability of non-inferiority Margin (ml)		
			75	100	125
FF/VI 92/22	FP/SAL 250/50	−36 (−92–19)	92 %	99 %	>99 %
FF/VI 92/22	BUD/FORM 320/9	−27 (−98–45)	91 %	98 %	>99 %
FF/VI 184/22	FP/SAL 500/50	147 (48–247)	>99 %	>99 %	>99 %
FF/VI 184/22	BUD/FORM 640/18	118 (−19–255)	>99 %	>99 %	>99 %
C					
Treatment	Comparator	Rate ratio (95 % CrI)	Probability of non-inferiority Margin (event rate ratio)		
			10 %		20 %
FF/VI 92/22	FP/SAL 250/50	1.164 (0.428–3.333)	74 %		78 %
FF/VI 92/22	BUD/FORM 320/9	0.985 (0.336–2.574)	82 %		86 %
D					
Treatment	Comparator	Mean difference, units (95 % CrI)	Probability of non-inferiority Margin (units)		
			0.25		0.5
FF/VI 92/22	FP/SAL 250/50	0.060 (−0.104–0.224)	>99 %		>99 %
FF/VI 92/22	BUD/FORM 320/9	0.203 (−0.461–0.867)	90 %		96 %

Svedsater et al. Asthma Research and Practice (2016) 2:4
DOI 10.1186/s40733-015-0016-0

RESEARCH Open Access

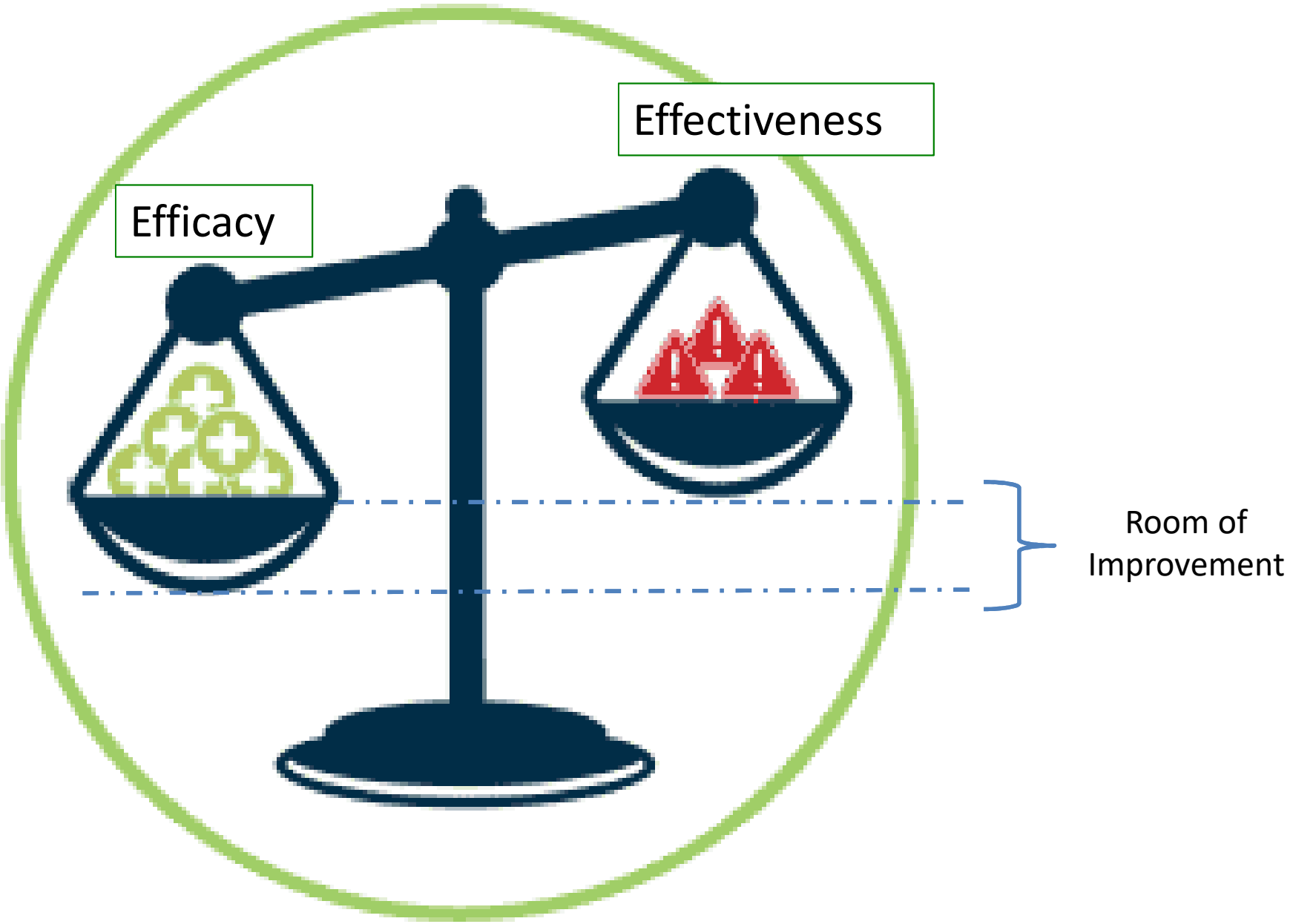
Once-daily fluticasone furoate/vilanterol versus twice daily combination therapies in asthma–mixed treatment comparisons of clinical efficacy

Henrik Svedsater[1*], Gillian Stynes[1], Jaro Wex[1], Lucy Frith[2], David Leather[2], Emanuela Castelnuovo[3], Michelle Detry[4] and Scott Berry[4]

Conclusions

The findings of the MTC suggest that the efficacy of both strengths of once-daily FF/VI in asthma is broadly comparable to that of corresponding doses of established twice-daily ICS/LABA combinations, FP/SAL and BUD/FORM, on lung function and health status outcomes of interest in the primary study populations. The MTC supported the findings of a previously-reported head-to-head randomised controlled trial of FF/VI 92/22 mcg vs FP/SAL 250/50 mcg in which it was shown that the efficacy of these treatments in improving lung function and health status endpoints is similar [7]. It should be borne in mind that the MTC findings are obtained through the analysis of outcomes from RCTs and any potential efficacy benefits that may derive from treatment attributes such as once- vs twice-daily dosing in real-world clinical practice will not be reflected in these data.

NEED
WANT


Effectiveness
Efficacy
Room of
Improvement


Needs
Awareness
Disease
Symptoms
Care
Care
What can I do?
How to find help?
What symptoms I need to be aware of?
Help
Whom to contact?
Where can I find more?
How to ask proper questions?
Treatment
Benefits
Risks
Option
Medication
Risks
Benefits
Why do I need it?
Side Effects
Alternatives
Couter - Effects
Lifestyle
What to avoid?
How will it affect me?
What can I do?
Behavioural Change
What do I do?
Revise decisional needs

THE REAL WORLD

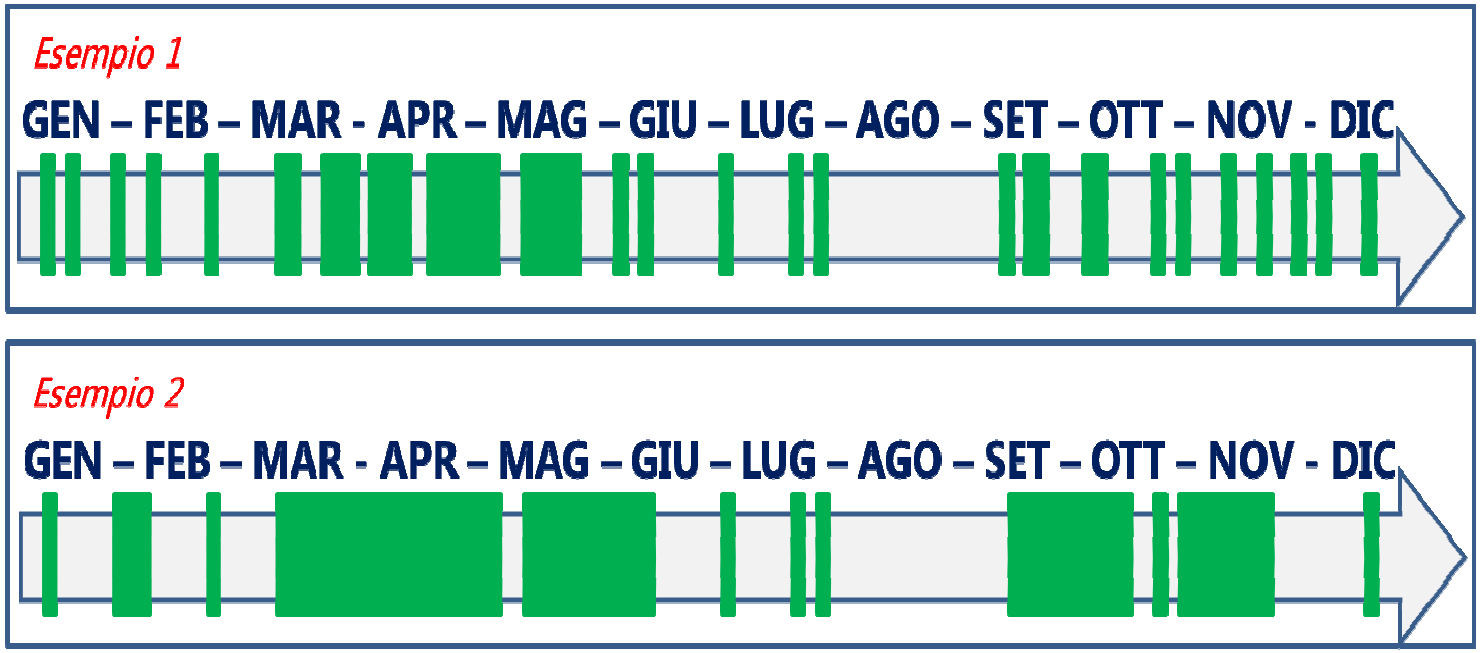
La terapia dell'Asma dovrebbe essere regolare e continuativa, ma il

dei pazienti fa terapia

«**occasionale**»,

L'uso dei Farmaci **in Italia.** Rapporto Nazionale Anno 2015

Symptoms relievers



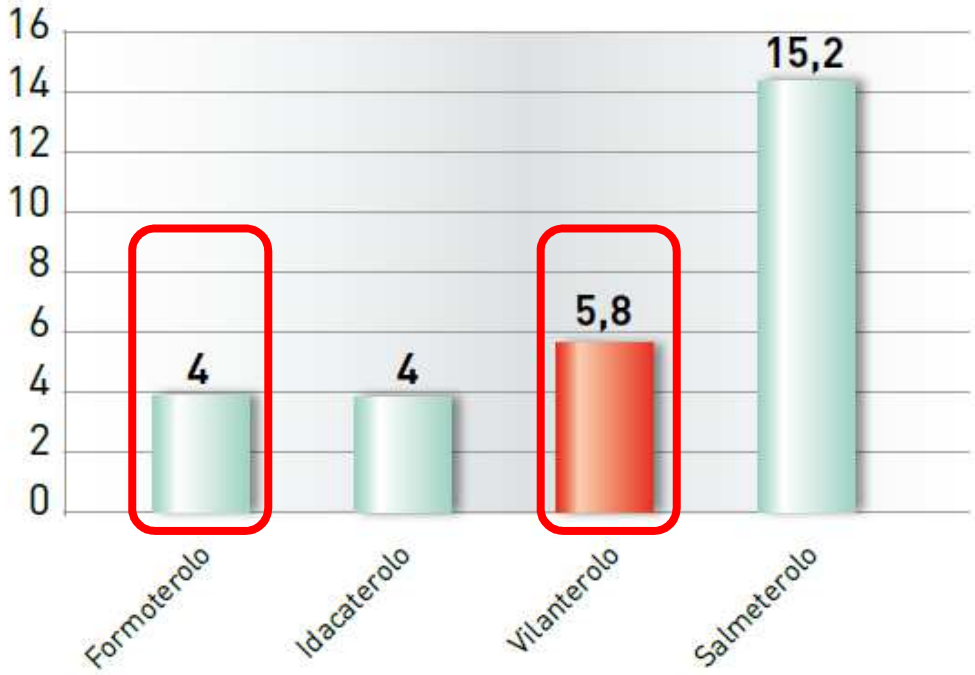
Aim: move from short term treatment cycles to longer treatment cycles

Strategy: drugs able to induce a fast symptoms relief

1521-0103/344/1/218–230$25.00
THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS

http://dx.doi.org/10.1124/jpet.112.198481
J Pharmacol Exp Ther 344:218–230, January 2013

In Vitro Pharmacological Characterization of Vilanterol, a Novel Long-Acting β_2-Adrenoceptor Agonist with 24-Hour Duration of Action



> β2/β1 sectivity

FEV_1

Does use of a corticosteroid/long-acting beta-agonist combination inhaler increase adherence to inhaled corticosteroids?

Table 1. Characteristics of subjects.

	ICS/LABA	ICS
N	25	57
Median age (IQR)	40 (36 to 42)	33 (26 to 40)
Gender, % female	62.5	63.8
Inhalers		
Seretide	21	
Symbicort	4	
Beclomethasone		51
Fluticasone		5
Budesonide		1
Adherence % (IQR)	72.2 (54.8 to 98.6)	40.5 (27.4 to 82.2)
Median SABA use (IQR)	3 (2 to 7)	4 (2 to 6)

ICS/LABA = Inhaled corticosteroid/long-acting beta-agonist combined inhaler; ICS = Inhaled corticosteroid inhaler; IQR = Interquartile range; SABA = Short-acting beta-agonist inhaler

Foden et al, 2008

Primary Care RESPIRATORY JOURNAL
www.thepcrj.org

Respiratory Medicine (2013) 107, 1873–1880

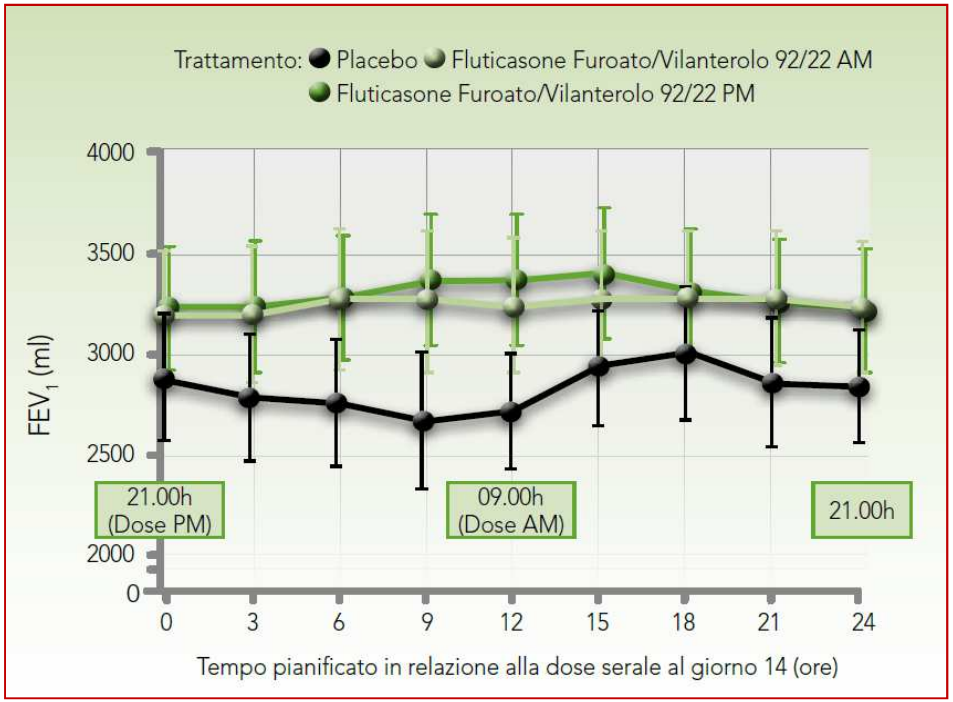
Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/rmed

The efficacy of once-daily fluticasone furoate/vilanterol in asthma is comparable with morning or evening dosing

Rodger D. Kempsford [a,*], Amanda Oliver [b], Joanne Bal [b], Lee Tombs [c], Dean Quinn [d]



Tailoring timing of administration according with patient's needs

Kempsford R et al. *Respir Med (2013)*

Lowest treatment burden

Adherence = inversely related to doses needed

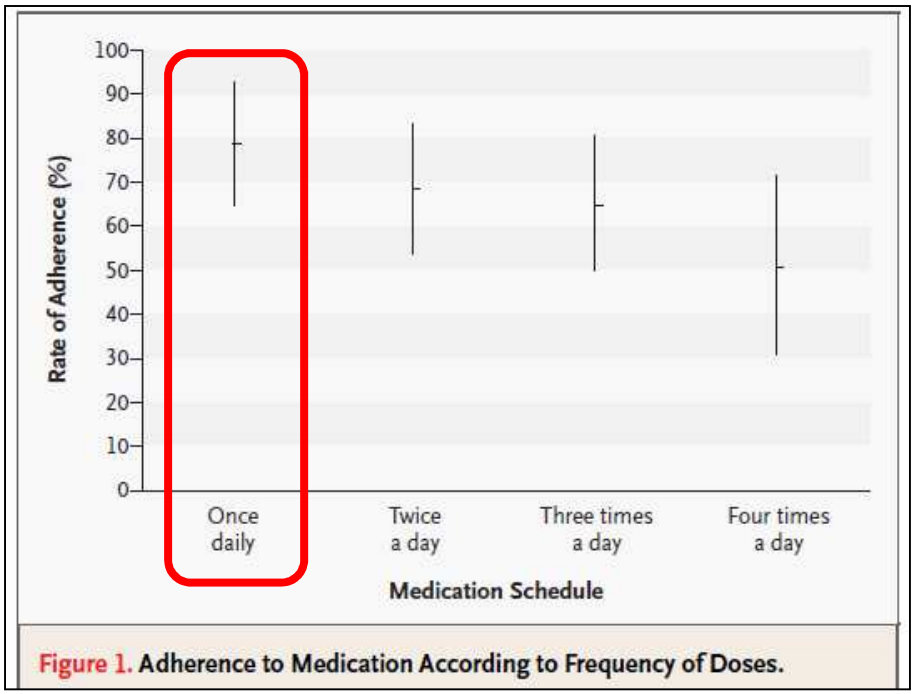


Figure 1. Adherence to Medication According to Frequency of Doses.

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

DRUG THERAPY

Adherence to Medication

Osterberg L et al. N Engl J Med 2005

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Patient Preference and Adherence

Patient Preference and Adherence

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Open Access Full Text Article

ORIGINAL RESEARCH

Impact of reducing dosing frequency on adherence to oral therapies: a literature review and meta-analysis

This article was published in the following Dove Press journal:
Patient Preference and Adherence
21 May 2013
Number of times this article has been viewed

Kunal Srivastava[1]
Anamika Arora[1]
Aditi Kataria[1]
Joseph C Cappelleri[2]
Alesia Sadosky[3]
Andrew M Peterson[4]

[1]HERON Health PVT, Chandigarh, India; [2]Pfizer Inc, Statistics, Groton, CT, USA; [3]Pfizer Inc Global Health Economics and Outcomes Research, New York, NY, USA; [4]Mayes College of Healthcare Business and Policy, University of the Sciences, Philadelphia, PA, USA

Objectives: To assess the impact of reduced frequency of oral therapies from multiple-dosing schedules to a once-daily (OD) dosing schedule on adherence, compliance, persistence, and associated economic impact.

Methods: A meta-analysis was performed based on relevant articles identified from a comprehensive literature review using MEDLINE® and Embase®. The review included studies assessing adherence with OD, twice-daily (BID), thrice-daily (TID), and four-times daily (QID) dosing schedules and costs associated with optimal/suboptimal adherence among patients with acute and chronic diseases. Effect estimates across studies were pooled and analyzed using the DerSimonian and Laird random-effect model.

Results: Forty-three studies met inclusion criteria, and meta-analyzable data were available from 13 studies. The overall results indicated that OD schedules were associated with higher adherence rates (odds ratio [OR] 3.07, 95% confidence interval [CI] 1.80–5.23; $P < 0.001$ for OD versus > OD dosing) and compliance rates (OR 3.50, 95% CI 1.73–7.08; $P < 0.001$ for

Srivastava et al. Pat Pref Adh 2013

Conclusion: Current meta-analyses suggested that across acute and chronic disease states, reducing dosage frequency from multiple dosing to OD dosing may improve adherence to therapies among patients. Improving adherence may result in subsequent decreases in health care costs.

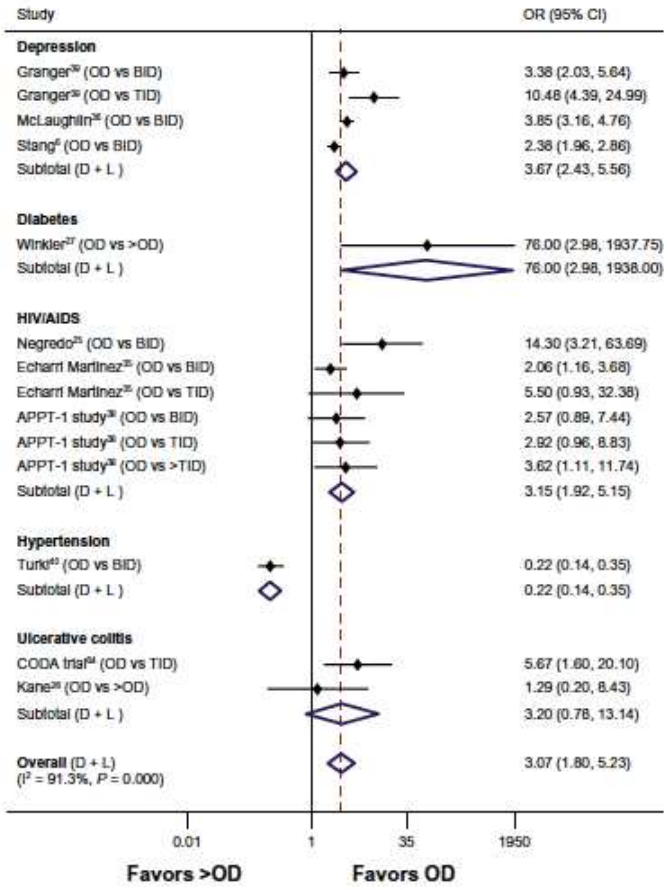


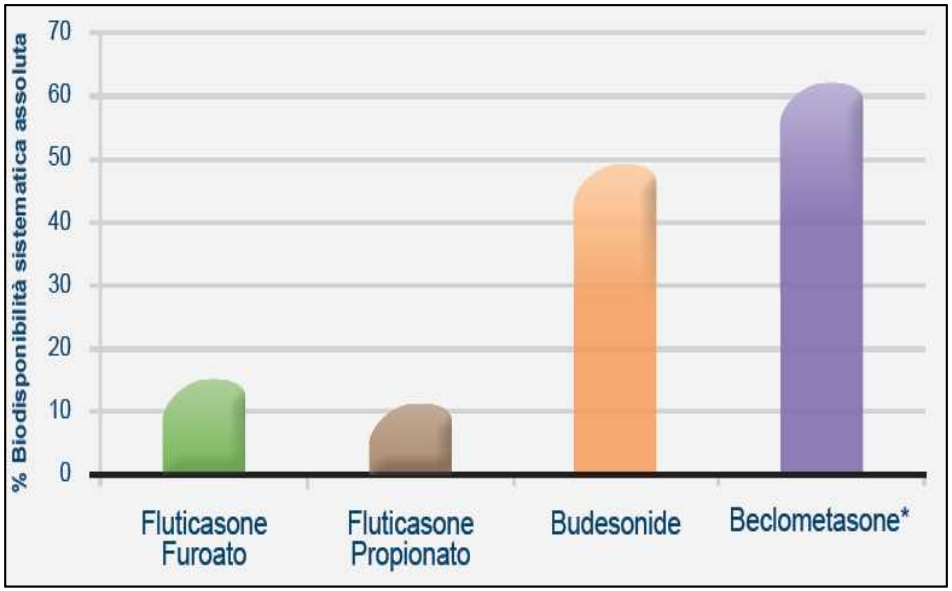
Figure 2 Forest plot of the odds ratios and 95% CIs for adherence rates associated with dosing schedules (once daily versus > once daily) of medications in all diseases.
Note: The broken line indicates overall effect relative to the comparator.
Abbreviations: BID, twice daily; CI, confidence interval; D + L, DerSimonian and Laird technique for meta-analysis; OD, once daily; OR, odds ratio; TID, three times daily; vs, versus; I^2, statistical heterogeneity.

Srivastava et al.
Pat Pref Adh 2013

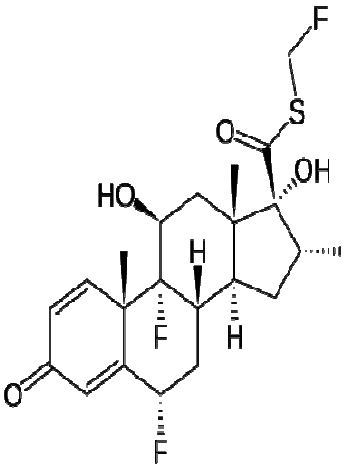
Side effects fear

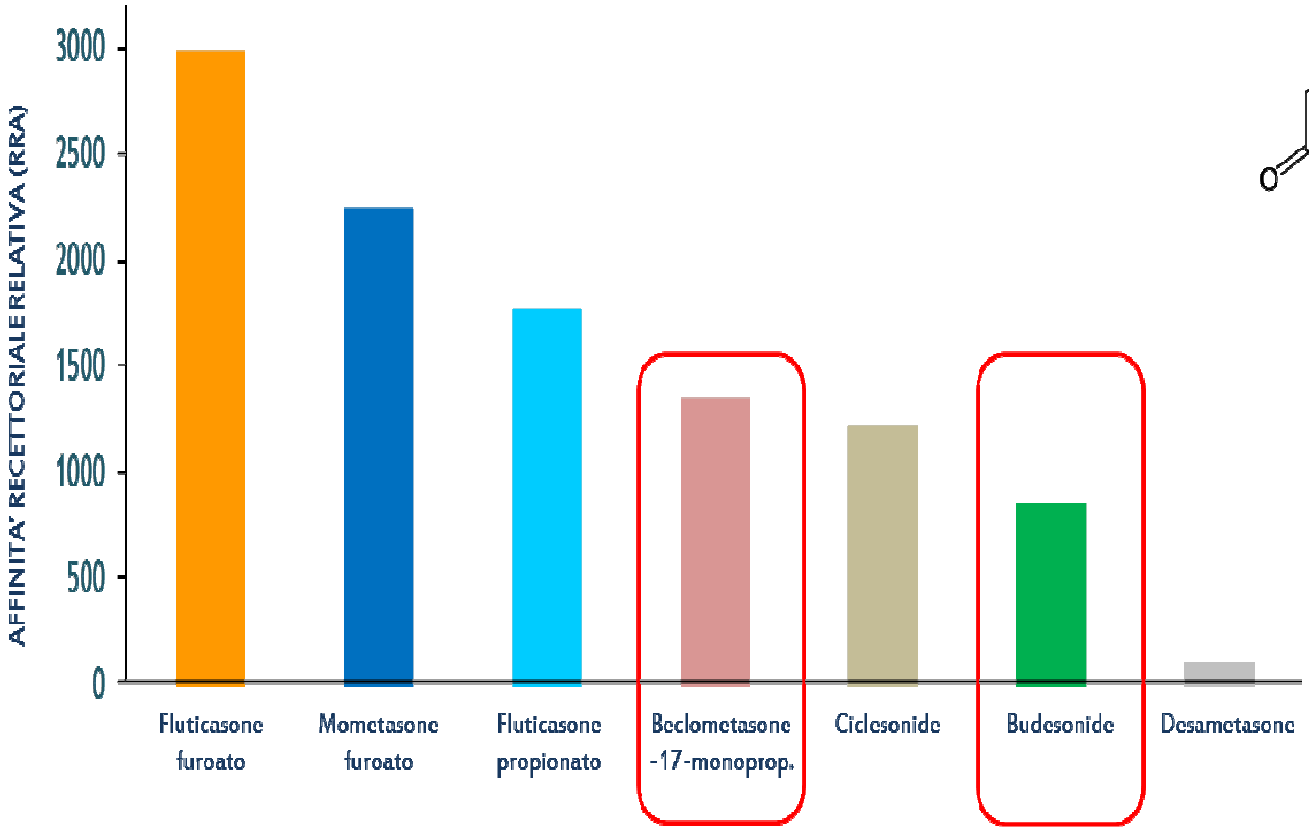
Fluticasone propionate to Fluticasone furoate

500-1000 mcg to 92 mcg daily



FLUTICASONE FUROATE (FF): receptor affinity





Valotis et al. *Respiratory Research (2007). Elaborazione grafica da testo.*

Simplest treatment schedule

1 drug = 1 schedule

Drug intake associated with ritual actions (wake up, tooth brushing, breakfast etc).

Brooks TL et al. *J Gen Intern Med 2014*

npj | Primary Care Respiratory Medicine

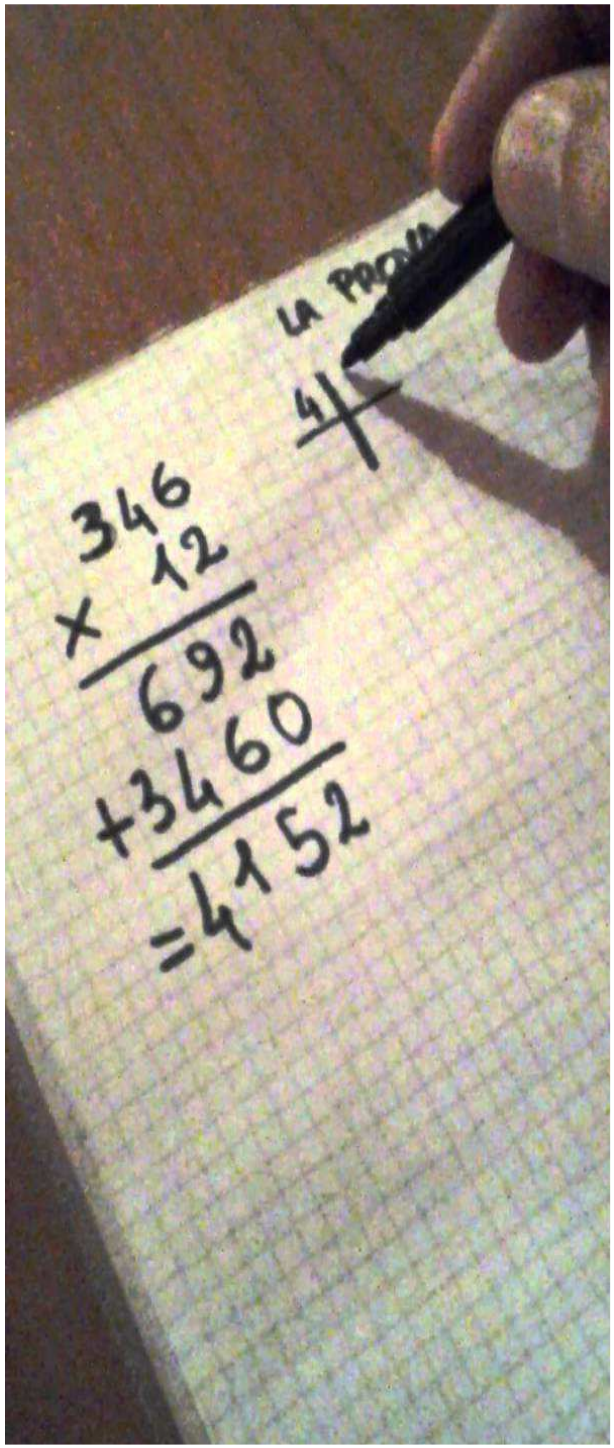
www.nature.com/npjpcrm

ARTICLE OPEN

The frequency of, and adherence to, single maintenance and reliever therapy instructions in asthma: a descriptive analysis

Rachael L DiSantostefano[1], Nada Boudiaf[2], David A Stempel[3], Neil C Barnes[4] and Andrew P Greening[4]

Luglio 2016



npj | Primary Care Respiratory Medicine

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*Analisi descrittiva condotta in UK, su un database di **14,000** paz, che ha valutato la frequenza d'uso della posologia SMART, l'aderenza e l'uso di SABA vs terapia regolare*

Luglio 2016

Il paziente è poco aderente alla terapia indipendentemente dalla posologia prescritta:

N°/anno di confezioni <5

Table 3. SABA (rescue medication) and BFC use by dosing instructions

	SMART dosing instructions	*Maintenance dosing instructions*
	N = *173*	N = *14,645*
SABA in the year following index date (includes index date) n (%):		
No prescription	82 (47.4)	2,677 (18.3)
Prescription	91 (52.6)	11,968 (81.7)
SABA on the index date n (%)		
No prescription	146 (84.4)	8,457 (57.8)
Prescription	27 (15.6)	6,188 (42.3)
Total users of SABA	N = *91*	N = *11,968*
Mean number of inhalers in year (s.d.)	5.7 (6.0)	5.5 (5.1)
Median	3	4
Min, max[a]	1, 40	1, 64
Total users of BFC	N = *173*	N = *14,645*
Mean number of inhalers in year (s.d.)	4.7 (4.3)	4.8 (3.6)
Median	4	4
Min, max[a]	1, 35	1, 36

npj | Primary Care Respiratory Medicine www.nature.com/npjpcrm

ARTICLE OPEN

The frequency of, and adherence to, single maintenance and reliever therapy instructions in asthma: a descriptive analysis

Rachael L DiSantostefano[1], Nada Boudiaf[2], David A Stempel[3], Neil C Barnes[4] and Andrew P Greening[4]

Il **53%** dei pazienti asmatici trattati con posologia

regolare + al bisogno con lo stesso inalatore

utilizza anche un **SABA**

Table 3. SABA (rescue medication) and BFC use by dosing instructions

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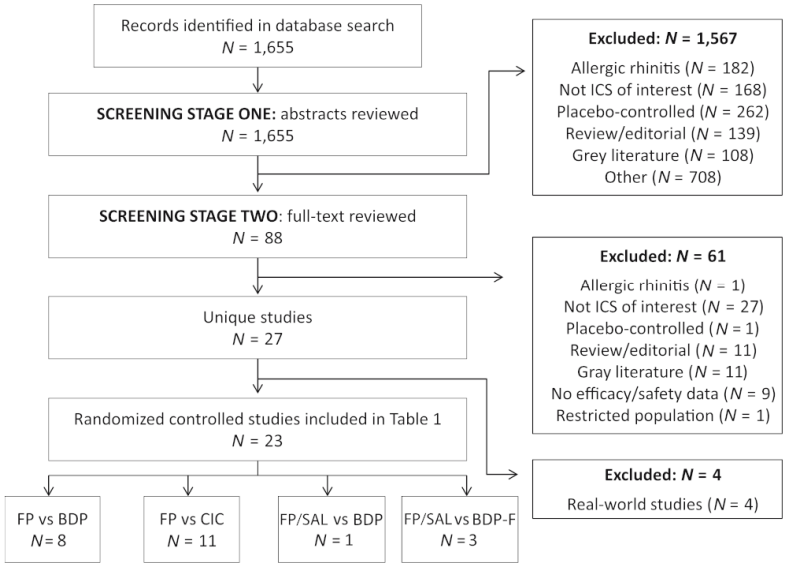
Min, max[a]	1, 35	1, 36

RESEARCH ARTICLE Open Access

Effect of inhaled corticosteroid particle size on asthma efficacy and safety outcomes: a systematic literature review and meta-analysis

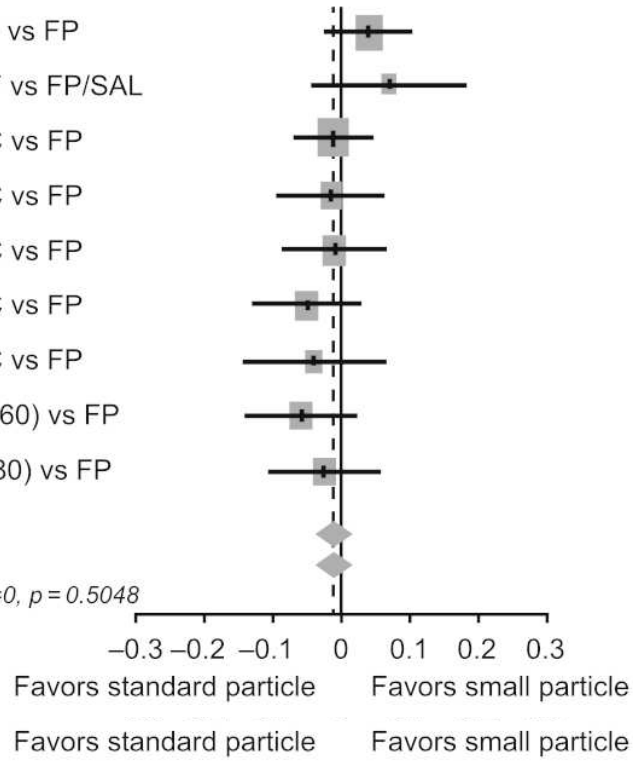
Céline El Baou[1,11*], Rachael L. Di Santostefano[2,9], Rafael Alfonso-Cristancho[3,4], Elizabeth A Suarez[5,10], David Stempel[2], Mark L Everard[6] and Neil Barnes[7,8]



FEV_1 (L) change from baseline between treatments

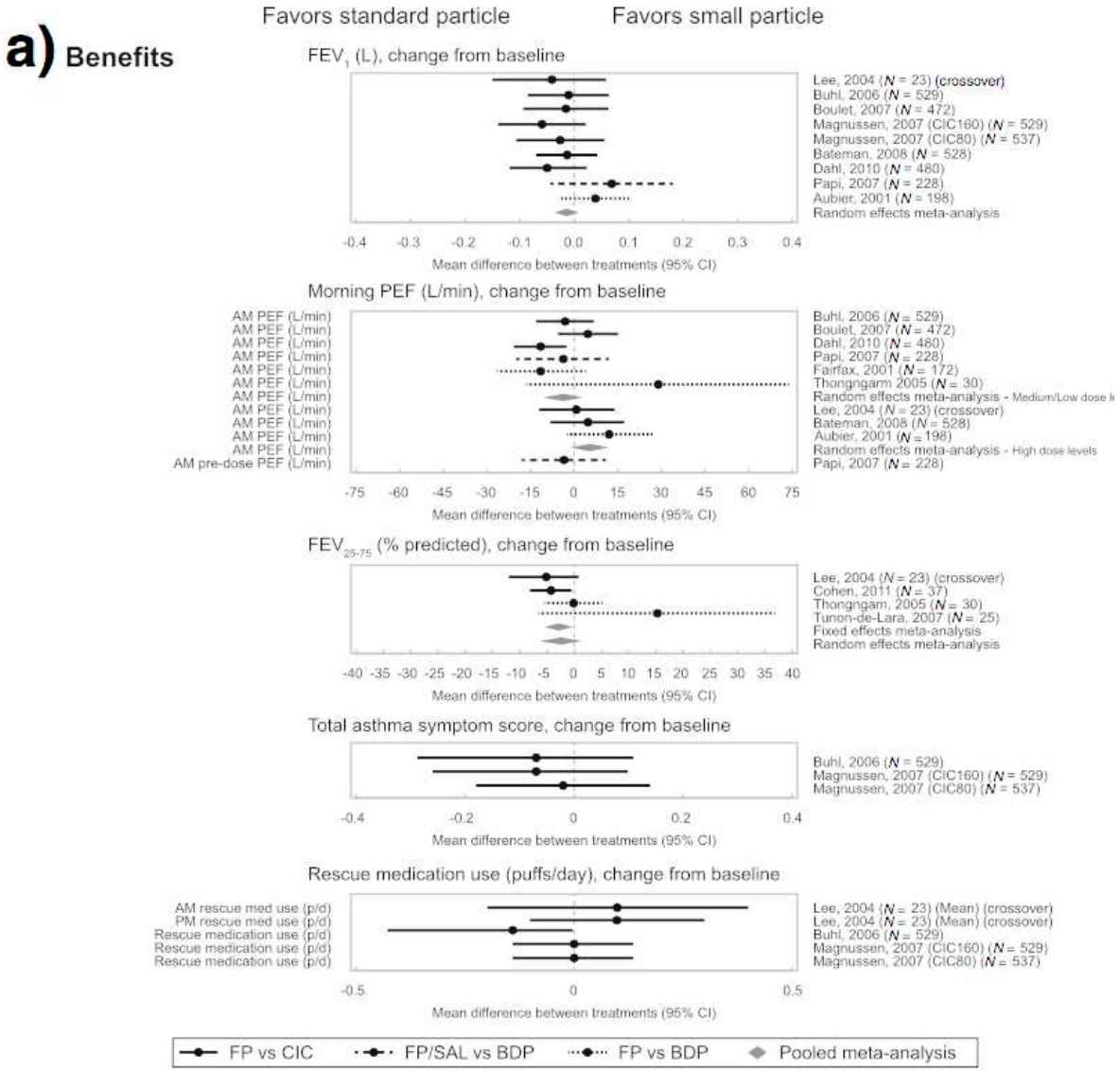
Study	*N*	Comparator	Mean difference (95% CI)		Weight, % (fixed)	Weight, % (random)
Aubier, 2001	198	BDP vs FP	0.040	[–0.022, 0.102]	16.7	16.7
Papi, 2007	228	BDP-F vs FP/SAL	0.070	[–0.043, 0.183]	5.1	5.1
Bateman, 2008	528	CIC vs FP	–0.013	[–0.070, 0.044]	20.0	20.0
Boulet, 2007	472	CIC vs FP	–0.015	[–0.093, 0.063]	10.5	10.5
Buhl, 2006	529	CIC vs FP	–0.010	[–0.086, 0.066]	11.3	11.3
Dahl, 2010	480	CIC vs FP	–0.050	[–0.128, 0.028]	10.5	10.5
Lee, 2004	23	CIC vs FP	–0.040	[–0.144, 0.064]	6.0	6.0
Magnussen, 2007	529	CIC (160) vs FP	–0.059	[–0.140, 0.022]	9.9	9.9
Magnussen, 2007	537	CIC (80) vs FP	–0.025	[–0.106, 0.056]	9.9	9.9
Fixed effect model			**–0.011**	**[–0.037, 0.014]**	**100**	**--**
Random effects model			**–0.011**	**[–0.037, 0.014]**	**--**	**100**

Heterogeneity: I–squared=0%, tau–squared=0, p = 0.5048



Favors standard particle
Favors small particle

Benefit-risk plot in adolescents and adults by particle size.



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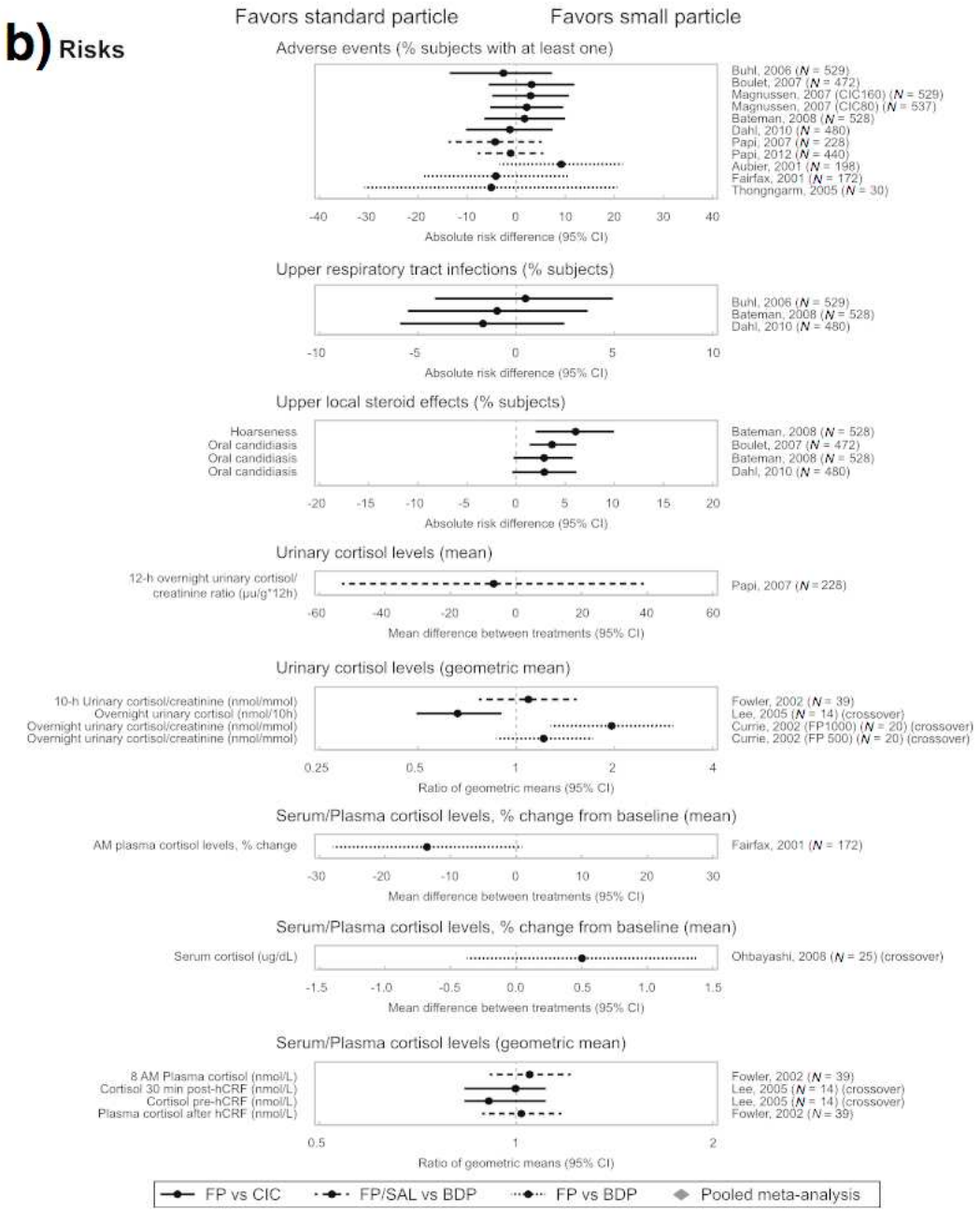

Come scegliere la terapia:
Focus sull'associazione Fluticasone furoato/vilanterolo

Farmaco o associazione di farmaci in grado di garantire il miglior controllo possibIle

Farmaco o associazione di farmaci in grado di garantire da incontrare le esigenze dei pazienti:

- Rapidità d'azione
- Indipendenza dell'effetto dall'ora di assunzione
- Lunga durata d'azione
- Bassa esposizione farmacologica
- Iper-semplificazione dello schema terapeutico

Come scegliere la terapia:
Focus sull'associazione Fluticasone furoato/vilanterolo

Fulvio Braido

Allergy and Respiratory Diseases Department
University of Genoa