



Behandeling van Astma:
update GINA 2021 richtlijnen

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Dienst Longziekten
UZ Gent

24/11/2021

Disclosure: Guy Brusselle

- GINA: Member of Scientific Committee and Board of Directors
- Member of Advisory boards for AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, MSD, Novartis, Sanofi and Teva.
- Lecture fees from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Sanofi and Teva.
- Several drugs or treatment strategies discussed in this presentation are off-label (in EU [EMA]).

S. B., jongen, 16 jaar; 09/09/2021



- Allergisch astma (HSM, kat)
- Flixotide gestopt (op eigen houtje)
- 5 puffers (pMDI) van **SABA** Ventolin in 7 weken tijd!

S. B., jongen, 16 jaar; 14/09/2021

- Extubatie op 12/09
- Transfer van IZ naar pneumo op 14/09
- Ontslag naar huis op 16/09 (normale longfunctie)
- Behandeling bij ontslag uit UZ Gent:

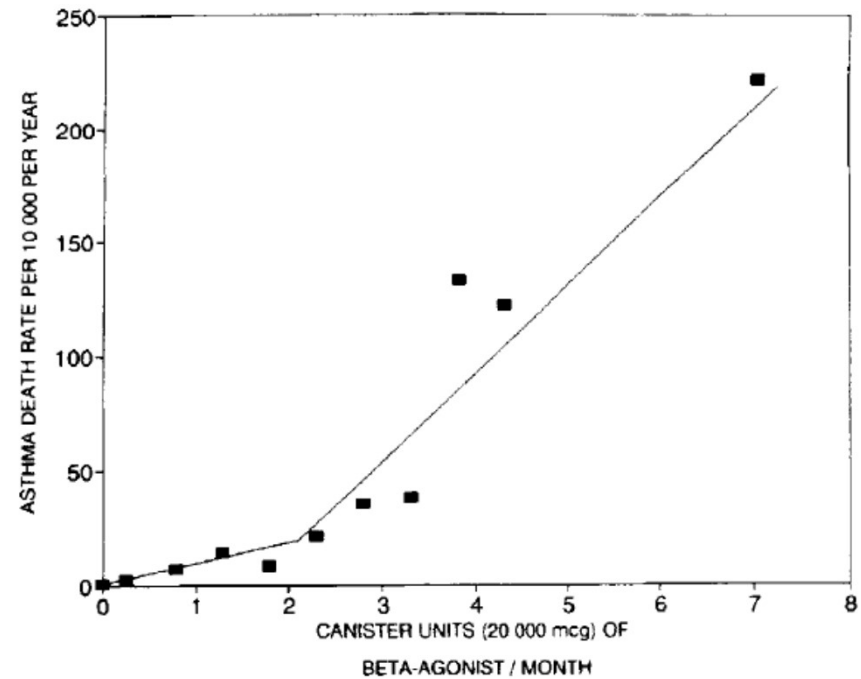
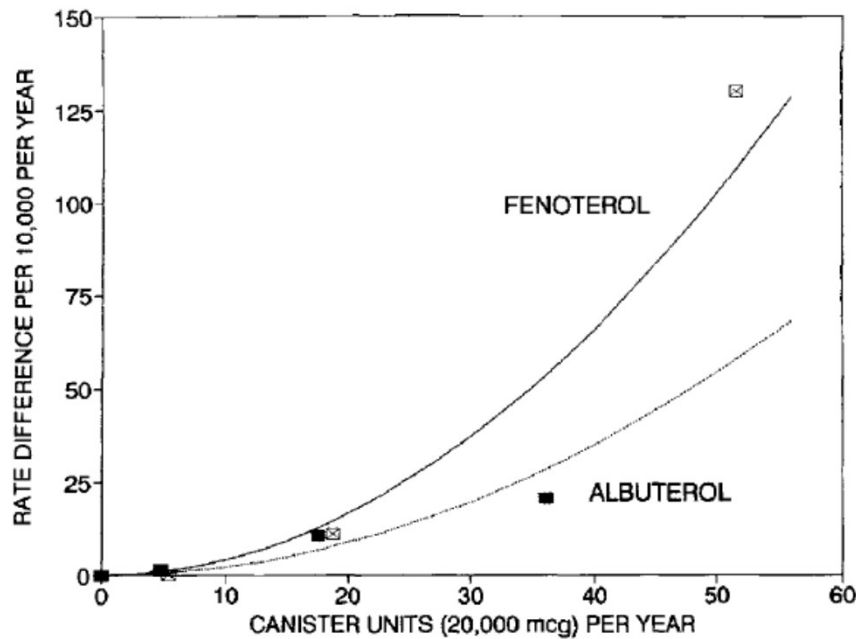
Symbicort MART:

Maintenance *and* Anti-inflammatory Reliever

Therapie met Symbicort (budesonide/formoterol):

2x daags 2 puffs *plus* 1 à 2 puffs extra zo nodig,
als kortademig.

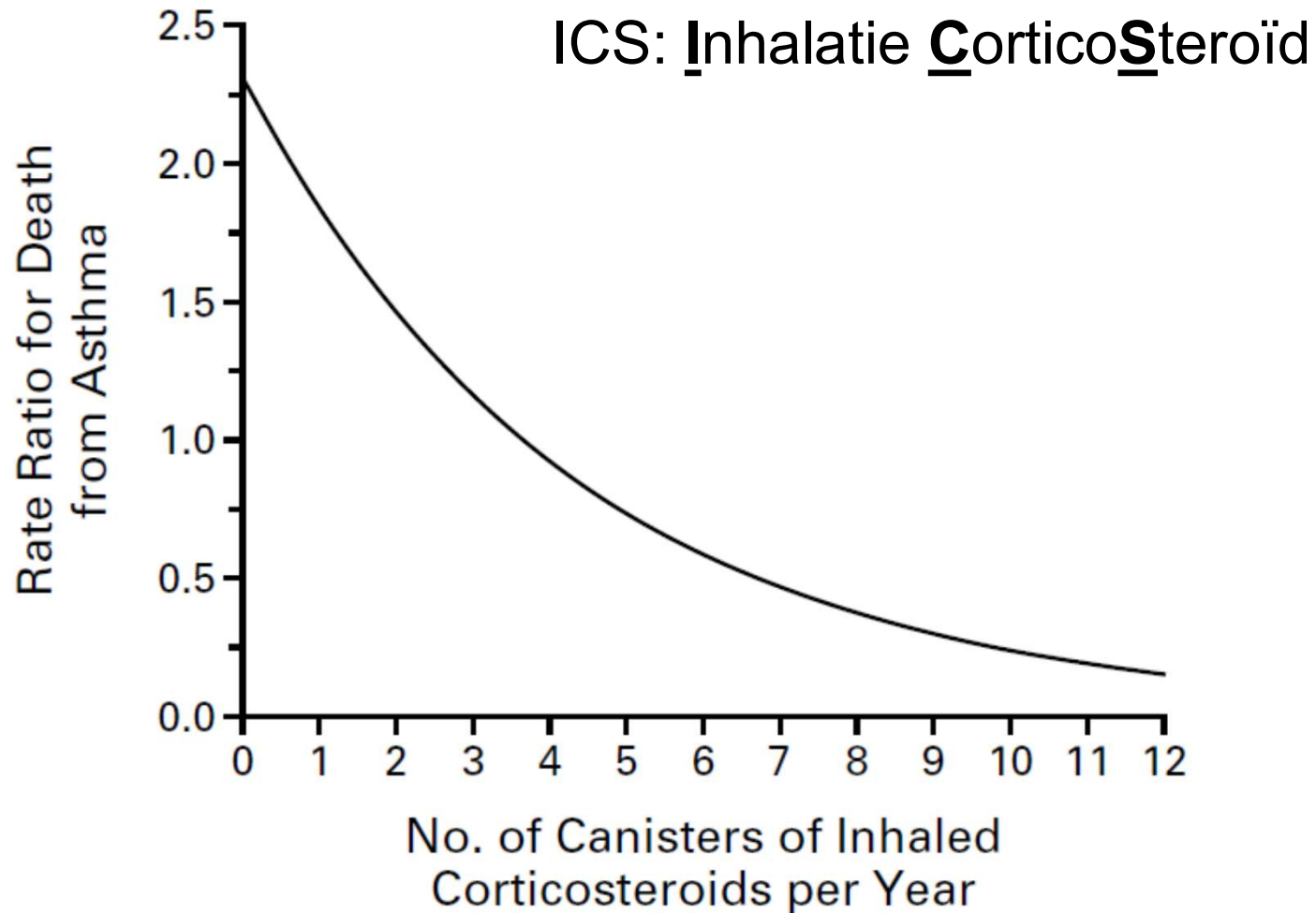
Increased use of inhaled SABA and excess risk of asthma death



SABA: Short-Acting Beta2-Agonist: e.g. salbutamol (Ventolin)

Suissa S. et al, AJRCCM 1994.

Regular use of ICS is associated with a decreased risk of death from asthma

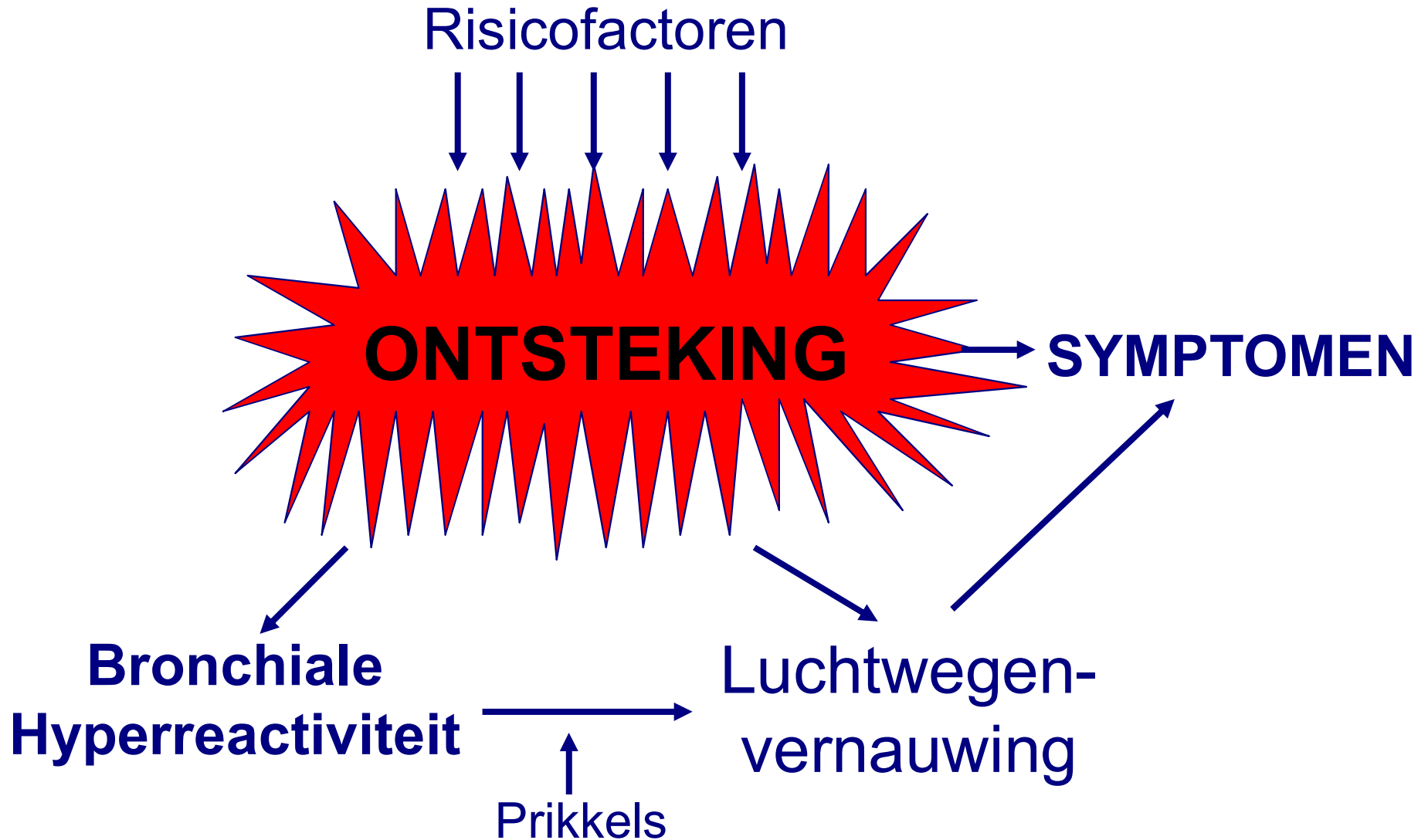


Suissa S. et al, NEJM 2000.

Astma: GINA 2021

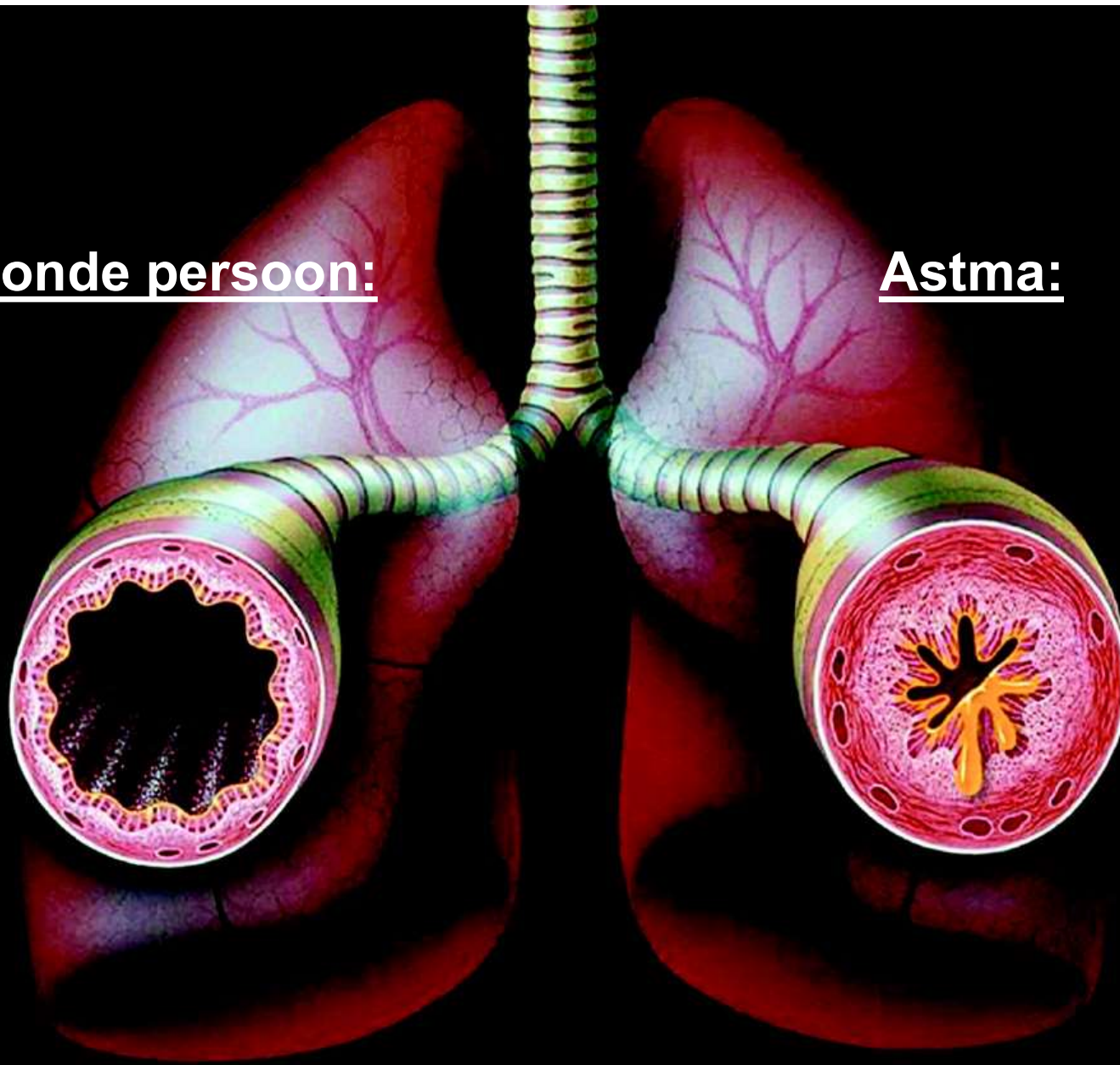
- Astma: diagnose
- Inhalatie medikatie: therapeutische klassen
- GINA richtlijnen 2021
- Behandeling van mild astma: AIR
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- Conclusie

Definitie van astma



Gezonde persoon:

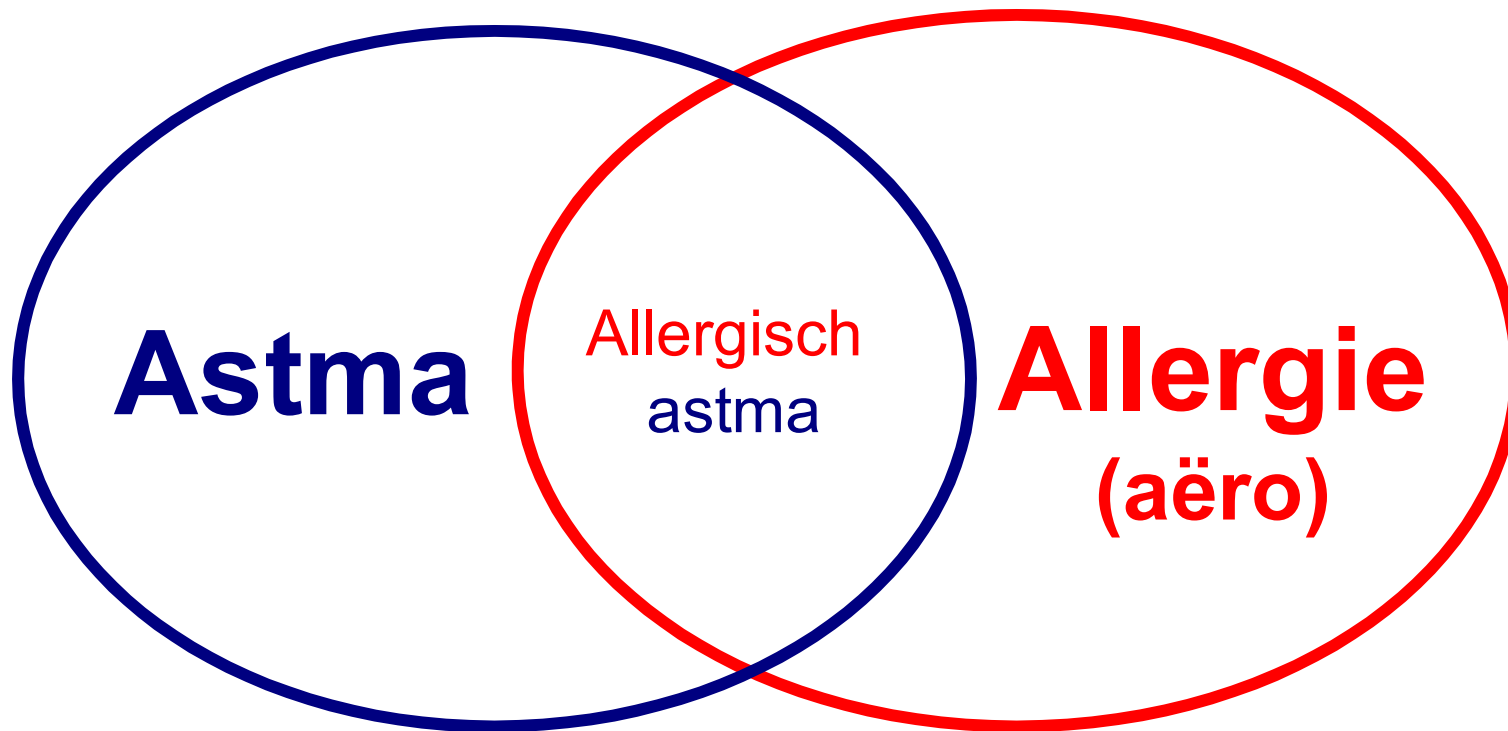
Astma:



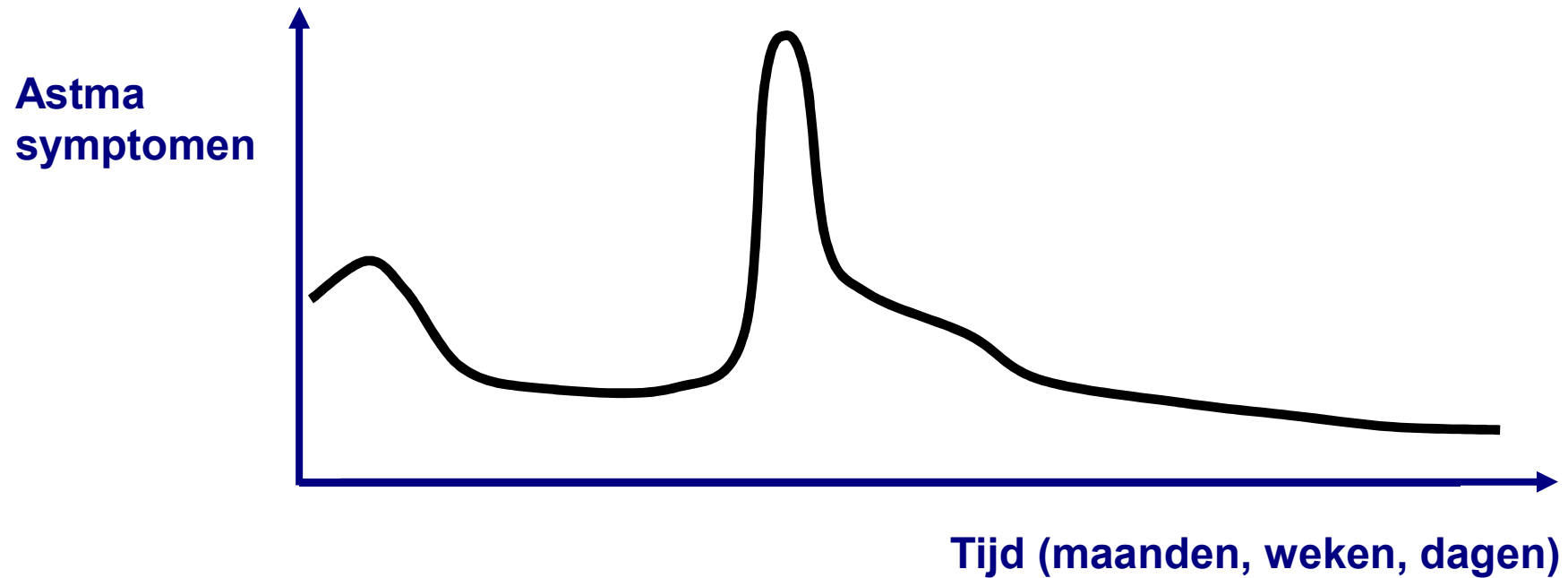
Diagnose van astma

- Anamnese (BHR)
- Klinisch Onderzoek
- Longfunctie:
 - aantonen van reversibele luchtwegenvernauwing
 - aantonen van bronchiale hyperreactiviteit (BHR)
- Allergietesten
- Bloedonderzoek: eosinofilie, serum IgE
- FeNO

Astma en Allergie



Astma is een variabele aandoening



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Inhalatie CorticoSteroïden (ICS)

<u>ICS</u>	<u>Merksnaam</u>	<u>Inhalator</u>	<u>Dosis</u>	<u>Dosering</u>
Beclometason	Qvar ®	Dosisaërosol Autohaler	50 µg 100 µg	2x 2x
Budesonide	Pulmicort ® Miflonide ® Budesonide Budesonide	<i>Turbohaler</i> <i>Aerolizer</i> <i>Easyhaler</i> <i>Novolizer</i>	200 µg 200 µg 200 µg 200 µg	2x 2x 2x 2x
Fluticason propionaat	Flixotide ®	<i>Diskus</i> Dosisaërosol pMDI	100 µg 250 µg 500 µg 50 µg 250 µg	2x 2x 2x 2x 2x
Fluticason furoaat		<i>Ellipta</i>	92 µg 184 µg	1x 1x

DroogPoederInhalatoren (DPI):

Aerolizer, Diskus, Ellipta, Easyhaler, Novolizer, Turbohaler.

Beta2-agonisten (BA): short-acting (SABA); long-acting (LABA)

	Merksnaam	Inhalator	Dosis	Dosering
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SABA: NOOIT als enige behandeling bij astma!

Salbutamol	Ventolin ®	dosisaërosol	100 µg	zo nodig
Fenoterol	Berotec ®	dosisaërosol	100 µg	zo nodig

LABA: NOOIT als enige behandeling bij astma!

Formoterol	Foradil ®	<i>Aerolizer</i>	12 µg	2x
	Formoterol	<i>Novolizer</i>	12 µg	2x
	Oxis ®	<i>Turbohaler</i>	6 of 12 µg	2x
Salmeterol	Serevent ®	Dosisaërosol	25 µg	2x 2 puffs
		<i>Diskus</i>	50 µg	2x 1 inhalatie
Indacaterol	Onbrez ®	<i>Breezhaler</i>	150 µg	1x 1 capsule
			300 µg	1x 1 capsule

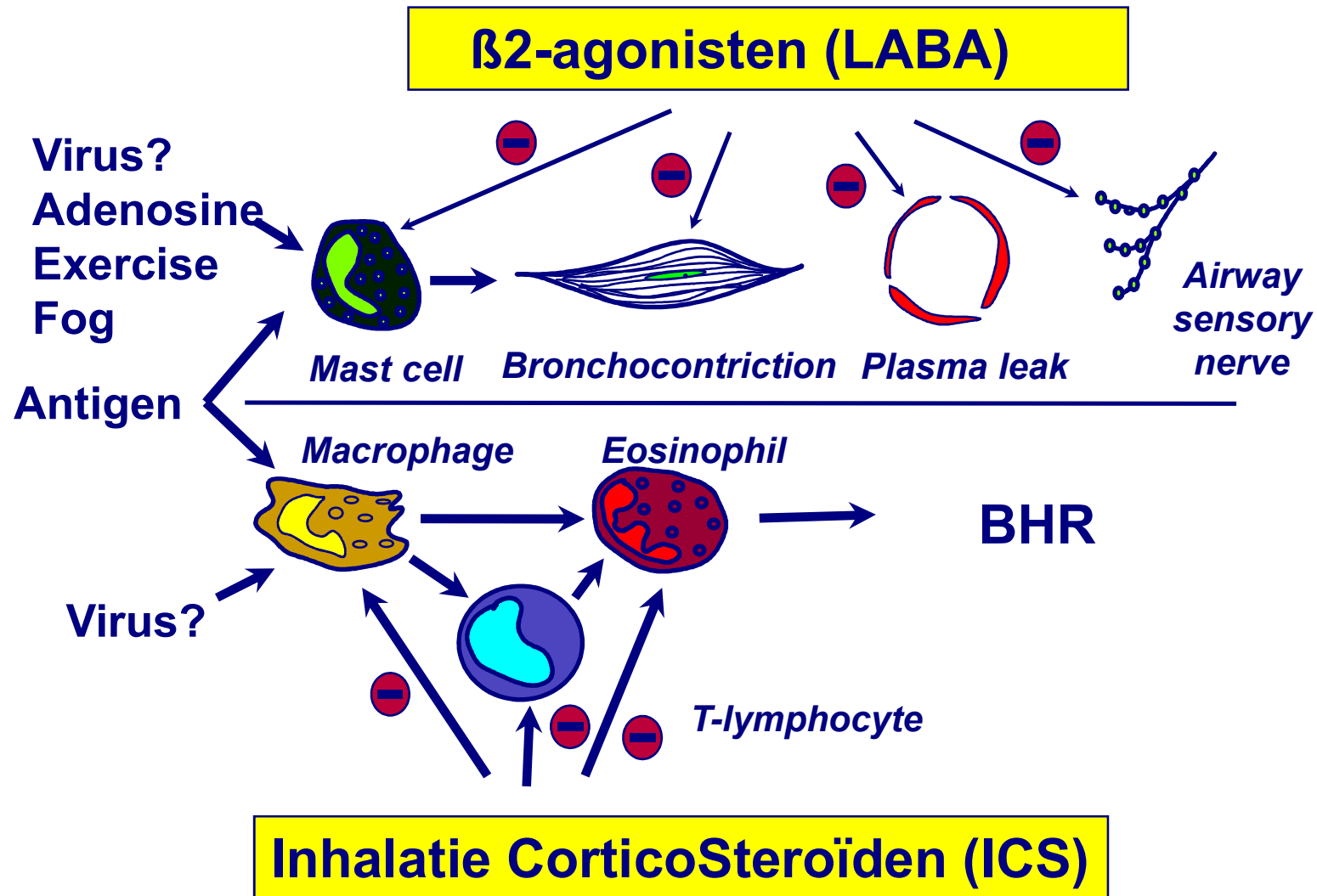
Indicatie (SABA): reliever use (as needed): “hoe minder, hoe liever”

Indicatie (LABA): COPD!; NOOIT als monotherapie bij astma!

LABA + ICS vaste combinaties

ICS	LABA	Merknaam	Inhalator	Dosis	Dosering
<u>Fluticason</u>	Salmeterol	Seretide ®	Dosisaërosol <i>Diskus</i>	<u>25/50</u> <u>25/125</u> <u>25/250</u> <u>50/100</u> <u>50/250</u> <u>50/500</u>	2x 2 puffs 2x 1 inhalatie
<u>Fluticason</u>	Formoterol	Flutiform ®	Dosisaërosol	<u>50/5</u> <u>125/5</u> <u>250/10</u>	2x 2 puffs
<u>Budesonide</u>	Formoterol	Symbicort ® Symbicort Forte Bufomix ®	<i>Turbohaler</i> <i>Easyhaler</i>	<u>160/4,5</u> <u>320/9</u> <u>200/6</u>	2x 1 à 2 inh. 2x 1 inhalatie
<u>Beclometason</u>	Formoterol	Inuvair ®	Dosisaërosol <i>Nexthaler</i>	<u>100/6</u> <u>100/6</u>	2x 1 à 2 puffs 2x 1 à 2 inh.
<u>Fluticasonfuroaat</u>	Vilanterol	Relvar ®	<i>Ellipta</i>	<u>92/22</u> <u>184/22</u>	1x 1 inhalatie 1x 1 inhalatie
<u>Fluticason</u>	Salmeterol	Airflusal ®	Dosisaërosol <i>Forspiro DPI</i>	<u>125/25</u> <u>250/50</u> <u>500/50</u>	2x 1 à 2 puffs 2x 1 inh. 2x 1 inh.

Vaste combinatie van LABA + ICS



Indeling van inhalatie β_2 -agonisten (+ ICS: Inhalatie CorticoSteroïd)

Snelheid van
werking

snel

terbutaline
salbutamol

**Formoterol
+ ICS**

traag

**Salmeterol
+ ICS**

kort

lang

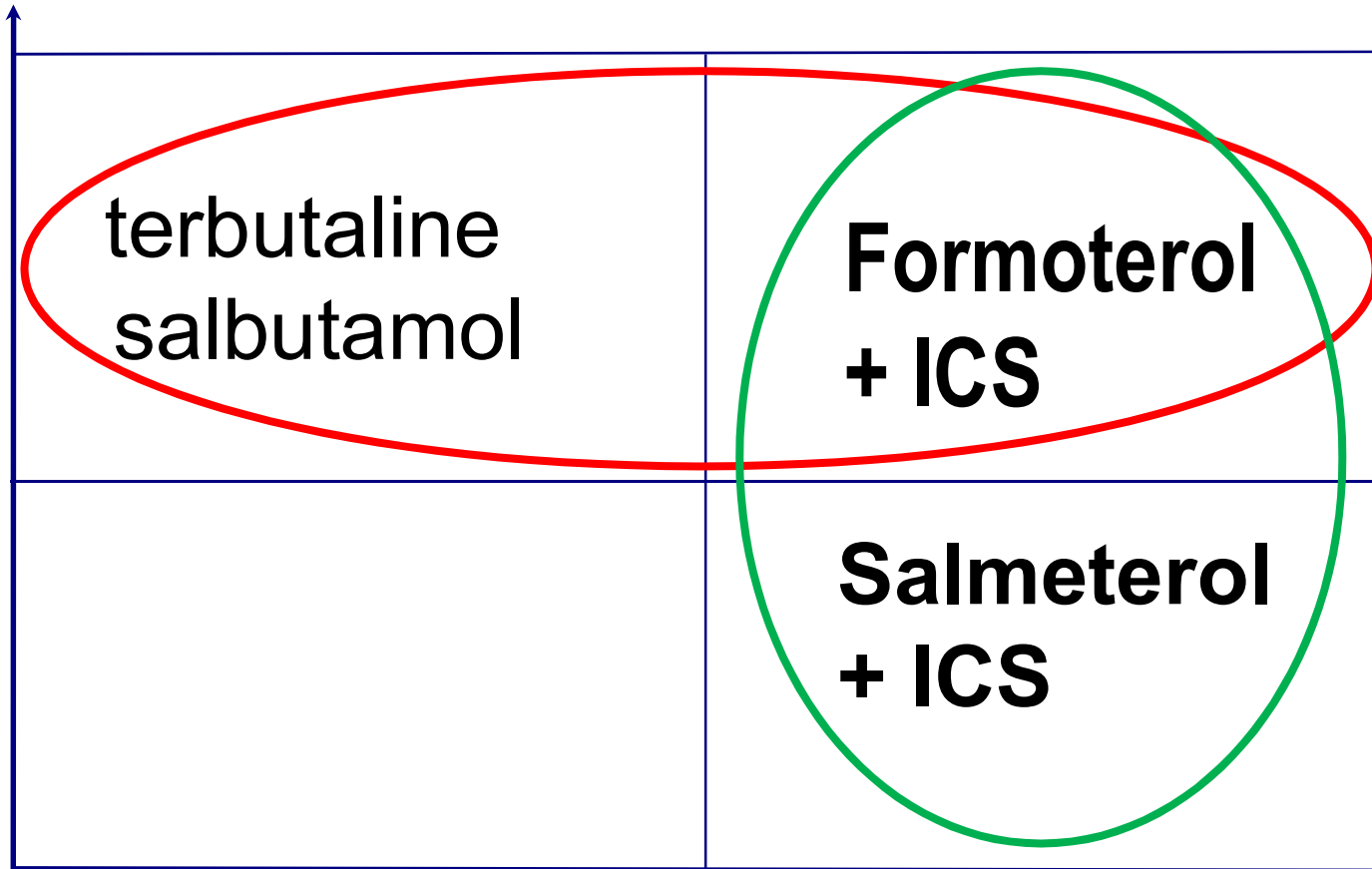
Duur van werking

Indeling van inhalatie β_2 -agonisten (+ ICS: Inhalatie CorticoSteroïd)

Snelheid van
werking

Snel
→ Als
reliever

traag



kort

Lang → Als onderhoudsR/

Duur van werking

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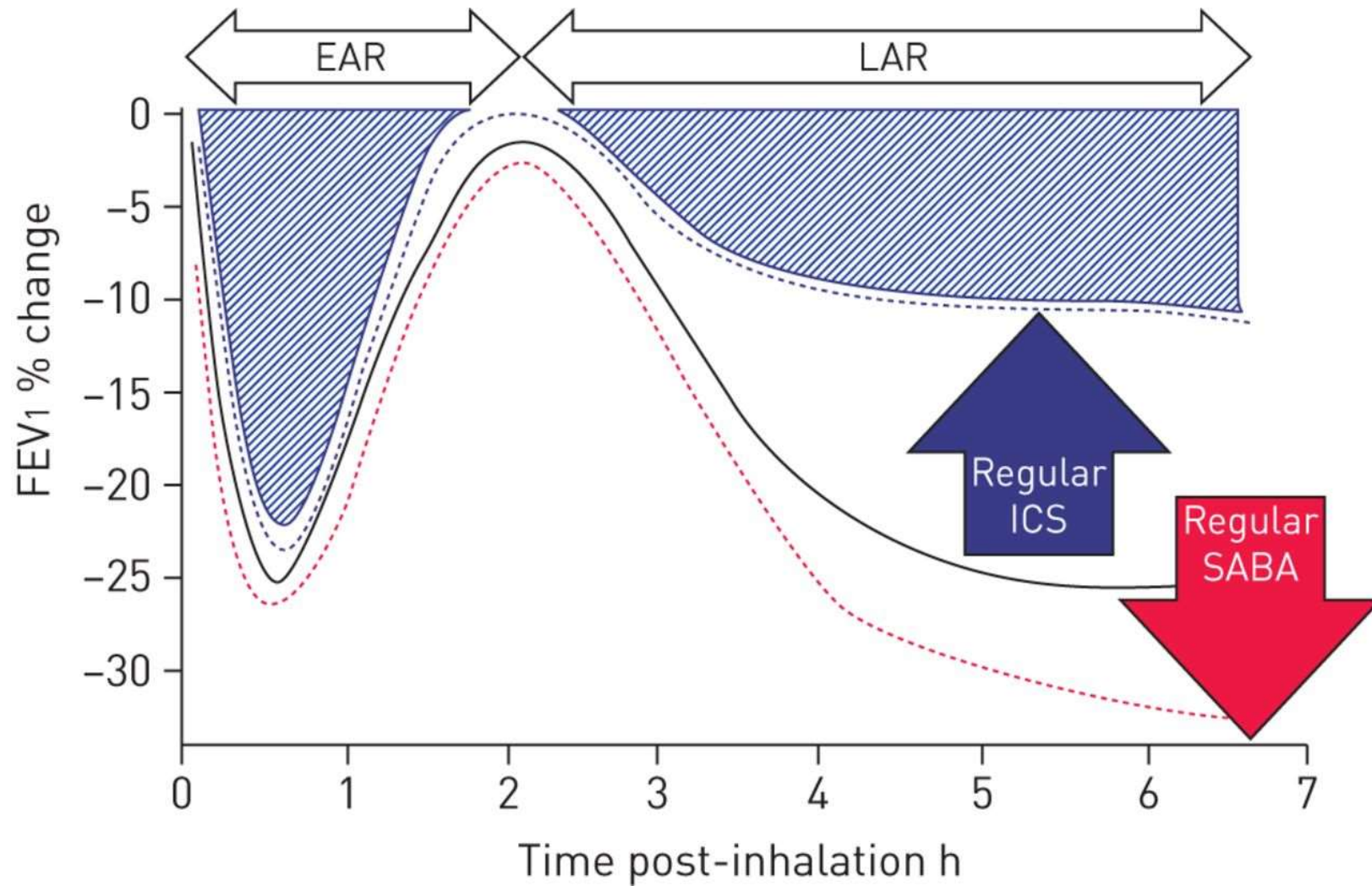


Asthma Management and Prevention Program

Goals of Long-term Management

1. Achieve and maintain control of symptoms
2. Maintain normal activity levels, including exercise
3. Maintain pulmonary function as close to normal levels as possible
- 4. Prevent asthma exacerbations**
- 5. Prevent asthma mortality**
6. Avoid adverse effects from asthma medications





Allergen-induced airway responses



G. Gauvreau et al, Eur Respir J 2015.

GINA 2019: a fundamental change in asthma management

Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents

Helen K. Reddel ¹, J. Mark FitzGerald², Eric D. Bateman³, Leonard B. Bacharier⁴, Allan Becker⁵, Guy Brusselle⁶, Roland Buhl⁷, Alvaro A. Cruz⁸, Louise Fleming ⁹, Hiromasa Inoue¹⁰, Fanny Wai-san Ko ¹¹, Jerry A. Krishnan¹², Mark L. Levy ¹³, Jiangtao Lin¹⁴, Søren E. Pedersen¹⁵, Aziz Sheikh¹⁶, Arzu Yorgancioglu¹⁷ and Louis-Philippe Boulet¹⁸



@ERSpublications

GINA no longer recommends treating adults/adolescents with asthma with short-acting bronchodilators alone. Instead, they should receive symptom-driven (in mild asthma) or a daily corticosteroid-containing inhaler, to reduce risk of severe exacerbations. <http://bit.ly/310LLzE>

H. Reddel et al, ERJ 2019.

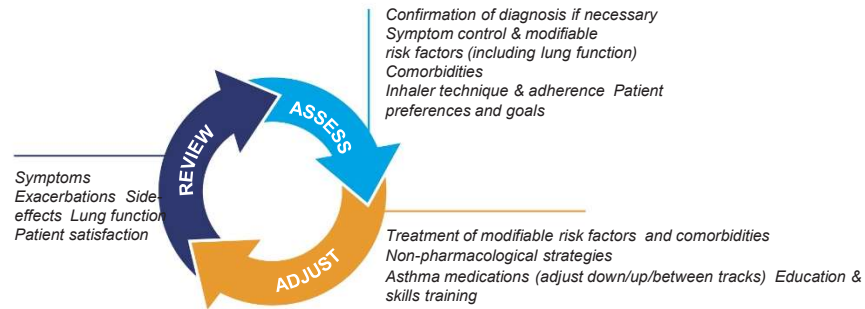
GINA 2021: Management van astma



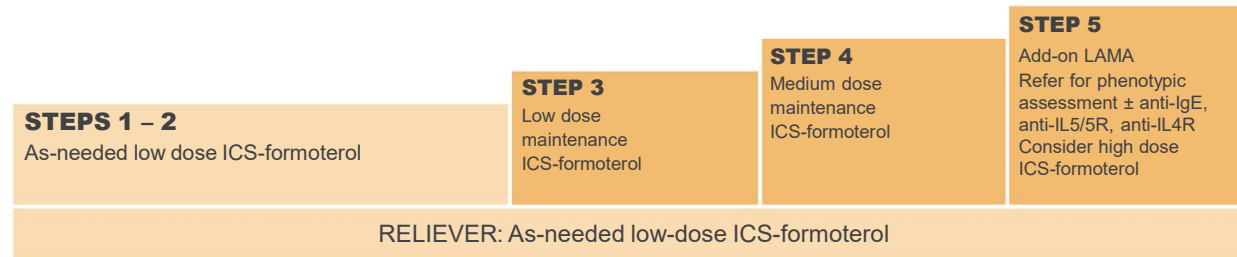
Adults & adolescents 12+ years

Personalized asthma management

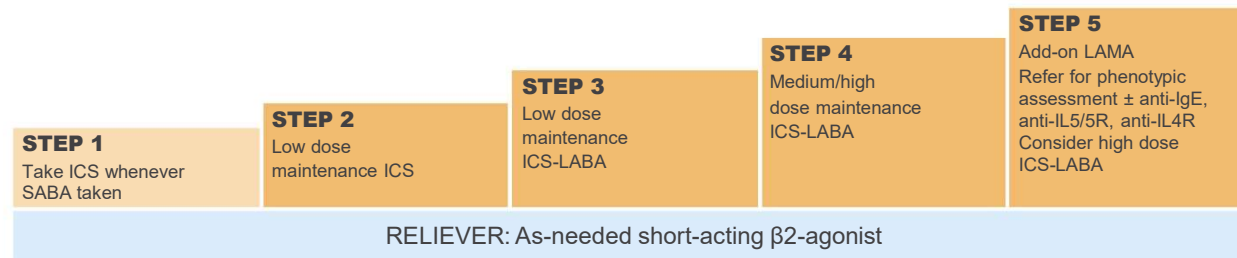
Assess, Adjust, Review
for individual patient needs



CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever



CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller



Other controller options for either track

Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA, or switch to high dose ICS	Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects
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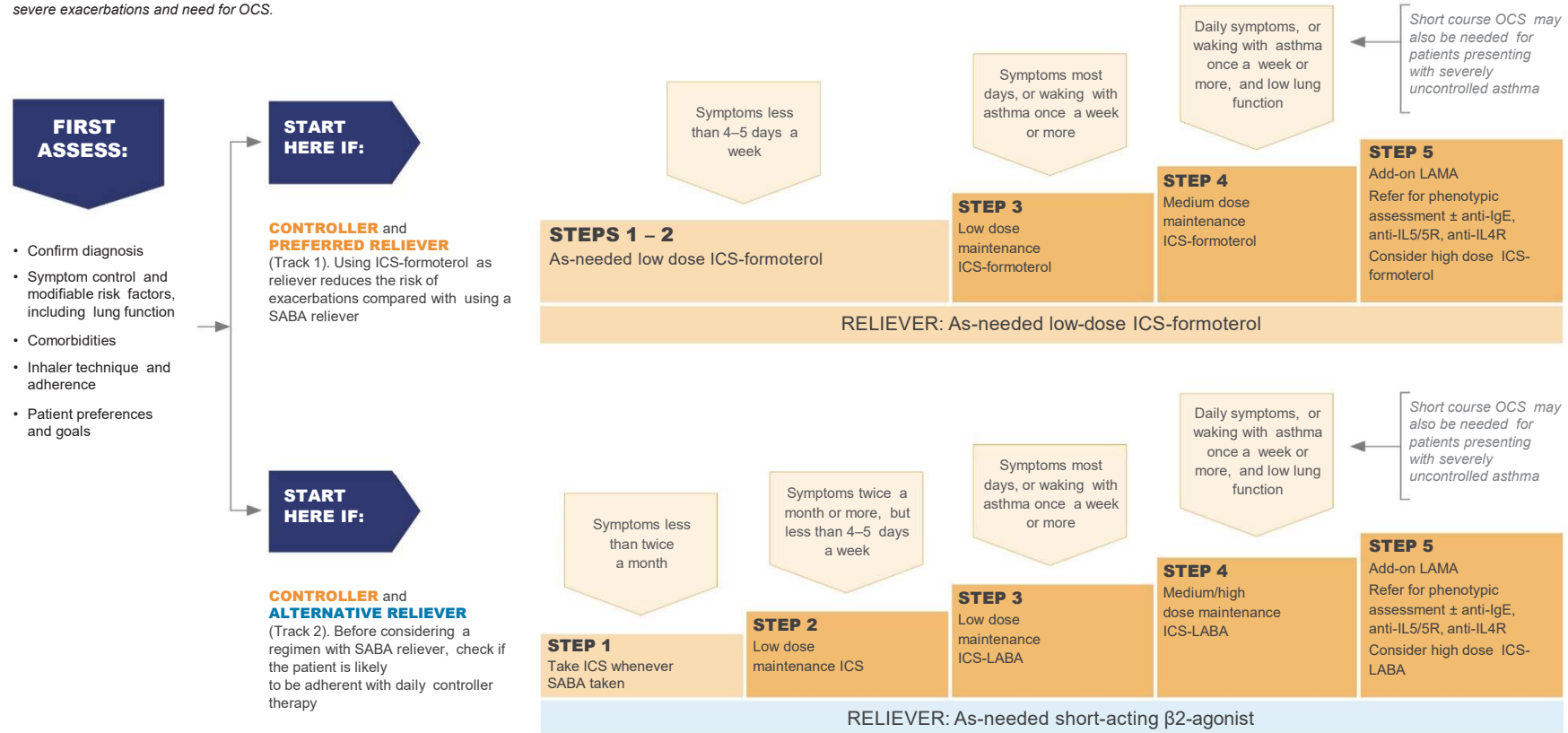
GINA 2021: Management van astma



STARTING TREATMENT

in adults and adolescents with a diagnosis of asthma

Track 1 is preferred if the patient is likely to be poorly adherent with daily controller. ICS-containing therapy is recommended even if symptoms are infrequent, as it reduces the risk of severe exacerbations and need for OCS.

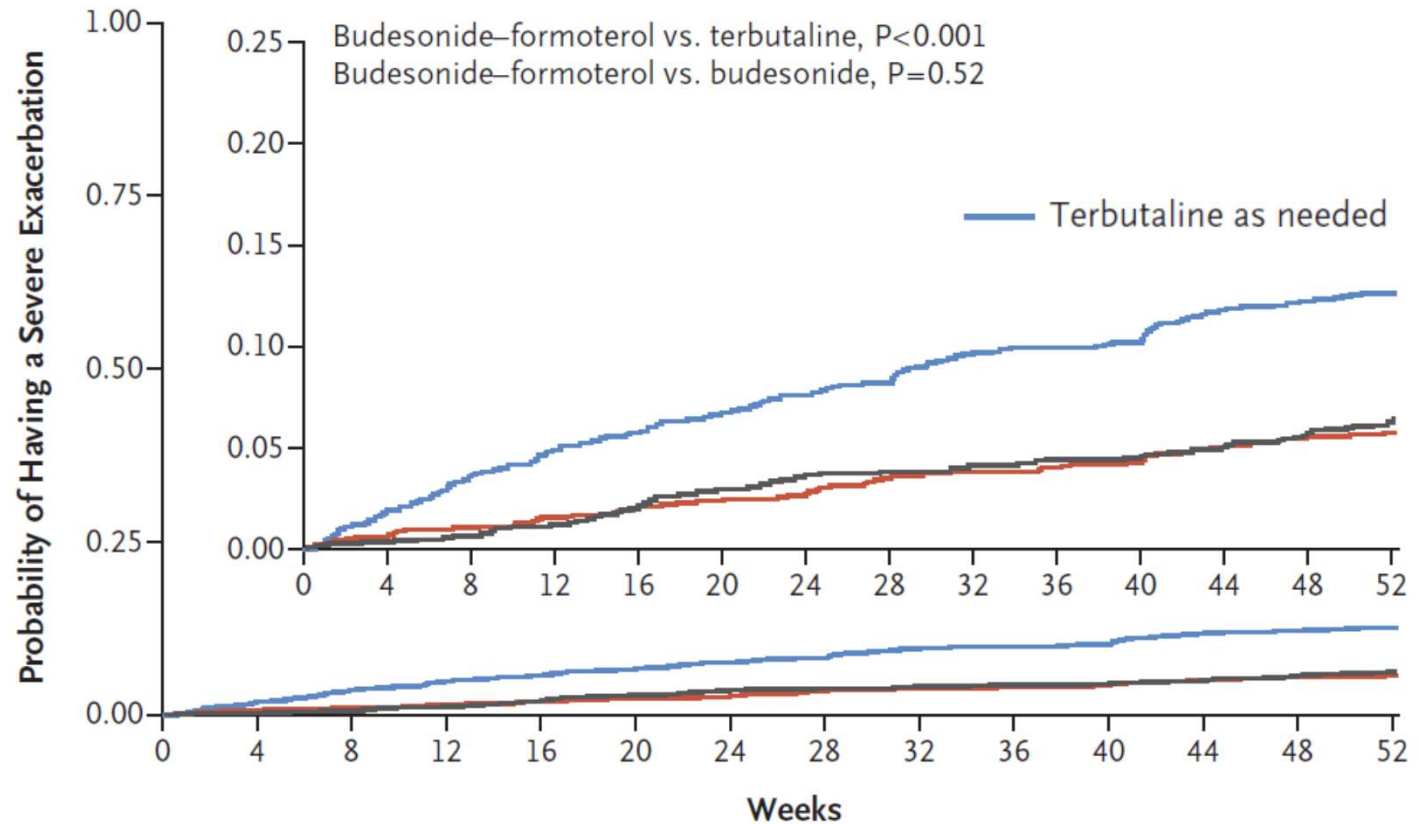


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Anti-Inflammatoire Reliever (AIR; Symbicort zo nodig) vermindert ernstige astma exacerbaties met 65% tov SABA

Severe Exacerbation



— Budesonide-formoterol as needed

— Budesonide maintenance

P. O'Byrne et al, SYGMA 1 trial; NEJM 2018.

SYGMA 1 trial: severe exacerbations

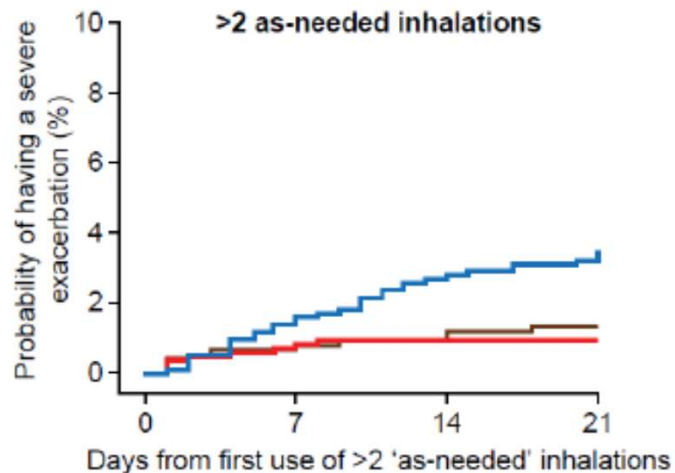
Table 2. Summary of Asthma Exacerbations, According to Treatment Group.

Variable	Terbutaline as Needed (N=1277)	Budesonide–Formoterol as Needed (N=1277)	Budesonide Maintenance Therapy (N=1282)
All severe exacerbations			
Patients with ≥1 exacerbation — no. (%)	152 (11.9)	71 (5.6)	78 (6.1)
Total no. of exacerbations	188	77	89
Annualized exacerbation rate	0.20	0.07	0.09
Comparison between as-needed budesonide–formoterol and other regimen			
Rate ratio	0.36	—	0.83
95% CI	0.27–0.49	—	0.59–1.16
P value	<0.001	—	0.28
Severe exacerbation leading to hospitalization			
Patients with ≥1 exacerbation — no. (%)	15 (1.2)	6 (0.5)	8 (0.6)
Total no. of exacerbations	21	6	8

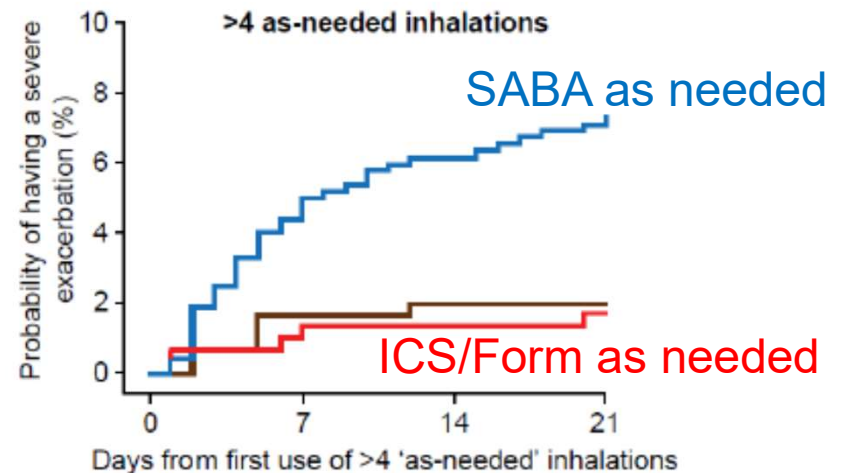
P. O’Byrne et al, NEJM 2018.

A single day of higher as-needed ICS/form reduces short-term risk of a severe exacerbation in mild asthma

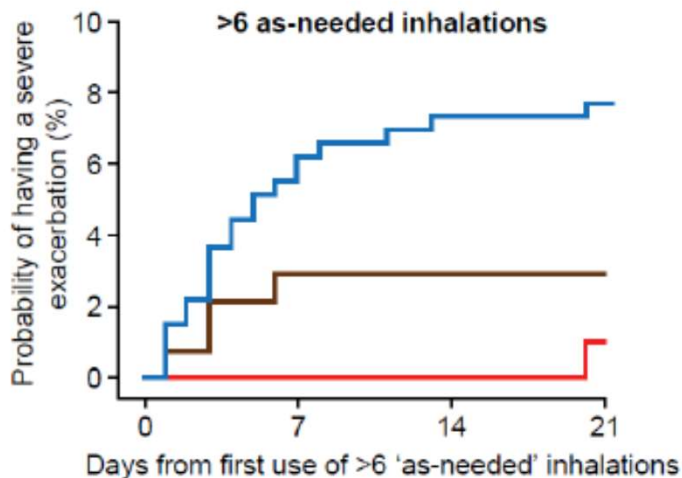
A)



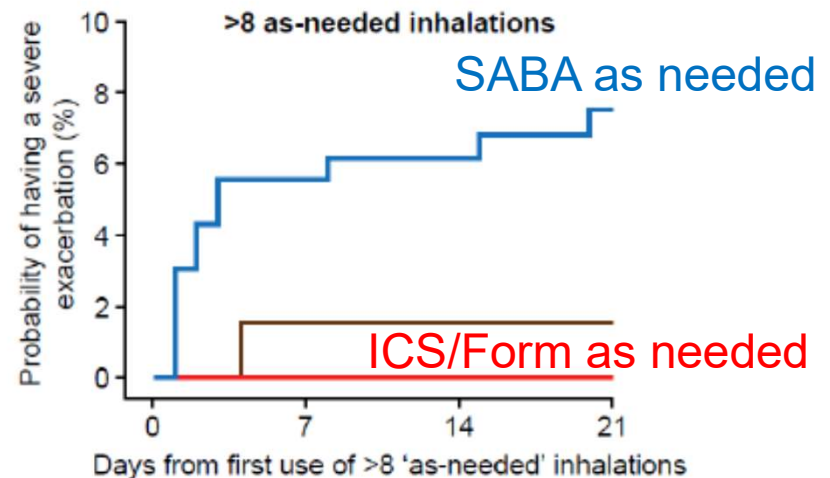
B)



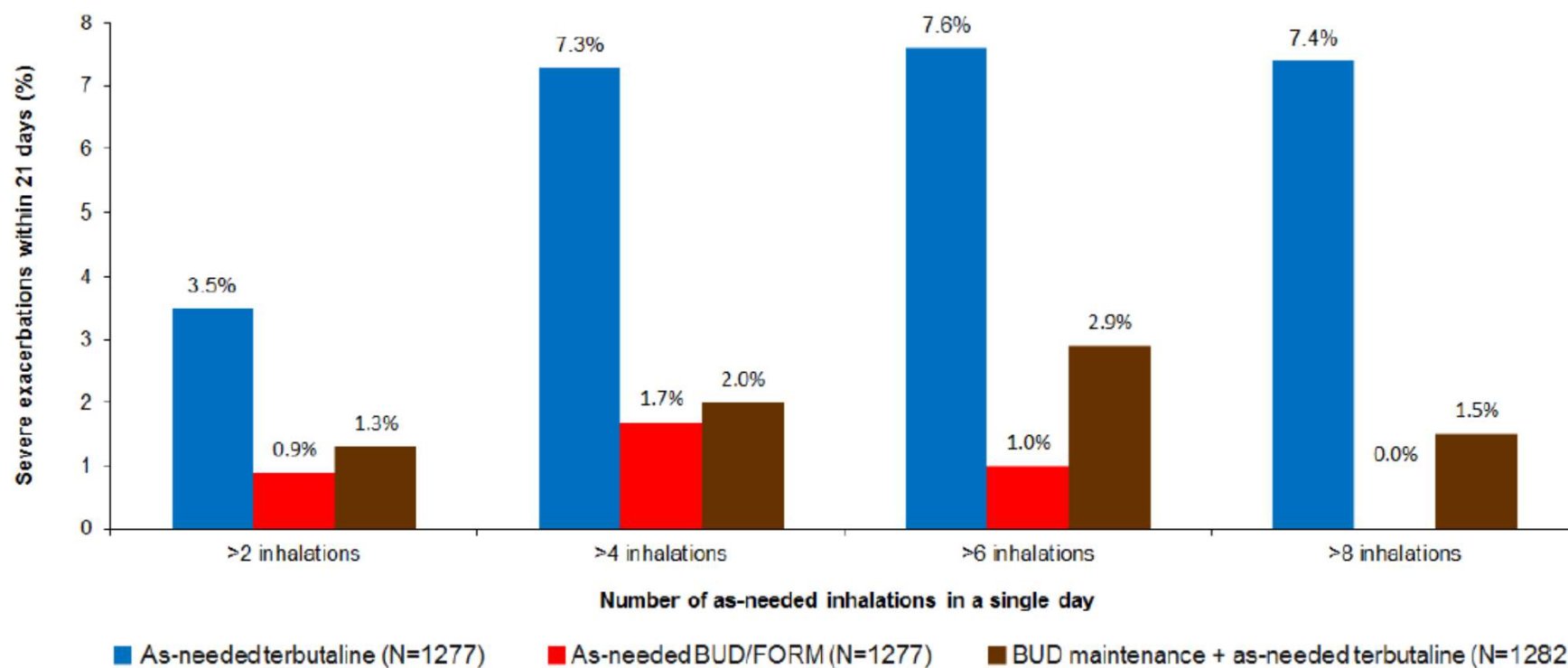
C)



D)



Anti-Inflammatoire Reliever (AIR: Symbicort zo nodig) vermindert ernstige astma exacerbaties op korte termijn tov SABA



SABA

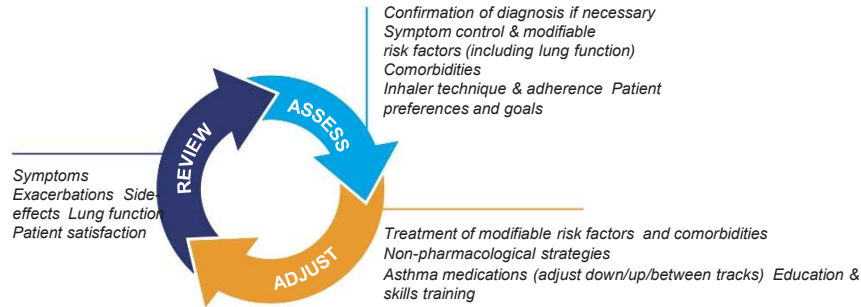
Anti-Inflammatoire Reliever (AIR):
Symbicort zo nodig als kortademig

P. O'Byrne et al, Lancet RM 2020.

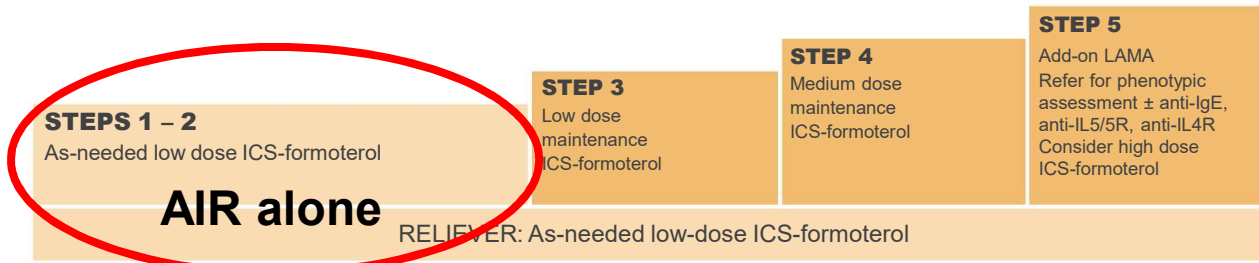
GINA 2021: Management of asthma: AIR alone

**Adults & adolescents
12+ years**

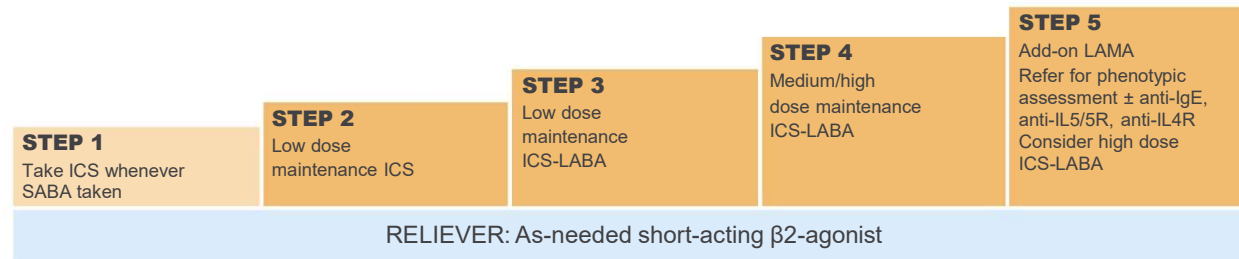
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Maintenance en Anti-inflammatoire Reliever Therapie (MART)

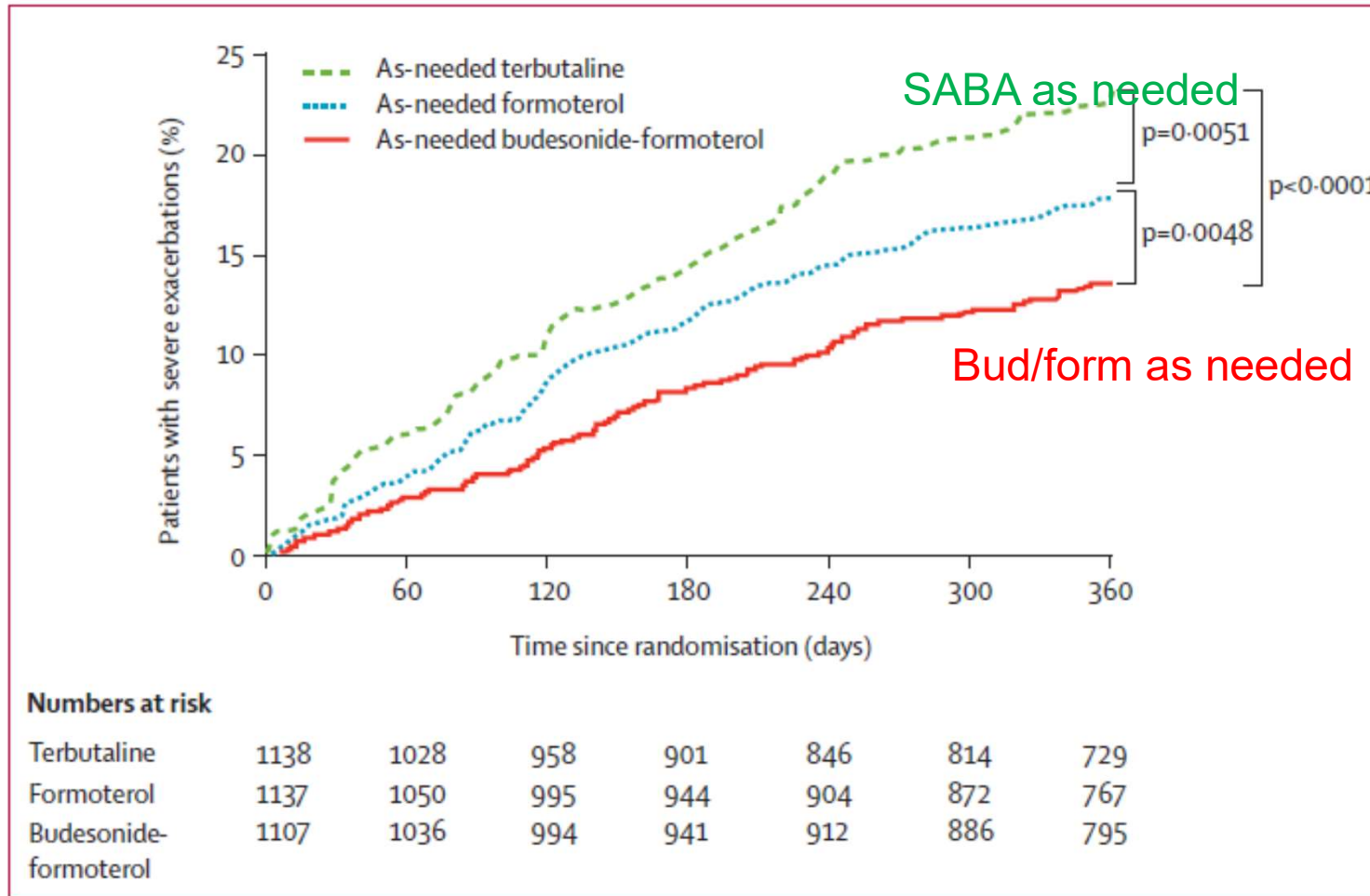
ICS	LABA	Merknaam	Inhalator	Dosis	Dosering
<u>Budesonide</u>	Formoterol	Symbicort ®	Dosisaërosol <i>Turbohaler</i>	<u>160/4,5</u> <u>160/4,5</u>	2x 1 à 2 puffs 2x 1 à 2 inh. plus extra zo nodig
<u>Beclometason</u>	Formoterol	Inuvair ®	Dosisaërosol <i>Nexthaler</i>	<u>100/6</u> <u>100/6</u>	2x 1 à 2 puffs 2x 1 à 2 inh. plus extra zo nodig

Symbicort of Inuvair MART:

als onderhoudsbehandeling

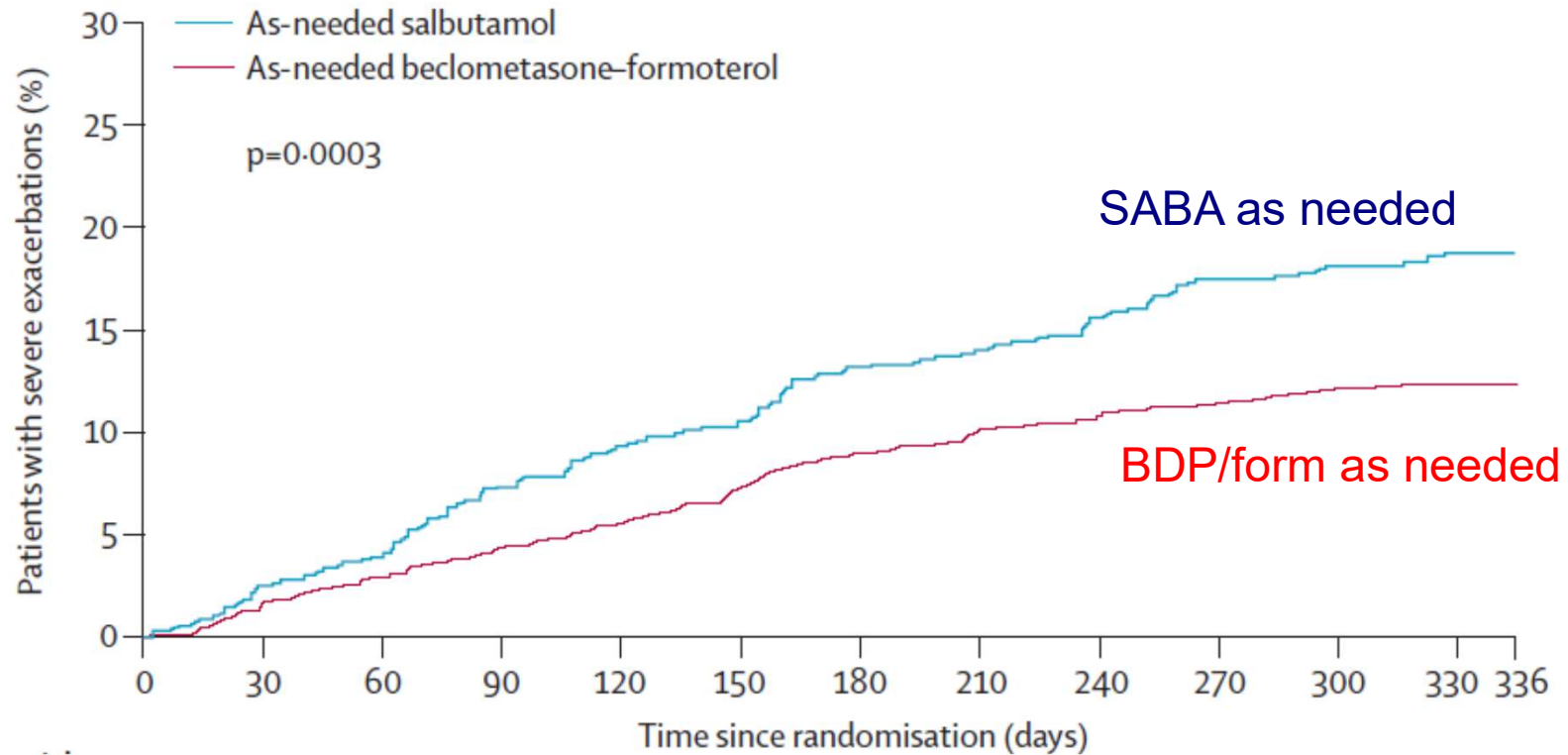
EN als “reliever” therapie (zo nodig als kortademig).

Bud/form Maintenance and Anti-inflammatory Reliever Treatment (MART) in moderate-to-severe asthma



K. Rabe et al, Lancet 2006.

BDP/form Maintenance and Anti-inflammatory Reliever Treatment (MART) in moderate-to-severe asthma



A. Papi et al, Lancet RM 2013.

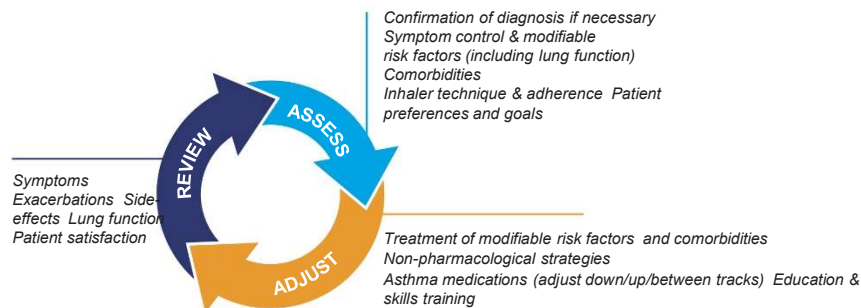
GINA 2021: Management of asthma: MART



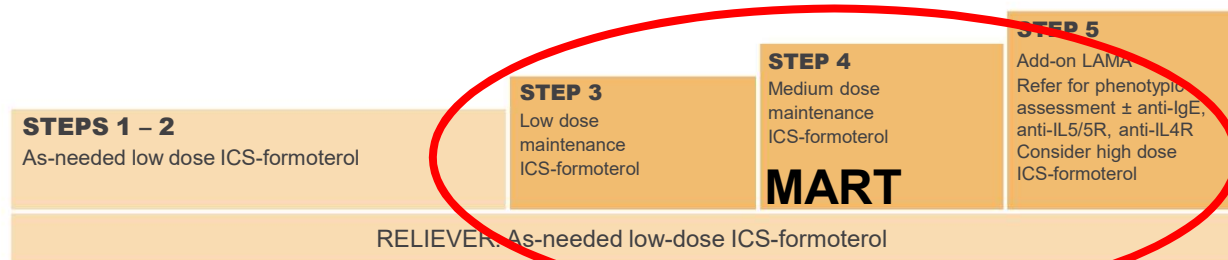
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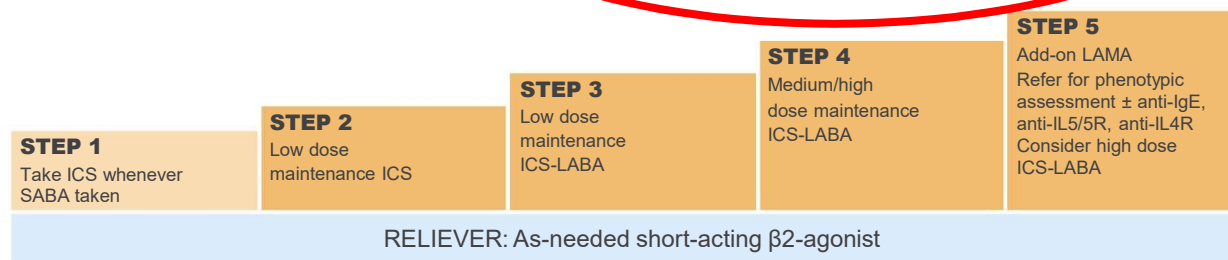
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CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever



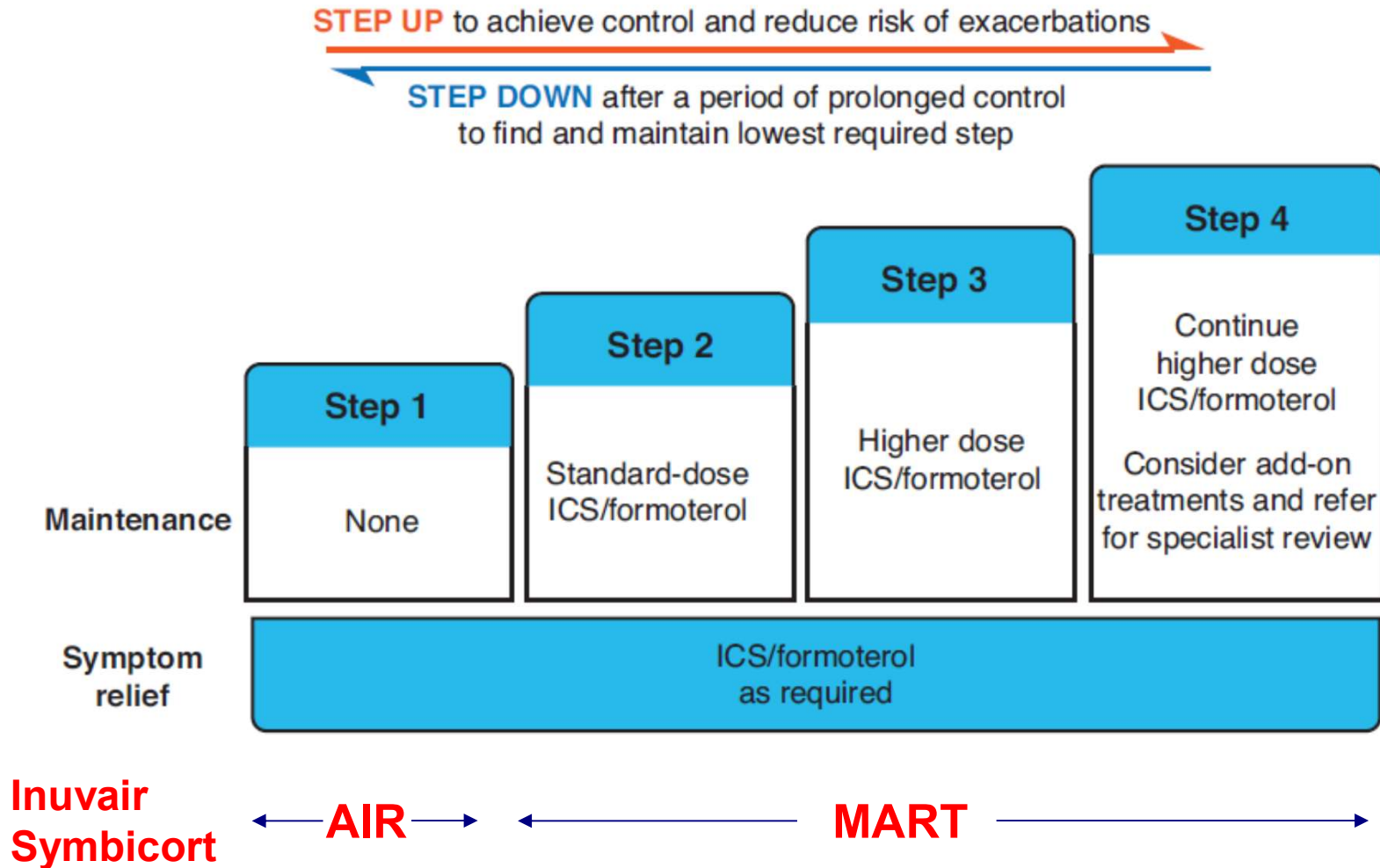
CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller



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A Anti-inflammatory Reliever therapy (AIR) based algorithm using ICS/formoterol



GINA: Track 1: AIR versus MART met ICS/formoterol (Inuvair of Symbicort)

	AIR (alone) (GINA steps 1 and 2)	MART (GINA steps 3, 4 and 5)
Acronym	<u>A</u> nti- <u>I</u> nflammatory <u>R</u> eliever (AIR)	<u>M</u> aintenance and <u>A</u> nti-inflammatory <u>R</u> eliever <u>T</u> herapy (MART)
Definition	As-needed low dose ICS-formoterol used as reliever	Daily low or medium (or high) dose maintenance ICS-formoterol <i>plus</i> As-needed low dose ICS-formoterol used as reliever
Aim	To treat asthma symptoms and prevent exacerbations	To treat and control asthma symptoms and prevent exacerbations
Indication	Mild asthma: GINA steps 1 and 2	Moderate-to-severe asthma: GINA steps 3, 4 and 5
Age categories	Adults and adolescents (12+ years)	Adults, adolescents (12+ years) and children (6-11 years)
Clinical characteristics (before start of treatment)	Infrequent asthma symptoms (≤ 2 x/week) AND No waking with asthma at night	Daily or most days asthma symptoms OR Waking with asthma at night
Lung function (spirometry or PEF)	Normal or near-normal lung function	Low or normal lung function



Levels of Asthma Control

Characteristic	Controlled	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	None (2 or less / week)	More than twice / week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for rescue / "reliever" treatment	None (2 or less / week)	More than twice / week	
Lung function (PEF or FEV₁)	Normal	< 80% predicted	
Exacerbation	None	One or more / year	

Als astma niet onder controle is

- **Slechte therapietrouw (ICS)**
- **Slechte inhalatietechniek**
- **Roken**
- **Blijvende blootstelling aan allergenen**
- **Significante comorbiditeit**
- **Foute diagnose**
- **Ernstig astma**

Asthma dat niet onder controle is: first things first: adherentie en inhalatietechniek verbeteren

■ In patiënten met ongecontroleerd astma,
is het zeer belangrijk om:

1) **Adherentie** te checken en optimaliseren:

- * tov onderhoudsbehandeling (ICS; ICS+LABA),
- * idealiter als **ICS/formoterol MART**

en

2) **Inhalatietechniek** te checken en optimaliseren:

- * **GGG: Goed Gebruik Geneesmiddelen**
- * App: **My puff.**

www.apb.be

App: My Puff



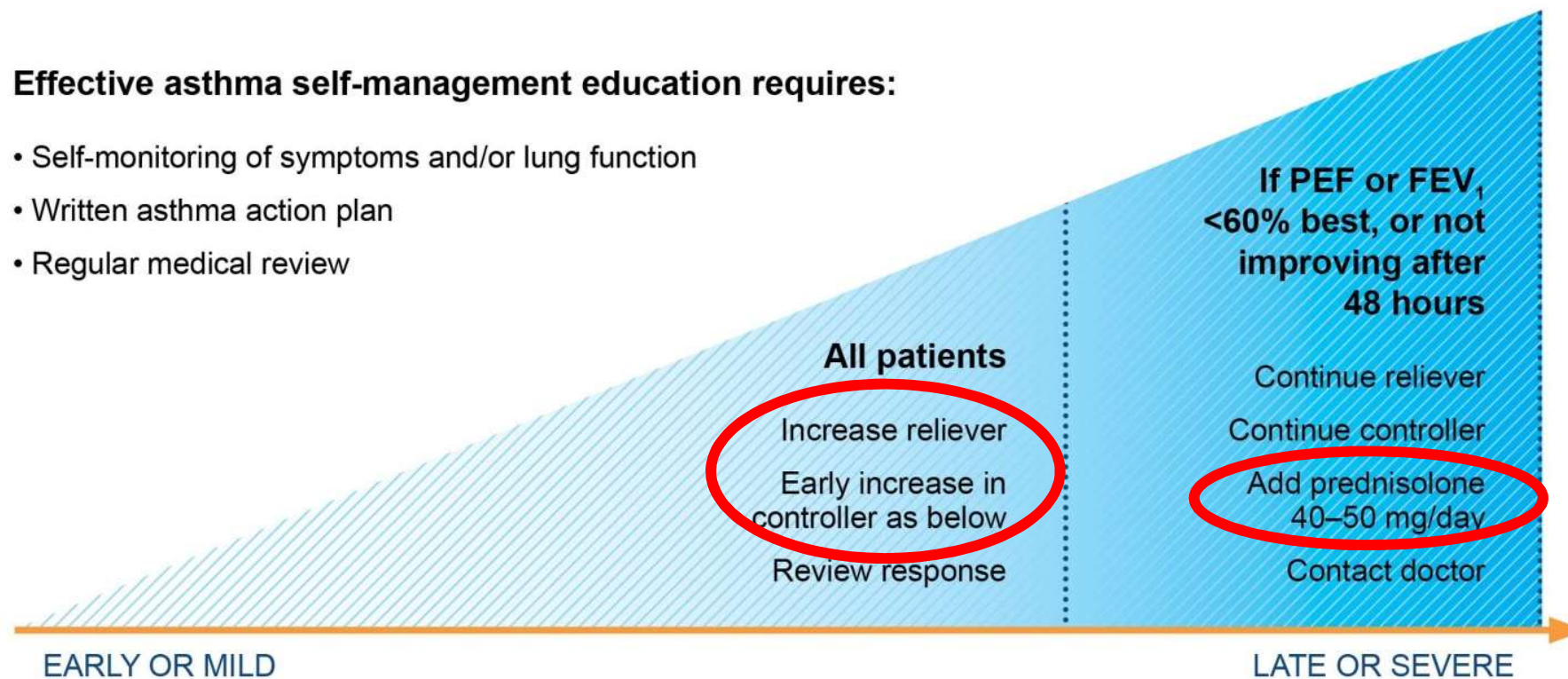
Voorschrift: R/ GGG = Goed Gebruik Geneesmiddelen

Behandeling van Acute Exacerbatie van Astma



Effective asthma self-management education requires:

- Self-monitoring of symptoms and/or lung function
- Written asthma action plan
- Regular medical review



Inuvair MART!
Symbicort MART!

Zo nodig: zuurstof
spoedopname
hospitalisatie

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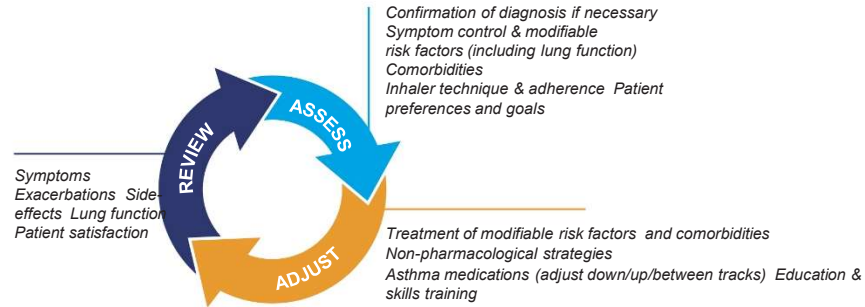
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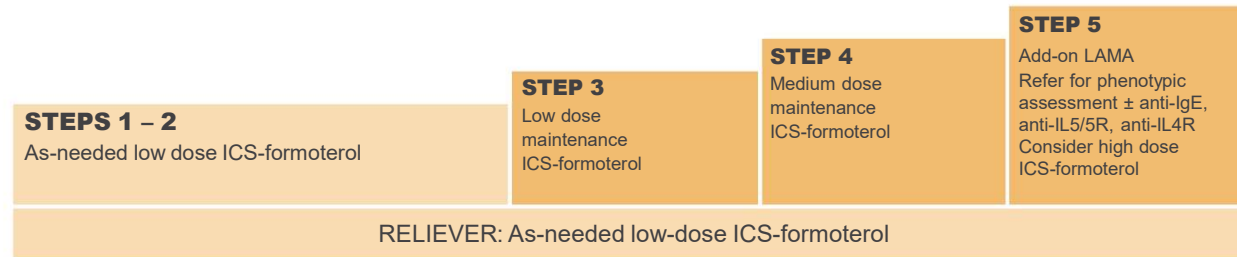
Adults & adolescents 12+ years

Personalized asthma management

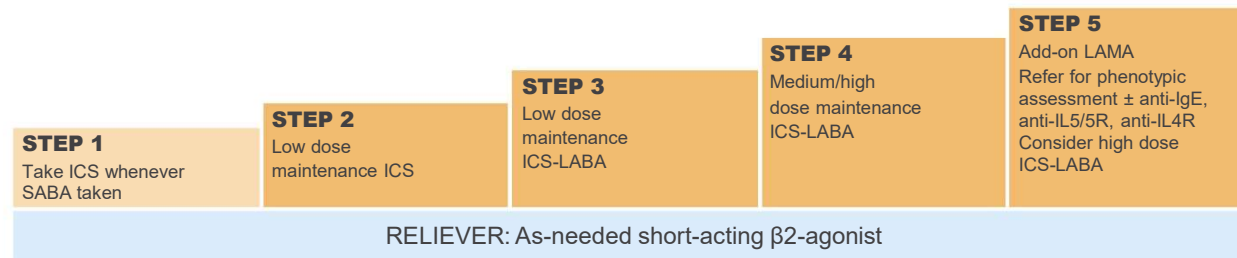
Assess, Adjust, Review
for individual patient needs



CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever



CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller



Other controller options for either track

Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	Medium dose ICS, or add LTRA, or add HDM SLIT	Add LAMA or LTRA, or switch to high dose ICS	Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects
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Behandeling van Astma in 2022

- ICS/formoterol (Symbicort of Inuvair):
 - als **AIR** (Anti-Inflammatoire Reliever) bij mild astma;
 - als **MART** bij matig-tot-ernstig astma.
- ICS/LABA (bv Relvar of Seretide):

als onderhoudsbehandeling bij matig-tot-ernstig astma;
- SABA (Ventolin)? uitsluitend “as needed” bij patiënten met goed gecontroleerd astma (die SABA zelden nodig hebben); nooit als monotherapie bij astma!
- LABA? nooit als monotherapie bij astma!

Bij adolescenten en volwassenen met astma, wanneer is gebruik van SABA aangewezen?

- A. Als acute behandeling van een astma aanval op Spoedopname of Huisartsen wachtpost
- B. Om reversibiliteit te testen in het longfunctie labo (als de spirometrie obstructief is)
- C. Als reliever bij patiënten met goed gecontroleerd astma die hun reliever (zeer) zelden nodig hebben
- D. Als profylaxie voor zware inspanningen (\leq éénmaal per week) bij patiënten met goed gecontroleerd astma
- E. Alle bovenstaande

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- E. **Alle bovenstaande**

**Bij adolescenten en volwassenen met astma,
wanneer is gebruik van SABA uit den boze?**

- A. Abusus van SABA (vele keren per dag)
- B. Regelmatig gebruik van SABA (b.v. tweemaal daags)
- C. Profylactisch gebruik van SABA voor de minste inspanning
- D. Frequent gebruik van SABA als reliever wegens kortademigheid (meerdere keren per week)
- E. Alle bovenstaande

**Bij adolescenten en volwassenen met astma,
wanneer is gebruik van SABA uit den boze?**

- A. Abusus van SABA (vele keren per dag of nacht)
- B. Regelmatig gebruik van SABA (b.v. tweemaal daags)
- C. Profylactisch gebruik van SABA voor de minste inspanning
- D. Frequent gebruik van SABA als reliever wegens kortademigheid (meerdere keren per week)
- E. Alle bovenstaande**



Global Initiative for Asthma

www.ginasthma.com



Global Initiative for Chronic Obstructive Lung Disease

www.goldcopd.com

