

The ERS/ATS severe asthma guidelines

Nicola Scichilone

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The ERS/ATS severe asthma guideline

The patient journey

Female, 51 yrs old, never smoker, asthma since adolescence.

Worsening in the last 2 yrs (several visits to ED, uncontrolled asthma under high dose ICS/LABA)

Nasal polyps, MRGE, Obesity.

Regione Siciliana
Azienda Ospedaliera
OSPEDALI RIUNITI VILLA SOFIA - CERVELLO
Legge Regionale n.5 del 14/04/2009
Sede Legale: Viale Strasburgo n.233 - 90146 Palermo. Tel.0917801111 - P.I. 05841780827

PRONTO SOCCORSO - P.O. V. CERVELLO

Verbale n. 008032

Pagina 1 di 2
Accettazione 23/01/2014 09:52
Ora Ingresso PS 23/01/2014 11:02
Dimissione 23/01/2014 14:53

Sig. [redacted] Sesso Femmina
Nato a [redacted] il 24/12/1972
Domiciliato a PALERMO in VIA S. FRAGAPANE N. 10
Residente a PALERMO in VIA S. FRAGAPANE N. 10
Cod. Sanitario Cod. Fiscale VNZDNL72T64G273X Tel. 0916840683
Nazionalità ITALIA Professione Casalinga
Modalità di arrivo AUTONOMO:
Sintomo RIF. DISPNEA E FAME D'ARIA IN PAZ. CON STORIA DI ASMA BRONCHIALE ALLERGICO.
Proven. paziente ALTRO
Modalità di trauma
Triagista CIOLINO GIUSEPPE Colore Triage GIALLO
Medico Accettante ROTOLO GASPARE ANTONIO
Rilevi rilevati 23/01/2014 09:54 CIOLINO GIUSEPPE FREQUENZA CARDIACA 84 bpm r
23/01/2014 09:54 CIOLINO GIUSEPPE SAT. O2 99% in a.a.
23/01/2014 09:56 CIOLINO GIUSEPPE PRESSIONE ARTERIOSA 125/75

Anamnesi
23/01/2014 11:19 ROTOLO GASPARE AN NON ESIBITA DOCUMENTAZIONE.
ASMA BRONCHIALE. NEGA DI ESSERE INCINTA.
RIFERISCE DI AVERE PRATICATO TERAPIA CON ZITROMAX E
VELAMOX (?) FINO A QUALCHE GIORNO ADDIETRO.
VIENE IN PRONTO SOCCORSO PER INCREMENTO DELLA DISPNEA E
TOSSE CON ESPETTORATO BIANCASTRO. NON FEBBRE.

Esame Obiettivo
23/01/2014 11:20 ROTOLO GASPARE AN PZ COLLABORANTE. LUCIDA, ORIENTATA. DISPNOICA A RIPOSO. AL
TORACE: REPERTO DI BRONCOSPASMO DIFFUSO. ATTIVITÀ
CARDIACA RITMICA NORMOFREQUENTE. PAO 120/70 MMHG.
23/01/2014 12:05 ROTOLO GASPARE AN EGA IN A.A. PH 7.465 PCO2 30.9 PO2 65.6 SO2 95.2 LAC 0.7
HCO3 21.9

Prestazioni 23/01/2014 11:02 897 VISITA GENERALE
23/01/2014 12:19 91492 PRELIEVO DI SANGUE VENOSO

Laboratorio 23/01/2014 14:33 ESEGUITI ESAMI EMATOCHIMICI: VEDI ALLEGATI
23/01/2014 14:33
23/01/2014 14:35

Radiologici 23/01/2014 12:20 87441 RX TORACE

Consulenza VC - PNEUMOLOGIA 1
23/01/2014 13:25 897 CONSULENZA PNEUMOLOGICA

Regione Siciliana
Azienda Ospedaliera
OSPEDALI RIUNITI VILLA SOFIA - CERVELLO
Legge Regionale n.5 del 14/04/2009
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PRONTO SOCCORSO - P.O. V. CERVELLO

Verbale n. 023727

Pagina 1 di 3
Accettazione 09/03/2014 10:43
Ora Ingresso PS 09/03/2014 11:52
Dimissione 10/03/2014 13:09

Sig. [redacted] Sesso Femmina
Nato a PALERMO il 24/12/1972
Domiciliato a PALERMO in VIA S. FRAGAPANE N. 10
Residente a PALERMO in VIA S. FRAGAPANE N. 10
Cod. Sanitario Cod. Fiscale VNZDNL72T64G273X Tel. 0916840683
Nazionalità ITALIA Professione Casalinga
Modalità di arrivo ACCOMPAGNATO DA:
Sintomo RIF. DISPNEA IN PAZ CON STORIA DI ASMA BRONCHIALE ALLERGICO
Proven. paziente ALTRO
Modalità di trauma
Triagista LIBRO FABIO Colore Triage GIALLO
Medico Accettante D.ssa GUZZETTA GIUSEPPA
Rilevi rilevati 09/03/2014 10:45 LIBRO FABIO FREQUENZA CARDIACA 90 bpm rit
09/03/2014 10:45 LIBRO FABIO SAT. O2 95% in aa
09/03/2014 10:46 LIBRO FABIO PRESSIONE ARTERIOSA 110/80 mmhg
09/03/2014 11:40 LIBRO FABIO FREQUENZA CARDIACA 100 bpm
09/03/2014 11:40 LIBRO FABIO SAT. O2 94% in aa
10/03/2014 09:00 ROTOLO GASPARE AN PRESSIONE ARTERIOSA 105/65 mmhg
10/03/2014 09:01 ROTOLO GASPARE AN SAT. O2 95% con O2 a 2 l'

Anamnesi
09/03/2014 11:52 GUZZETTA GIUSEPPA RIFERITA DISPNEA DA STANOTTE E DOLORE IN EMICOSTATO
DESTRO. IN PZ CON STORIA DI ASMA

Esame Obiettivo
09/03/2014 11:55 GUZZETTA GIUSEPPA PZ. DISPNOICA TORACE REPERTO DI BRONCOSPASMO TONI
CARDIACI NETTI IN SUCCESSIONE RITMICA
09/03/2014 12:45 GUZZETTA GIUSEPPA RX TORACE. TENUE ADDENSAMENTO ILARE EMIDIAFRAMMI
REGOLARI CON SENI COSTO FRENICI LIBERI (MERCADANTE GISELLA
GILDA)
09/03/2014 17:01 RESTIVO PANTALONE IT 37.4°C. SAO2 IN OSSIGENOTERAPIA 96%.
09/03/2014 19:37 RESTIVO PANTALONE SAO2 IN OSSIGENOTERAPIA 96%. REPERTO BRONCOSPASTICO E
DISPNEA A RIPOSO.

Prestazioni 09/03/2014 11:52 897 VISITA GENERALE
09/03/2014 11:59 91492 PRELIEVO DI SANGUE VENOSO
10/03/2014 11:17 91492 PRELIEVO DI SANGUE VENOSO

Laboratorio 09/03/2014 12:46 ESEGUITI ESAMI EMATOCHIMICI: VEDI ALLEGATI
09/03/2014 13:33
10/03/2014 12:26

Radiologici 09/03/2014 17:03 87441 RX TORACE

Regione Siciliana
Azienda Ospedaliera
OSPEDALI RIUNITI VILLA SOFIA - CERVELLO
Legge Regionale n.5 del 14/04/2009
Sede Legale: Viale Strasburgo n.233 - 90146 Palermo. Tel.0917801111 - P.I. 05841780827

PRONTO SOCCORSO - P.O. V. CERVELLO

Verbale n. 024800

Pagina 1 di 2
Accettazione 12/03/2014 12:30
Ora Ingresso PS 12/03/2014 16:32
Dimissione 12/03/2014 22:24

Sig. [redacted] Sesso Femmina
Nato a PALERMO il 24/12/1972
Domiciliato a PALERMO in VIA S. FRAGAPANE N. 10
Residente a PALERMO in VIA S. FRAGAPANE N. 10
Cod. Sanitario Cod. Fiscale VNZDNL72T64G273X Tel. 0916840683
Nazionalità ITALIA Professione Casalinga
Modalità di arrivo AUTONOMO:
Sintomo TORANI PER IL PERSISTERE DELLA SINTOMATOLOGIA:
VERBALE N° 23727
RILIEVI
Proven. paziente ALTRO
Modalità di trauma
Triagista CUCCHIARA GIOVANNI Colore Triage GIALLO
Medico Accettante Dott. VAGLICA SAVERIO
Rilevi rilevati 12/03/2014 12:32 CUCCHIARA GIOVANNI PRESSIONE ARTERIOSA 180/80
12/03/2014 12:32 CUCCHIARA GIOVANNI FREQUENZA CARDIACA 102
12/03/2014 12:32 CUCCHIARA GIOVANNI SAT. O2 97
12/03/2014 22:20 ROTOLO GASPARE AN SAT. O2 99% in a.a.
12/03/2014 22:21 ROTOLO GASPARE AN PRESSIONE ARTERIOSA 100/65 mmhg a dx e

Anamnesi
12/03/2014 16:51 VAGLICA SAVERIO RITORNA PER IL PERSISTERE DEL DOLORE EMITRACE DX.
PROBABILE ASMA ESTRINSECA. UDIVERSI ACCESSI IN PS PER
ANALOGA SINTOMATOLOGIA. ULTIMO ACCESSO INDICATO IL
RICOVERO MA PER MANCANZA DI POSTI LETTO HA RIFIUTATO
OSSERVAZIONE

Esame Obiettivo
12/03/2014 16:55 VAGLICA SAVERIO BRONCOSTENOSI DIFFUSA.
DOLROE TRA IV E VI SPAZIO INTERCOSTALE DX SULL'ASCELLARE
MEDIA E AMTERIORE, NON LESIONI ERPETICHE

12/03/2014 22:07 ROTOLO GASPARE AN
DA REFERATO TAC:-> Indagine eseguita in urgenza, nelle sole condizioni di
base. Non significative alterazioni della densità pare nchmale aventi
carattere di attivita'. li di volume medio. Non versamento pleurico e/o faldi di
pnx. La trachea ed i bronchi principali sono pervi. Note di spondiloartrite
dorsale. Nodulo ipodensito di circa 1,8 cm. nella mammella di destra.

12/03/2014 22:11 ROTOLO GASPARE AN
IN ATTO ASINTOMATICA. D-DIMERO 110. SI ESEGUE ECG:
SOVRAPPONIBILE A QUELLO ESEGUITO IL 10 MARZO. AL TORACE: MV
RIDOTTO + MODESTO BRONCOSPASMO. PAO 100/65 MMHG A DX E A
SX (NB.: SI TRATTA DI VALORI PRESSORI GIÀ NOTI ALLA PAZIENTE).

Prestazioni 12/03/2014 16:32 897 VISITA GENERALE
12/03/2014 16:53 91492 PRELIEVO DI SANGUE VENOSO
12/03/2014 20:13 91492 PRELIEVO DI SANGUE VENOSO
12/03/2014 22:20 8952 ELETTROCARDIOGRAMMA

Why does she suffer from severe asthma?

- **Frequent severe exacerbations**
- **Poor symptom control in the last years**
- **Coexistence of concomitant diseases**
- **Other factors...**

bronchiectasie, OSAS, ...

ERS/ATS definition of severe asthma

- A patient is deemed to have **uncontrolled asthma** if at least one of the following features is present:

Poor symptom control	Frequent severe exacerbations
Serious exacerbations	Airflow limitation

A patient is deemed to have **severe asthma** if he/she has:

Uncontrolled asthma while on high-dose therapy

OR

Controlled asthma that becomes uncontrolled on tapering of high-dose corticosteroids

ERS 1999 “Difficult asthma”

- **“asthma, poorly controlled in terms of chronic symptoms, with episodic exacerbations, persistent and variable airway obstruction and continued requirement for short-acting beta-2-agonists and a reasonable dose of inhaled corticosteroids”**

Eur Respir J 1999

ATS 2000: Refractory asthma

Major criteria

- **Treatment with oral corticosteroids > 50% of the time**
- **high doses inhaled corticosteroids (>1200 µg beclomethasone equivalent)**

Minor criteria

- **requirement for daily treatment with LABA, theophylline or LTRAs**
- **daily asthma symptoms requiring rescue medication**
- **persistent airway obstruction (FEV1 < 80% predicted); diurnal PEF variability > 20%**
- **1 or more urgent care visits for asthma per year**
- **3 or more oral steroid bursts per year**
- **prompt deterioration with > 25% reduction in oral or ICS dosing**
- **near fatal asthma event in the past**



UNIVERSITÀ
DEGLI STUDI
DI PALERMO

Dipartimento Biomedico di Medicina
Interna e Specialistica (Di.Bi.MIS)
SEZIONE di PNEUMOLOGIA

Palermo, 11/11/2015

V1 Screening Visit 380009101

Paziente: [REDACTED]

Data della visita: [REDACTED]

Data di nascita: [REDACTED] Razza: Caucasica Telefono: [REDACTED]

Il paziente viene adeguatamente informato sulla possibilità di partecipare allo studio clinico Sanofi EFC13579 e viene valutato come possibile candidato.

Il paziente firma:

- Informativa e manifestazione del consenso Informato Asthma Quest – EFC13579 e informativa per il paziente versione V1 del 25 febbraio 2015.
- Consenso informato supplementare per il test HIV versione V1 del 25 febbraio 2015

La paziente rifiuta di dare il consenso alle valutazioni di farmaco-genetica, alle analisi di risposta al vaccino e alla raccolta dei campioni per usi futuri.

Si consegna al paziente:

- Copia informativa e manifestazione del consenso Informato Asthma Quest – EFC13579 e informativa per il paziente versione V1 del 25 febbraio 2015
- Copia consenso informato supplementare per il test HIV versione V1 del 25 febbraio 2015
- Modulo informativo per il medico curante versione V1 del 25 febbraio 2015

La paziente rispetta tutti i criteri di inclusione ed esclusione previsti dal protocollo pertanto si contatta il sistema IVRS per registrare la visita di screening. Il sistema assegna alla paziente il numero 380009101.

Report Date: 11/Nov/2015
Time: 13:26:59

Biomedical Systems Centralized Spirometry
AZIENDA OSPEDALIERA OSPEDALI RIUNITI VILLA
SOFIA CERVELLO 380009
Sanofi EFC13579
CPS V2.8.2.5_C70-I_IP
NM09 SN: 34901_07962_2302_508

Subject ID: 380009101

Test Date: 11/Nov/2015 13:20:29

Visit: Visit 1 (Wk -4 +/- 1)

Interval: PreDose

Session ID: 5

Dose Time: N/A

Tech: federicas

FeNO Rep: 14.3 %

Repeatability NOT Achieved (Pair NOT within 2.5 ppb or 10% whichever is greater)

Number of Efforts: 2

Gender: F Age: 52
Height: 150.0 cm

Date of Birth: 01-Oct-1963

Race: Caucasian/White

Ethnicity: Non-Hispanic/Latino

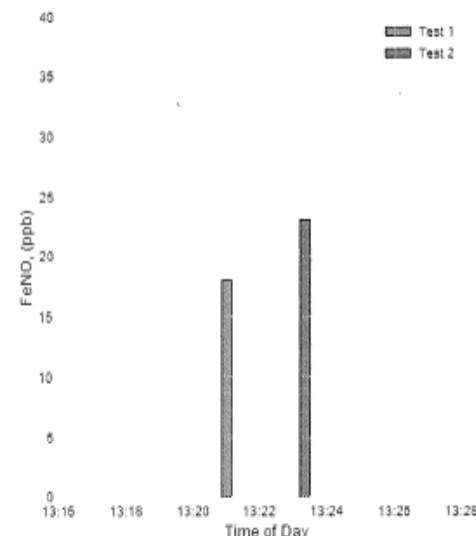
Parameters	Test*1	Test*2	Avg
FeNO	ppb	18	23

'+' = Accepted, '-' = NotAccepted, '*' = Used for average value

Repeat #2 Reason: the first exam isn't correct

Comments:

Has the patient fasted for at least 1 hour? YES



Signature: [Signature]

Print: ALBA BENFANTE

Date: 11 Nov 2015

Federica Scaduto

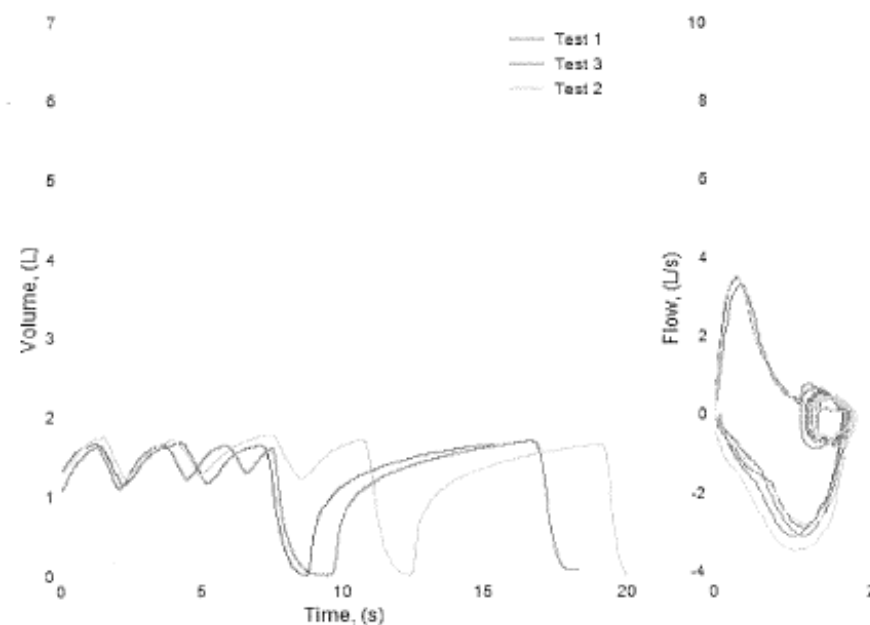
FEDERICA SCADUTO

11-NOV-2015

Subject ID: 380009101
Visit: Visit 4 (Wk 4) Interval: PreBD
Test Date: 07/Jan/2016 10:26:48 Session ID: 19
Tech: federicas Cal. Check Date/Time: 07/Jan/2016 08:26:5
Gender: F Age: 52 Date of Birth: 01/Oct/1963 Height: 150.0 cm
Race: Caucasian/White Correction %: 100
Ethnicity: Non- Hispanic/Latino Predicted Values: NHANES-III.Caucasian
Number of Efforts: 3 FEV1 Rep: 0.00 L FVC Rep: 0.04 L

ATS/ERS							
Parameters		Pred	Test+1	Test+3	Test+2	Best	%Pred
FVC	L	2.92	1.70	1.66	1.66	1.70	58
FEV1	L	2.31	1.08	1.08	1.07	1.08	47
FEV1/FVC	%	80	64	65	64	64	80
PEF25-75	L/s	2.41	0.48	0.53	0.51	0.48	20
PEF	L/s	5.93	3.30	3.46	3.52	3.52	59
TPEF	ms	-	100	78	75	75	-
FET	s	-	6.92	6.45	6.61	6.92	-
VEVT	ml	-	80	49	42	42	-
VEVT/FVC	%	-	4.71	2.95	2.53	2.47	-

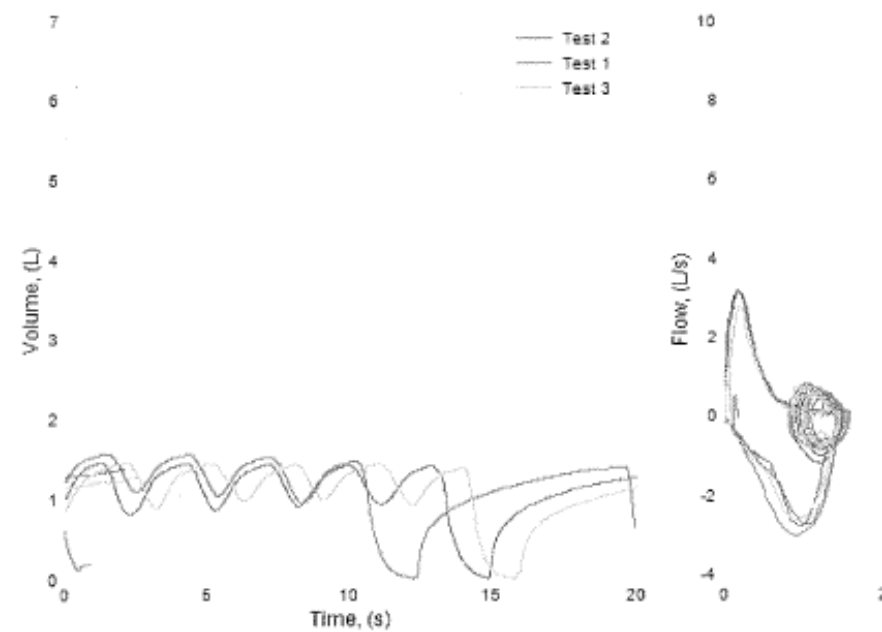
Comments:



Subject ID: 380009101
Visit: Visit 12 (Wk 28) Interval: PreDose
Test Date: 20/Jun/2016 09:40:34 Session ID: 41
Tech: Benfante Cal. Check Date/Time: 20/Jun/2016 09:15:27
Gender: F Age: 52 Date of Birth: 01/Oct/1963 Height: 150.0 cm
Race: Caucasian/White Correction %: 100
Ethnicity: Non- Hispanic/Latino Predicted Values: NHANES-III.Caucasian
Number of Efforts: 3 FEV1 Rep: 0.00 L FVC Rep: 0.03 L

ATS/ERS							
Parameters		Pred	Test+2	Test+1	Test+3	Best	%Pred
FVC	L	2.92	1.40	1.37	1.27	1.40	48
FEV1	L	2.31	0.82	0.82	0.77	0.82	35
FEV1/FVC	%	80	59	60	61	59	74
PEF25-75	L/s	2.41	0.32	0.34	0.31	0.32	13
PEF	L/s	5.93	3.16	3.17	2.76	3.17	53
TPEF	ms	-	58	50	69	50	-
FET	s	-	7.23	7.26	6.57	7.26	-
VEVT	ml	-	29	15	83	15	-
VEVT/FVC	%	-	2.07	1.09	6.54	1.07	-

Comments:



Report Date: 12/Jun/2017
Time: 10:29:29

Biomedical Systems Centralized Spirometry
AZIENDA OSPEDALIERA OSPADALI RIUNITI VILLA
SOFIA CERVELLO 380099
Sanofi LTS12551

Subject ID: 380009101

Visit: Visit 11 (Wk 24)

Test Date: 12/Jun/2017 10:14:45

Tech: chiarac

Gender: F Age: 53 Date of Birth: 01/Oct/1963

Race: Caucasian/White

Ethnicity: Non- Hispanic/Latino

Number of Efforts: 3

Interval: PreDose

Session ID: 6

Cal. Check Date/Time: 12/Jun/2017 09:24:03

Height: 150.0 cm

Correction %: 100

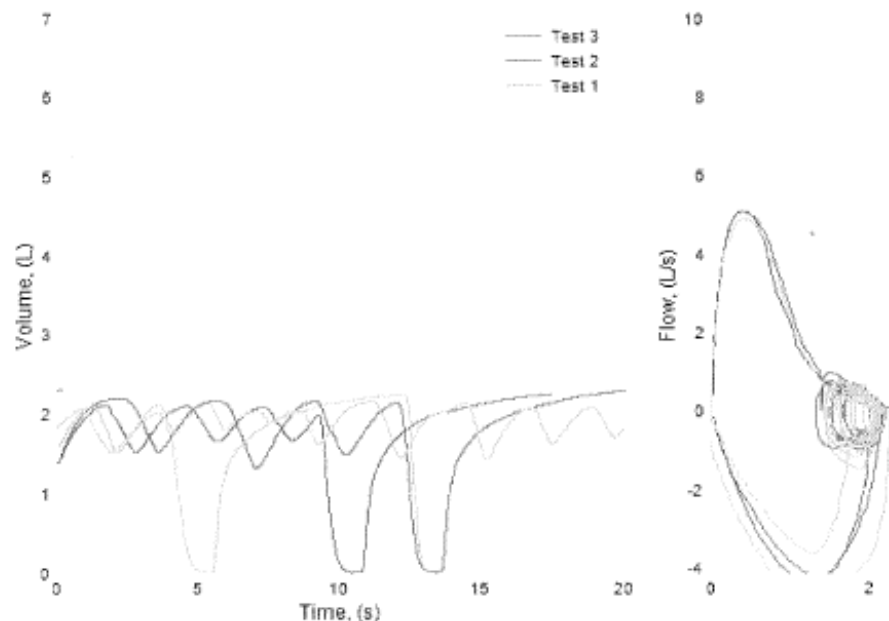
Predicted Values: NHANES-III.Caucasian

FEV1 Rep: 0.04 L

FVC Rep: 0.05 L

		ATS/ERS					
Parameters		Pred	Test+3	Test+2	Test+1	Best	%Pred
FVC	L	2.90	2.31	2.26	2.26	2.31	80
FEV1	L	2.28	1.68	1.64	1.62	1.68	74
FEV1/FVC	%	80	73	73	72	73	91
PEF	L/s	5.89	5.07	5.07	4.88	5.07	86
FEF25_75	L/s	2.37	1.13	1.11	1.05	1.13	48
PET	s	-	6.52	6.60	6.64	6.64	-
TPEF	ms	-	79	86	83	79	-
VEXT	ml	-	51	48	44	44	-
VEXT/FVC	%	-	2.21	2.12	1.95	1.90	-

Comments:



Report Date: 16/Apr/2018
Time: 12:09:05

Biomedical Systems Centralized Spirometry
AZIENDA OSPEDALIERA OSPADALI RIUNITI VILLA
SOFIA CERVELLO 380099
Sanofi LTS12551

Subject ID: 380009101

Visit: Visit 15 (Month 18)

Test Date: 16/Apr/2018 10:06:11

Tech: sitesuper

Gender: F Age: 54 Date of Birth: 01/Oct/1963

Race: Caucasian/White

Ethnicity: Non- Hispanic/Latino

Number of Efforts: 3

Interval: PreDose

Session ID: 10

Cal. Check Date/Time: 16/Apr/2018 09:56:24

Height: 150.0 cm

Correction %: 100

Predicted Values: NHANES-III.Caucasian

FEV1 Rep: 0.03 L

FVC Rep: 0.03 L

CAL T

UND: S

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ia who f

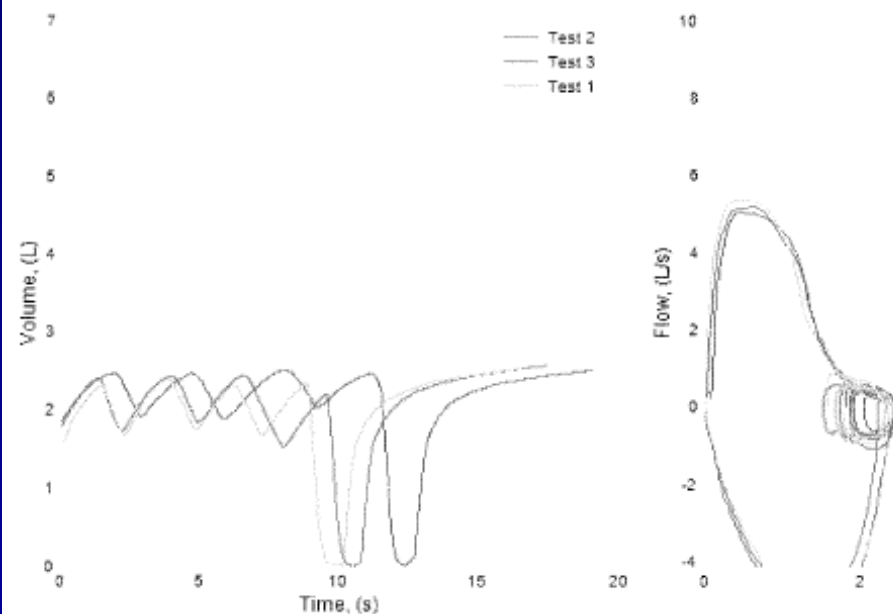
na clinic

NUMBER

3ERTY,

		ATS/ERS					
Parameters		Pred	Test+2	Test+3	Test+1	Best	%Pred
FVC	L	2.87	2.56	2.50	2.53	2.56	89
FEV1	L	2.26	1.96	1.99	1.95	1.99	88
FEV1/FVC	%	79	77	80	77	78	99
PEF	L/s	5.85	5.15	5.03	5.35	5.35	91
FEF25_75	L/s	2.33	1.65	1.92	1.66	1.65	71
PET	s	-	6.58	6.35	6.34	6.58	-
TPEF	ms	-	109	84	87	84	-
VEXT	ml	-	67	99	43	43	-
VEXT/FVC	%	-	2.62	3.96	1.70	1.68	-

Comments:

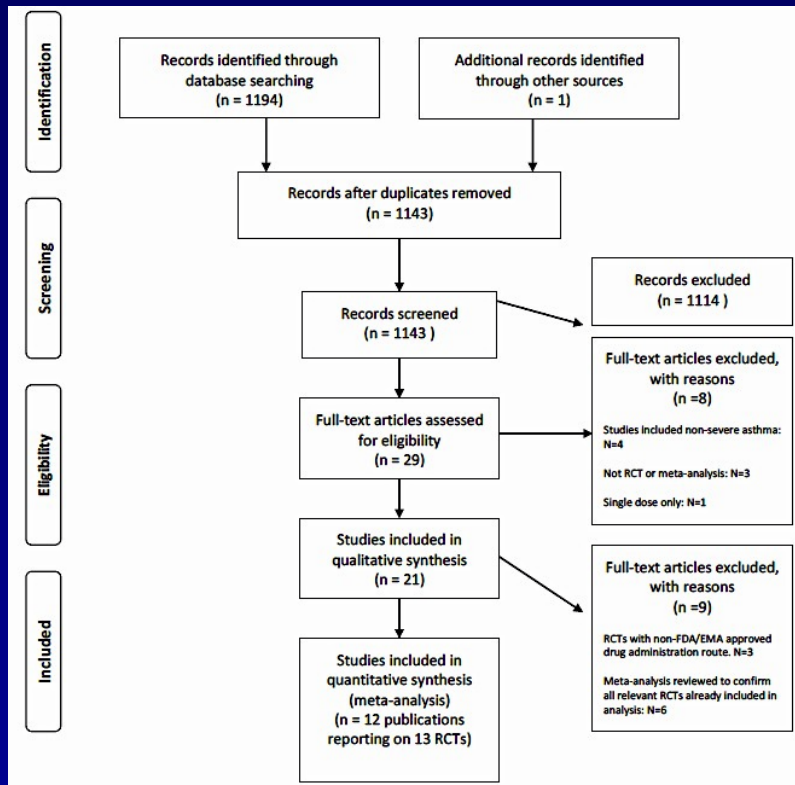


The ERS/ATS severe asthma guideline

The patient journey

The target treatment

The Task Force was focused on specific PICOs, and, unlike the first Task Force, did not consider general management strategies for severe asthma



Asthma exacerbations

Symptoms

Asthma control

Quality of life

Use of systemic corticosteroids

Adverse events

**CRITICAL
OUTCOMES**

Change in lung function

**IMPORTANT
OUTCOME**

Question 1: Should a monoclonal anti-IL5 antibody be used in adults and children with severe asthma?

MEPOLIZUMAB therapy was associated with a 50% reduction in the rate of any exacerbation

**SIRIUS
MUSCA
MENSA**

- **64% reduction in exacerbations requiring emergency department (ED) visit or hospitalization**
- **50% median reduction in the dose of maintenance oral corticosteroids (OCS)**
- **0.43-point decrease in ACQ-5 and an absolute 7.14 decrease in the SGRQ scale**
- **The effect of mepolizumab on FEV1 was less than the minimal clinically important difference (MCID)**

Bel EH, NEJM 2014; Chupp GL, Lancet Resp Med 2017; Ortega HG, NEJM 2014

Question 1: Should a monoclonal anti-IL5 antibody be used in adults and children with severe asthma?

QUESTION 1: ANTI-IL5 STRATEGIES

RECOMMENDATION

We suggest using anti-IL5 strategies as add-on therapy for adults with severe uncontrolled eosinophilic asthma

CONDITIONAL

Studies not *homogenously* severe

Not cost effective, reduced equity and feasibility

Insufficient evidence in adolescents

SAFETY

All three anti-IL5 strategy drugs were well tolerated. Frequency of adverse effects was similar when compared with placebo.

Participants experienced a lower risk of serious adverse events when assigned to anti-IL5 strategy drugs. The lower risk for having any adverse events is likely driven by the reduction in severe asthma exacerbations by these drugs.

Question 2: Should a measurement of a specific biomarker be used to guide initiation of treatment with a monoclonal anti-IL5 antibody or anti-IL5-R α in adults and children with severe asthma?

QUESTION 2: BIOMARKERS FOR ANTI-IL5

RECOMMENDATION

We suggest using blood eosinophil cut-off $\geq 150/\mu\text{L}$ to guide anti-IL5 therapy initiation in adults with severe asthma and a history of prior asthma exacerbations

CONDITIONAL

Low quality of evidence

Limited data on sputum eosinophils and no data on FeNO or serum periostin

Question 3: Should a measurement of a specific biomarker be used, in addition to total IgE level, to guide initiation of treatment with a monoclonal anti-IgE antibody in adults and children with severe asthma?

BLOOD EOS COUNT

FENO

SERUM PERIOSTIN

ACLQ

QUESTION 3: BIOMARKERS FOR ANTI-IGE TREATMENT

RECOMMENDATION

We suggest using a blood eosinophil cutoff of 260/mcL and a FENO cut-off of 19.5 ppb to identify adolescents and adults with severe allergic asthma more likely to benefit from anti-IgE treatment

CONDITIONAL

Low quality of evidence

Periostin data was omitted due to low clinical availability

Question 6: Should an anti-interleukin 4/13 strategy be used for adults and children with severe asthma?

QUESTION 6: ANTI-IL4/13 TREATMENT

RECOMMENDATION

We suggest dupilumab as add-on therapy for adult patients with severe eosinophilic asthma, and for those with severe corticosteroid-dependent asthma regardless of eosinophil levels

CONDITIONAL

Due to limited number of adolescents treated with anti-IL4/13, the TF was unable to provide a recommendation for this age group and no available evidence exists for children < 12 yrs

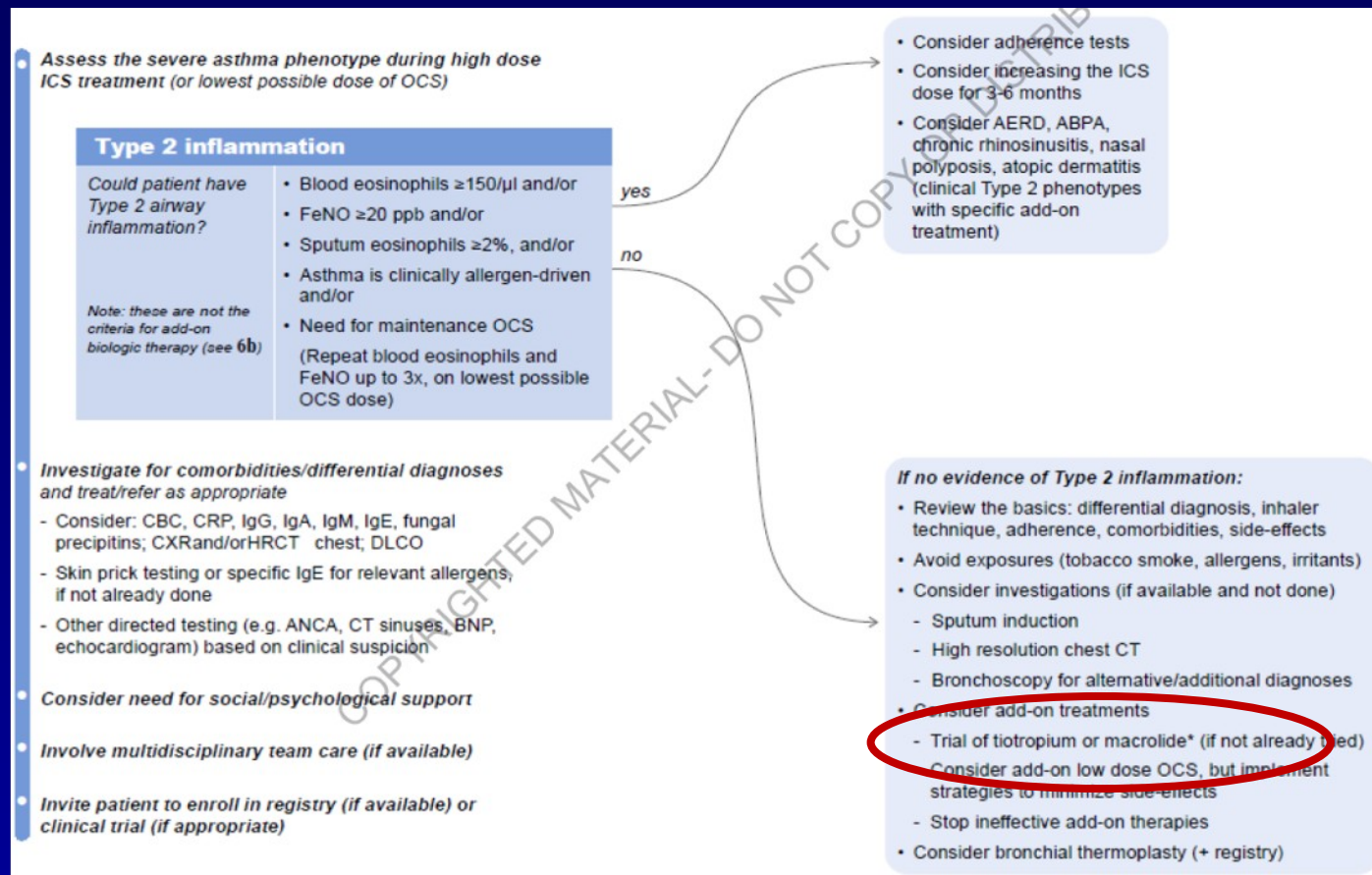
Key changes to GINA severe asthma guide in 2022

- **Anti-IL4R* (dupilumab)** for severe eosinophilic/Type 2 asthma
 - Not suggested if blood eosinophils (current or historic) >1500/ μ l
 - Dupilumab now also approved for children ≥ 6 years with severe eosinophilic/Type 2 asthma, not on maintenance OCS (Bacharier, NEJMed 2021)
- **Anti-TSLP (tezepelumab)** now approved for severe asthma (age ≥ 12 years)
 - Greater clinical benefit with higher blood eosinophils and/or higher FeNO
 - Insufficient evidence in patients taking maintenance OCS

Class	Name	Age*	Asthma indication*	Other indications*
Anti-IgE	Omalizumab (SC)	≥ 6 years	Severe allergic asthma	Nasal polyposis, chronic spontaneous urticaria
Anti-IL5	Mepolizumab (SC)	≥ 6 years	Severe eosinophilic/Type 2 asthma	Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome
Anti-IL5R	Reslizumab (IV)	≥ 18 years		
	Benralizumab (SC)	≥ 12 years		
Anti-IL4R	Dupilumab (SC)	≥ 6 years	Severe eosinophilic/Type 2 asthma, or maintenance OCS	Moderate-severe atopic dermatitis, CRSwNP
Anti-TSLP	Tezepelumab (SC)	≥ 12 years	Severe asthma	

Question 4: Should a long-acting inhaled muscarinic antagonist be used in adults and children with severe asthma?

Question 5: Should a macrolide be used in adults and children with severe asthma?



QUESTION 4 and 5: ADDITION OF LAMA AND MACROLIDE

RECOMMENDATION

We *recommend* the addition of tiotropium for adolescents and adults with severe asthma uncontrolled despite GINA step 4-5 therapies.

RECOMMENDATION

We suggest a trial of macrolide treatment to reduce asthma exacerbations in adult asthma subjects on GINA step 5 therapy that remain persistently symptomatic or uncontrolled.

CONDITIONAL

We suggest against the use of chronic macrolide treatment in children and adolescents with severe uncontrolled asthma.

ERS/ATS recommendations and future challenges

The ERS/ATS severe asthma guideline

The patient journey

The target treatment

Toward precision medicine

Treatable traits: toward precision medicine of chronic airway diseases

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ABSTRACT Asthma and chronic obstructive pulmonary disease (COPD) are two prevalent chronic airway diseases that have a high personal and social impact. They likely represent a continuum of different diseases that may share biological mechanisms (*i.e.* endotypes), and present similar clinical, functional, imaging and/or biological features that can be observed (*i.e.* phenotypes) which require individualised treatment. Precision medicine is defined as “treatments targeted to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations”. In this Perspective, we propose a precision medicine strategy for chronic airway diseases in general, and asthma and COPD in particular.

Triple therapy vs. biologics

Subjects enrolled in triple therapy trials are older, more obstructed and with lower rate of exacerbations compared to those under biologic trials.

Triple therapy vs. biologics

**On ICS/LABA
with persistent
bronchial obstruction**



ICS/LABA/LAMA

**On ICS/LABA
with reversible bronchial obstruction
AND
frequent exacerbations (T2 high)**



BIOLOGICS

Omic sciences to identify new target treatments in severe asthma