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Worsening asthma in adults

Part 1: Preventing exacerbations and developing an action plan

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Despite recent significant advances in the control of asthma, exacerbations still cause significant morbidity and mortality. The first part of this two-part article discusses strategies for the prevention of exacerbations, the early identification of worsening asthma, and patient self-management using a written action plan.

Key points

- **Ensure patients are taking preventer medication regularly.**
- **Check and provide skills training for optimal use of inhaler devices.**
- **Identify avoidable patient-specific triggers of worsening asthma.**
- **Educate patients to recognise early signs of worsening asthma through self-monitoring of symptoms or objective measures such as peak expiratory flow.**
- **Provide a written asthma action plan, tailored to the individual patient, that includes details of preventers and relievers for use when asthma is under control, an escalation plan for when asthma worsens and advice on when to seek medical or emergency care.**
- **Review the asthma action plan annually or when maintenance treatment changes.**

Asthma is a common and widespread chronic disease, affecting millions of people worldwide. Asthma is defined as 'a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.'[1]

Asthma exacerbations have been defined in several ways, but consensus guidelines define them as events characterised by a change in symptoms and lung function from the patient's previous status; in clinical practice, they are recognised as episodes that are troublesome to patients and that prompt a need for a change in treatment.[2] Despite recent significant advances in the control of asthma, exacerbations still cause significant morbidity and mortality.

In this two-part article, we present a practical guide to the prevention and management of worsening asthma in adults, based on current guidelines and the practices at our institution. The management of worsening asthma in children will not be discussed as the signs, symptoms, investigation and management are significantly different and beyond the scope of this review. Whereas most literature focuses on in-hospital care of acute severe asthma, this article highlights the need for continuity in management of asthma across the spectrum,

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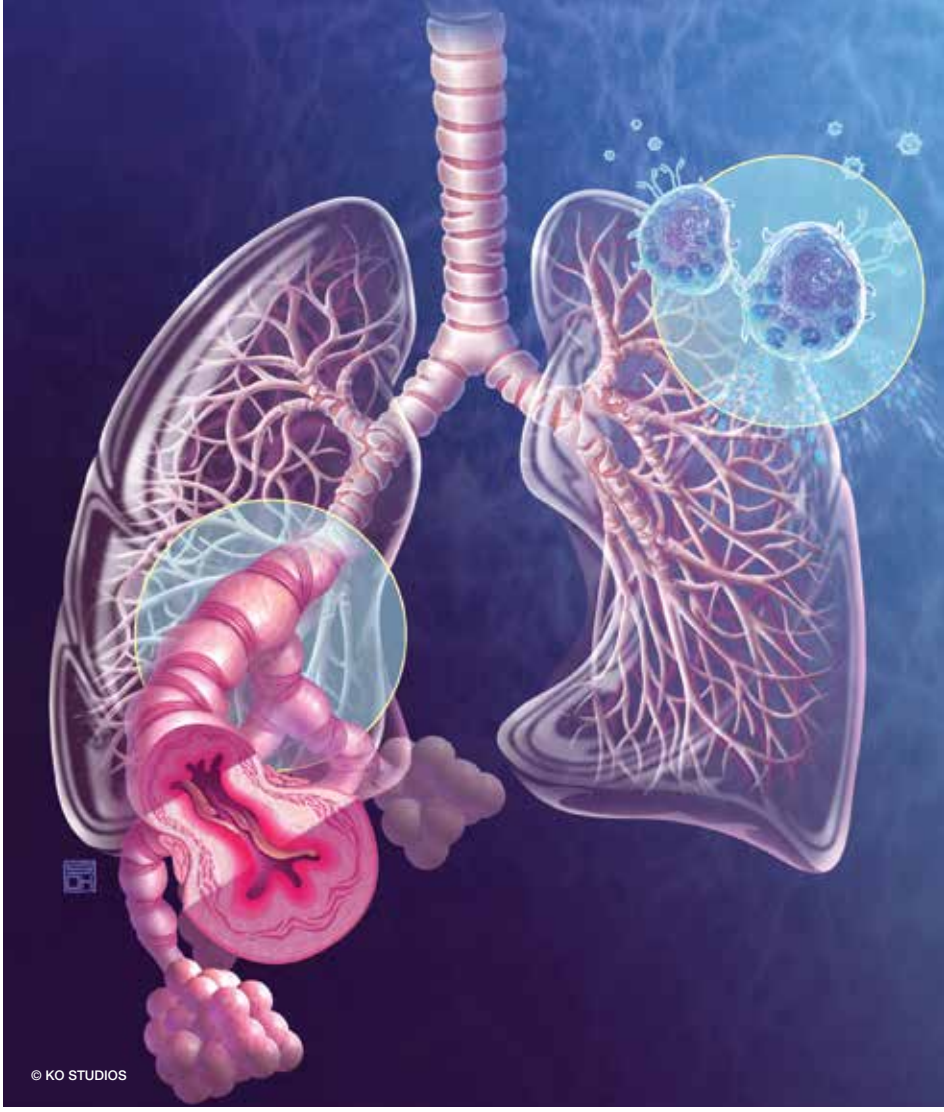
from prevention of exacerbations, monitoring and early self-management of worsening asthma using a written asthma action plan (Part 1) through to primary care and hospital treatment of exacerbations, and then the transition back to stable treatment (Part 2).

Good asthma management should include providing the patient with:

- strategies to prevent exacerbations, through
  - prescribing an effective preventer medication regimen
  - checking inhaler technique and adherence
  - identifying avoidable exacerbation triggers
- strategies to identify and manage worsening asthma, through
  - encouraging regular self-monitoring
  - developing a written asthma action plan
  - conducting regular medical review, including review of the action plan.

These aspects of the management of worsening asthma in adults are the focus of the first part of this two-part article.



PREVENTING EXACERBATIONS

Ensure patients take regular preventer medication

The most effective strategy for preventing asthma exacerbations is to ensure that patients are taking a preventer medication regularly. Inhaled corticosteroids, even at very low doses, are remarkably effective in reducing asthma deaths and hospitalisations.[3,4] In Australia, currently available inhaled corticosteroids for maintenance therapy in asthma are beclomethasone, budesonide, ciclesonide and fluticasone. In patients whose asthma is not adequately controlled with inhaled corticosteroids alone, a further small reduction in exacerbations can be achieved by adding a long-acting β_2-agonist, preferably as a combination inhaler (e.g. budesonide/eformoterol, fluticasone/salmeterol or fluticasone/eformoterol).[5]

In patients who have had an exacerbation in the previous 12 months, who are therefore at higher risk of another exacerbation in coming months, the greatest reduction in exacerbations is seen with the use of budesonide/eformoterol as a 'Single Maintenance and Reliever Therapy' (SMART) regimen.[6] This regimen prescribes use of the low-dose combination inhaler not only for regular twice-daily maintenance treatment but also for relief of any day-to-day symptoms. This allows for the early uptitration of both the inhaled corticosteroid budesonide and the rapid-onset, long-acting bronchodilator eformoterol at the earliest symptoms of worsening asthma. Available therapies of budesonide/eformoterol that been approved for a SMART regimen are the 100/6 μg and 200/6 μg dry powder inhalers (one inhalation at a time) and the 50/3 μg and 100/3 μg pressurised metered-dose inhalers (two puffs at a time).

Although patients are sometimes fearful of regular inhaled corticosteroid treatment, these medications have a highly favourable risk–benefit ratio as most of the benefit for asthma is seen at low doses, at which the risk of systemic or local side effects is very low.[7] Long-term use of high-dose inhaled corticosteroids is associated with an increase in the normal age-related risk of osteoporosis, cataract and glaucoma, but for asthma, high doses are needed in only a small proportion of patients, and the risk is small compared with the risk

of leaving asthma uncontrolled.[1] The local side effects of dysphonia and oral thrush are also dose-related and can be minimised by correct inhaler technique and (for oral thrush) by rinsing the mouth with water and spitting out after use. For pressurised metered-dose inhalers, the risk of local side effects can be reduced by always using a spacer.

Check inhaler technique and adherence

It is essential that patients understand the importance of regular use of their prescribed preventer medication and are trained in optimal inhaler technique. Common delivery devices include pressurised metered-dose inhalers, with or without a spacer, and dry powder inhalers (either multidose or single-dose delivery). Each delivery system has its advantages and disadvantages.

Poor drug delivery as a result of poor technique can lead to recurrent exacerbations, emergency department presentations and hospitalisations.[8] It is essential that patients are educated in inhaler use at the time of prescribing, and that their technique is checked regularly, particularly if symptom control seems inadequate or an exacerbation occurs.

Similarly, poor adherence with preventer medications is also associated with an increased risk of exacerbations.[9,10] Asking about medication use in an empathic, accepting way will often elicit a more honest response about adherence than a confrontational approach.[11]

Recognise avoidable exacerbation triggers

An important strategy for reducing exacerbations is for patients to recognise and avoid where appropriate their potential exacerbation triggers. Common triggers include (but are not restricted to):

- viral upper respiratory tract infections
- organic or inorganic particulate matter or vapour
- certain foods
- cold air.

Some triggers can be identified through thorough history taking, and some can be specifically tested for by allergen testing.

Although some triggers may be difficult to avoid, such as viral upper respiratory tract infections, asking patients about the context of their exacerbations may help to identify avoidable triggers such as running out of medication or, for cat-allergic patients, staying overnight in a house with cats. Avoidance is important with food allergy, as this is an important risk factor for asthma death, particularly in children and young adults.[12] Patients who are allergic to rye grass pollen should avoid being outdoors during spring and summer thunderstorms.[13] However, for perennial allergens such as house dust mite, or for patients with multiple allergies, avoidance strategies have not been shown to be effective in preventing exacerbations.[1]

IDENTIFYING AND MANAGING WORSENING ASTHMA

Educate patients to recognise early symptoms

Good patient education about symptom recognition is essential for the early identification of asthma exacerbations. For most patients, self-monitoring of symptoms is sufficient.[14] However, a subset of patients are poor perceivers of airflow limitation – either high- or low-perceiving.[15]

High-perceiving patients may inappropriately initiate additional therapy and unnecessarily overuse β_2-agonists and inhaled or oral corticosteroids, thereby exposing themselves to avoidable side effects. High-perceivers may be identified by measuring lung function when symptoms are present.

Low-perceiving patients may not recognise the early onset of worsening asthma, leading to late presentation and more severe exacerbations. Low-perceivers may be identified by a lack of change in symptoms with a 20% rise in lung function (e.g. after bronchodilator use) or with a 15 to 20% fall in lung function (e.g. after exercise, or during a bronchial provocation test in a respiratory function laboratory).

Both high- and low- perceivers, together with patients with severe asthma, may benefit from monitoring with objective measures such as peak expiratory flow in addition to symptoms. Recording peak flow values on a standardised chart with a low aspect ratio (i.e. horizontally compressed) improves recognition of exacerbations.[16] An example of a suitable peak flow chart is available for free download from the National Asthma Council website (www.nationalasthma.org.au/uploads/content/197-Woolcock-peak-flow-chart.pdf).

Develop a written asthma action plan

It has long been recognised that a written asthma action plan is an important tool in the long-term management of asthma.[17] An action plan empowers patients by providing written instructions about how to recognise worsening asthma and how to escalate asthma treatment and/or seek medical care. By changing therapy early, it is hoped exacerbations will remain mild, rather than progressing to the severe category. However, when an exacerbation does progress, or if it develops rapidly, the action plan helps the patient to recognise severe or life-threatening asthma and to know how to access appropriate emergency care.

Ownership of a written asthma action plan, when accompanied by education in self-management and regular review, is associated with strikingly improved asthma outcomes and reduced health care utilisation.[17] Despite this, and despite asthma guidelines strongly recommending provision of a written action plan for every patient with asthma, ownership of an action plan remains disturbingly low in Australia, around 20 to 30%.[18] Do all of your patients with asthma have a written asthma action plan?

How to construct a written asthma action plan

Aspects generally included in a written asthma action plan are listed in Box 1. The

1. INCLUSIONS IN A WRITTEN ASTHMA ACTION PLAN

- A list of the patient's usual medications
- A list of symptoms of worsening asthma or, for a small proportion of patients, a level of peak flow at which the patient should take action (both should be tailored to the patient)
- A plan of the medications (relievers and preventers) to be used for worsening asthma
- A plan for appropriate escalation of therapy if the initial treatment fails to control symptoms or improve peak flow readings, by increasing bronchodilators and inhaled and/or oral corticosteroids
- When to contact or visit the primary care physician or the emergency department

plan should be individualised and explained to the patient during the consultation. A prescription should be provided for any additional medications required to implement the action plan, and the patient should be advised to have the prescription filled in advance if they are planning travel or have a history of rapid deterioration.

Templates for written asthma action plans may be found on the websites of many asthma-related professional and consumer organisations (e.g. www.nationalasthma.org.au), and brief action plans are sometimes included in electronic health record software. Clinicians should become familiar with one or two templates so that they can complete them quickly during an asthma review.[19] A sample template is shown in the Figure.

An action plan template specific for the budesonide/eformoterol maintenance and reliever SMART regimen was developed by Australian clinicians and approved by the National Asthma Council. It is simple to complete, and is available in several languages on the Council website (www.nationalasthma.org.au/asthma-tools/asthma-action-plans/asthma-action-plan-library#ssaap) and on some medical software.

Choice of medication and escalation of therapy

The medications recommended within a written asthma action plan should be tailored according to the patient's usual medications, their risk of side effects, their preferred level of autonomy in self-management, and in some cases, cost considerations.[20,21] However, a typical action plan may recommend the following.

Reliever medication

- For patients using short-acting β_2-agonist reliever medication (e.g. salbutamol, terbutaline), it should be increased to relieve symptoms; for those using a pressurised metered-dose inhaler, use of a spacer improves delivery.
- For patients prescribed low-dose budesonide/eformoterol maintenance and reliever SMART therapy, the β_2-agonist eformoterol component provides rapid-acting and long-lasting (up to 12 hours) relief and the budesonide component rapidly treats additional airway inflammation. Extra doses of budesonide/eformoterol should be taken as needed as soon as symptoms worsen. The total dose (maintenance plus reliever) should not exceed 72 µg eformoterol in a 24-hour period.

Preventer medication: fixed-dose maintenance inhaled corticosteroids (e.g. beclomethasone, budesonide, ciclesonide, fluticasone) or maintenance inhaled corticosteroid/long-acting β_2-agonist combinations (e.g. budesonide/eformoterol, fluticasone/salmeterol, fluticasone/eformoterol).

- Reinforce regular use of preventer medication. This may serve as a reminder to re-start this medication if recent adherence has been poor. In a study with electronic inhaler monitoring, patients whose reliever medication was budesonide/eformoterol (as part of a single inhaler maintenance and reliever regimen) had fewer days with no inhaled corticosteroid than those on fixed-dose budesonide/eformoterol therapy who were using the short-acting β_2-agonist salbutamol as their reliever.[22]
- Our practice in writing action plans for patients taking maintenance inhaled corticosteroids is to increase the inhaled corticosteroid dose without delay when asthma symptoms start to worsen and to add two to four puffs of an inhaled β_2-agonist via a spacer up to every two to four hours for symptomatic relief. Evidence supporting an increase in inhaled corticosteroid dose when asthma worsens is based on studies of self-management education, and studies in which patients took extra inhaled corticosteroid whenever they took reliever medication.[14,23,24]
- Although many guidelines do not currently recommend doubling of the inhaled corticosteroid dose, based on placebo-controlled clinical trials, the intervention in these trials may have been too late (five to seven days after onset of worsening asthma) to be effective.[25]
- There is evidence that it is effective to quadruple the inhaled corticosteroid dose for seven to 14 days when asthma worsens or at the onset of a cold.[26] In clinical practice, this may be achieved for patients using an inhaled corticosteroid alone or fixed-dose maintenance budesonide/eformoterol by quadrupling the number of maintenance puffs, or for patients using fluticasone/salmeterol, by adding a high-dose corticosteroid

ASTHMA ACTION PLAN

Take this **ASTHMA ACTION PLAN** with you when you visit your doctor

NAME

DATE

NEXT ASTHMA CHECK-UP DUE

DOCTOR'S CONTACT DETAILS

EMERGENCY CONTACT DETAILS

Name

Phone

Relationship

WHEN WELL

Asthma under control (almost no symptoms)

ALWAYS CARRY YOUR RELIEVER WITH YOU

Peak flow* (if used) above:

Your preventer is: ..... (NAME & STRENGTH)

Take ..... puffs/tablets ..... times every day

☐ Use a spacer with your inhaler

Your reliever is: ..... (NAME)

Take ..... puffs .....

When: You have symptoms like wheezing, coughing or shortness of breath

☐ Use a spacer with your inhaler

OTHER INSTRUCTIONS

(e.g. other medicines, trigger avoidance, what to do before exercise)

WHEN NOT WELL

Asthma getting worse (needing more reliever e.g. more than 3 times per week, waking up with asthma, more symptoms than usual, asthma is interfering with usual activities)

Peak flow* (if used) between ..... and .....

Keep taking preventer: ..... (NAME & STRENGTH)

Take ..... puffs/tablets ..... times every day

☐ Use a spacer with your inhaler

Your reliever is: ..... (NAME)

Take ..... puffs .....

☐ Use a spacer with your inhaler

OTHER INSTRUCTIONS ☐ Contact your doctor

(e.g. other medicines, when to stop taking extra medicines)

IF SYMPTOMS GET WORSE

Asthma is severe (needing reliever again within 3 hours, increasing difficulty breathing, waking often at night with asthma symptoms)

Peak flow* (if used) between ..... and .....

Keep taking preventer: ..... (NAME & STRENGTH)

Take ..... puffs/tablets ..... times every day

☐ Use a spacer with your inhaler

Your reliever is: ..... (NAME)

Take ..... puffs .....

☐ Use a spacer with your inhaler

OTHER INSTRUCTIONS ☑ **Contact your doctor today**

(e.g. other medicines, when to stop taking extra medicines)

Prednisolone/prednisone:

Take ..... each morning for ..... days

DANGER SIGNS

Asthma emergency (severe breathing problems, symptoms get worse very quickly, reliever has little or no effect)

DIAL 000 FOR AMBULANCE

Peak flow (if used) below:

Call an ambulance immediately

Say that this is an asthma emergency

Keep taking reliever as often as needed

National Asthma Council Australia

leading the attack against asthma

www.nationalasthma.org.au

* Peak flow not recommended for children under 12 years.

Figure. The National Asthma Council Australia template for an asthma action plan, which is downloadable from the NAC website (www.nationalasthma.org.au/uploads/content/341-nac_asthma_action_plan_colour_a4.pdf).

inhaler for seven to 14 days.[20,27] However, quadrupling the inhaled corticosteroid dose may not be appropriate for patients who might find the cost of an extra inhaler to be an issue or those who need to avoid the possibility of dysphonia, such as singers and teachers.

- For patients using conventional fixed-dose inhaled corticosteroid/long-acting β_2-agonist therapy, doubling the dose also doubles the long-acting β_2-agonist component. For budesonide/eformoterol, the extra eformoterol may provide additional bronchodilatation, as eformoterol shows a dose–response relationship above 12 μg per day. For fluticasone/salmeterol, there is little added benefit from a dose of salmeterol above 100 μg per day, but short-term treatment with 200 μg per day is well tolerated.

Preventer and reliever medication regimen: budesonide/eformoterol as single maintenance and reliever therapy.

- For patients prescribed this treatment regimen, the use of the specific Australian-designed SMART action plan is recommended.
- With this regimen, the initial instruction on the SMART action plan for worsening asthma is the same as the instruction for everyday symptoms; that is, to continue taking maintenance budesonide/eformoterol (as prescribed) morning and night, and to increase use of the same medication as needed for relief of symptoms.
- A maximum dose of 72 μg eformoterol is allowed in a 24-hour period, whether the patient is taking 100/6 or 200/6 dry powder inhalers (i.e. a maximum of 12 inhalations) or the 50/3 or 100/3 pressurised metered-dose inhalers (i.e. a maximum of 24 puffs). Few patients should require such high doses, and medical attention should be sought if symptoms are not controlled at or close to these maximal doses.

Oral corticosteroids: prednisolone.

- If symptoms progress (e.g. reliever is needed every three hours or the patient has difficulty carrying out normal activity), then patients should commence oral corticosteroids (prednisolone), and an inhaled β_2-agonist may be taken via a spacer at up to six to eight puffs every two to three hours. Early review should be advised if symptoms do not respond rapidly because of the risk of fatal asthma or β-receptor downregulation.
- The recommended dose of prednisolone is 1 mg/kg per day (maximum 50 mg per day) for adults, to be taken

for five to 10 days. No tapering is needed, except for patients with troublesome side effects[20] or those who need oral corticosteroids for more than 14 days.
- Add-on high-dose inhaled corticosteroid (as above) may provide an alternative strategy for patients who experience severe side effects with oral corticosteroids.[20,25]
- For patients prescribed budesonide/eformoterol as maintenance and reliever therapy, the SMART action plan generally recommends oral corticosteroids if the patient requires more than 36 µg of eformoterol in as-needed inhalations for two to three days in a row.

Presenting for urgent medical review

- Patients should be advised when to present to their primary care physician; this will depend on factors such as their preference for autonomy in self-management and the speed of onset and severity of previous exacerbations.[21]
- If symptoms are not controlled despite the above strategies, or symptoms deteriorate, then patients must present to an emergency department for review and further management.
- Reliever medication should continue to be taken as needed en route to the hospital.

WHEN SYMPTOMS CONTINUE TO WORSEN

If patients adhere to their prescribed action plan, including commencing oral corticosteroids if indicated, they can often avoid progression to a more severe exacerbation.[17] Those whose condition deteriorates despite implementing their action plan, or those who experience sudden severe exacerbations, should be considered at high risk. However, the many factors that may influence the apparent failure of an asthma action plan should be explored before labelling the patient 'high risk,' or 'treatment resistant'. Possible contributors to the failure of an asthma action plan are shown in Box 2. High-risk patients often require early and more frequent review by medical practitioners, and may also require monitoring with objective measures such as peak flow. There should also be a low threshold for referral to an emergency department in those who are considered high risk or treatment resistant, as the condition of these patients can deteriorate faster. This will be covered in more detail in Part 2 of this article.

The key components for clinical effectiveness of written asthma action plans have been identified by a systematic review as:[14]

- use of two to four action points

2. POSSIBLE CONTRIBUTORS TO FAILURE OF AN ASTHMA ACTION PLAN

- Poor inhaler technique, leading to decreased drug delivery
- Out-of-date medications, leading to decreased drug potency
- Poor adherence to maintenance preventer treatment or to the action plan, perhaps because of poor education or social circumstances such as poor access to the prescribed medications
- Respiratory viral infection, which may be associated with severe exacerbations, even in patients with mild or well-controlled asthma
- (Rarely) bacterial infection contributing to respiratory deterioration
- Inappropriate 'action points' specified for the patient's asthma severity or usual level of control

- inclusion of both inhaled and oral corticosteroids on the action plan
- (for peak flow-based plans) use of personal best rather than predicted peak flow values.

HOW TO REVIEW AN ASTHMA ACTION PLAN

A patient's written asthma action plan should be reviewed annually or when maintenance treatments are changed. Review of the action plan is a specified component of the Asthma Cycle of Care GP incentive program. A review should include the following:

- Does the patient know where their action plan is?
- Have the patient's usual asthma medications been changed since the action plan was written?
- If the patient's asthma has flared up since the action plan was issued, did the patient use their action plan? If not, what were the barriers? If it was used, were there any problems or side effects?
- Do the action points or medications need to be modified?

CONCLUSION

Patient education, optimisation of inhaler technique and planning are essential in the management of worsening asthma, to allow early identification of an exacerbation and implementation of appropriate therapy to prevent progression to a more severe exacerbation. The management of more severe asthma exacerbations, including assessment of exacerbation severity, treatment modalities available and post-exacerbation follow up, will be discussed in Part 2 of this article, to be published in a future issue of *Medicine Today*. MT

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A list of references is included in the website version (www.medicinetoday.com.au) and the iPad app version of this article.

COMPETING INTERESTS: Dr Yan has received honoraria for giving lectures from AstraZeneca, GlaxoSmithKline, Novartis and Takeda (Nycomed). Associate Professor Reddel has participated in advisory boards for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis; has received consultancy fees from GlaxoSmithKline and research funding from AstraZeneca and GlaxoSmithKline; has provided independent continuing medical education for AstraZeneca, GlaxoSmithKline and Novartis; and is participating in a data safety monitoring committee for AstraZeneca, GlaxoSmithKline, Merck and Novartis. Dr Hamor: None.

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