Indacaterol: Maximizing bronchodilation in COPD

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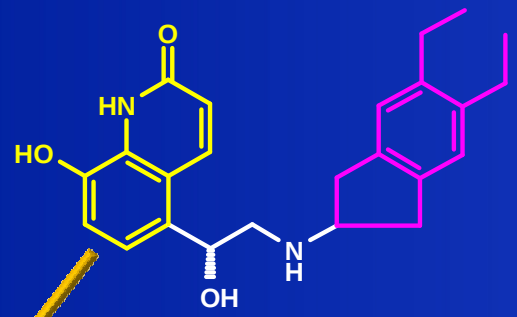


New drug

Manufacturer

Research, clinical trials

Negotiation

Payers

Regulatory Authorities

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

What's more important for drug effectiveness in COPD ?

Lung function parameters (e.g. FEV1)

or

Patient centered outcomes ?

or

Both ?

Different outcome parameters

Surrogate

- FEV1
- FVC, RV
- Exercise parameters (?)
- 6-Minute walking distance
- Biomarkers (serum, breath, sputum, biopsies, urine)
- pO2 / pCO2
- Combined parameters (BODE)
- Time to first exacerbation (?)

Patient centered outcome

- Mortality
- COPD-Exacerbation rate
- Hospitalization
- QoL (e.g. SGRQ*)
- Dyspnoea (TDI, Borg*)

**Problem*: Acceptance of questionnaire be authorities ?

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

FDA

Regulatory Authorities Require

Lung function data

Payers Require

Patient centered outcomes

Indacaterol

Lung function

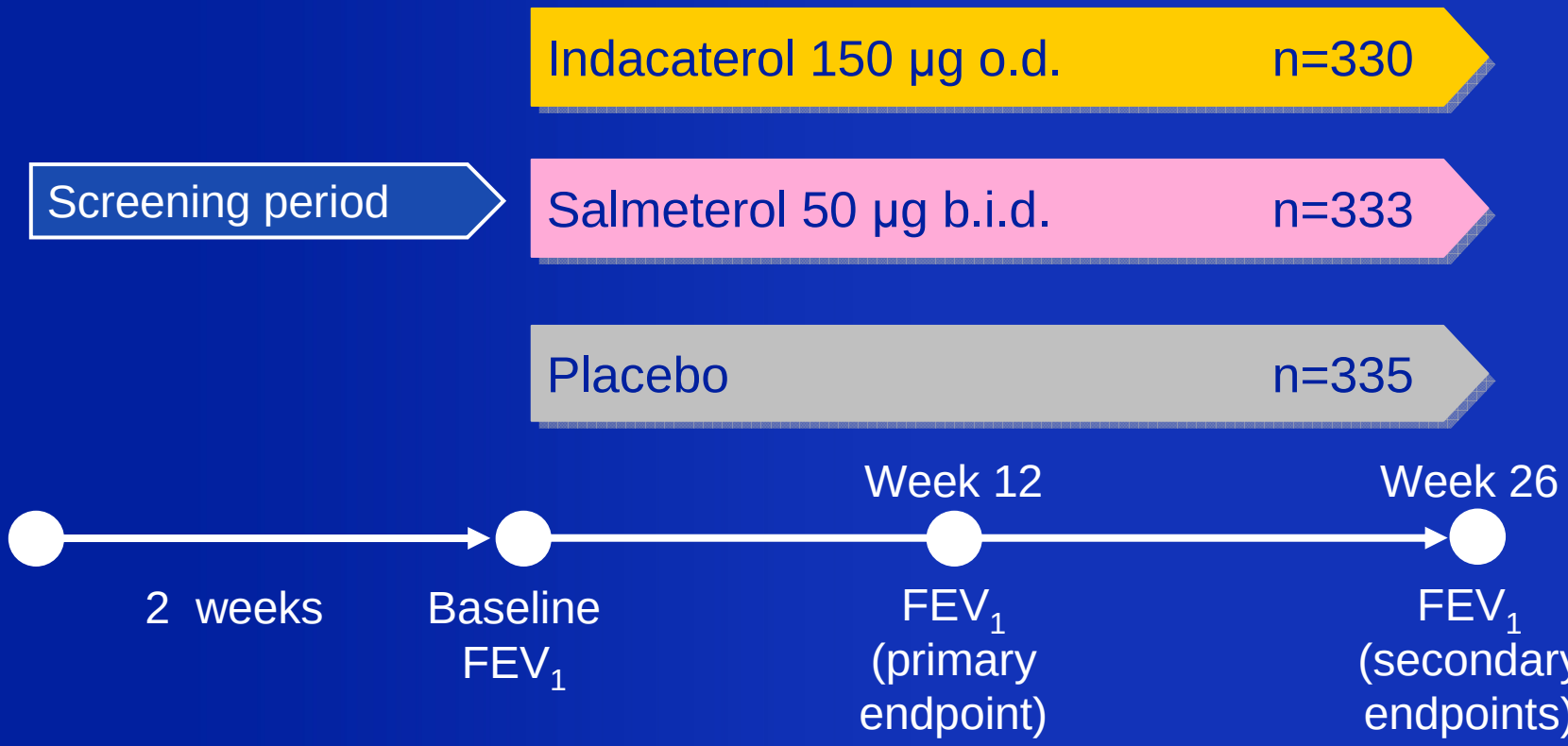
Indacaterol vs Salmeterol

INLIGHT 2

26-week efficacy and safety

Kornmann et al. Eur Respir J 37:273-279, 2011

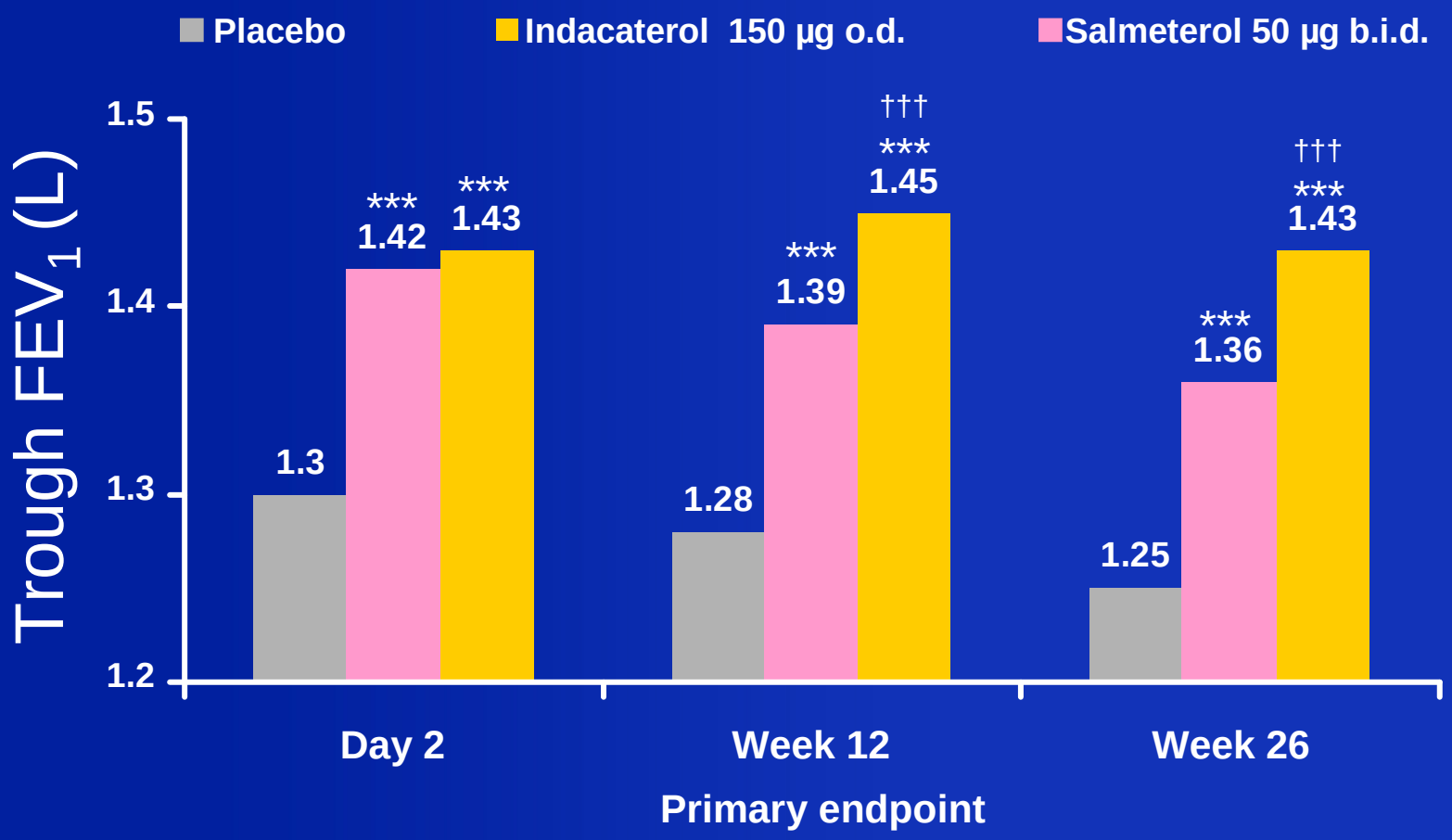
Double-blind, double-dummy, randomized, placebo-controlled, parallel-group study



INLIGHT 2

Indacaterol provided significant sustained improvement in trough FEV_1 over 26 weeks versus placebo and salmeterol

Kornmann et al. Eur Respir J 37:273-279, 2011

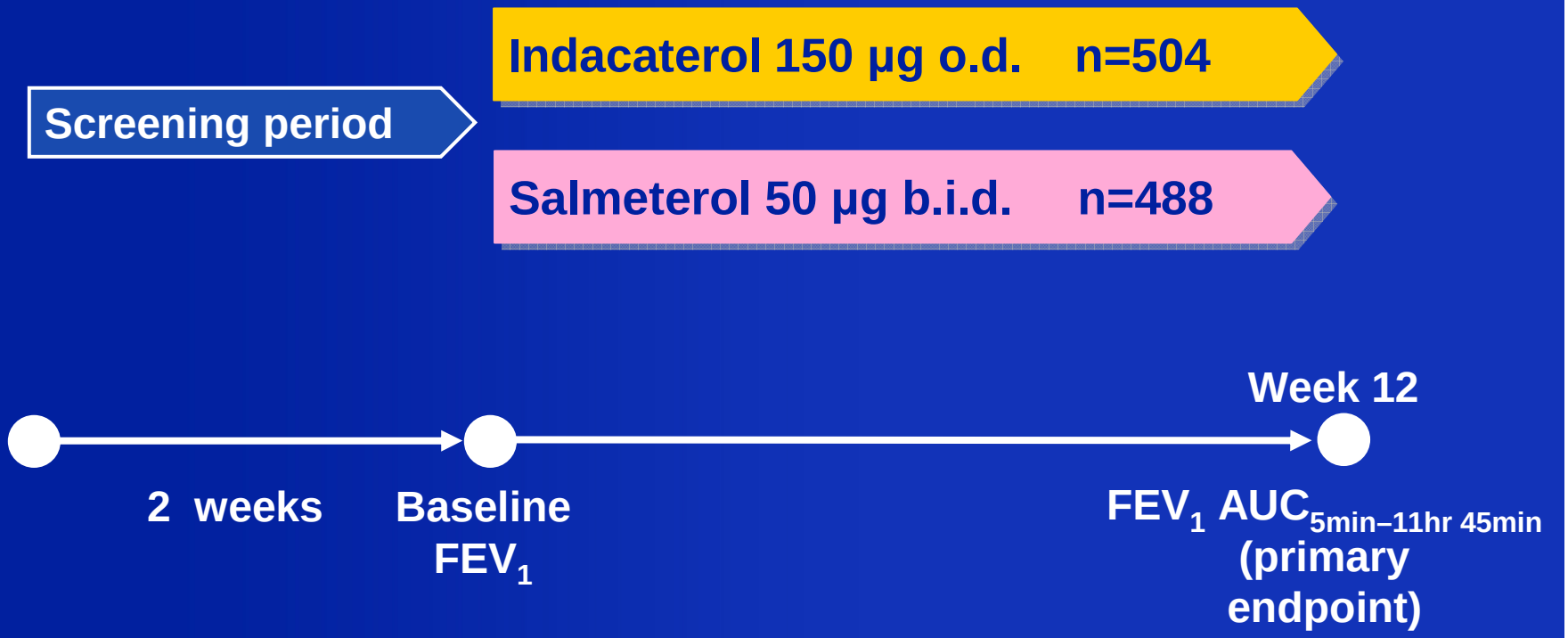


***p<0.001 vs placebo; †††p<0.001 vs salmeterol; Data are LSM

INSIST: 12-week efficacy and safety

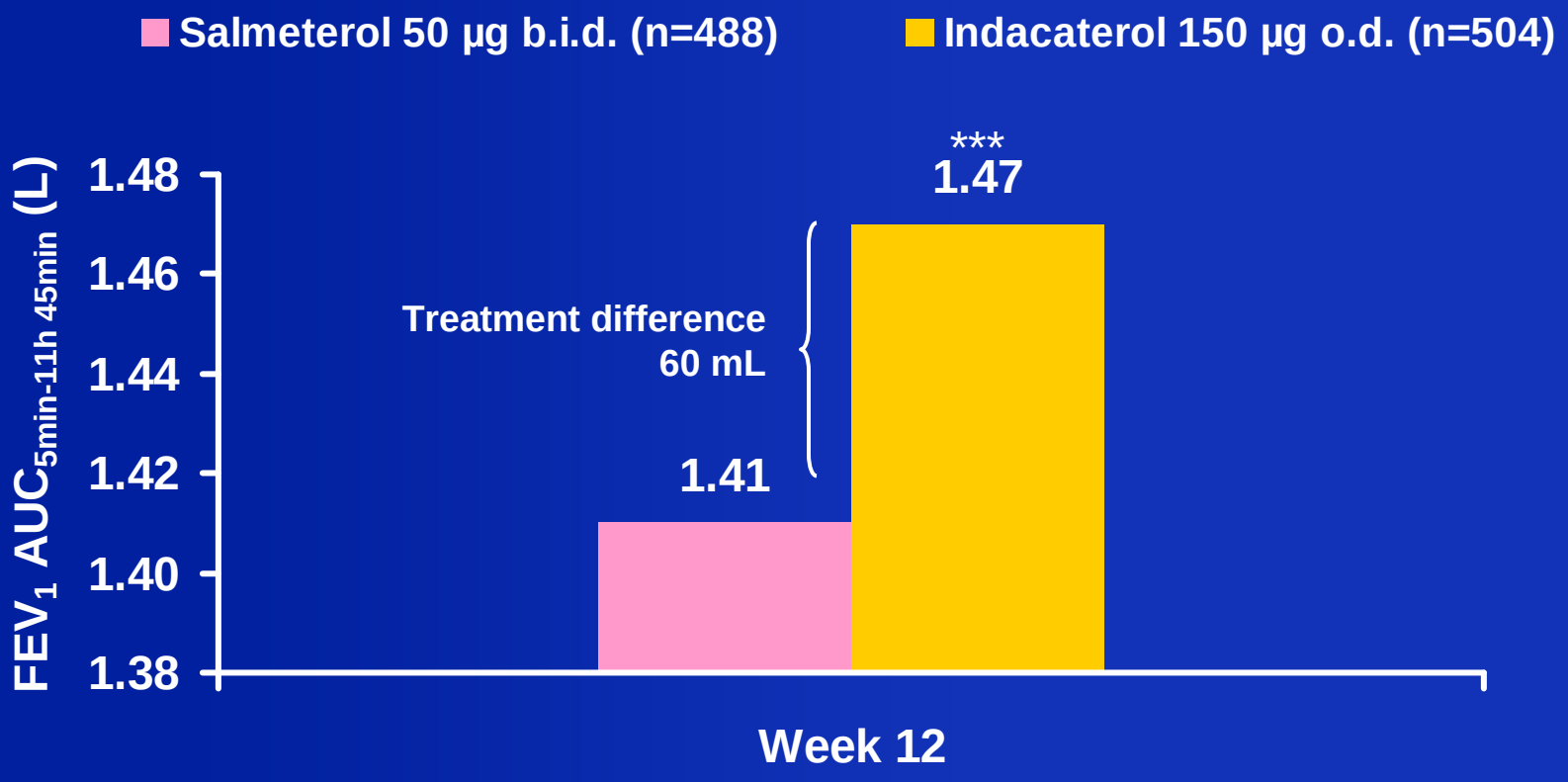
Korn et al. ERS 2010 (Abstract)

Double-blind, double-dummy, randomized, parallel-group study



Indacaterol improved FEV_1 AUC compared with salmeterol

Korn et al. ERS 2010 (Abstract)



***p<0.001 vs salmeterol. Data are LSM
AUC = area under the curve

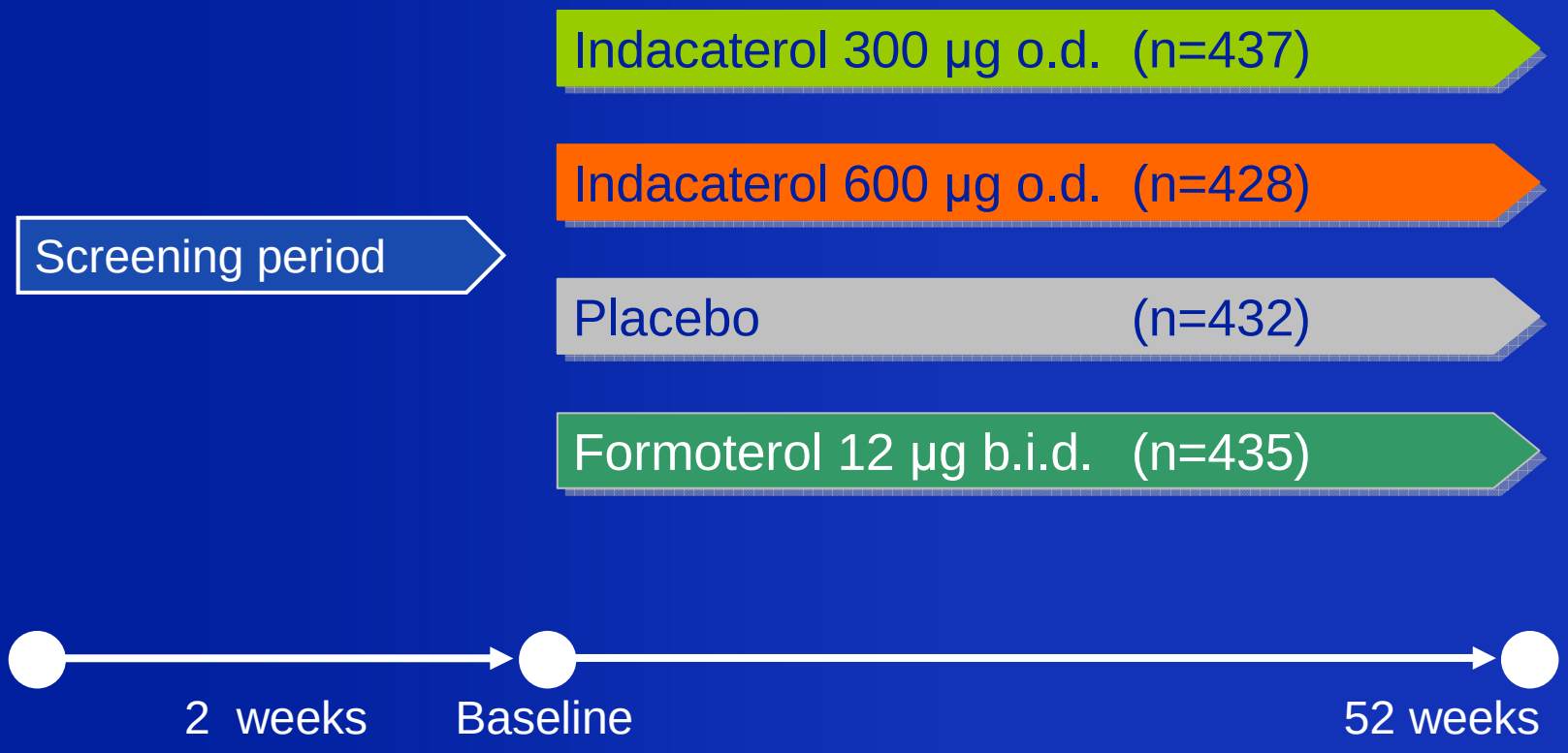
Indacaterol vs Formoterol

INVOLVE

52-week efficacy and safety

Dahl et al. Thorax 65:473-479, 2010

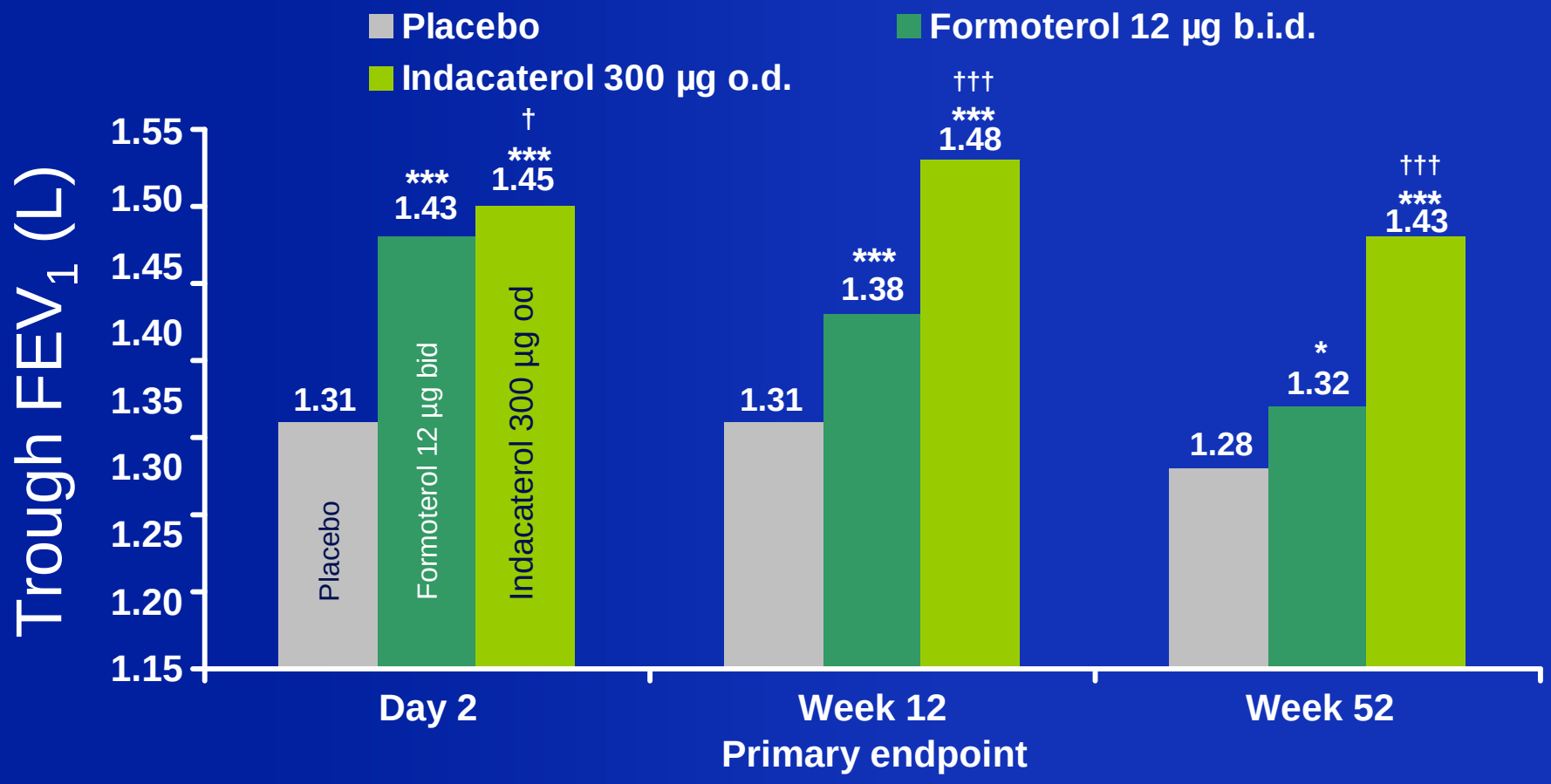
Double-blind, randomized, placebo-controlled, parallel-group study



Indacaterol 300 µg vs. Formoterol 12 µg

→ Superiority in trough FEV_1 over 52 weeks

Dahl et al. Thorax 65:473-479, 2010



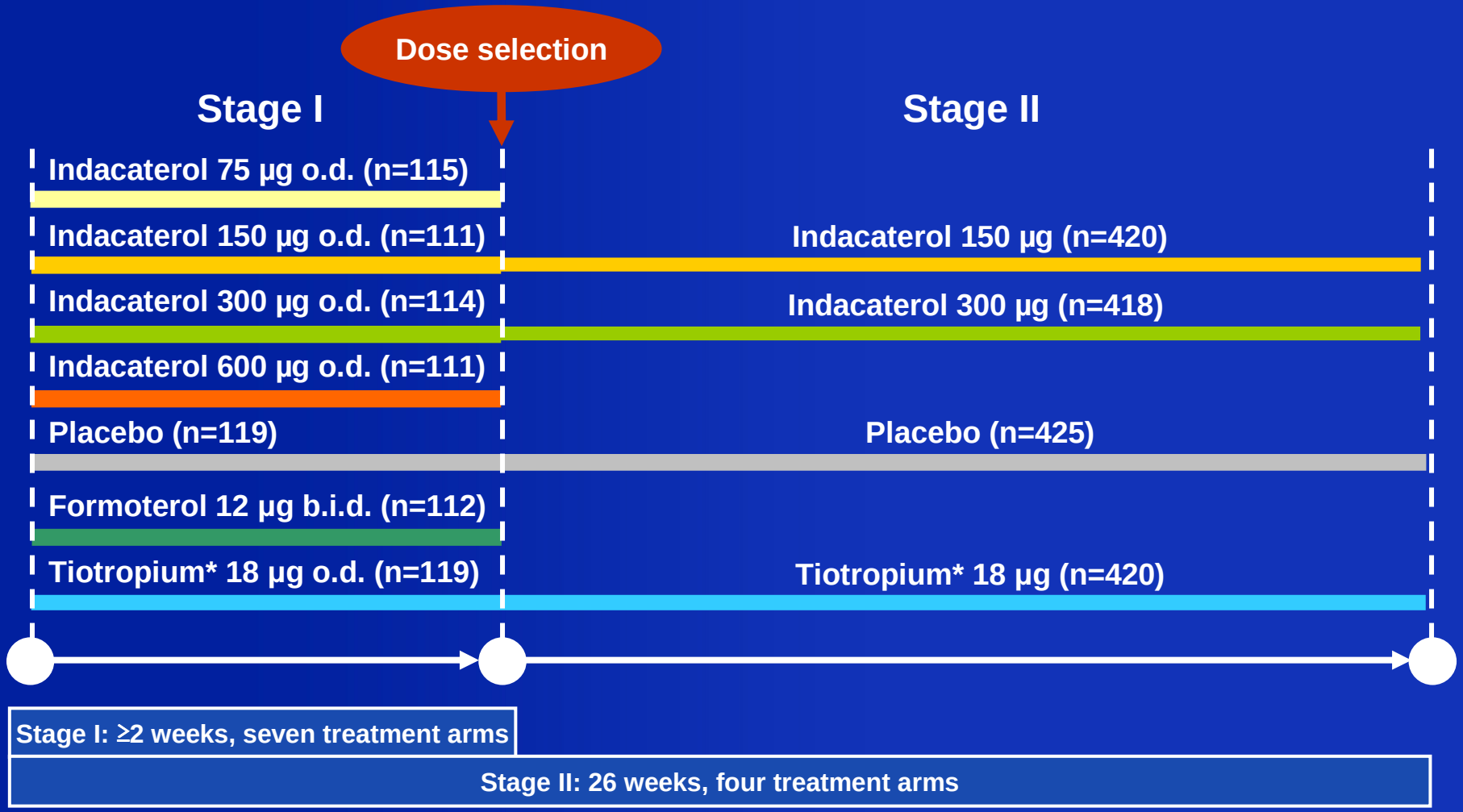
*p<0.05, ***p<0.001 vs placebo; †p<0.05, †††p<0.001 vs formoterol; Data are LSM in the modified intent-to-treat population
Trough = average of 23 h 10 min and 23 h 45 min post-dose values

Indacaterol vs Tiotropium

INHANCE

26-week efficacy and safety

Barnes et al PPT 23:165-171, 2010; Donohue et al AJRCCM 182:155-162, 2010

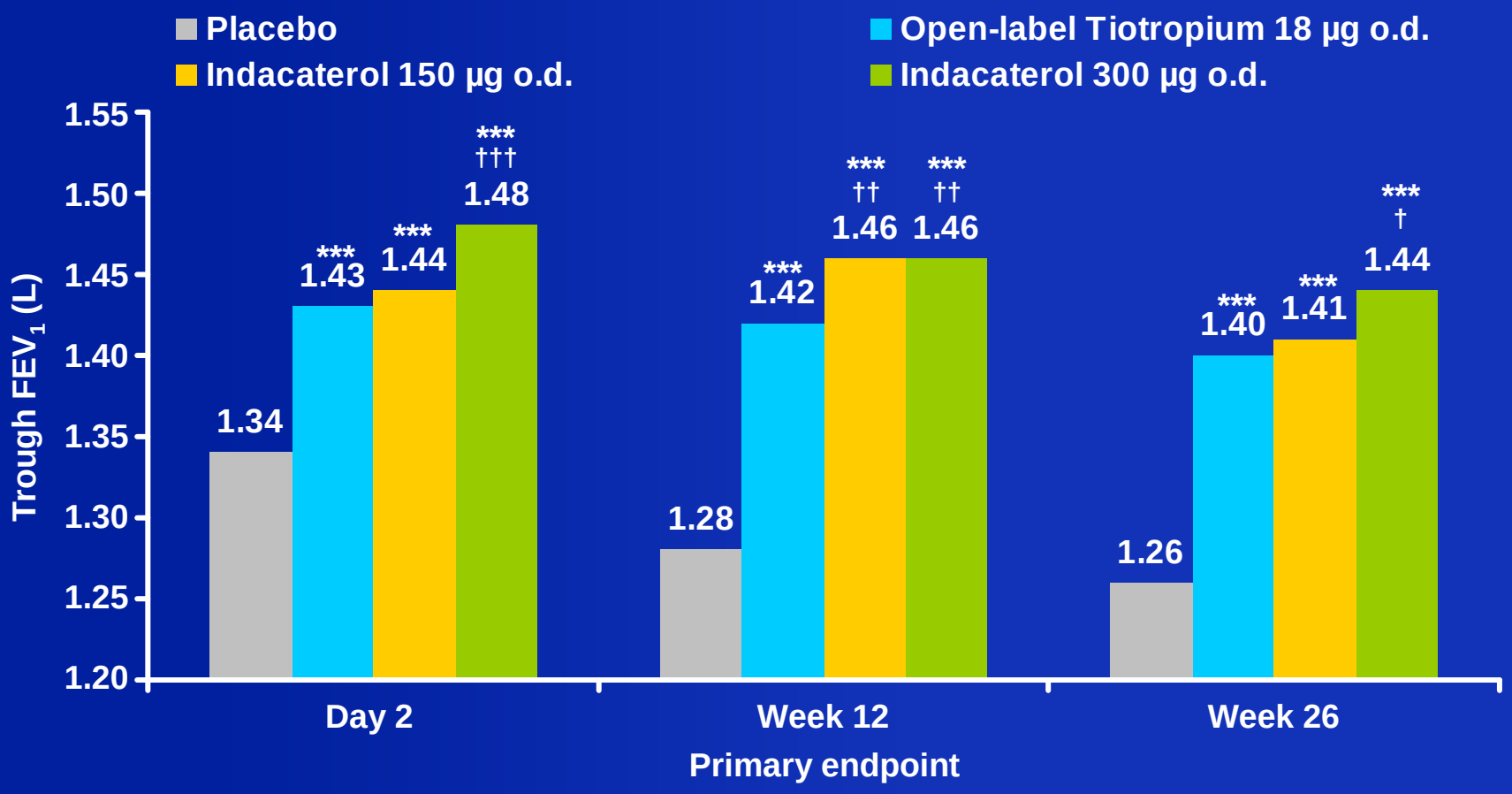


*Open-label. All drugs were delivered via proprietary single-dose dry powder inhalers

INHANCE

Indacaterol: improvement of FEV_1 over 26 weeks

Donohue et al AJRCCM 182:155-162, 2010

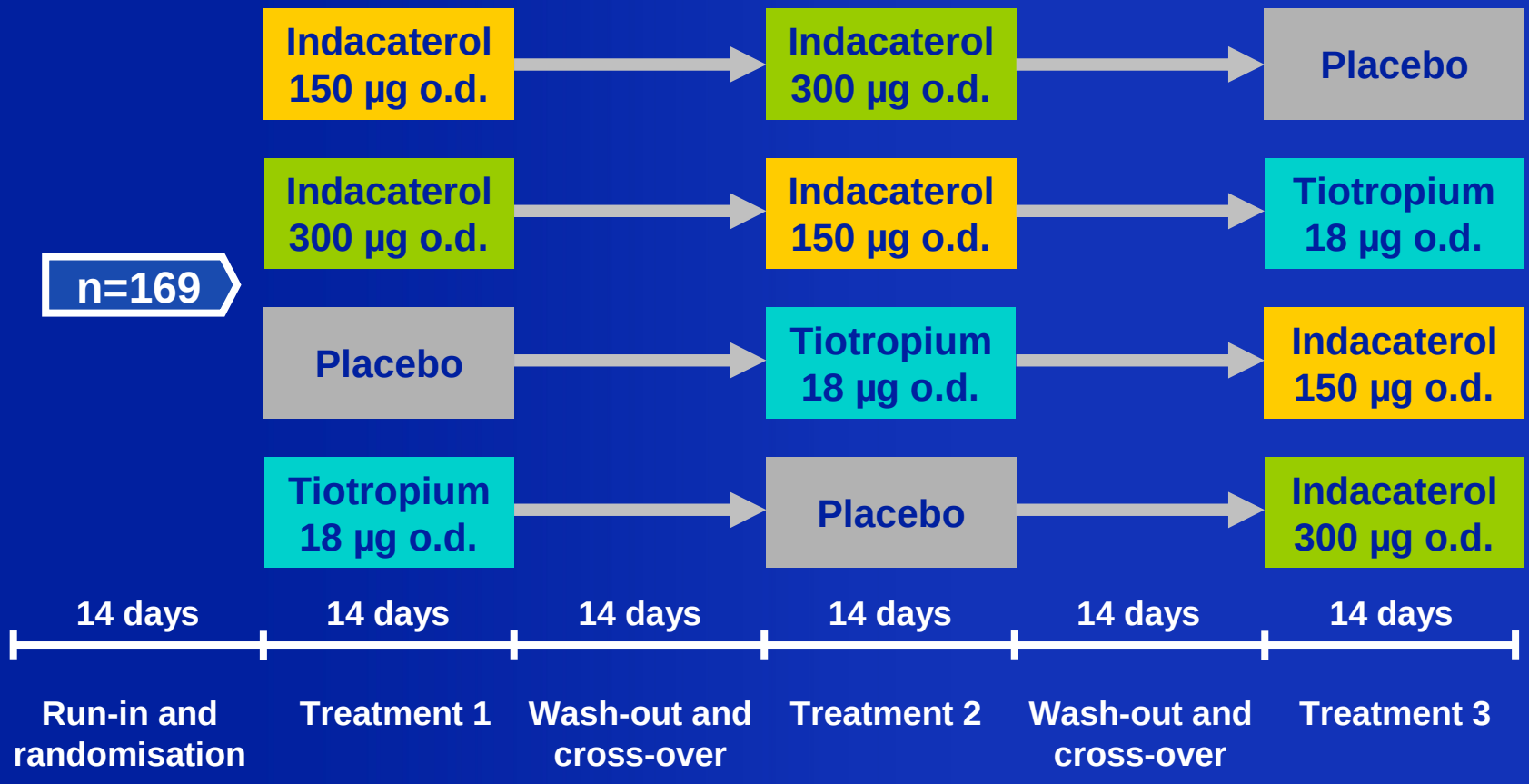


***p<0.001 vs placebo; †p<0.05, ††p≤0.01, †††p<0.001 vs tiotropium
Indacaterol-tiotropium comparisons are for superiority.
Data are LSM , Trough = average of 23 h 10 min and 23 h 45 min post-dose values

INTIME

14-day double-blind cross-over study

Vogelmeier et al. Respir Res 11:135, 2010

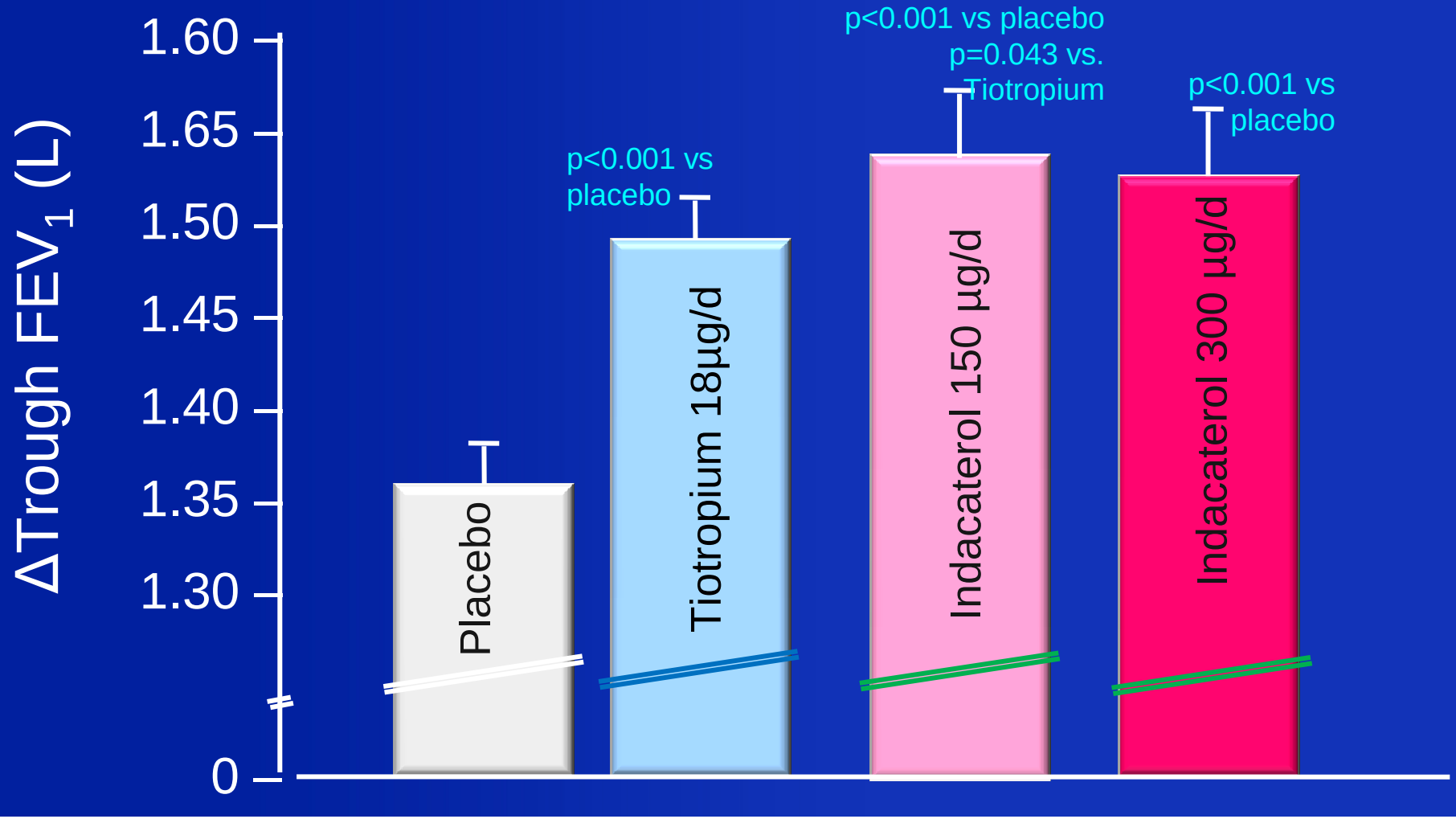


Study treatments taken via SDDPI

Indacaterol (150+300 µg vs. Tiotropium vs. Placebo) in COPD

Vogelmeier et al. Respir Res 11:135, 2010

moderate to severe COPD (n=69), FEV1 56%pred., 14 days cross-over (3 period), rand., placebo-controlled, multicenter

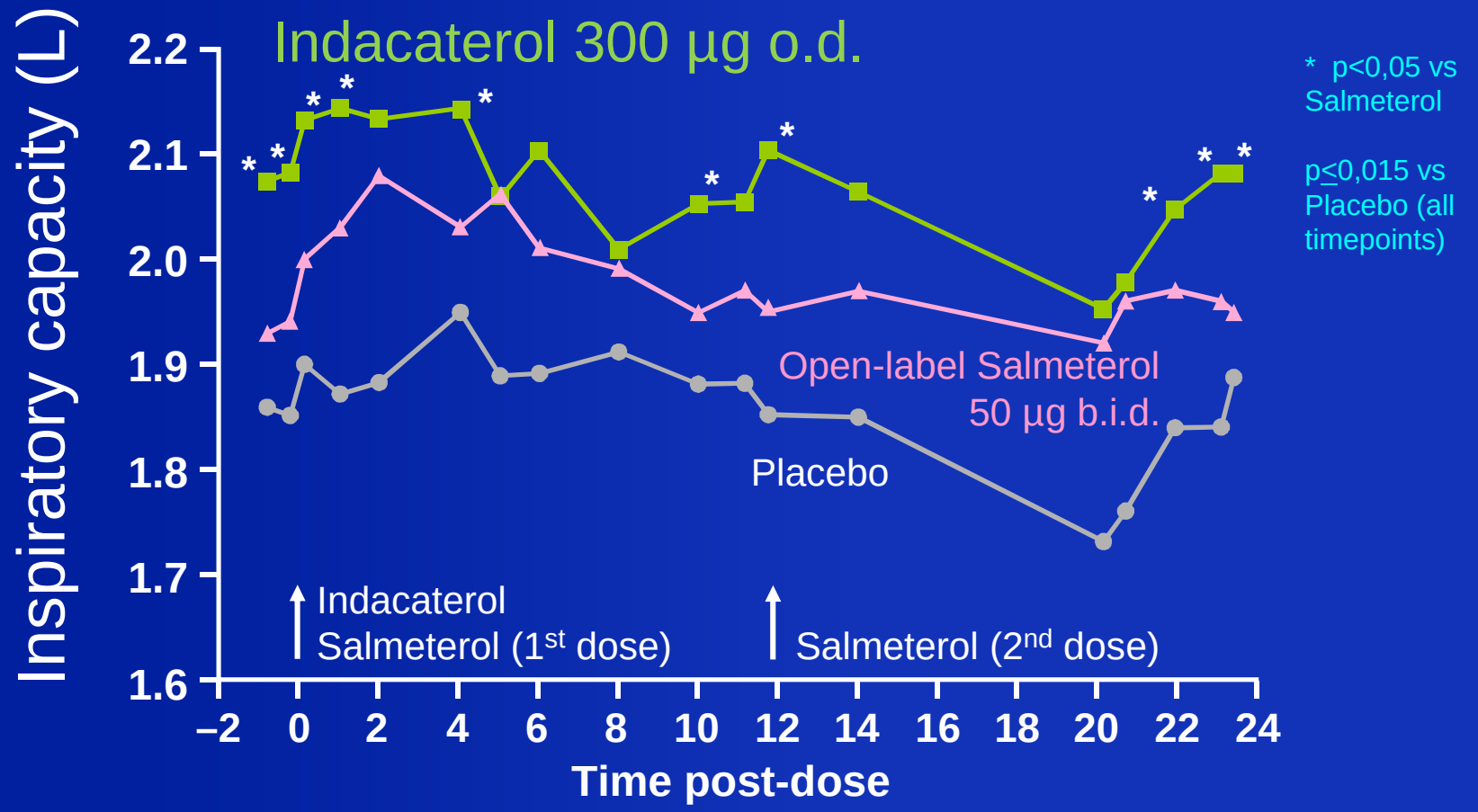


INTEGRAL

Indacaterol improved inspiratory capacity over 24 hr

LaForce et al Pulm Pharmacol Ther. 24:162-168, 2011

moderate to severe COPD (n=61), 14 days cross-over, rand., placebo-controlled, multicenter

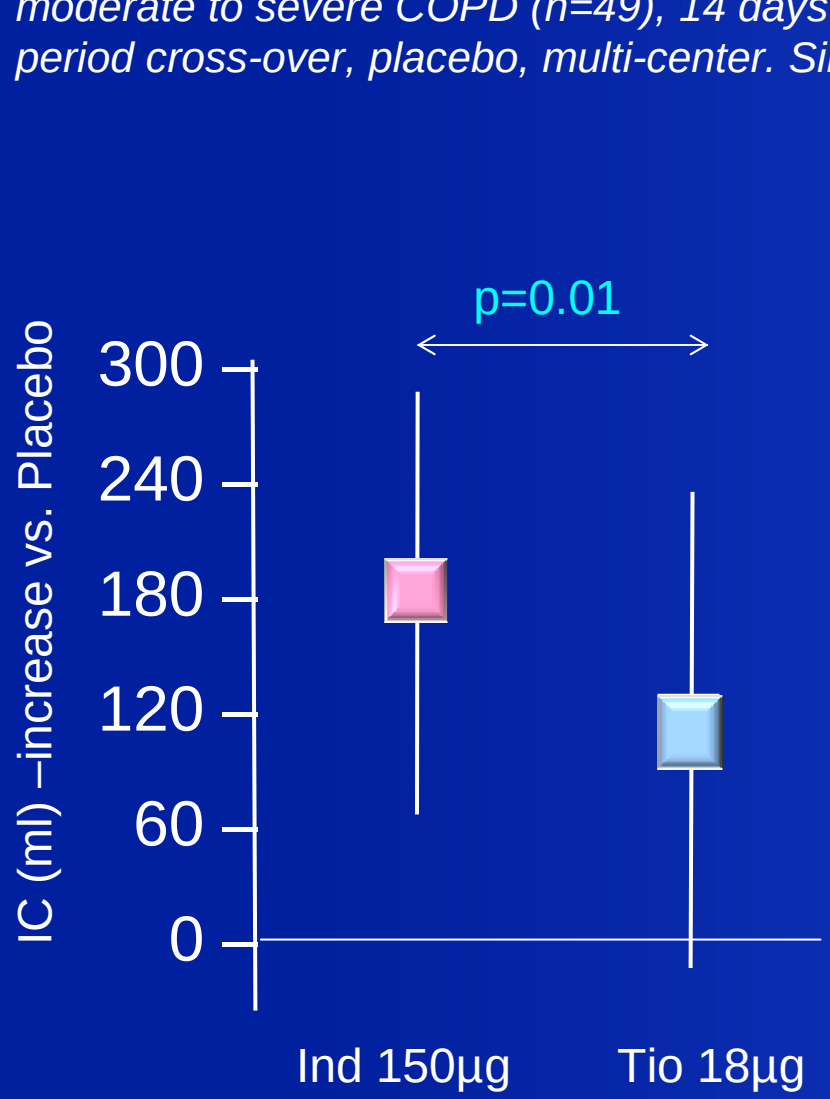


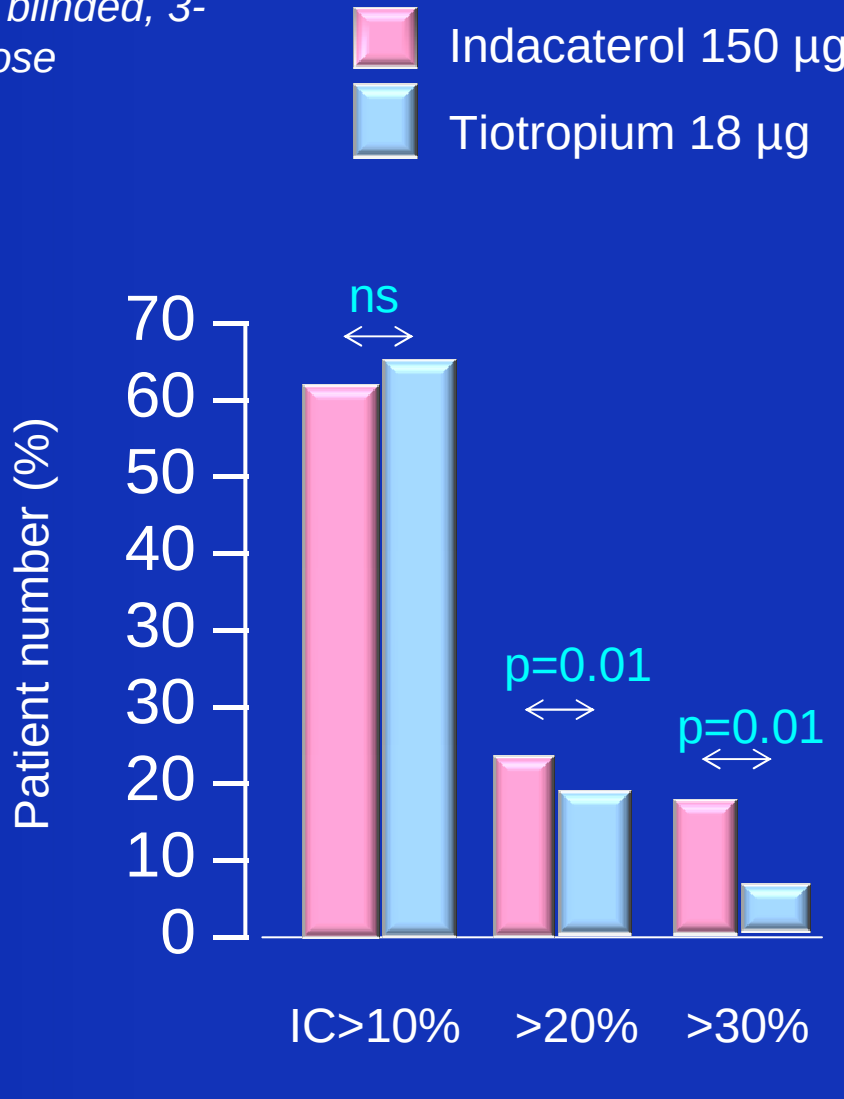
*p<0.05 indacaterol vs salmeterol; p≤0.015 for indacaterol vs placebo at all time points; p<0.05 for salmeterol vs placebo at all time points except –50 minutes, 3 hours, 8 hours, 10 hours, 11 hours 10 minutes and 23 hours 45 minutes. Data are LSM±SE

Indacaterol improved inspiratory capacity over 24 hr

Rossi Respir.Med., 2011 (online first)

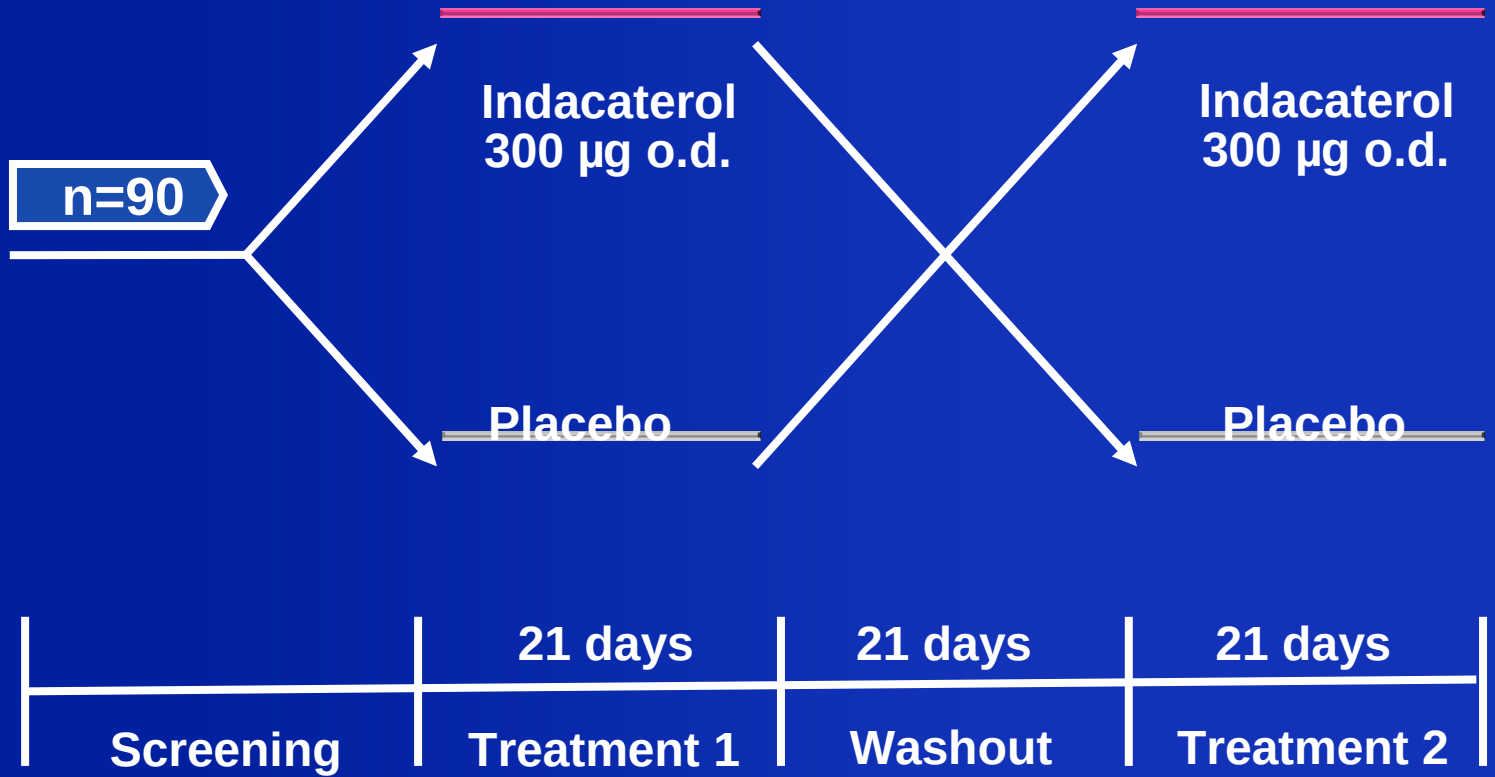
moderate to severe COPD (n=49), 14 days rand., blinded, 3-period cross-over, placebo, multi-center. Single dose





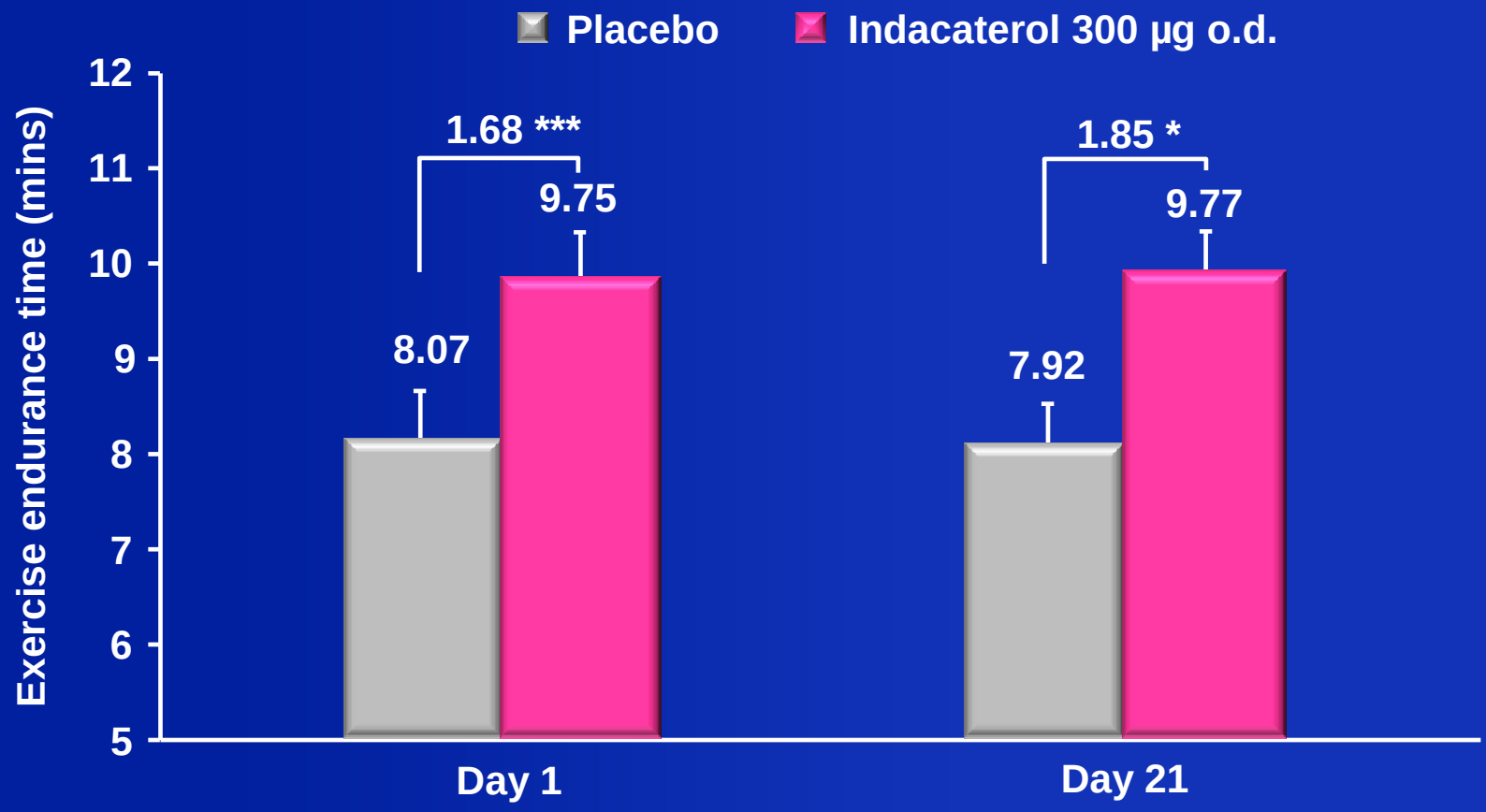
21-day exercise endurance study

O'Donnell et al. ATS 2010 (Abstract)

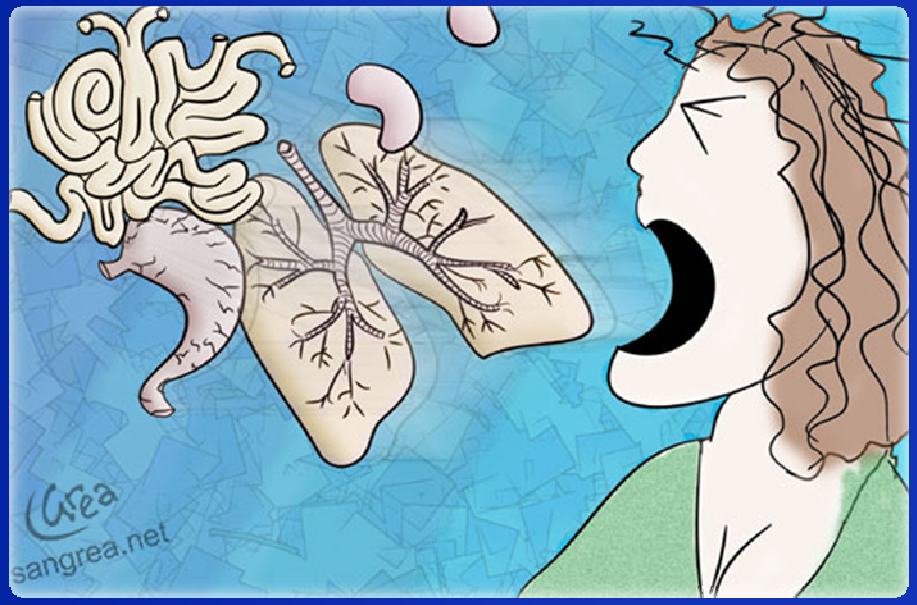


Indacaterol improved exercise endurance time on Days 1 and 21, compared with placebo

O'Donnell et al. ATS 2010 (Abstract)



*p=0.011, ***p<0.001 Data are LSM and SE



Control of symptoms and patient centered outcome parameters

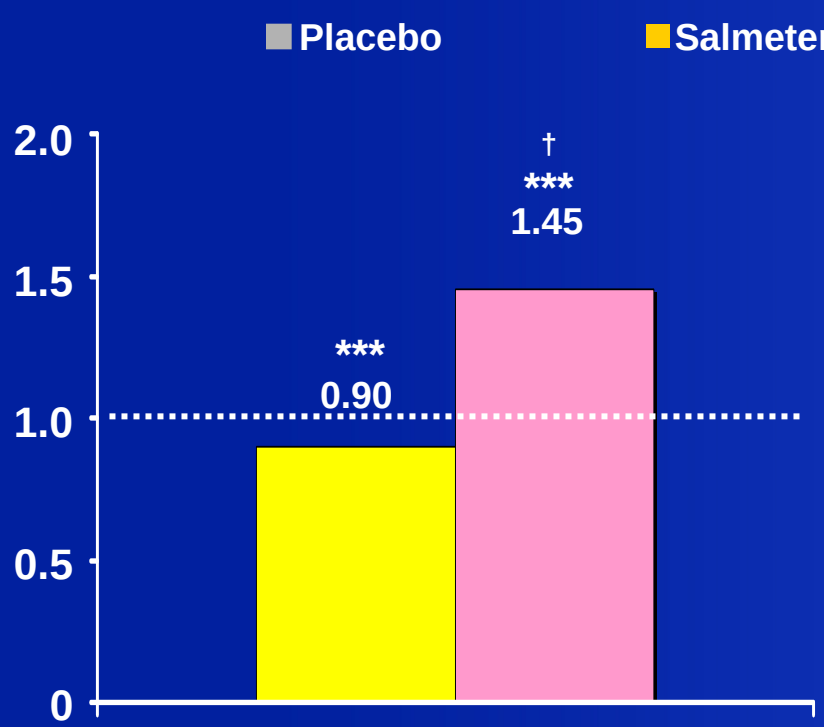
- ✓ Shortness of breath / dypnea
- ✓ QoL
- ✓ Rescue medication (short acting ß2-agonists)
- ✓ Exacerbations

INLIGHT 2

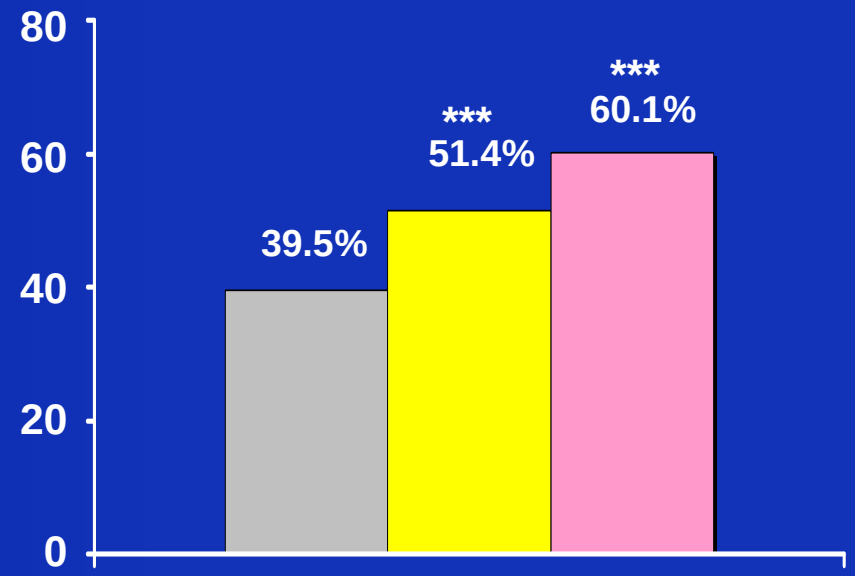
Indacaterol improves dyspnea (TDI total score) over 12 weeks

Kornmann et al. Eur Respir J 37:273-279, 2011

TDI total score versus placebo



Patients (%) with clinically important change (≥1 point) in TDI total score

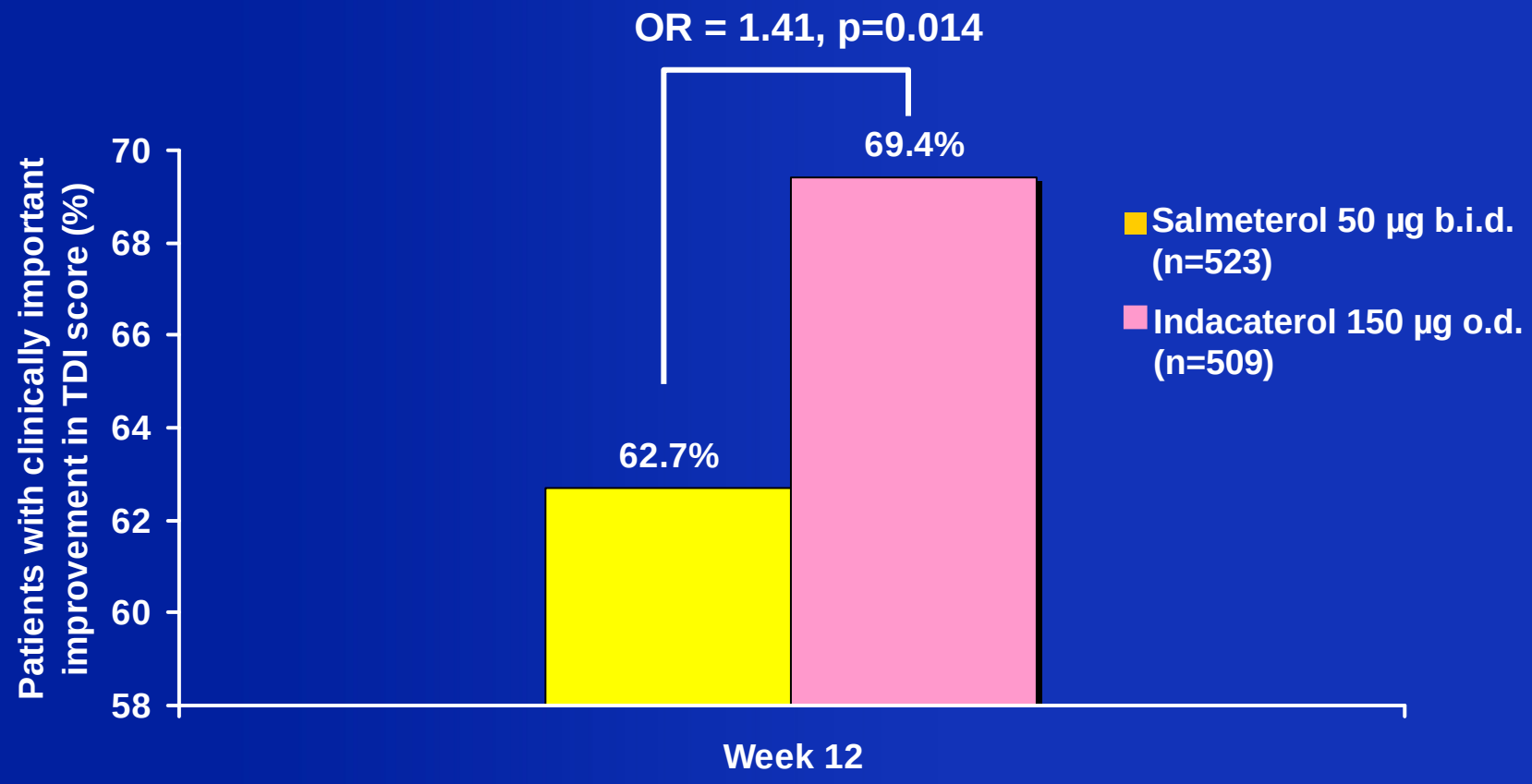


***p<0.001 vs placebo; ††p<0.01, †p<0.05 vs salmeterol, Data are LSM.
Difference of ≥1 = clinically important improvement in the Transition Dyspnoea Index (TDI) total score (dotted line)

INSIST

Indacaterol improves TDI dyspnea Index

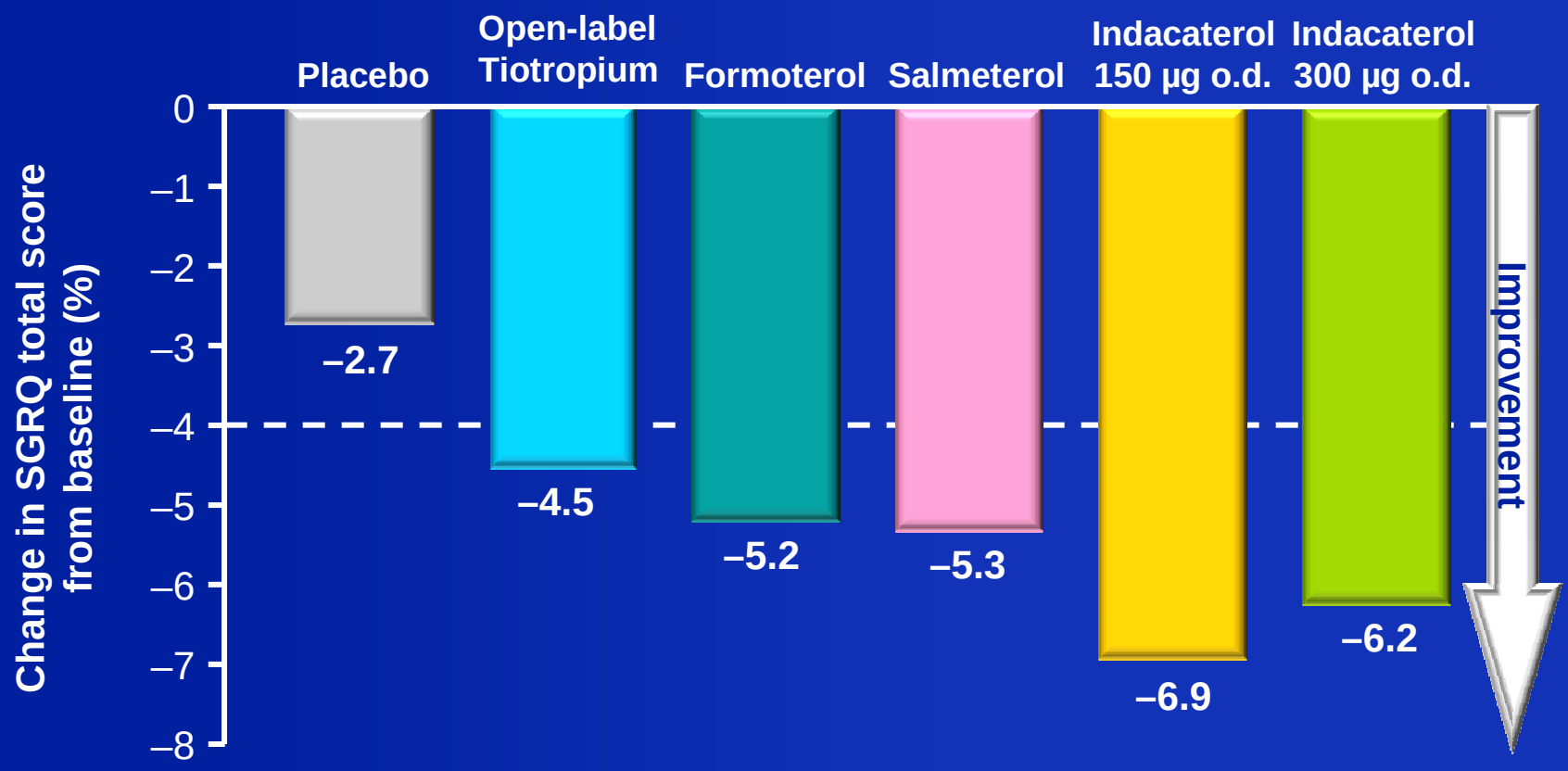
Korn et al. ERS 2010 (Abstract)



*Responder = patient with clinically important improvement in TDI score (≥1 unit)
OR = odds ratio; TDI = Transition Dyspnea Index

Indacaterol improved quality of life (SGRQ Total Score) over 6 months (pooled analysis)

Kleerup et al. ATS 2010 (Abstract)



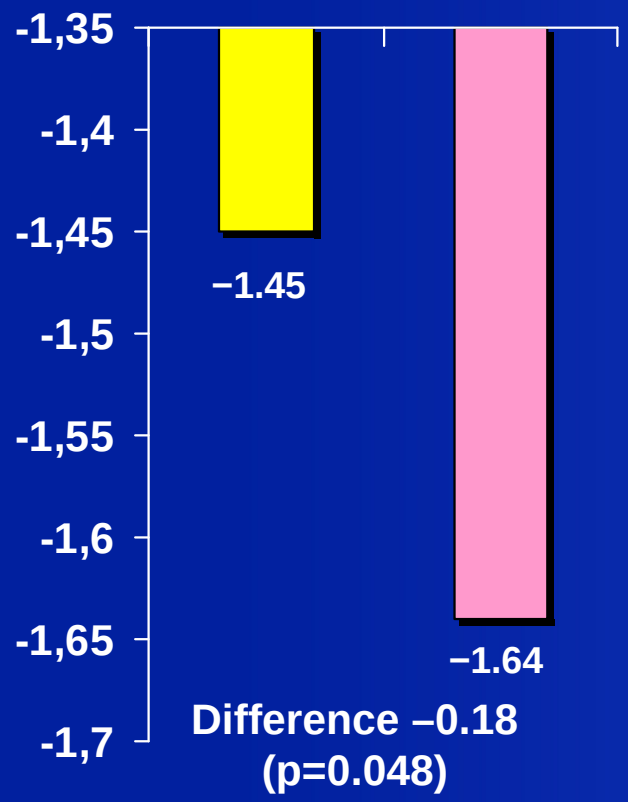
Plotted data are unadjusted means

INSIST

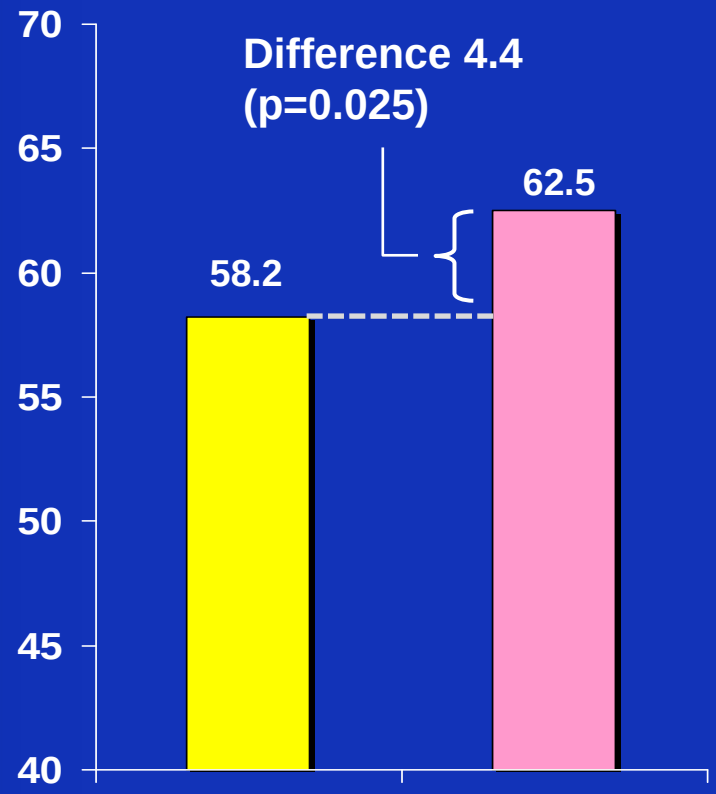
Indacaterol resulted in fewer days with rescue medication use, compared with **salmeterol**

Korn et al. ERS 2010 (Abstract)

Change from baseline in number of daily albuterol puffs



Days (%) with no rescue use



Salmeterol 50 µg b.i.d. (n=530) Indacaterol 150 µg o.d. (n=528)

INTENSITY

Indacaterol resulted in fewer days with rescue medication use, compared with **tiotropium**

Buhl et al ERJ Express 2011, e-pub, doi:10.1183/09031936.00191810

Comparison Indacaterol vs.Tiotropium

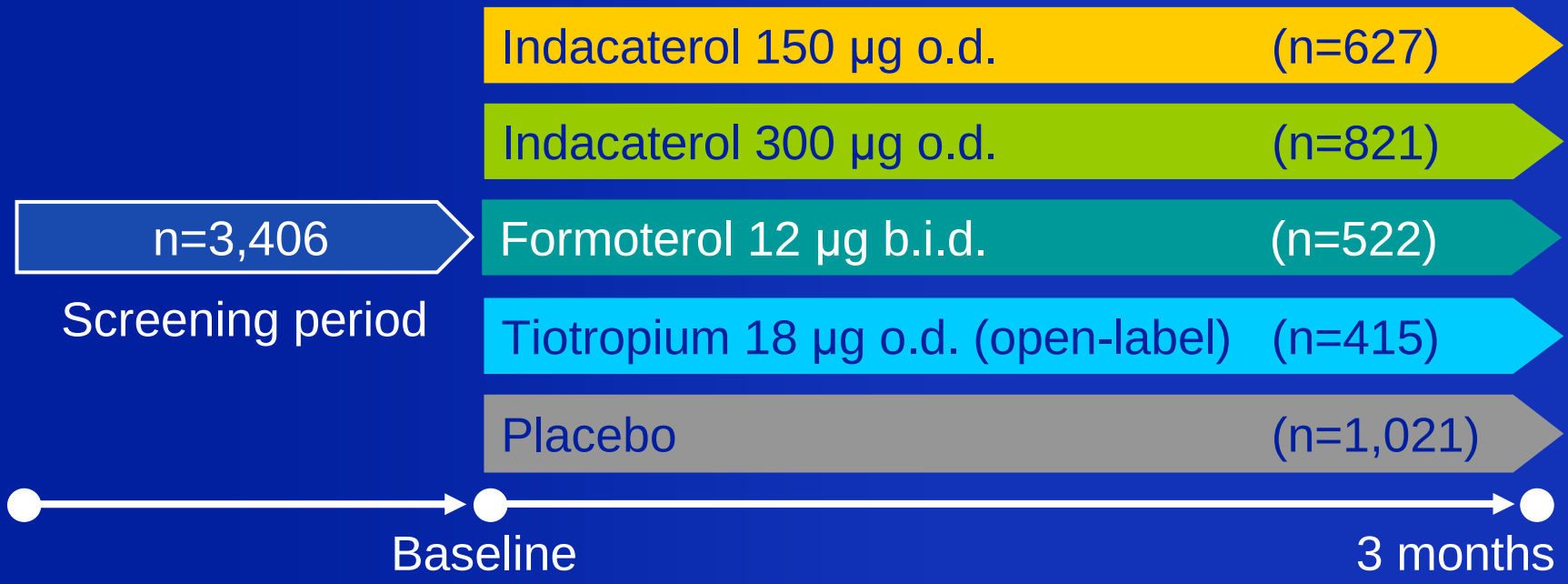
Parameter	Indacaterol	Tiotropium	Δ	p-value
Δ from baseline **Daily** No puffs	-1.40	-0.85	-0.54	<0.001
Δ from baseline **Mean Daily** No puffs	-0.90	-0.59	-0.32	<0.001
Δ from baseline **Mean nightime** No puffs	-0.52	-0.28	-0.24	<0.001
% Days **without rescue** medication	46.1	41.4	4.8	=0.004

Rates of COPD exacerbations

3 months pooled data

Siler et al. ATS 2010 (Abstract)

Pooled analysis of three randomized, placebo-controlled studies*



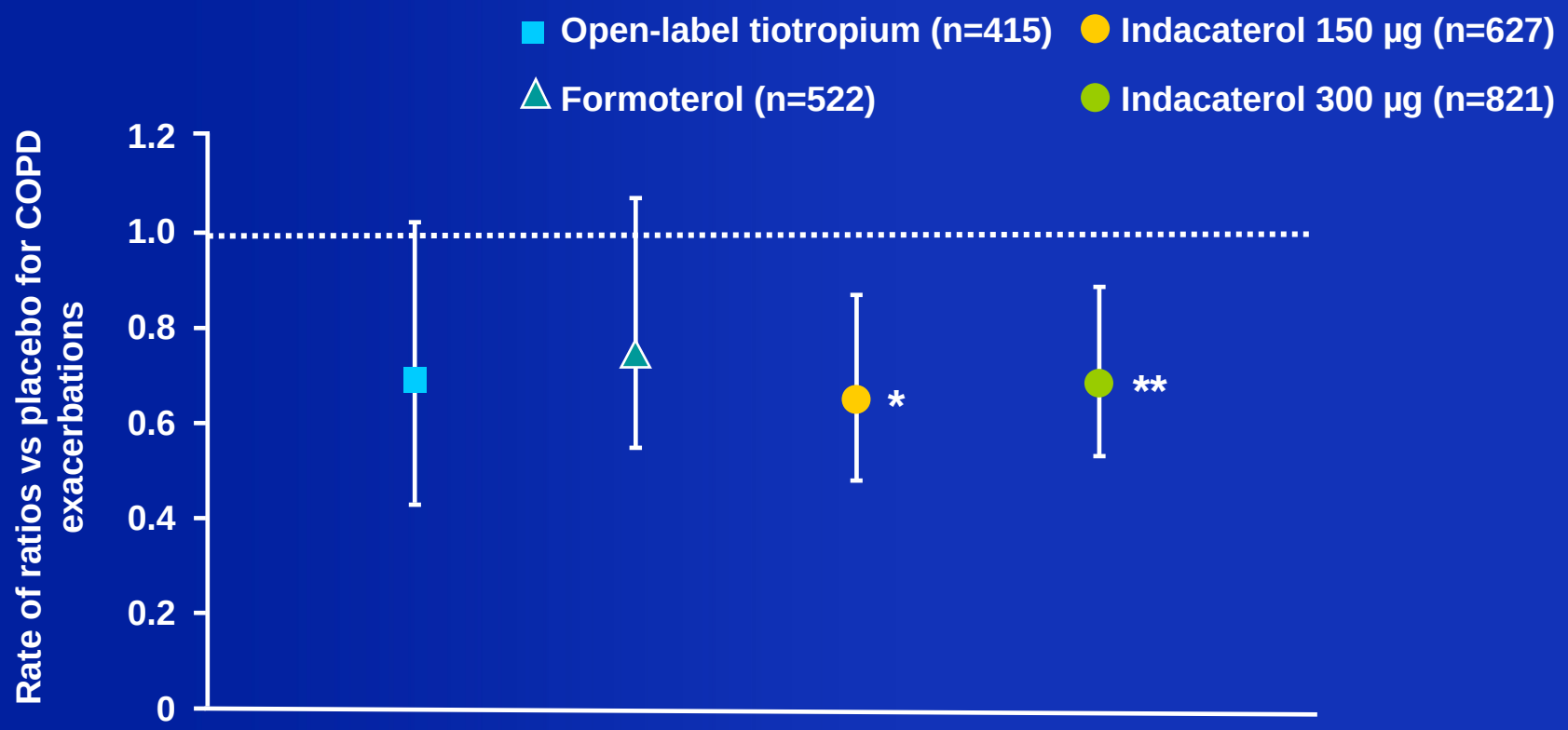
***Indacaterol 150 µg o.d. vs placebo (3 months)**
Indacaterol 150 µg and 300 µg o.d. vs placebo and tiotropium 18 µg o.d. (6 months)
Indacaterol 300 µg o.d. vs placebo and formoterol 12 µg b.i.d. (1 year)

Siler et al. ATS 2010

Rates of COPD exacerbations

3 months pooled data

Siler et al. ATS 2010 (Abstract)



*p<0.05, **p<0.01 vs placebo

Data are from Poisson regression analysis of rates of COPD exacerbations with 95% CI

Indacaterol in COPD

a Case Report
a one year experience

Real Life COPD Patient

Age	76 years old
Admission	11th Jan 2011
Smoking History	65 pack-years
Ex Smoking	Quit: Oct. 2010
Current	COPD Exacerbation
Concomitant Diseases	Diabetes (oral) Hypertension Heart failure
COPD Therapy at admission	Salbutamol (as needed) Seretide (2puffs/day)

Photo: Jan.13, 2011 (Hospital)

COPD-Patient: a case presentation

Lung function at admission

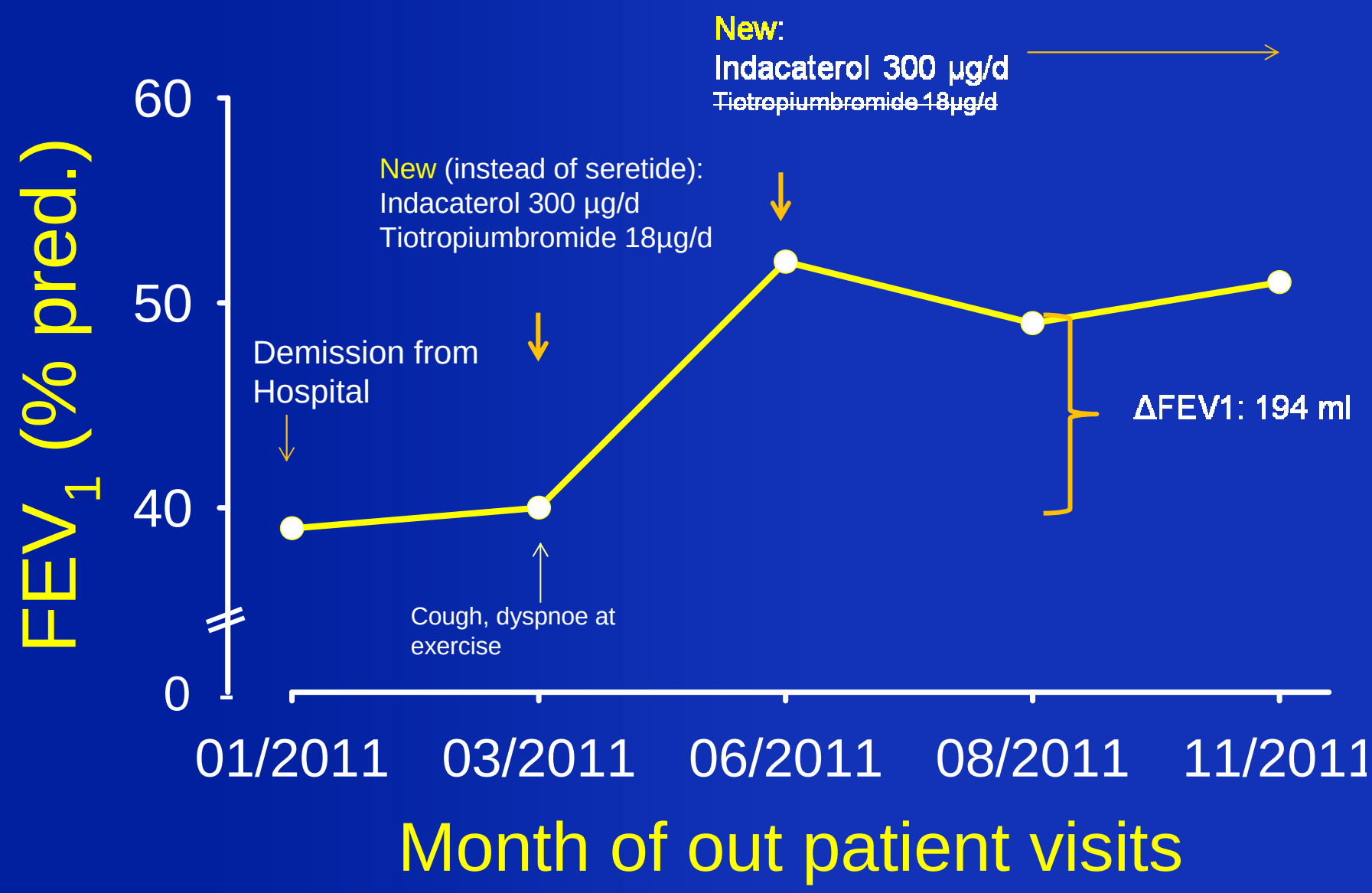
FEV1 pred	28%
FVC pred	41%
RV pred	160%

Lung function at demission

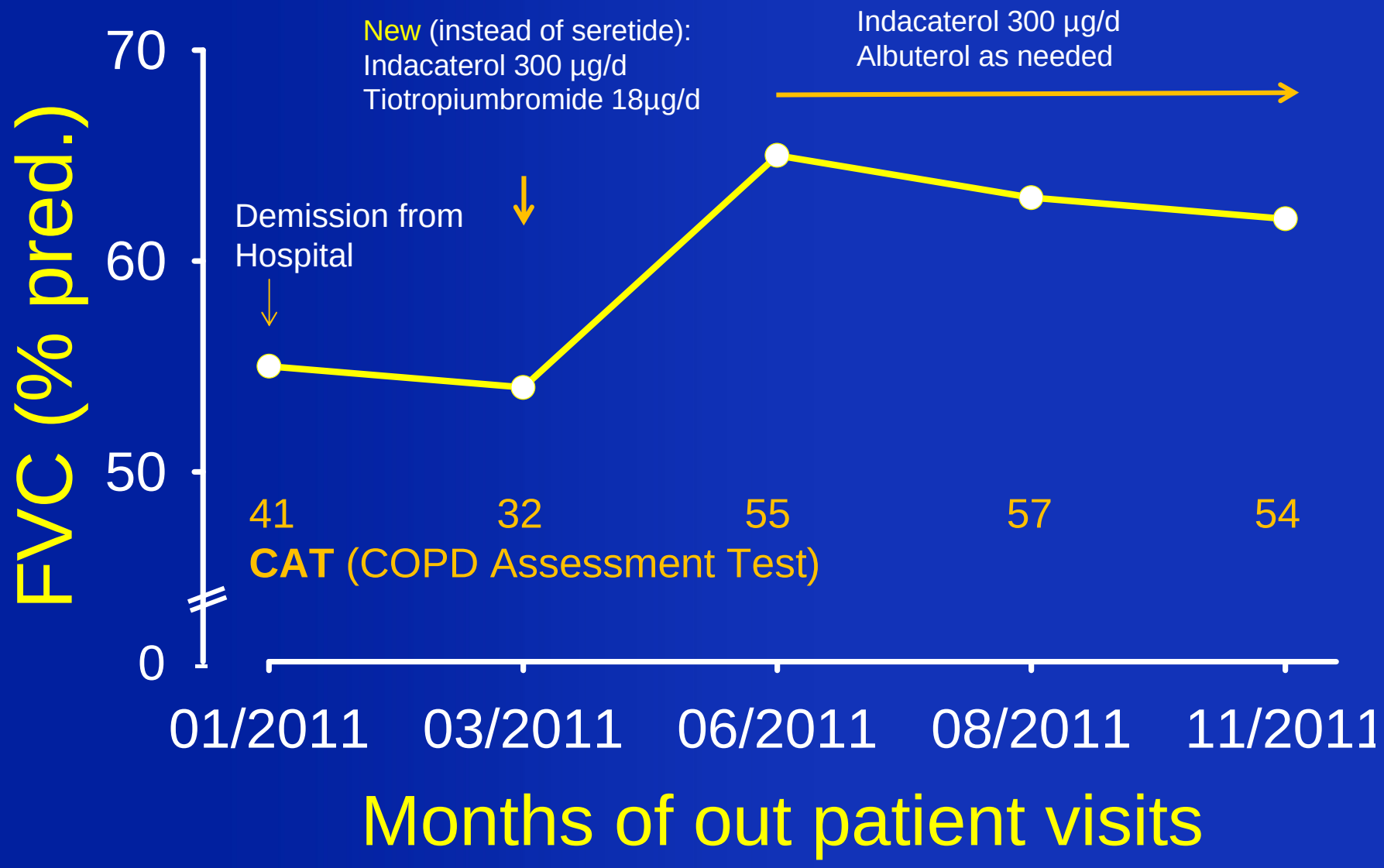
FEV1 pred	39%
FVC pred	55%
RV pred	153%

Blood gases (at hospital demission)
pO2: 53 (59) mmHg, pCO2: 42 (39) mmHg

COPD-Patient: a case presentation

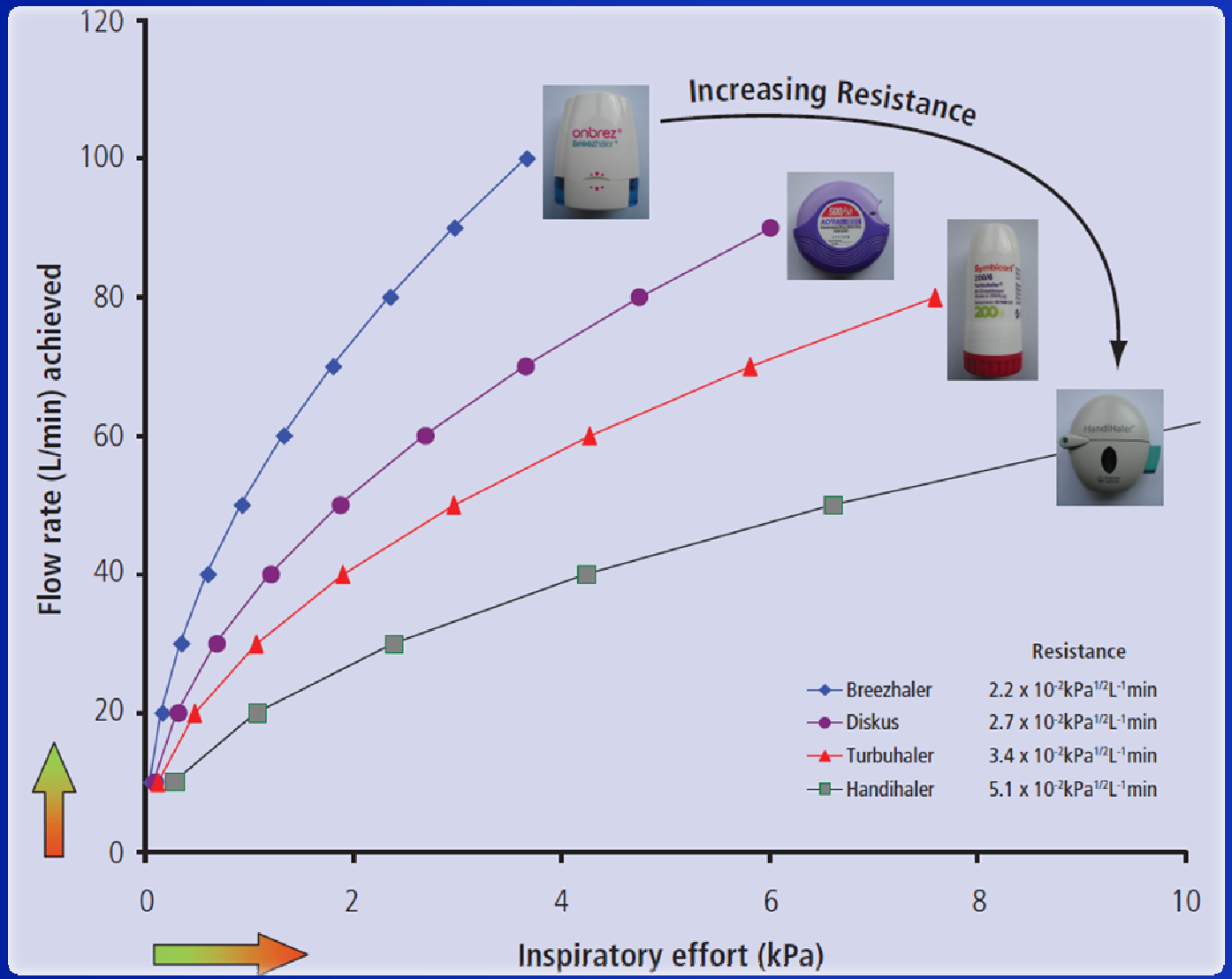


COPD-Patient: a case presentation



Breezehaler: an easy way to inhale

Singh et al Poster at ATS 2010



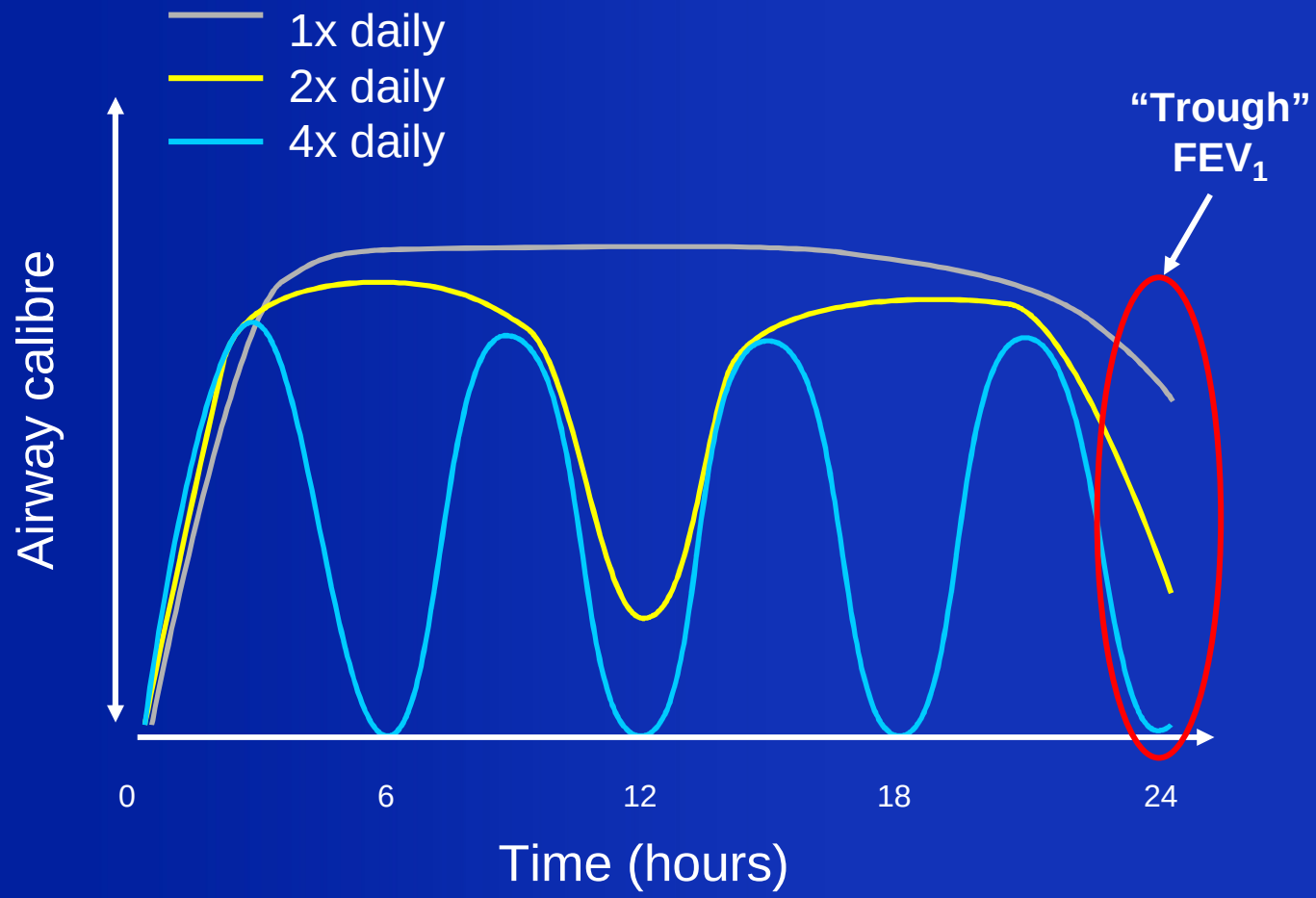
Indacaterol: Safety aspects

*Chapman et al Chest 2011 e-pub

- Cough
  - 17–20% of patients experienced a sporadic cough within 15 seconds following inhalation of indacaterol
  - higher frequency among females vs males and current smokers versus ex-smokers
  - Cough was not associated with higher drop-outs
- Headache (IND 150/300/Placebo*): 10.4% / 4.8% / 4.0%
- No evidence of bronchospasm, exacerbations, deteriorations of disease or loss of efficacy
- No evidence of cardiac AEs (QTc, tachycardia, blood pressure)

Usefulness of long-acting versus short-acting bronchodilators on 24-hour airway tone

Beeh , Beier Adv.Ther. 27:150-159, 2010



Conclusions

- Once-daily indacaterol provided
  - significant, consistent and clinically important improvements in lung function (FEV_1)
  - significant improvements in breathlessness and health status at least as good as or better than tiotropium, salmeterol and formoterol
  - reduction in relief medication compared with tiotropium, salmeterol and formoterol
- Efficacy of indacaterol was maintained over the full treatment period (up to 52 weeks in Phase III)
- Indacaterol was shown to have a satisfactory safety and tolerability profile in studies of up to 1 year's duration

Indacaterol: maximizing bronchodilation

A. Gillissen