Asthma Control: Setting Goals

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Presenter Disclosures

Eric D Bateman

Lecture Fees: AstraZeneca, Alk Abello, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Nycomed, Pfizer, TEVA

Consultancy or Advisory Boards: Almirall, AlkAbello, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Forest, Hoffmann la Roche, GlaxoSmithKline, Merck, Morria Biopharmaceuticals, Novartis, Nycomed, Pfizer, ScheringPlough

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Asthma Control: Setting Goals

Learning objectives

- To review current thinking on what defines acceptable asthma control
- To review tools that are available to evaluate control
- To review how to set goals to achieve asthma control
GINA 2006 treatment approach

Control-driven management
“to achieve and maintain control”

“Treating to target”
Asthma Control: Setting Goals

What do you view as

- Acceptable control of asthma?
- Optimal control?
- Ideal control?
- Are they different?
Baseline characteristics in two studies

<table>
<thead>
<tr>
<th>Chuchalin <em>et al</em></th>
<th>STUDY A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Mean PEF (FEV1) % pred.</strong></td>
</tr>
<tr>
<td>Salm-FP qd</td>
<td>87 (97)</td>
</tr>
<tr>
<td>FP bid</td>
<td>87 (96)</td>
</tr>
<tr>
<td>Placebo</td>
<td>88 (98)</td>
</tr>
</tbody>
</table>

Mean age = 34 years

<table>
<thead>
<tr>
<th>Papi <em>et al</em></th>
<th>STUDY B</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDP-Alb prn</td>
<td>89</td>
</tr>
<tr>
<td>Alb prn</td>
<td>89</td>
</tr>
<tr>
<td>BDP bid</td>
<td>89</td>
</tr>
<tr>
<td>BDP-Alb bid</td>
<td>87</td>
</tr>
</tbody>
</table>

Mean age = 37 years

Chuchalin A *et al*. 2008
Papi et al: % days without symptoms

- Baseline
- Wks 23-24

P = 0.04

No placebo!

Once-daily low-dose Salm-FP in Mild Asthma: Symptom-free days

Chuchalin A et al. 2008
ATS/ERS Statement: Asthma Control and Exacerbations


Standardizing Endpoints for Clinical Asthma Trials and Clinical Practice


This Joint Statement of the American Thoracic Society and European Respiratory Society was approved by the ATS Board of Directors on March 13, 2009 and by the ERS Executive Committee on November 27, 2008.

Asthma goals are based on:

- What is possible to achieve with treatment
- Benefit — the immediate and long-term benefits of treatment
- Cost — financial / short and long-term side-effects of treatment
Percentage of patients achieved “total control” and “well-controlled” asthma with Salm-FP and FP


All strata (8-week assessment at end of phase 2)
ACT score and GINA categories in outpatients with asthma in five European countries and the USA

Study date: Q1 2007
France, Italy, UK, Spain, Germany and USA
N = 2949 patients: 10 consecutive from each doctor
GP 50, Pulmonologists 50 and Allergists 20 in each country

GOAL: Who is less likely to achieve Well-Controlled asthma?

- Smokers < ex-smokers
- Men
- Longer duration of asthma
- Lower lung function
- Lack of control on ICS

Pedersen SE et al, JACI 2007
Measures of Clinical Control of Chronic Diseases

Overall Control

- Achieve and maintain Current Control
- Achieve and maintain Glycaemic control
- Achieve and maintain Blood Pressure

Future Risk

- Reduce Microvascular complications
- Reduce Cardiovascular complications

Bateman ED et al, JACI 2010
Goals of asthma management

Overall Asthma Control

Current Control
- Symptoms
- Activity
- Reliever use
- Lung function

Future Risk
- Instability/Worsening
- Exacerbations
- Loss of lung function
- Adverse effects of Medication

Bateman ED et al, JACI 2010
Measures of Asthma Control: categorical *versus* continuous measures?

“Control should preferably be described using continuous variables”

Examples – ACQ, ACT, ACSS, ATAQ

“… if categorical descriptors are used, they should be based on clinically meaningful cut points”

Examples – controlled, partly controlled, uncontrolled (GINA 2006)

Taylor DR *et al*, *ERJ* 2008; 32:545-554
The Asthma Control Questionnaire (ACQ) is the most widely used assessment tool in clinical practice.

<table>
<thead>
<tr>
<th>Q1.</th>
<th>On average, during the past week, how often were you woken by your asthma during the night?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Never</td>
</tr>
<tr>
<td>1</td>
<td>Hardly ever</td>
</tr>
<tr>
<td>2</td>
<td>A few times</td>
</tr>
<tr>
<td>3</td>
<td>Several times</td>
</tr>
<tr>
<td>4</td>
<td>Many times</td>
</tr>
<tr>
<td>5</td>
<td>A great many times</td>
</tr>
<tr>
<td>6</td>
<td>Unable to sleep</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q2.</th>
<th>On average, during the past week, how bad were your asthma symptoms when you woke up in the morning?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>Very mild symptoms</td>
</tr>
<tr>
<td>2</td>
<td>Mild symptoms</td>
</tr>
<tr>
<td>3</td>
<td>Moderate symptoms</td>
</tr>
<tr>
<td>4</td>
<td>Quite severe symptoms</td>
</tr>
<tr>
<td>5</td>
<td>Severe symptoms</td>
</tr>
<tr>
<td>6</td>
<td>Very severe symptoms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q3.</th>
<th>In general, during the past week, how limited were you in your activities because of your asthma?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not limited at all</td>
</tr>
<tr>
<td>1</td>
<td>Very slightly</td>
</tr>
<tr>
<td>2</td>
<td>Slightly limited</td>
</tr>
<tr>
<td>3</td>
<td>Moderately limited</td>
</tr>
<tr>
<td>4</td>
<td>Very limited</td>
</tr>
<tr>
<td>5</td>
<td>Extremely limited</td>
</tr>
<tr>
<td>6</td>
<td>Totally limited</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q4.</th>
<th>In general, during the past week, how bad were your asthma symptoms when you woke up in the morning?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Very little</td>
</tr>
<tr>
<td>2</td>
<td>A little</td>
</tr>
<tr>
<td>3</td>
<td>A moderate amount</td>
</tr>
<tr>
<td>4</td>
<td>Quite a lot</td>
</tr>
<tr>
<td>5</td>
<td>A great deal</td>
</tr>
<tr>
<td>6</td>
<td>A very great deal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q5.</th>
<th>In general, during the past week, how much of the time did you wheeze?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Not at all</td>
</tr>
<tr>
<td>1</td>
<td>Hardly any of</td>
</tr>
<tr>
<td>2</td>
<td>A little of the time</td>
</tr>
<tr>
<td>3</td>
<td>A moderate</td>
</tr>
<tr>
<td>4</td>
<td>A lot of the time</td>
</tr>
<tr>
<td>5</td>
<td>Most of the time</td>
</tr>
<tr>
<td>6</td>
<td>All the time</td>
</tr>
</tbody>
</table>

Questions taken from ACQ-5 a shortened version of the ACQ-7

### Levels of Asthma Control

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controlled (All of the following)</th>
<th>Partly controlled (Any present in any week)</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td>3 or more features of partly controlled asthma present in any week</td>
</tr>
<tr>
<td>Limitations of activities</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Nocturnal symptoms / awakening</td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>Need for rescue / “reliever” treatment</td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td>Lung function (PEF or FEV₁)</td>
<td>Normal</td>
<td>&lt; 80% predicted or personal best (if known) on any day</td>
<td></td>
</tr>
</tbody>
</table>
ACQ-5 score at study end by control state as defined by GINA criteria

ACQ = Asthma Control Questionnaire
GINA: U = Uncontrolled, P = Partly Controlled, C = Controlled

O'Byrne P et al, ERJ 2010
What do our patients want?

- No fear of Exacerbations (attacks)
- Less medicines
- Less cost
- Less side effects
- More stability/predictability

No symptoms (Normal life)
Future risk ... in relation to current control
Natural History of Asthma: Outcomes and Treatment Regimens (TENOR)

Asthma Therapy Assessment Questionnaire (ATAQ) in relation to “asthma events” over subsequent 12 months

Outcome
- Unscheduled contacts
- Oral steroid “bursts”
- ER visits
- Nights in hospital

ATAQ score (vs 0)
1
2
3

Odds ratio
1 3 5 7 9 11 13 15 25

(compared to ATAQ score 0) (n = 987)

Chen H et al, JACI 2007; 120: 376-402
Exacerbation rate in maintenance phase
(according to control status achieved in phase I)

Mean exacerbation rate per patient per year

Stratum 1: ICS-naive
- Not TC or WC
  - Fluticasone: 0.13
  - Salm-FP: 0.05
  - Total control: 0.01
- Well controlled
  - Fluticasone: 0.28
  - Salm-FP: 0.09
  - Total control: 0.02
- Total control
  - Fluticasone: 0.23
  - Salm-FP: 0.19
  - Total control: 0.13

Stratum 3: Moderate ICS
- Not TC or WC
  - Fluticasone: 0.42
  - Salm-FP: 0.19
  - Total control: 0.13
- Well controlled
  - Fluticasone: 0.42
  - Salm-FP: 0.19
  - Total control: 0.13
- Total control
  - Fluticasone: 0.42
  - Salm-FP: 0.19
  - Total control: 0.13

Historical = 0.70

*Requiring either oral steroids or hospitalisation / emergency visit

GOAL Study
Predicting asthma exacerbations from current level of Asthma Control

* Markov Model: Transitional probability independent of time (homogeneous)

- Controlled
  - 75%
- Partly Controlled
  - 20%
- Uncontrolled
  - 5%
- Exacerbation
  - 0.05%

SMART Studies: Bateman ED et al, JACI 2010
Predicting asthma exacerbations from current level of Asthma Control

* Markov Model: Transitional probability independent of time (homogeneous)


SMART Studies: Bateman ED et al, JACI 2010
Predicting asthma exacerbations from current level of Asthma Control

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SMART Studies: Bateman ED et al, JACI 2010
Asthma Control: Setting Goals

**Summary**

- What is acceptable asthma control? - Partly controlled or better
- How to measure control? – Composite measure (e.g. ACT) or categorical method (e.g. GINA)
- How to set goals? Individualize but understand risks and benefits, and differential effects of drugs