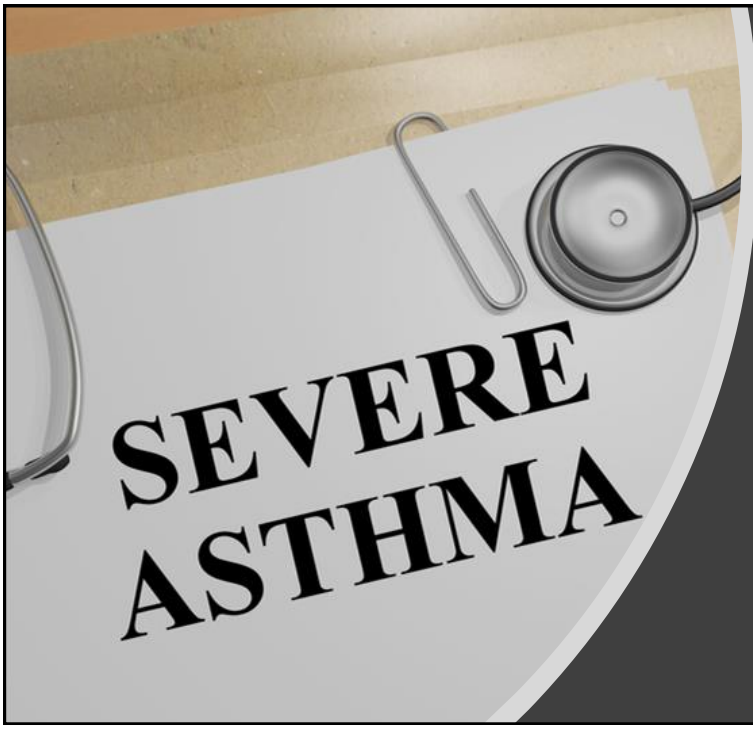


從A到Z線上藥學論壇

# 防範嚴重氣喘過度依賴口服類固醇

三軍總醫院臨床藥學部
林麗卿

2022/03/19

## 大綱

- 嚴重氣喘的簡介
- 案例分享
- 生物製劑用於嚴重氣喘及防範口服類固醇過度依賴

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# 大綱

- 嚴重氣喘的簡介
- 案例分享
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## About asthma

- Asthma is the most common chronic non-communicable disease, affecting over 260 million people globally in 2019
- The Taiwan National Health Insurance database, prevalence of asthma among residents older than 18 years has increased from 7.57% in 2000 to 10.57% in 2011.

GINA Update 2021
Severe asthma casebook, 2020

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- Asthma is characterized by **variable respiratory symptoms** such as wheeze, shortness of breath, chest tightness and cough, and **variable expiratory airflow limitation**. It is usually associated with **airway inflammation**
- People with asthma often have periods of worsening symptoms and worsening airway obstruction, called **exacerbations** (also called attacks or flare-ups), that can be fatal
- Most of the morbidity and mortality associated with asthma is preventable, particularly with use of inhaled corticosteroids


https://toolkit.severeasthma.org.au/severe-asthma/symptoms/

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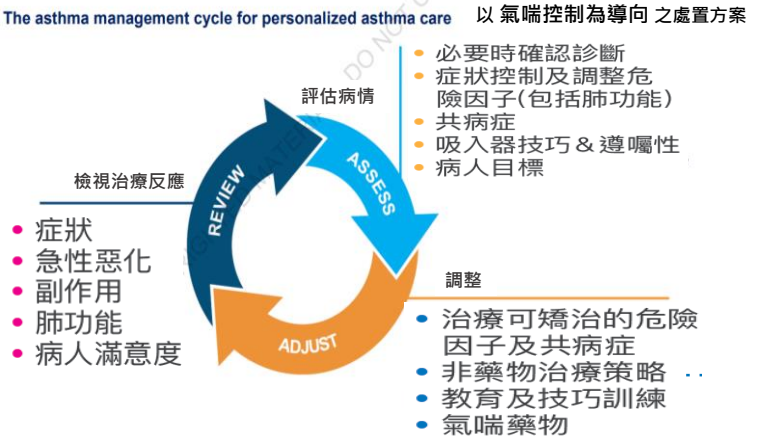
# 氣喘治療控制目標

◆**控制症狀**
- 達到並維持症狀的控制
- 維持正常活動

◆**降低風險**
- ●避免氣喘發作
- ●避免藥物副作用
- ●預防氣喘相關死亡

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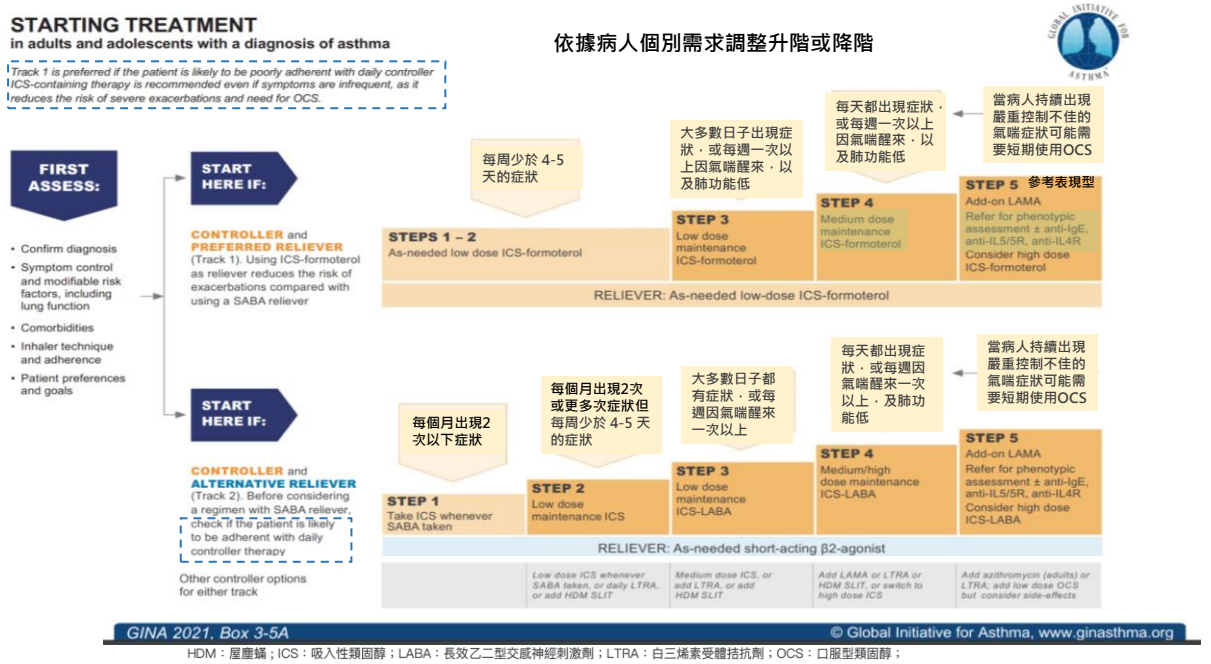


HDM：屋塵蟎；ICS：吸入性類固醇；LABA：長效乙二型交感神經刺激劑；LTRA：白三烯素受體拮抗劑；OCS：口服型類固醇；
SABA：短效乙二型交感神經刺激劑；SLIT：舌下免疫療法

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# Low, medium and high ICS doses: adults/adolescents

**Adults and adolescents (12 years and older)**

| Inhaled corticosteroid | Total daily ICS dose (mcg) – see notes above Low | Medium | High |
|---|---|---|---|
| Beclometasone dipropionate (pMDI, standard particle, HFA) | 200-500 | >500-1000 | >1000 |
| Beclometasone dipropionate (DPI or pMDI, extrafine particle, HFA) Foster (100) | 100–200 | >200–400 | >400 |
| Budesonide (DPI, or pMDI, standard particle, HFA) Pulmicort (200) , Symbicort (160[200]), Duasma (200) | 200–400 | >400–800 | >800 |
| Ciclesonide (pMDI, extrafine particle, HFA) Alvesco(160) | 80–160 | >160–320 | >320 |
| Fluticasone furoate (DPI) Relvar ellipta (92[100]) | 100 | | 200 |
| Fluticasone propionate (DPI, or pMDI, standard particle, HFA) | 100–250 | >250–500 | >500 |
| Mometasone furoate (DPI) Seretide (125 or 250 ) | Depends on DPI device – see product information | | |
| Mometasone furoate (pMDI, standard particle, HFA) | 200-400 | | >400 |

This is NOT a table of equivalence. These are suggested total daily doses for the 'low', 'medium' and 'high' dose treatment options with different ICS.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; ICS: inhaled corticosteroid; pMDI: pressurized metered dose inhaler; * see product information

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# Severe asthma

Approximately 3–10% of people with asthma have severe asthma

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# Terminology and Definitions

**Uncontrolled asthma: ≥1 of the following:**

- Poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma)
- Frequent exacerbations (≥2/year) requiring oral corticosteroids (OCS), or serious exacerbations (≥1/year) requiring hospitalization

**Difficult-to-treat asthma:**

- Uncontrolled despite GINA Step 4/5 treatment ( e.g. medium or high dose ICS with a 2nd controller ( eg . LABA) or maintain OCS) .
- Contributory factors may include incorrect inhaler technique, poor adherence, comorbidities or incorrect diagnosis.

**Severe asthma: (a retrospective label)**

- Uncontrolled despite adherence with maximal optimized (high dose ICS-LABA) therapy and treatment of contributory factors, or
- Worsens when high dose treatment is decreased.

OCS: Oral corticosteroids

GINA 2021, DIFFICULT-TO-TREAT & SEVERE ASTHMA IN ADULT AND ADOLESCENTS

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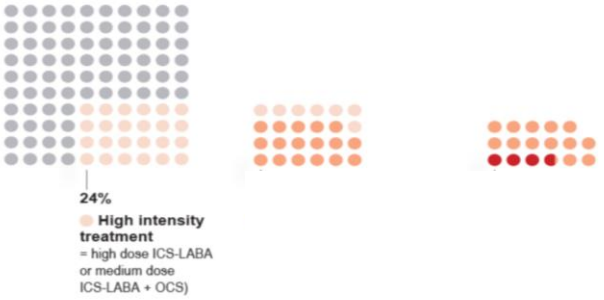
# What proportion of adults have severe asthma?




GINA Step 4~5

*Data from Hekking et al, JACI 2015*

ICS: inhaled corticosteroids; LABA: long-acting beta$_2$-agonist; OCS: oral corticosteroids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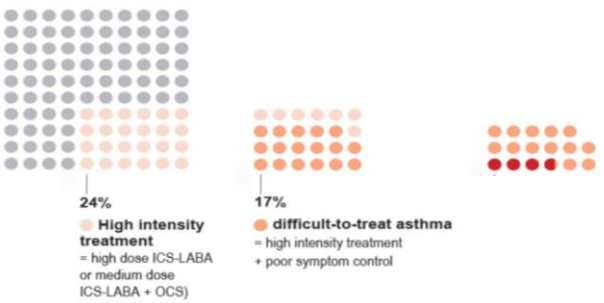
# What proportion of adults have severe asthma?




GINA Step 4~5

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ICS: inhaled corticosteroids; LABA: long-acting beta$_2$-agonist; OCS: oral corticosteroids


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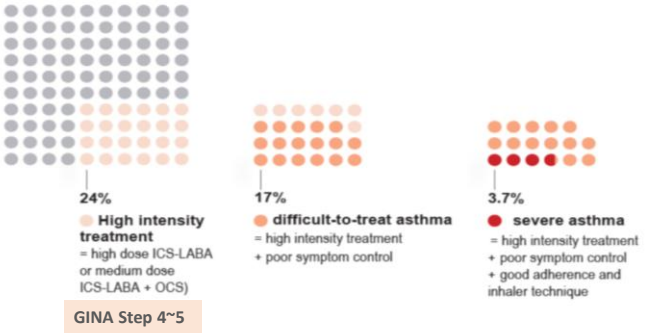
# What proportion of adults have severe asthma?




GINA Step 4~5

*Data from Hekking et al, JACI 2015*
*Study in the Netherlands*

ICS: inhaled corticosteroids; LABA: long-acting beta$_2$-agonist; OCS: oral corticosteroids

GINA 2021, Box 3-15

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嚴重氣喘決策圖

## 成年人與青少年難治氣喘病人之調查與管理

於任何階段考慮轉介至專科醫師或嚴重氣喘門診

診斷：「難治氣喘」

對於即使接受GINA第四階治療或使用維持性OCS，仍有症狀和/或急性惡化的青少年和成人

**1** 確定診斷（氣喘/鑑別診斷）

**2** 探尋與評估造成症狀、急性惡化及生活品質變差的原因：

評估

- 吸入性藥物使用技術不正確
- 不佳的遵囑性
- 共病症：肥胖、胃食道逆流、慢性鼻竇炎、阻塞型睡眠呼吸中止症
- 居家或工作環境中，可改變的危險因子及誘發因子，例如：抽菸、環境暴露、過敏原暴露(若皮膚針刺試驗或特異性IgE呈現陽性)；藥物使用，例如：乙型交感神經阻斷劑或非類固醇類消炎止痛藥
- 過量使用緩解型藥物SABA
- 藥物副作用
- 焦慮、憂鬱及社交困難

**3** 優化氣喘處置包括：

- 氣喘衛教
- 優化治療(例如：檢查及矯正吸入性藥物使用技術和遵囑性；若適用，改為使用ICS-formoterol做為維持與緩解治療的藥物)
- 治療共病症和可矯治的危險因子
- 考慮非生物製劑的附加治療(若未曾使用過，可考慮例如：LABA、tiotropium、LM/LTRA)
- 考慮非藥物治療(例如：戒菸、運動、減重、清痰、接種流感疫苗)
- 若未曾使用過，可考慮嘗試高劑量ICS

於任何階段考慮轉介至專科醫師或嚴重氣喘門診

**4** 3~6個月後檢視治療反應

氣喘仍然控制不良？ 是 → 診斷：「難治氣喘」 → 如氣喘仍未控制，可能的話請轉介專科醫師

否 → 考慮降階治療，從OCS開始(如已使用)

降階治療後，氣喘變成控制不良？ 是 → 恢復先前劑量

否 → 繼續優化氣喘處置

圖例：決定/篩選點、介入/治療、確診


2020台灣成人氣喘照護指引補充版;https://www.tspccm.org.tw/media/7785

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## 評估與治療嚴重氣喘之表現型

持續步驟 3 的優化氣喘處置(包括吸入藥物使用技術、遵囑性、共病症)

**5 評估嚴重氣喘表現型和其他致病因子**

*評估嚴重氣喘表現型在高劑量ICS治療下(或可能的最低OCS治療劑量下)*

**第二型發炎反應**

*病人有第二型呼吸道發炎反應嗎？*

*注意：這些不是附加生物治療的使用標準(見6b)*

- 血液嗜酸性白血球 ≥150μL 和/或
- FeNO ≥20ppb 和/或
- 痰液嗜酸性白血球≥2% 和/或
- 氣喘是臨床過敏原所導致和/或
- 需要維持使用OCS
  (在可能的最低OCS劑量治療下，重複血液嗜酸性白血球和FeNO檢測最多三次)

是 / 否

*調查合併症/鑑別診斷，並視情況治療/轉介*

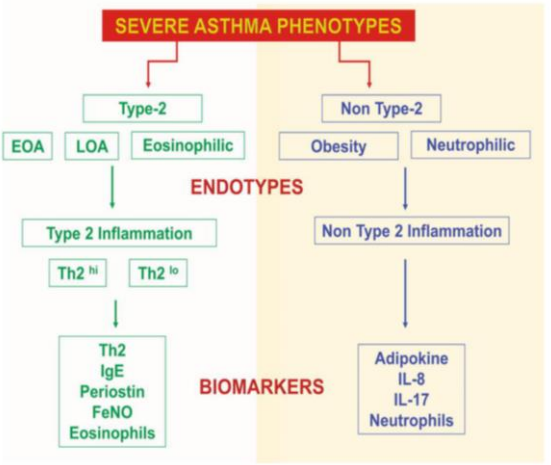
- 考慮：CBC、CRP、IgG、IgA、IgM、真菌抗體；胸部X光和/或高解析度胸部電腦斷層掃描HRCT；DLCO
- 皮膚點刺試驗或相關過敏原的特異性IgE (若先前未測試)
- 基於臨床懷疑可進行相關測試(例如抗中性球細胞質ANCA、鼻竇CT、B型利納利尿胜肽、心臟超音波)

*考慮社會及心理支持的需要*

*參與多專科團隊照護(若可獲得)*

*邀請病人參與收案登記(若可獲得)或臨床試驗(若符合試驗條件)*

Phenotypes, endotypes, and biomarkers in severe asthma.




early onset asthma (EOA), late onset asthma (LOA), FeNO (fraction of nitric oxide expired)

2020台灣成人氣喘照護指引補充版;https://www.tspccm.org.tw/media/7785
https://www.intechopen.com/chapters/60274



## 評估與治療嚴重氣喘之表現型

持續步驟 3 的優化氣喘處置(包括吸入藥物使用技術、遵囑性、共病症)

**5 評估嚴重氣喘表現型和其他致病因子**

**6a 考慮非生物製劑治療**

- 考慮遵囑性測試
- 考慮增加ICS劑量3~6個月
- 考慮AERD、ABPA、慢性鼻竇炎、鼻息肉、異位性皮膚炎(臨床第二型發炎反應表現型可使用特定的附加治療)

*附加第二型生物製劑可取得/負擔的起？* 是 / 否

*評估嚴重氣喘表現型在高劑量ICS治療下(或可能的最低OCS治療劑量下)*

**第二型發炎反應**

*病人有第二型呼吸道發炎反應嗎？*

*注意：這些不是附加生物治療的使用標準(見6b)*

- 血液嗜酸性白血球 ≥150μL 和/或
- FeNO ≥20ppb 和/或
- 痰液嗜酸性白血球≥2% 和/或
- 氣喘是臨床過敏原所導致和/或
- 需要維持使用OCS
  (在可能的最低OCS劑量治療下，重複血液嗜酸性白血球和FeNO檢測最多三次)

是 / 否

*調查合併症/鑑別診斷，並視情況治療/轉介*

- 考慮：CBC、CRP、IgG、IgA、IgM、真菌抗體；胸部X光和/或高解析度胸部電腦斷層掃描HRCT；DLCO
- 皮膚點刺試驗或相關過敏原的特異性IgE (若先前未測試)
- 基於臨床懷疑可進行相關測試(例如抗中性球細胞質ANCA、鼻竇CT、B型利納利尿胜肽、心臟超音波)

*考慮社會及心理支持的需要*

*參與多專科團隊照護(若可獲得)*

*邀請病人參與收案登記(若可獲得)或臨床試驗(若符合試驗條件)*

*如果附加第二型生物製劑治療不可取得/負擔不起*

- 如果沒使用過，考慮使用更高劑量的ICS
- 考慮非生物製劑附加療法(例如LABA、tiotropium、LM/LTRA、大環內酯抗生素macrolide*)
- 考慮添加低劑量OCS，但是實施減少副作用的策略
- 停止無效的附加治療

*如果沒有第二型發炎反應的證據：*

- 回顧基準點：鑑別診斷、吸入器使用技術、遵囑性、合併症、副作用
- 避免接觸(菸草煙、過敏原、刺激物)
- 考慮進行(如果可進行檢查但還沒作)
  - 痰誘導
  - 高解析度胸部電腦斷層掃描
  - 支氣管鏡檢查，用於替代/額外診斷
- 考慮附加治療
  - 若尚未使用過，可嘗試使用tiotropium或大環內酯抗生素macrolide*
  - 考慮添加低劑量OCS，但要實施減少副作用的策略
  - 停止無效的附加療法
- 考慮支氣管熱整形導管手術(支氣管燒灼術)(需註冊)

*目前資格不符合使用生物製劑*

★藥品仿單標示外使用

AERD: aspirin-exacerbated respiratory disease
ABPA: Allergic bronchopulmonary aspergillosis

2020台灣成人氣喘照護指引補充版;https://www.tspccm.org.tw/media/7785

## Add-on long-acting muscarinic antagonists (LAMA)

- Step 5 recommendations for add-on LAMA have been expanded to include combination ICS-LABA-LAMA, if asthma is persistently uncontrolled despite ICS-LABA
  - Add-on tiotropium in separate inhaler (ages ≥6 years) TRIMBOW TRELEGY
  - Triple combinations (ages ≥ 18 years): beclometasone-formoterol-glycopyrronium; fluticasone furoate-vilanterol-umeclidinium; mometasone-indacaterol-glycopyrronium
- Lung function:
  - Adding LAMA to medium or high dose ICS-LABA modestly improves lung function (Evidence A) but not symptoms
- Severe exacerbations
  - In some studies, add-on LAMA modestly increased the time to severe exacerbation requiring OCS (Evidence B)
  - For patients with exacerbations, it is important to ensure that the patient receives sufficient ICS, i.e. at least medium dose ICS-LABA, before considering adding a LAMA

ICS: inhaled corticosteroids; LABA: long-acting beta$_2$-agonist; LAMA: long-acting muscarinic antagonist; OCS: oral corticosteroids

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## Add-on azithromycin

- Add-on azithromycin three days a week has been confirmed as an option for consideration after specialist referral
  - Significantly reduces exacerbations in patients taking high dose ICS-LABA
  - Significantly reduces exacerbations in patients with eosinophilic or non-eosinophilic asthma
  - No specific evidence published for azithromycin in patients taking medium dose ICS-LABA *(Hiles et al, ERJ 2019)*
- Before considering add-on azithromycin
  - Check sputum for atypical mycobacteria
  - Check ECG for long QTc (and re-check after a month of treatment)
  - Consider the risk of increasing antimicrobial resistance (population or personal)

ICS: inhaled corticosteroids; LABA: long-acting beta$_2$-agonist

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## 評估與治療嚴重氣喘之表現型 (續)

持續步驟 3 的優化氣喘處置(包括吸入藥物使用技術、遵囑性、共病症)

**6b** 考慮以*第二型發炎反應為標的之生物製劑*附加治療

- 考慮以第二型發炎反應為標的之生物製劑附加治療用於病情惡化的病人或於高劑量ICS–LABA使用下，症狀控制不佳，病人有：●
- 有嗜酸性白血球或過敏性生物標誌物，或
- 需要維持使用OCS
- 考慮醫療給付條件 ● 和各治療反應的預測因子
- 同時考慮成本，劑量頻率，給藥方式(SC或IV)，病人偏好

*哪種生物製劑適合先開始?*

**Anti–IgE**

*病人是否有資格接受嚴重過敏性氣喘的Anti–IgE治療?*

- 對皮膚點刺試驗或特異性IgE敏感 ●
- 劑量範圍內的總血清IgE和體重 ●
- 過去一年間的惡化 ●

否 否

**Anti–IL5/Anti–IL5R**

*病人是否有資格接受嚴重嗜酸性球性氣喘Anti–IL5/Anti–IL5R治療?*

- 過去一年間的惡化 ●
- 血液嗜酸性白血球≥300顆/μL ●

否 否

**Anti–IL4R**

*病人是否有資格獲得Anti–IL4R治療 ...針對嚴重嗜酸性白血球/第二型氣喘?*

- 過去一年間的惡化 ●
- 血液嗜酸性白血球≥150顆/μL ● 或FeNO≥25ppb ●

...還是因為需要持續OCS? ●

沒有資格嗎? 返回第6a

*哪些因素可以預測Anti–IgE能改善氣喘症狀?*

- 血中嗜酸性白血球 ≥260顆/μL++
- FeNO≥20ppb+
- 因過敏造成的氣喘症狀+
- 兒時發病的氣喘+

*哪些因素可能預測氣喘對Anti–IL5/IL5R有好的反應?*

- 高血液嗜酸性白血球+++
- 過去一年多次的惡化+++
- 成人發病的氣喘++
- 鼻息肉++

*哪些因素可能預測氣喘對Anti–IL4R有好的反應?*

- 高血液嗜酸性白血球+++
- 更高的FeNO+++

Anti–IL4R也可用於治療

- 中度/重度異位性皮膚炎
- 鼻息肉

● 檢查當地的特定生物製劑資格標準 這些療法可能與列出的療法不同




## Add-on biologic therapy for severe Type 2 asthma

- When assessing eligibility, repeat blood eosinophils if low at first assessment
  - One study found that 65% patients on medium or high dose ICS-LABA shifted their eosinophil category during 12 months' follow-up *(Lugogo et al, Ann Allergy Asthma Immunol 2020)*
- Additional indications for these therapies in Europe and/or USA have been listed
  - Omalizumab: chronic idiopathic urticaria, nasal polyposis
  - Mepolizumab: hypereosinophilic syndrome, eosinophilic granulomatosis with polyangiitis (EGPA)
  - Benralizumab: no additional indications at present
  - Dupilumab: chronic rhinosinusitis with nasal polyposis (CRSwNP); atopic dermatitis
- Check local regulatory approvals and eligibility criteria

ICS: inhaled corticosteroids; LABA: long-acting beta$_2$-agonist

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## 觀察及監控嚴重氣喘治療

**持續優化氣喘處置**

**7 評估對治療的反應和影響**

- 氣喘本身；症狀的控制、症狀惡化、肺功能
- 第二型發炎反應共病症，例如鼻息肉、異位性皮膚炎
- 藥物：治療強度、副作用、經濟負擔
- 病人的滿意度

是 →

***對於治療反應良好***

- 每3–6個月評估一次病人情況 ●
- 口服藥物的調整：考慮先行降低/停用OCS，然後逐漸停用其他附加治療
- 吸入型藥物的調整：3~6個月後可考慮降低劑量；建議至少維持中等劑量之ICS
- 再次評估是否需要持續使用生物製劑
- 在減藥時須考量藥物本身的好處、潛在副作用、花費、以及病人本身的喜好

否 →

***對於治療反應不佳***

- 停用生物製劑
- 回顧基準點：鑑別診斷、吸入器使用技術、遵囑性、合併症、副作用、情緒支持
- 考慮安排高解析度胸部電腦斷層掃描HRCT(若之前沒有做過)
- 再次評估病人本身的氣喘表現型和治療選項
  - 收集痰液(若能夠取得)
  - 考慮加上大環內酯抗生素(macrolide)
  - 考慮給予低劑量OCS，但要實施減少副作用的策略
  - 考慮安排支氣管鏡檢查，用於替代/額外診斷
  - 考慮支氣管熱整形導管手術(支氣管燒灼術)(需註冊)
- 停止無效的附加療法
- 勿停用ICS


24

- 嚴重氣喘的簡介
- **案例分享**
- 生物製劑用於Type 2嚴重氣喘病患之介紹

25

49 year-old woman, Non-smoker

- Height: 157cm, Weight: 55kgw (BMI 22.3)
- History of Asthma ,regular OPD follow up
- Family history: grandmother had asthma
- Occupation: 行政工作
- Systemic disease: allergic rhinitis, sinusitis, nasal polyposis

## 氣喘急性惡化住院記錄

- 2014.04 - Admission due to asthma AE
- 2014.07 - Admission due to asthma AE
- 2015.04 - Admission due to asthma with AE
- 2016.01 - Admission due to influenza and asthma AE

## 胸腔科追蹤

| | | | |
|---|---|---|---|
| 2014 | 4/10<br>(4/11-4/25) | AE- WBC 9640, EOS : 5.9% (569) ; IgE 25.7IU/mL | # Controller- Symbicort 1puff bid , singulair |
| | 07/07 | Sneezing, running nose followed by **severe cough** with much sticky suptum for about one week. Nocturnal symptoms (3-4am/day), DOE(+)<br>**Pulmonary function test on 20140704:**<br>**FEV1/FVC:71%, FEV1:58%, TLc:67% and negative bronchodilator test.** | # Add Prednisolone 10 mg bid *7days |
| | 7/15<br>(7/17-7/22) | AE | |
| | 08/04 | F/u post discharged | #Controller- Symbicort 2puff bid , singulair |
| | 09/01 | **Dyspnea got worse;** used symbicort 6 puff /day , but tremor of hands and palpitation | # Add Prednisolone 15 mg bid 7days;<br>Xanthium 200mg 1#qd<br>other :nasal spray , anti-histamines |
| | 09/29 | **Severe cough,** stuffy nose, sore throat, **increased shortness of breath, subjective wheezing for 2-3 days. Nocturnal symptoms(every night), she could not sleep** at night due to **severe cough and chest tightness.** | # Controlle- Symbicort 2puff bid , singulair, Xanthium<br>Add on Spiriva respimat<br>Prednisolone 15 mg bid *7days |
| | 10/27 | **Insomnia, persistent shortness of breath, severe cough Nocturnal symptoms (everynight), daily activity limitation(+).** | # Controller - * 4 ( LABA + ICS+LAMA ,leukotriene antagonist )<br>keep Prednisolone 15 mg bid 14days |
| | 11/24<br>12/22 | | # Controller- * 4 ;<br>Regular Prednisolone 10 mg bid 28days |

dyspnea on exertion(DOE)



| | | | |
|---|---|---|---|
| 2015<br>ADMx1<br>Need OCS | 01/19 | Mildly improved SOB, cough, and **need symbicort 8-10 puff per day** | # Controller - * 4 ; Xanthium<br>keep Prednisolone 5mg bid<br>oral bata2 agonist |
| | 4/20<br>(4/20-4/29) | **Severe DOE, depended on systemic steroid** in recent 2-3 months. | |
| | 06/15 | **Severe cough, runny nose, shortness of breath** for 3-4 days. She took prednisolone 5mg po qd | # Controller - * 4 ;Xanthium, oral bata2 agonist<br>Prednisolone 10mg bid 28 days;<br>Rinderon 4mg stat IM |
| | 08/10 | **Wheezing, productive cough and dyspnea on exertion** | # Adjust Prednisolone 15mg bid 28 days |
| | 12/28 | Symptoms improved mildly and she changed her symbicort from 4puff bid to 6puff qd and her symptoms improved mildly since then on. | # Controller -LABA + ICS, leukotriene antagonist, Xanthium, oral bata2 agonist |
| 2016<br>ADMx1 | 1/17<br>(1/17-1/26) | Asthma with AE | # 會診藥師:確認病人能正確使用吸入劑<br>=>病人能清楚用藥目的,劑量頻次;能正確使用藥品及吸藥技巧 |
| | 02/01<br>06/27 | F/u post discharged | # Controller - *4 ; Xanthium, oral bata2 agonist<br>stop oral steroid |
| | 07/25 | **嗅覺異常,** intermittent low grade fever. Sneezing, runny nose got worse recently.<br>**Nocturnal symptoms (1-2 nights/month),** daily activity limitation(-), use of rescue medicine (1-2 times/week) | # Controller- *4 ; Xanthium *3M |
| | 10/17 | | # Controller - *4 ; Xanthium *3M |

| | | | |
|---|---|---|---|
| 2017 | 01/09 | DOE(-), Nocturnal symptoms (1-2 nights/month) | # Controller - Symbicort 2puff bid , singulair 3M |
| | 04/10 | | # Controller - Symbicort 2puff bid , singulair |
| ACT: 20 | 05/26 | | # Controller - Symbicort 2puff bid , singulair |
| | 06/13 | **She received surgery(鼻竇手術) for sinusitis and nasal polyp** DX: *. Chronic parasinusitis, bil ; Chronic hypertrophic rhinitis. | |
| | 07/10 | | # Controller - Symbicort 2puff bid , singulair |
| | 10/16 | Nocturnal symptoms (-), DOE(+, 快走). Cough(-). | # Controller - Symbicort 2puff bid , singulair *3M |
| 2018 | 01/08 | Nocturnal symptoms (1-2 times/month), occasional cough when exposure to cold air. | # Controller - Symbicort 2puff bid , singulair<br>Add Prednisolone 10 mg bid *7days |
| | 04/02 | | # Controller - Symbicort 2puff bid , singulair *3M |
| Frequent AE | 06/25 | She **use symbicort 4puff bid** during recent weeks. **Diffuse inspiratory and expiratory wheezing, bilateral** | # Add Spiriva ; Prednisolone 10 mg bid *7days |
| | 08/16 | | # Controller- *4 |
| | 09/17 | Just came back from Japan; **complained chest tightness, SOB** during this period. | # Controller - *4<br>Add Prednisolone 15 mg bid *14days |
| | 10/15 | **Worse symptoms** (Sore throat, stuffy nose) after URI spisode one week ago. | # Keep Prednisolone 15 mg bid *7 days;<br>Antibiotics. |
| | 11/12 | Less cough and dyspnea | # Controller - *4 |

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| | | | |
|---|---|---|---|
| 2019 | 01/28 | | # Controller - *4 |
| | 04/01 | Increased SOB since March, nocturnal symptoms **(+ every night)**, severe DOE persisted. | Controller - *4<br>Add Prednisolone 15 mg bid *10days<br>**Xanthium ; SABA+ SAMA prn** |
| Nocturnal symptoms, DOE | 04/27 | | # Controller: *4<br>SABA+SAMA prn |
| | 05/27 | Still DOE, nocturnal symptoms **(every night).** | # Controller: *4 ( 2M) |
| | 07/22 | Increased DOE even climbing upstair (2nd floor), nocturnal symptoms **(every night)**, audible wheezing. | Controller: *4<br>Add Prednisolone 10 mg bid *28days ;<br>Xanthium |
| | 08/20 | **Nocturnal symptoms > 4times/week.** Use berotec 2-3 times/week. | # Controller: *4 ; Xanthium (2M)<br>Adjust Prednisolone 5 mg bid *2M |
| | 10/15 | **Nocturnal cough still severe, chest tightness, shortness of breath every night** | # Controller: *4 ; Xanthium<br>Adjust Prednisolone 20mg bid<br>申請nucala(mepolizumab) |
| | 11/12 | **Nocturnal cough, audible wheezing, chest tightness persisted despite prednisolone 20mg po bid use.** | # Controller: *4 ; Xanthium ; Prednisolone 20mg bid<br>Add NUCALA 100mg Q4W SC |

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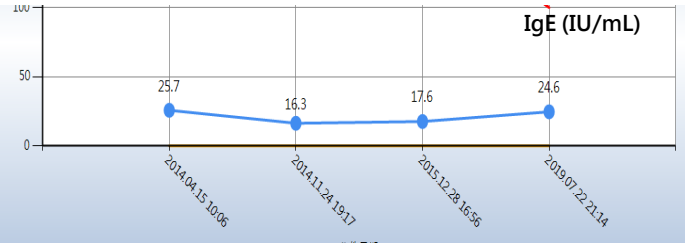
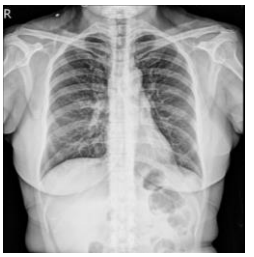
# Mast tests

| 檢驗名稱 | 結果值 | 參考值 | 單位 | 收件日期時間 |
|---|---|---|---|---|
| Latex | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Avocado | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Pork | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Beef | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Milk | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Cheese | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Shrimp | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Crab | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Clam | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Codfish | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Tuna | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Peanut | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Soybean | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Wheat | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Yeast | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Egg Yolk | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Egg White | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Chicken Feathers | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Bermuda Grass | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Willow, Black | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Eucalyptus | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Japanese Cedar | 0 | 0 - 4 | | 2014/11/24 19:18 |
| White Mulberry | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Pigweed | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Ragweed Mix I | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Timothy Grass | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Alternaria | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Aspergillus | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Cladosporium | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Penicillium | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Cat | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Dog | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Housedust | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Cockroach Mix | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Mite DF | 0 | 0 - 4 | | 2014/11/24 19:18 |
| Mite DP | 0 | 0 - 4 | | 2014/11/24 19:18 |

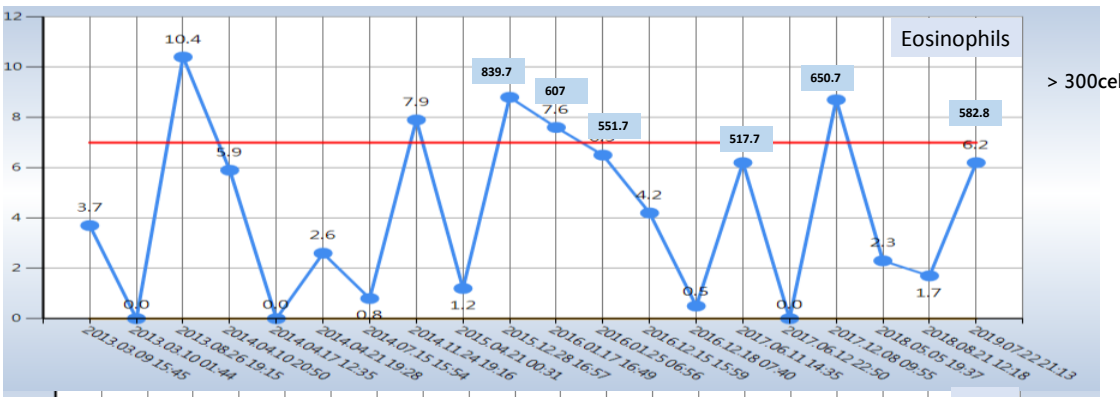



ANA, C3, C4, ANCA: normal

20211019 CV echo:
PA systolic pressure:24 mmHg
LVEF :82%
Minimal aortic regurgitation.
Minimal mitral regurgitation .
Minimal tricuspid regurgitation .



20190722

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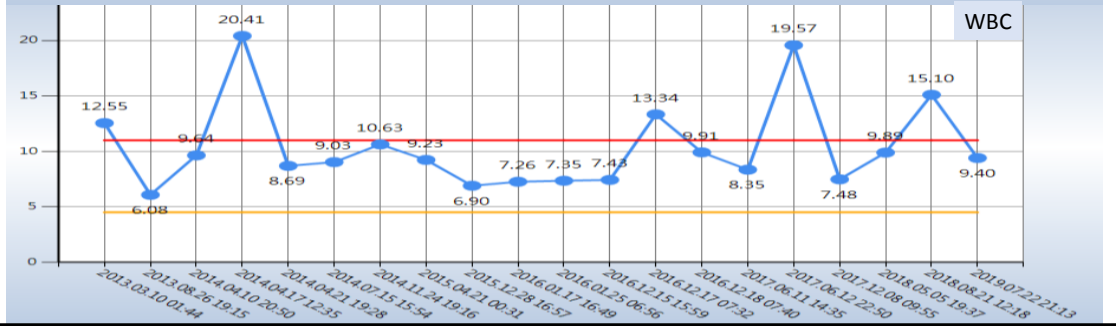

| | | | |
|---|---|---|---|
| 2019 | 12/10 | Less use of rescue medicine, use prednisolone 10mg 1-2 times/week. She used prednisolone 3# bid in the 1st week, much improved since 2nd week. 嗅覺明顯改善(聞得到廢氣味，食物). Less DOE (she could climb up to 4th floor without rest). | # Controller: Symbicort 2puff bid , singulair; NUCALA |
| 2020 | 01/07 | Stable condition, No nocturnal symptoms | # Controller: Symbicort 2puff bid, NUCALA |
| | 03/03 | Good response to nucala | # Controller: Symbicort 2puff bid, NUCALA |
| | 03/31 | Dyspnea with respiratory wheezing on weather changing lately -> could be relieved on symbicort | # Controller: Symbicort 2puff bid, NUCALA |
| | 04/28 | Occasional wheeze, could be relieved by symbicort use | # Controller: Symbicort 2puff bid, NUCALA |
| | 05/26 | | # Controller: Symbicort 2puff bid, NUCALA |
| | 06/23 | Severe intermittent chest pain for about 2 weeks, improved after 5 minutes. Mild intermittent cough, less subjective wheezing | # Controller: Symbicort 2puff bid, NUCALA add spiriva |
| | 07/21 | Intermittent cough with audible wheezing lasting 1-2 minutes 2-3 times/week. No obvious SOB. | # Controller: LABA + ICS+LAMA„ NUCALA |
| | 08/18 | Less cough, no audible wheezing, no nocturnal symptoms. Occasional wheeze. | # Controller: LABA + ICS+LAMA„ NUCALA |
| | 09/22 | Intermittent chest tightness (3-5 minutes) recently. used symbicort 1-2puff bid now. | # Controller: Symbicort 2puff bid, NUCALA |
| | 10/20 | Mild SOB during weather change | # Controller: Symbicort 2puff bid, NUCALA |
| | ~2021 | | |

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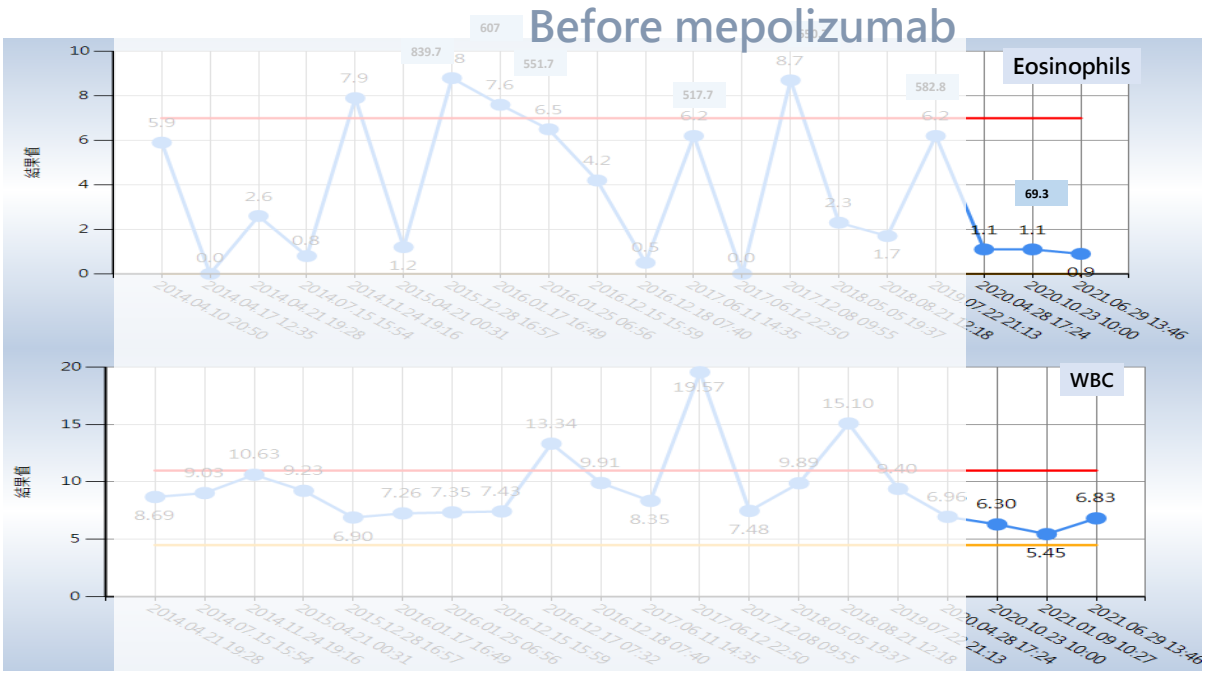
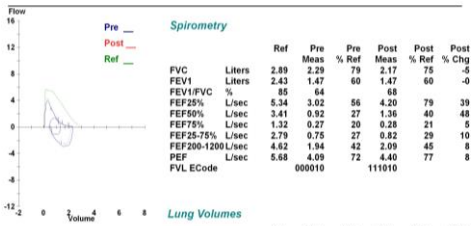


三軍總醫院,台北,中華民國 日期: 08/20/2019

三軍總醫院,台北,中華民國
肺功能室

20/05/26

**FEV1 60% --> 72.4%**
**(after mepolizumab)**




*Spirometry*

| | | Ref | Pre Meas | Pre % Ref | Post Meas | Post % Ref | Post % Chg |
|---|---|---|---|---|---|---|---|
| FVC | Liters | 2.89 | 2.29 | 79 | 2.17 | 75 | -5 |
| FEV1 | Liters | 2.43 | 1.47 | 60 | 1.47 | 60 | -0 |
| FEV1/FVC | % | 85 | 64 | | 68 | | |
| FEF25% | L/sec | 5.34 | 3.02 | 56 | 4.20 | 79 | 39 |
| FEF50% | L/sec | 3.41 | 0.92 | 27 | 1.36 | 40 | 48 |
| FEF75% | L/sec | 1.32 | 0.27 | 20 | 0.28 | 21 | 5 |
| FEF25-75% | L/sec | 2.79 | 0.75 | 27 | 0.82 | 29 | 10 |
| FEF200-1200 | L/sec | 4.62 | 1.94 | 42 | 2.09 | 45 | 8 |
| PEF | L/sec | 5.68 | 4.09 | 72 | 4.40 | 77 | 8 |
| FVL ECode | | | 000010 | | 111010 | | |

*Lung Volumes*

| | | Ref | Pre Meas | Pre % Ref | Post Meas | Post % Ref | Post % Chg |
|---|---|---|---|---|---|---|---|
| VC | Liters | 3.03 | 2.61 | 86 | | | |
| TLC | Liters | 4.61 | 2.87 | 62 | | | |
| RV | Liters | 1.58 | 0.26 | 16 | | | |
| FRC PL | Liters | 2.54 | 1.93 | 76 | | | |
| ERV | Liters | | 1.65 | | | | |
| IC | Liters | | 0.94 | | | | |
| Raw | cmH2O/L/sec | 1.57 | | | | | |
| RV/TLC | % | 34 | 9 | | | | |
| Vtg (Raw) | Liters | | | | | | |
| Vtg | Liters | | 1.78 | | | | |

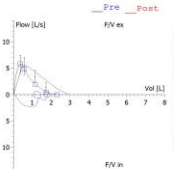
*Diffusion*

Hb:

| | | Ref | Pre Meas | Pre % Ref | Post Meas | Post % Ref |
|---|---|---|---|---|---|---|
| DLCO | mL/mmHg/min | 19.7 | | | | |
| DL Adj | mL/mmHg/min | 19.7 | | | | |
| VA | Liters | | | | | |
| DLCO/VA | mL/mHg/min/L | 3.93 | | | | |
| DL/VA Adj | mL/mHg/min/L | | | | | |
| IVC | Liters | | | | | |

Comment:

mildly obstructive ventilatory impairment
moderately restrictive ventilatory impairment
negative bronchodilator test




**Spirometry**

| | | Ref | Pre | Pr%Rf | Post | Po%Rf | Chg% |
|---|---|---|---|---|---|---|---|
| FVC | [L] | 2.90 | 2.30 | 79.3 | | | |
| FEV 1 | [L] | 2.44 | 1.77 | 72.4 | | | |
| FEV 1 % FVC | [%] | | 76.8 | | | | |
| FEF25 | [L/s] | 5.36 | 4.77 | 89.0 | | | |
| FEF 50 | [L/s] | 3.40 | 1.93 | 56.6 | | | |
| FEF75 | [L/s] | 1.39 | 0.43 | 31.1 | | | |
| FEF25/75 | [L/s] | 2.75 | 1.45 | 52.5 | | | |
| FEF 200-1200 | [L/s] | 4.56 | 3.44 | 75.3 | | | |
| PEF | [L/s] | 5.69 | 5.78 | 101.7 | | | |
| Error ATSplus | | | 0 | | | | |

**Lung Volumes**

| | | Ref | Pre | Pr%Rf | Post | Po%Rf | Chg% |
|---|---|---|---|---|---|---|---|
| VC | [L] | 2.90 | 2.30 | 79.3 | | | |
| TLC | [L] | 4.61 | 4.06 | 88.2 | | | |
| RV | [L] | 1.58 | 1.76 | 111.8 | | | |
| RV % TLC | [%] | 34.94 | 43.42 | 124.3 | | | |
| FRCpleth | [L] | 2.54 | 2.53 | 99.5 | | | |
| ERV | [L] | | 0.77 | | | | |
| IC | [L] | | 1.53 | | | | |
| R tot | [cmH2O/L/sec] | 3.00 | 3.87 | 129.1 | | | |
| BF Res | [1/min] | | 31.58 | | | | |
| FRCpl used in resis. | [L] | | 2.77 | | | | |

**Diffusion**

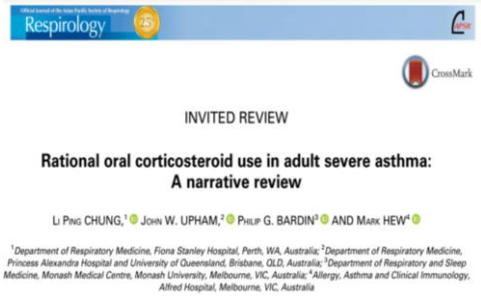
| | | Ref | Pre | Pr%Rf | Post | Po%Rf | Chg% |
|---|---|---|---|---|---|---|---|
| DLCO SB | [ml/mmHg/min] | 19.92 | | | | | |
| DLCOc SB | [ml/mmHg/min] | 19.92 | | | | | |
| VA | [L] | | | | | | |
| DLCO/VA | [ml/mmHg/min/L] | 4.15 | | | | | |
| DLCOc/VA | [ml/mmHg/min/L] | | | | | | |
| VIN | [L] | | | | | | |

Comment

- 嚴重氣喘的簡介
- 案例分享
- **生物製劑用於嚴重氣喘及防範口服類固醇過度依賴**

37

**Systematic reviews have demonstrated the effectiveness of OCS for treating asthma exacerbations, reducing relapses, lowering short-acting beta2-agonist (SABA) use and reducing hospital admissions by 60% in the acute setting. Additionally, daily maintenance (long-term, low-dose) OCS is a guideline-supported therapy for uncontrolled severe asthma.**




- Prior to the availability of new treatments, >50% of patients with uncontrolled severe asthma required maintenance OCS, in addition to conventional therapy to manage their symptoms.
- The International Severe Asthma Registry : for severe asthma patients were prescribed OCS maintenance treatment:

  --The UK :59.6% ; median prednisolone dose was 10–15 mg/day (Several specialist UK centres)
  --The USA : 23.3%
  --Australian: 25% ; the median daily dose is estimated to be 10 mg/day (prednisolone equivalent), although a wide dose range is reported (2–50 mg).
  --South Korea : 20.7%
  --Italy : 5.2%

Respirology (2020) 25, 161–172

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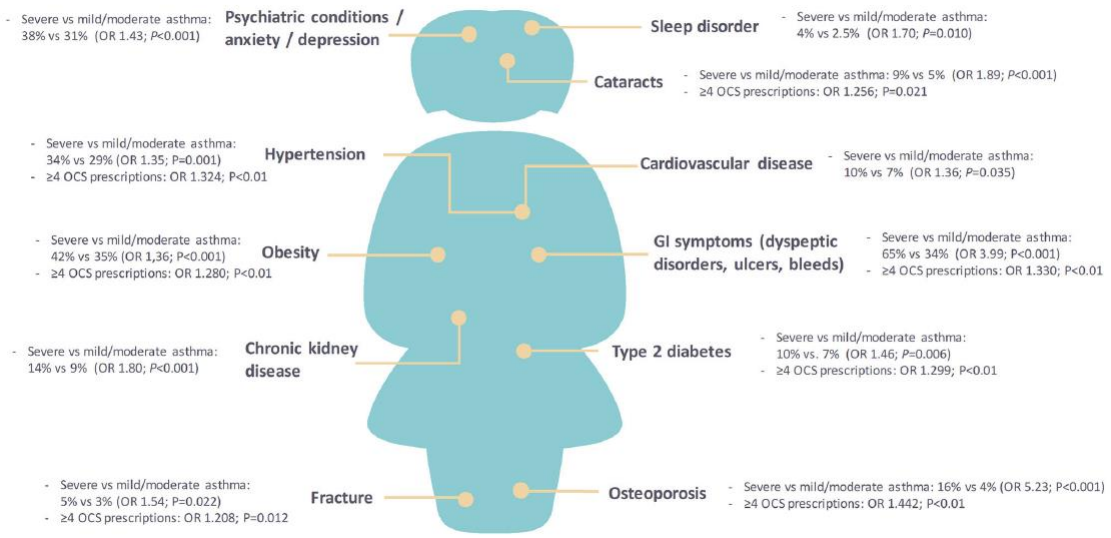
**Burden of OCS in severe asthma.**




OR, odds ratio; OCS, oral corticosteroids; GI, gastrointestinal.

JOURNAL OF ASTHMA 2021, VOL. 58, NO. 4, 448–458

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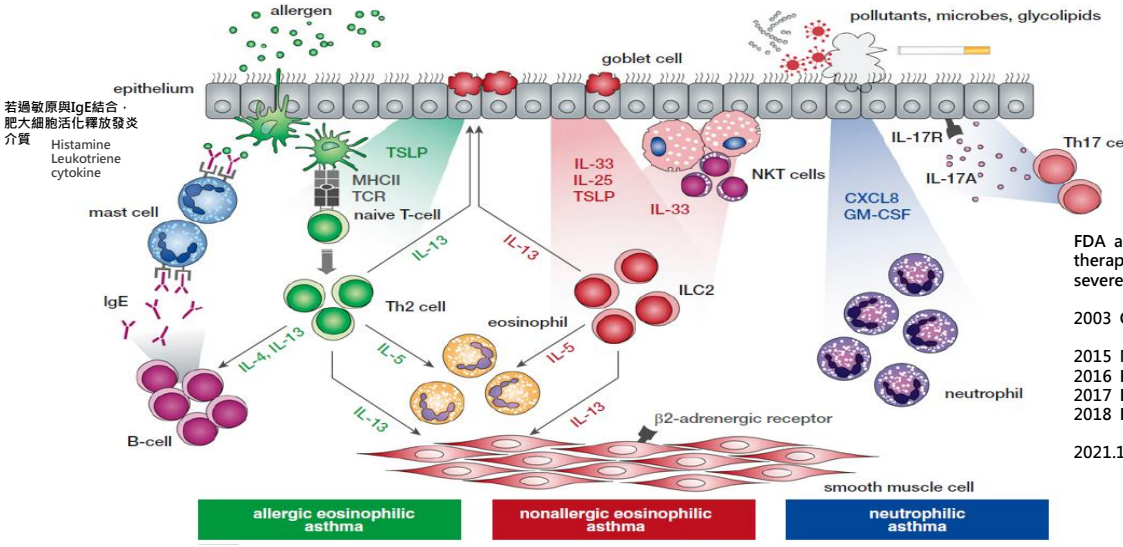
## Asthma is a heterogeneous disease ：many different endotypes and phenotypes




FDA approved biologic therapy for severe asthma :

2003 Omalizumab

2015 Mepolizumab
2016 Reslizumab
2017 Benralizumab
2018 Dupilumab

2021.12 Tezepelumab

Th2 cell: T helper cell 2; TSLP = thymic stromal lymphopoietin; TCR = T cell receptor; MHC = major histocompatibility complex;
NKT cells :natural killer T cells; CXCL8: formerly called IL-8 ; ILC2 :innate lymphoid cells type 2;
GM-CSF = granulocyte/macrophage colony-stimulating factor

Ann Am Thorac Soc Vol 11, Supplement 5, pp S322–S328, Dec 2014

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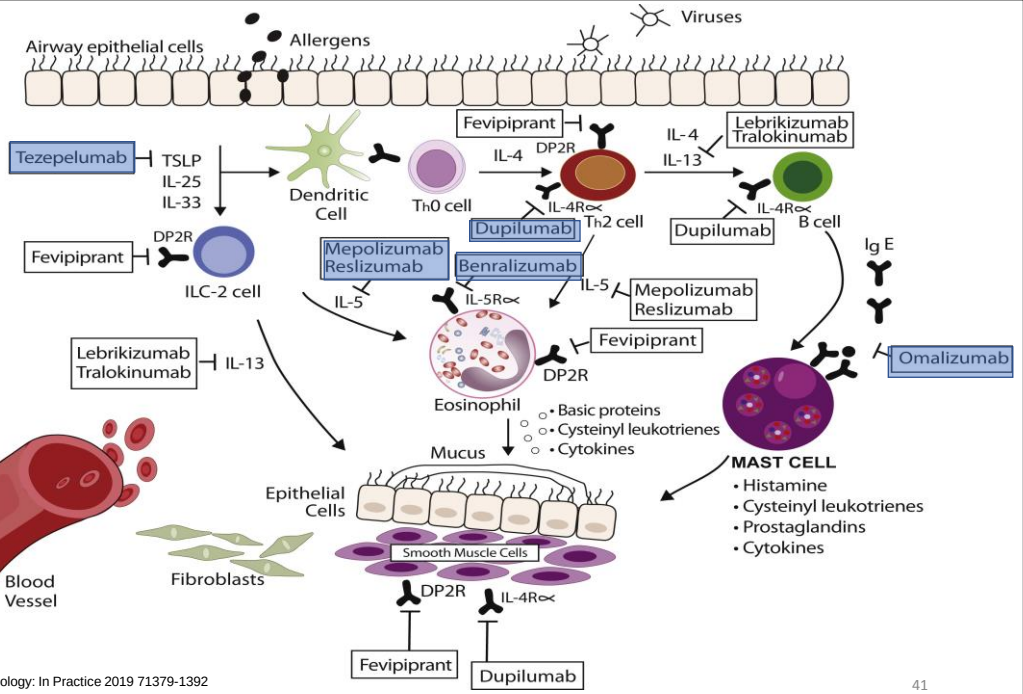
FDA approved biologic therapy for severe asthma :

2003 Omalizumab
2015 Mepolizumab
2016 Reslizumab
2017 Benralizumab
2018 Dupilumab

2021.12 Tezepelumab




The Journal of Allergy and Clinical Immunology: In Practice 2019 71379-1392
DOI: (10.1016/j.jaip.2019.03.008)

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## Efficacy of the biologics that are FDA-approved for the treatment of moderate-to-severe persistent asthma with a T2-high phenotype

| Medication | Frequency of exacerbations | |
|---|---|---|
| Omalizumab[29,54-61] (2003) | Reduces the risk of asthma exacerbations 25%-50% when compared with placebo | anti-IgE |
| Mepolizumab[20,91-93] (2015) | Reduces the risk of asthma exacerbations ~50% when compared with placebo | |
| Reslizumab[21-23,26,91-93] (2016) | Reduces the risk of asthma exacerbations ~50%-60% when compared with placebo | Anti-IL-5 ,anti-IL-5R |
| Benralizumab[24,25,93,106] (2017) | Reduces the risk of asthma exacerbations ~40%-50% when compared with placebo | |
| Dupilumab[27,28] (2018) | Reduces the risk of asthma exacerbations ~50%-70% when compared with placebo | Anti-IL-4R |

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## Efficacy of the biologics that are FDA-approved for the treatment of moderate-to-severe persistent asthma with a T2-high phenotype

| Medication | Frequency of exacerbations | Lung function improvement |
|---|---|---|
| Omalizumab[29,54-61] | Reduces the risk of asthma exacerbations 25%-50% when compared with placebo | Minimal improvement in lung function |
| Mepolizumab[20,91-93] | Reduces the risk of asthma exacerbations ~50% when compared with placebo | Some, but not all, studies showed some improvement in lung function |
| Reslizumab[21-23,26,91-93] | Reduces the risk of asthma exacerbations ~50%-60% when compared with placebo | All phase 3 clinical trials showed an improvement in lung function if patients had eosinophilia ≥400 cells/μL |
| Benralizumab[24,25,93,106] | Reduces the risk of asthma exacerbations ~40%-50% when compared with placebo | All phase 3 clinical trials showed an improvement in lung function |
| Dupilumab[27,28] | Reduces the risk of asthma exacerbations ~50%-70% when compared with placebo | All phase 3 clinical trials showed an improvement in lung function |

For Fixed airway obstruction

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## Efficacy of the biologics that are FDA-approved for the treatment of moderate-to-severe persistent asthma with a T2-high phenotype

For OCS resistance

| Medication | Frequency of exacerbations | Lung function improvement | Corticosteroid weaning |
|---|---|---|---|
| Omalizumab[29,54-61] | Reduces the risk of asthma exacerbations 25%-50% when compared with placebo | | Decreases total use of ICSs and OCSs; however, no clear evidence exists that it facilitates discontinuation of chronic OCSs |
| Mepolizumab[20,91-93] | Reduces the risk of asthma exacerbations ~50% when compared with placebo | Who has evidence of eosinophilia (150-300 cells/mL) | Has been shown to facilitate a decrease in total OCS use and facilitate discontinuation of chronic OCSs |
| Reslizumab[21-23,26,91-93] | Reduces the risk of asthma exacerbations ~50%-60% when compared with placebo | | OCS weaning has not been evaluated as an end point with reslizumab |
| Benralizumab[24,25,93,106] | Reduces the risk of asthma exacerbations ~40%-50% when compared with placebo | Who has evidence of eosinophilia (150-300 cells/mL) | Has been shown to facilitate a decrease in total OCS use and facilitate discontinuation of chronic OCS |
| Dupilumab[27,28] | Reduces the risk of asthma exacerbations ~50%-70% when compared with placebo | Who has evidence of eosinophilia (150-300 cells/mL), or a high FENO level | Has been shown to facilitate a decrease in total OCS use and facilitate discontinuation of chronic OCS |

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Main findings from key studies that aimed to reduce the use of oral corticosteroids (OCS).

| Citation | Design | Main findings | |
|---|---|---|---|
| **Omalizumab** | | | |
| Berger et al. [91] | 28-week, double-blind, RCT with a 24-week open-label extension in children (N = 225) with moderate-to-severe allergic asthma requiring ICS | There was a substantial reduction in ICS use in the double-blind period that was maintained in the open-label phase<br>Almost all patients who withdrew ICS at the end of the core study remained ICS-free at the end of the extension period | 降低ICS使用 |
| Teach et al. [82] | Three-arm, randomized, double-blind, double placebo controlled, multicenter clinical trial in asthmatic children aged ≥6 years with ≥1 recent exacerbation | A subgroup analysis from the PROSE study showed that omalizumab was significantly more efficacious than both placebo and ICS burst in patients with an exacerbation during the run-in phase | |
| Deschildre et al. [61] | One-year observational survey of atopic children and adolescents (N = 104) with severe allergic asthma who were given omalizumab as an add-on therapy to high level maintenance treatment | Over the year on treatment, a 30% reduction in ICS dose was reported ($P < 0.0001$). | |
| Brodlie et al. [17] | Interventional study in 34 children with severe asthma receiving maintenance oral prednisolone | There was a median daily prednisolone dose reduction from 20 mg to 5 mg ($P < 0.0001$), including 7 children who stopped taking prednisolone completely | |
| Rodrigo et al. [100] | Systematic review examined 8 RCTs (3429 participants), which compared subcutaneous omalizumab with placebo as an add-on to corticosteroids (inhaled or oral) in patients with allergic asthma. Six studies were in adults and adolescents (aged ≥12 years) and two were in children (aged < 12 years) | Compared with placebo, omalizumab resulted in significantly fewer asthma exacerbations (RR 0.57, 95% CI 0.48 to 0.66, NNTB = 10, 95% CI 7 to 13). Omalizumab significantly reduced asthma exacerbations per patient (WMD −0.19, 95% CI −0.23 to −0.14; eight RCTs), hospitalization rates (RR 0.44, 95% CI 0.23 to 0.83; 5 RCTs), inhaled or OCS dose (more than 50% dose reduction RR 1.34, 95% CI 1.23 to 1.46; 4 RCTs) and steroid use (complete withdrawal RR 1.80, 95% CI 1.42 to 2.28; 4 RCTs) | 降低ICS/OCS或停止OCS使用 |
| Molimard et al. [65] | Real-world evidence study assessing prescriptions of omalizumab for > 16 weeks by French and German clinicians to patients with severe persistent allergic asthma (N = 346) | Following omalizumab therapy, 50.6% patients on OCS at baseline reduced/stopped OCS dose at the time of data collection; 20.5% stopped and 30.1% reduced OCS. In all patients receiving maintenance OCS at baseline, mean reduction from baseline in daily OCS dose was 29.6% (7.1 mg prednisolone). In patients who reduced/stopped maintenance OCS, mean reduction from baseline in daily OCS dose was 74.3% (15.4 mg prednisolone). | |

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Main findings from key studies that aimed to reduce the use of oral corticosteroids (OCS).

| Citation | Design | Main findings |
|---|---|---|
| **Omalizumab** | | |
| Siergiejko et al. [63] | Randomized, open-label, placebo-controlled trial of omalizumab added to optimized asthma therapy, compared with standard therapy alone over 34 weeks (N = 82) | Change from baseline in mean maintenance OCS dose at the end of the study was significantly greater in the omalizumab-treated group compared with the standard therapy group (mean OCS dose at baseline [13.1 mg] vs at Week 32 [8.4 mg]; change from baseline, −45%; P = 0.002). Significantly more patients (n = 59) treated with omalizumab reduced or stopped OCS use at Week 32 |
| Rottern et al. [62] | Small study in a real-life setting in Israel that compared use of OCS in patients taking omalizumab with those taking placebo (N = 33) | The number of patients who used OCS significantly decreased for those receiving omalizumab therapy (84.8% vs 57.6%, P < 0.003), as did the median dosage of OCS for 33 patients (753 mg vs 662 mg; P < 0.002) |
| Lafeuille et al. [64] | Retrospective cohort study of patients (N = 644) with uncontrolled asthma based on a US health insurance claims database | Data showed 53.3% of those who initiated omalizumab therapy were able to reduce their OCS use |
| Braunstahl et al.– the eXpeRience registry [47] | 2-year multinational, observational study of 943 patients with uncontrolled allergic asthma who were taking omalizumab, 263 of whom were also receiving maintenance OCS therapy | The proportion of patients (n = 131) who had maintenance OCS therapy was lower at Month 24 (14.2%) compared with Month 12 (16.1%) and baseline (28.6%). The mean total daily OCS dose (prednisolone equivalent) decreased between baseline (15.5 mg) and Month 12 (7.7 mg), and continued to decrease between Months 12 and 24 (5.8 mg) |

降低OCS使用/劑量

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## Reduction in maintenance OCS dosing with biologicals from randomized, placebo-controlled registration trials in severe asthma

| Study name | Intervention dose/ duration | Intervention | Reduction in daily OCS dose from baseline (%)† | *P*-value | Patients achieving reduction in daily OCS dose from baseline by percentage category (%) ≥50% Reduction | ≥75% Reduction | ≥90% Reduction | 100% Reduction |
|---|---|---|---|---|---|---|---|---|
| SIRIUS[19] | Mepolizumab 100 mg SC Q4W for 20 weeks‡ | Placebo (*n* = 66) | 0 | — | 33 | 18 | 11 | 8 |
| | | Mepolizumab (*n* = 69) | 50 | 0.007 | 54 | 41 | 23 | 14 |
| ZONDA[20] | Benralizumab 30 mg SC Q4W or Q8W for 28 weeks§ | Placebo (*n* = 75) | 25 | — | 35 | 20 | 12 | 19 |
| | | Benralizumab Q4W (*n* = 72) | 75 | <0.001 | 67 | 53 | 33 | 56¶ |
| | | Benralizumab Q8W (*n* = 73) | 75 | <0.001 | 66 | 52 | 37 | 52¶ |
| LIBERTY ASTHMA VENTURE[54] | Dupilumab 300 mg SC Q2W (after a 600-mg loading dose) for 24 weeks†† | Placebo (*n* = 107) | 42 | — | 53 | 39 | 31 | 29 |
| | | Dupilumab (*n* = 103) | 70 | <0.001 | 80 | 69 | 55 | 52 |

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# Take home message

- Asthma is heterogeneous disease with multiple phenotypes that are caused by a variety of pathophysiologic mechanisms, or endotypes
- The targeted therapies have been shown to reduce asthma exacerbations, improve lung function, reduce oral corticosteroid use, and improve quality of life in appropriately selected patients.

| | 生物製劑 | 作用機制 | 試驗期別 | 生物標記 | 急性發作 | 肺功能 | 生活品質 | 減少類固醇 |
|---|---|---|---|---|---|---|---|---|
| 已核准 | Omalizumab | anti-IgE | 3 | allergen-specific IgE；BES ≥ 260 cells/μL、FeNO ≥ 20 ppb 反應較佳 | 降低 25% | 改善很少或意義不明確 | 改善 | 減少 ICS；OCS 無研究數據 |
| | Mepolizumab | anti-IL-5 | 3 | BES ≥ 300 cells/μL；在嗜酸性球較高、過去一年發作較多者反應較佳 | 可降低 50% | 改善；FEV1 無差異 | 改善 | 減少 OCS |
| | Reslizumab | anti-IL-5 | 3 | | 降低 50-60% | 改善 FEV1 | 改善 | 無評估研究 |
| | Benralizumab | anti-IL-5Rα | 3 | | 降低 25-60% | 改善 FEV1 | 改善 | 減少 OCS |
| | Dupilumab | anti-IL-4Rα | 3 | BES ≥ 150 cells/μL；FeNO ≥ 25 ppb | 降低 50-70% | 改善 FEV1 | 改善 | 減少 OCS |

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**藥品給付規定**

Anti-IgE

6. 2. 6. Omalizumab（如 Xolair）：（97/6/1、100/6/1、103/10/1）

1. 限用於

（1）12歲以上之青少年或成人經胸腔內科或小兒科或過敏免疫專科醫師診斷為「重度持續性氣喘」病患，為非抽煙或正積極戒煙者，需符合下列條件。

I. 臨床病史顯示對某過敏原過敏或經由體內試驗（如 skin prick test）或體外 IgE 試驗（如 CAP、MAST、RAST、FAST、ELISA test 等）呈陽性反應者。

II. 必須檢附「免疫球蛋白 IgE 檢驗結果」。免疫球蛋白 Total IgE 檢驗結果必須介於 30~1300IU/mL，但使用抗 IgE 製劑後 IgE 值降低者不在此限（103/10/1）。

III. 已接受高劑量類固醇藥物吸入劑（青少年大於400 mcg belcomethasone dipropionate/day 以上或他類固醇藥物吸入劑相等劑量；成人大於800mcg beclomethasone dipropionate/day 以上或其他類固醇藥物吸入劑相等劑量）及併用其他治療，如：長效乙二型作用劑（β2-agonist）、口服類固醇治療、口服 theophylline 或抗白三烯素類藥品仍控制不良者，且過去四週氣喘控制仍不穩定者(包括：日間症狀每週超過2次、且常活動受到限制、有夜間氣喘症狀發作或到醒來、需要緩解型藥物每週超過2次或以上，符合上述條件2者或以上者）（103/10/1）。

IV. 病歷記載有氣喘病史或需經證實為氣喘病患，支氣管擴張試驗顯示 FEV1 reversibility 超過12%與絕對值增加200mL 以上，或使用類固醇後 FEV1增加20%以上（103/10/1）。

2. 需經事前審查核准後使用。

3. 每月使用不得超過2次。

4. 應於病歷上詳細記載上個月發作次數、頻率及肺功能(如 PEFR 值或 $FEV_1$值)之變化。

5. 使用16週後需進行評估，與未使用前比較，症狀確實改善，方可繼續使用。

備註：「症狀改善」的定義為每日症狀或 PEFR 的改善，或減少口服或吸入性類固醇的使用，或減少非常規回診的次數或急診就醫或住院次數。

**藥品給付規定**

Anti-IL5, Anti-IL5R

6.2.8.Mepolizumab（如Nucala）、Benralizumab（如Fasenra）(107/11/1、109/3/1、109/11/1)：

1.限用於經胸腔專科或過敏免疫專科醫師診斷為嗜伊紅性(嗜酸性)白血球的嚴重氣喘且控制不良(severe refractory eosinophilic asthma)之18歲以上成人病患，投藥前12個月內的血中嗜伊紅性(嗜酸性)白血球≧300 cells/mcL，且需符合下列條件：(109/11/1)

(1)病患已遵循最適切的標準療法且過去6個月持續使用口服類固醇prednisolone每天至少5mg或等價當量(equivalence)。

(2)過去12個月內有2次或2次以上因氣喘急性惡化而需要使用全身性類固醇，且其中至少一次是因為氣喘惡化而需急診或住院治療。

2.需經事前審查核准後使用。

3.使用頻率：

(1)Mepolizumab每4週使用不得超過1次。

(2)Benralizumab第一個8週使用不得超過3次(第0、4、8週)，以後每8週使用不得超過1次。

4.使用32週後進行評估，與未使用前比較，若「惡化」情形減少，方可繼續使用。

備註：

1.「惡化」的定義為必須使用口服/全身性類固醇治療、或住院治療、或送急診治療的氣喘惡化現象。

2.「最適切的標準療法」係指符合GINA治療指引Step 5之規範。(109/11/1)

# Thanks for your attention

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