Exploring clinical remission in moderate asthma – perspectives from Asia, Middle East, and South America

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Supplementary Materials

Table S1: Physicians' countries and level of participation

	Country	Survey-1 answered (Y/N)	Scientific Workshop attended (Y/N)	Survey-2 answered (Y/N)
1	Abu Dhabi	N	N	N
2	Argentina	Y	Y	Y
3	Argentina	N	N	N
4	Argentina	Y	N	Y
5	Argentina	Y	Y	Y
6	India	Y	N	Y
7	India	Y	N	N
8	India	Y	N	N
9	Kuwait	Y	Y	Y
10	Kuwait	Y	Y	Y
11	Kuwait	Y	N	Y
12	Mexico	Y	N	Y
13	Mexico	Y	N	N
14	Mexico	Y	N	Y
15	Oman	Y	N	Y
16	Philippines	Y	N	Y
17	Philippines	Y	Y	Y
18	Philippines	Y	Y	Y
19	Thailand	Y	Y	Y
20	Thailand	Y	Y	Y
21	Thailand	N	N	N
22	United Arab Emirates	N	N	Y
23	United Arab Emirates	N	N	N
24	Vietnam	Y	Y	Y
25	Vietnam	Y	Y	Y

Figure S1: Study and participant flow diagram

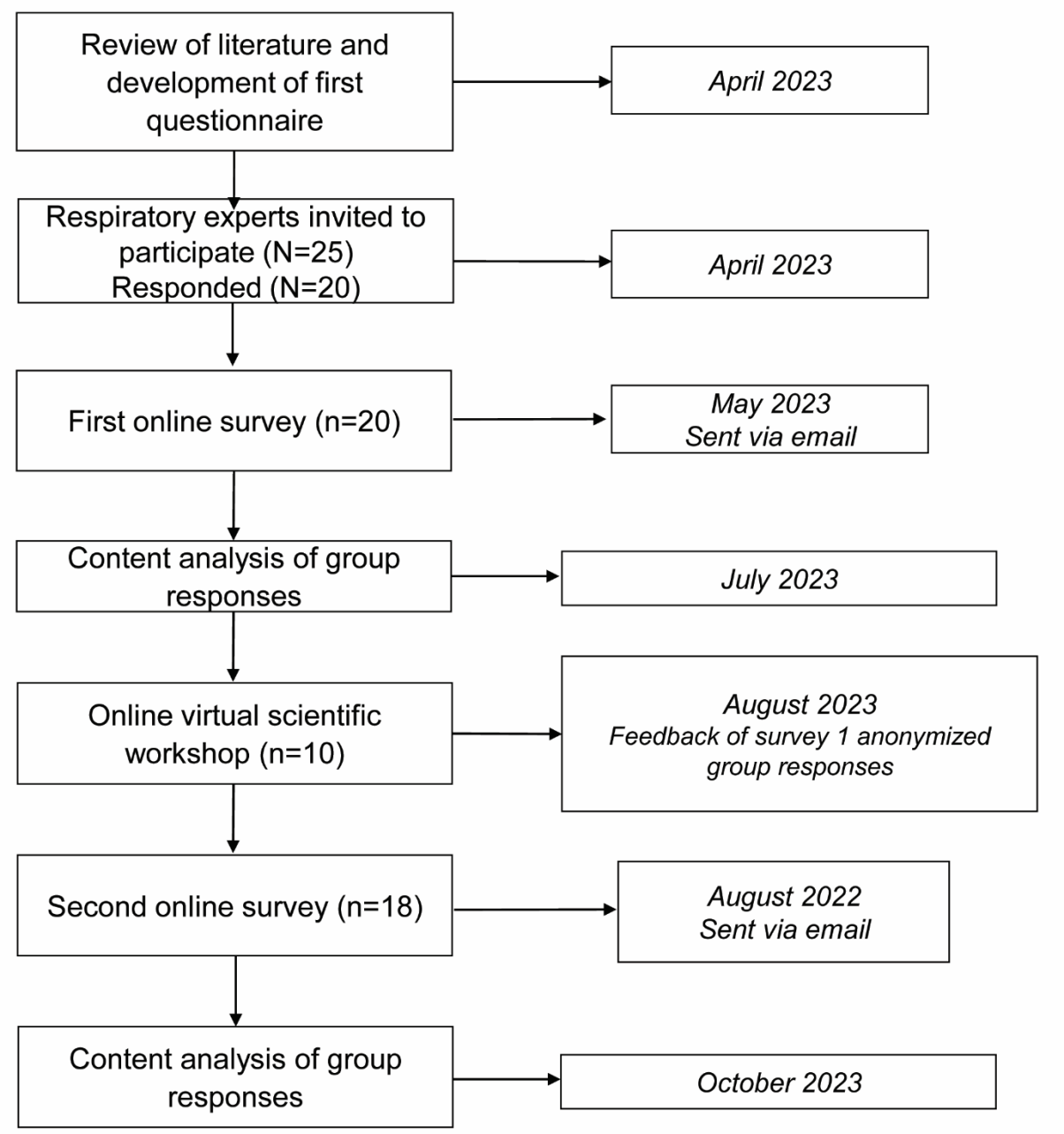
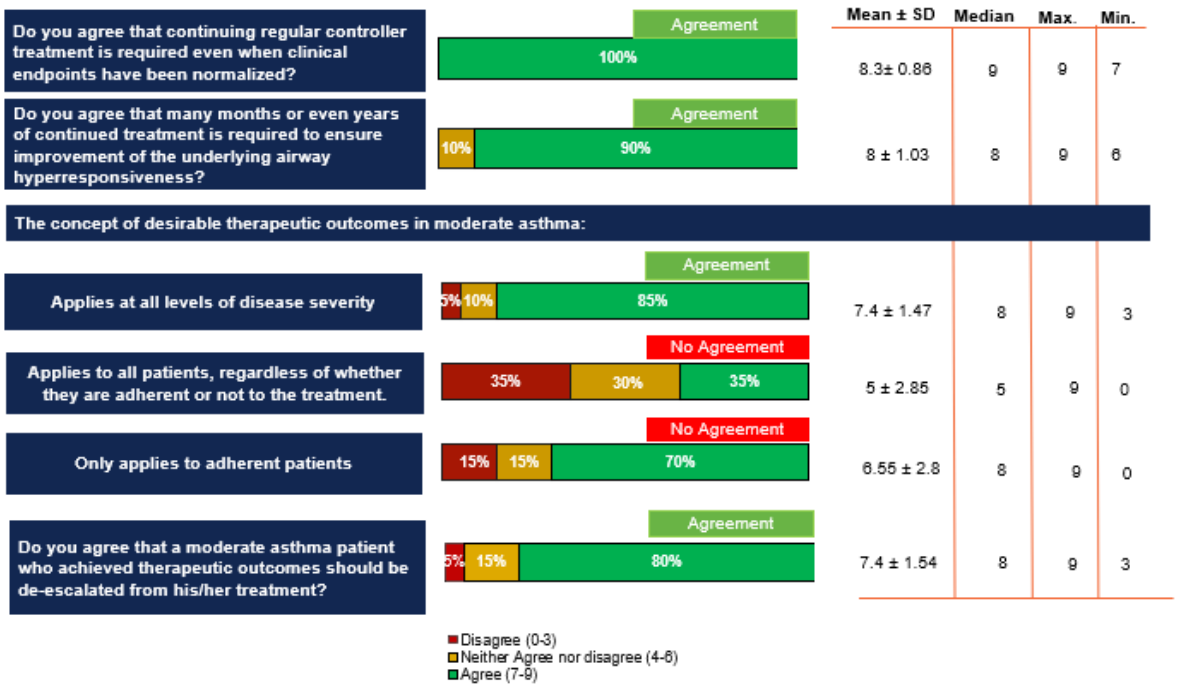


Figure S2: Responses on concepts of desirable therapeutic outcomes

a. Survey 1



b. Changes between survey 1 and survey 2

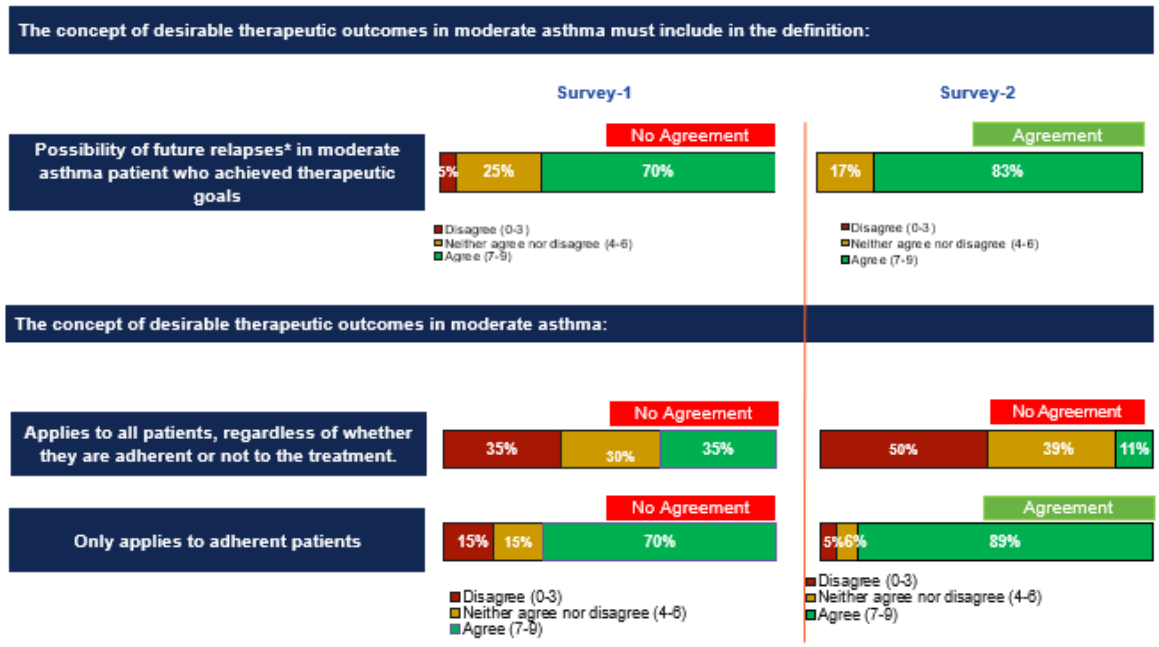
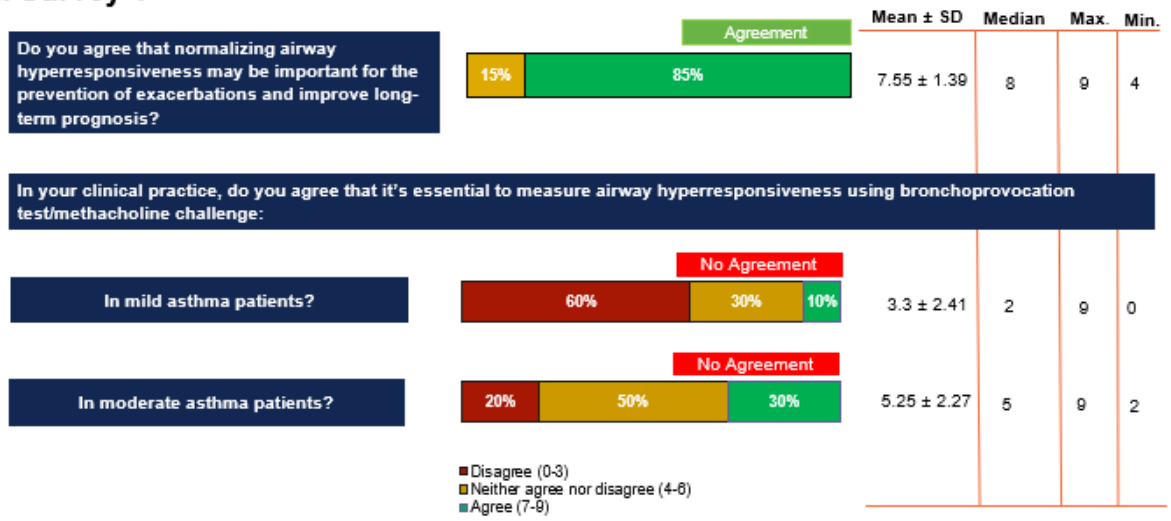


Figure S3: Role of airway responsiveness measure in defining desirable therapeutic outcomes

a. Survey 1



b. Changes between survey 1 and survey 2

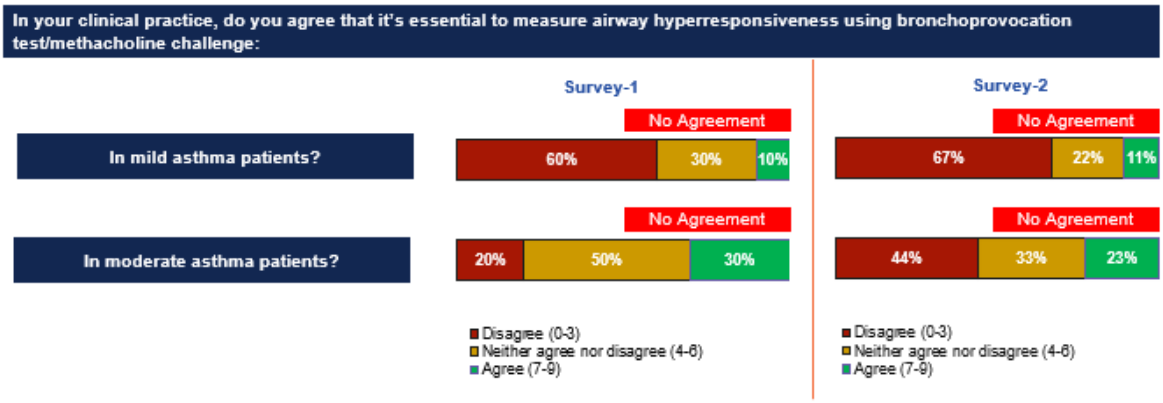


Figure S4: Duration of treatment in concepts of desirable therapeutic outcomes (survey 1)

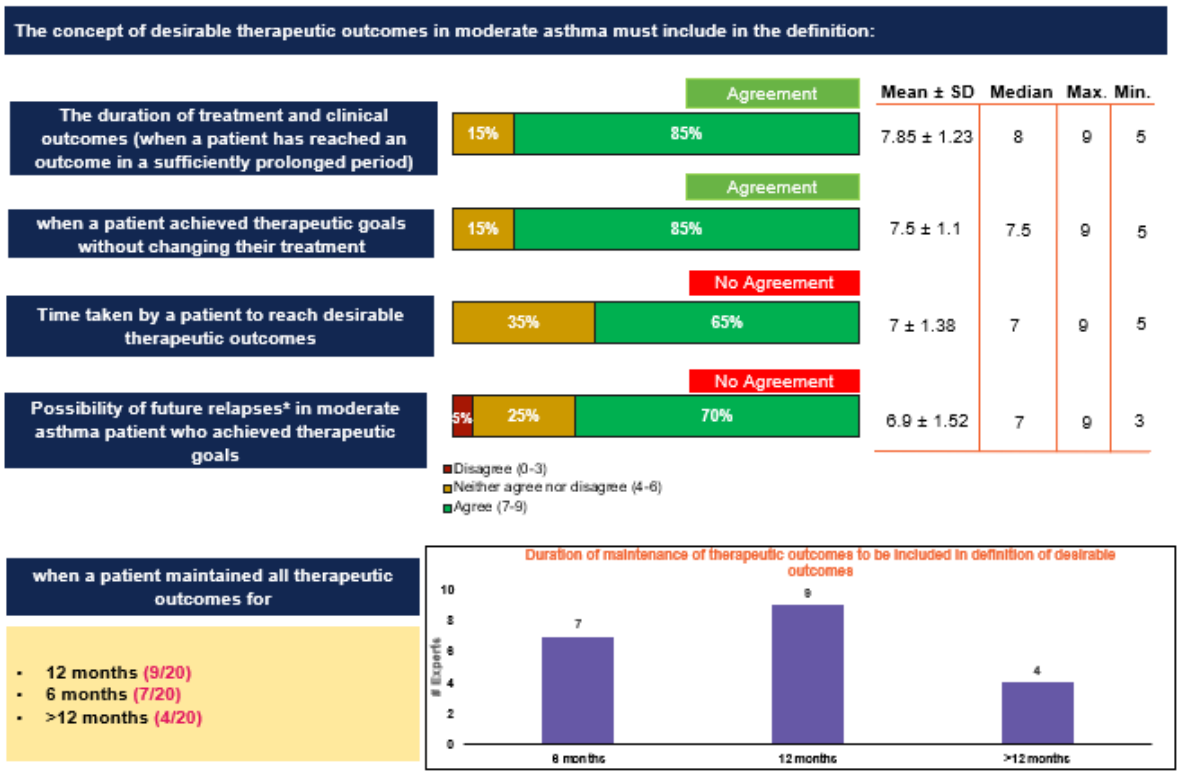
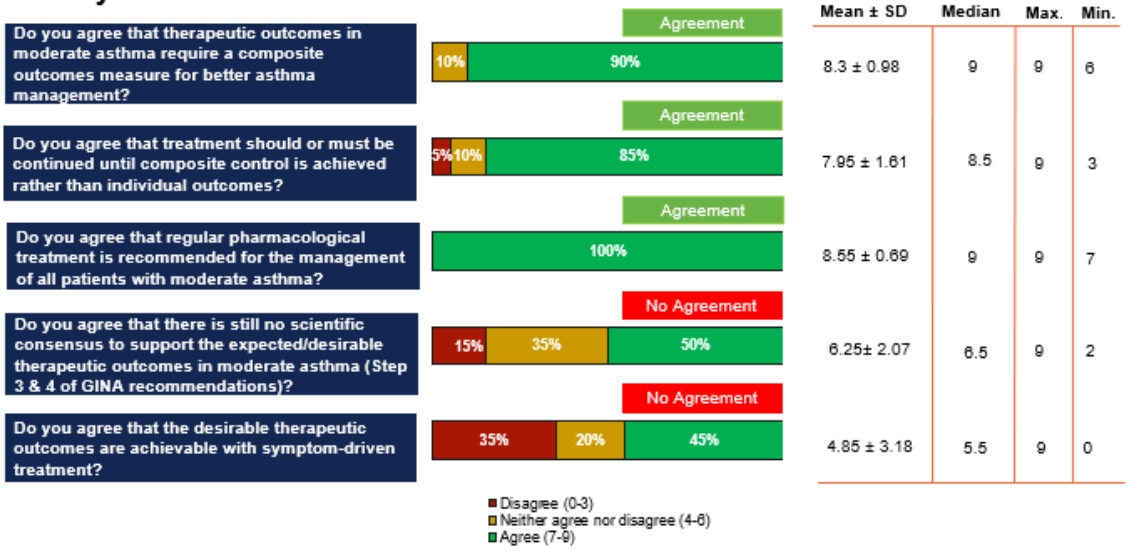


Figure S5: Views on treatment in relation to desirable therapeutic outcomes

a. Survey 1



b. Survey 2

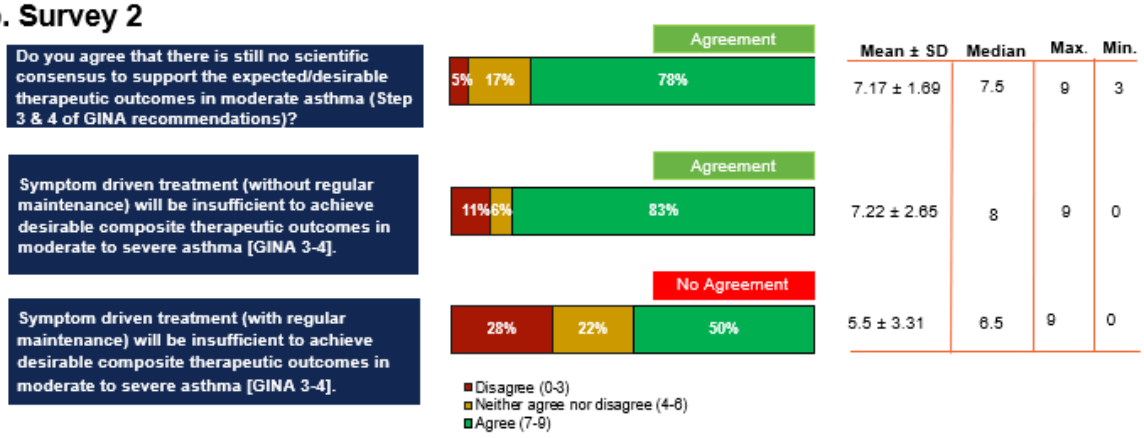


Figure S6: Most important outcomes for a composite measure (survey 1)

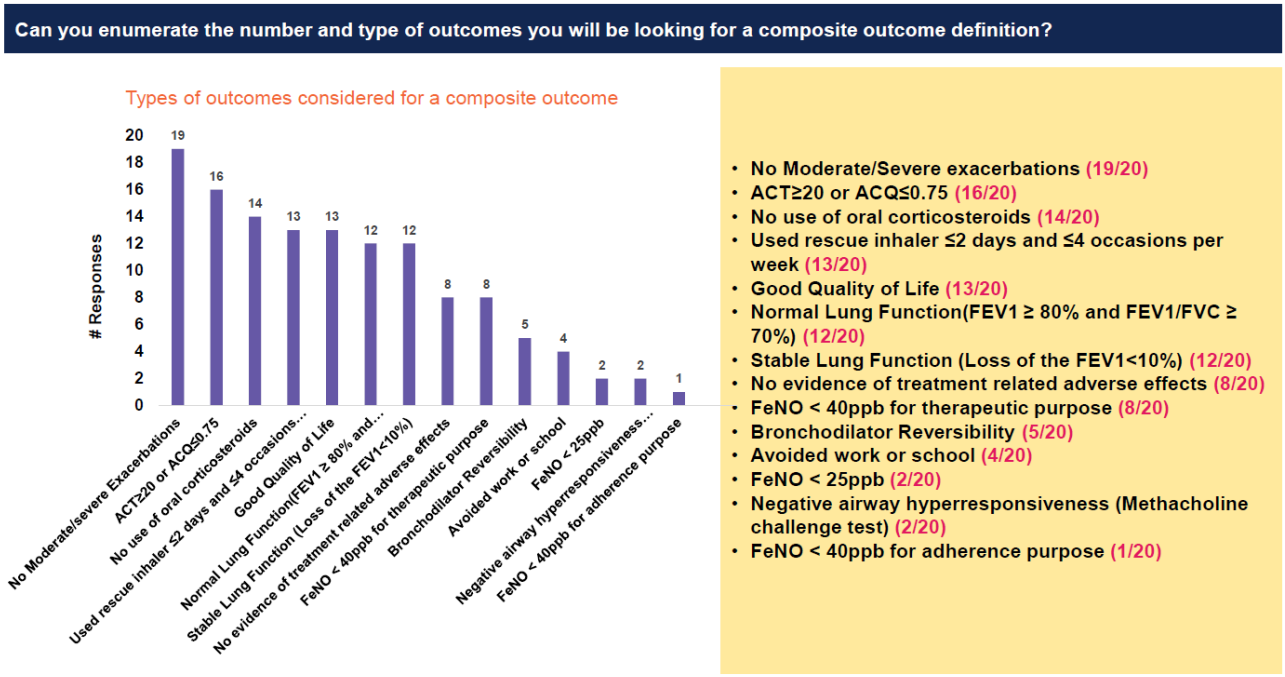
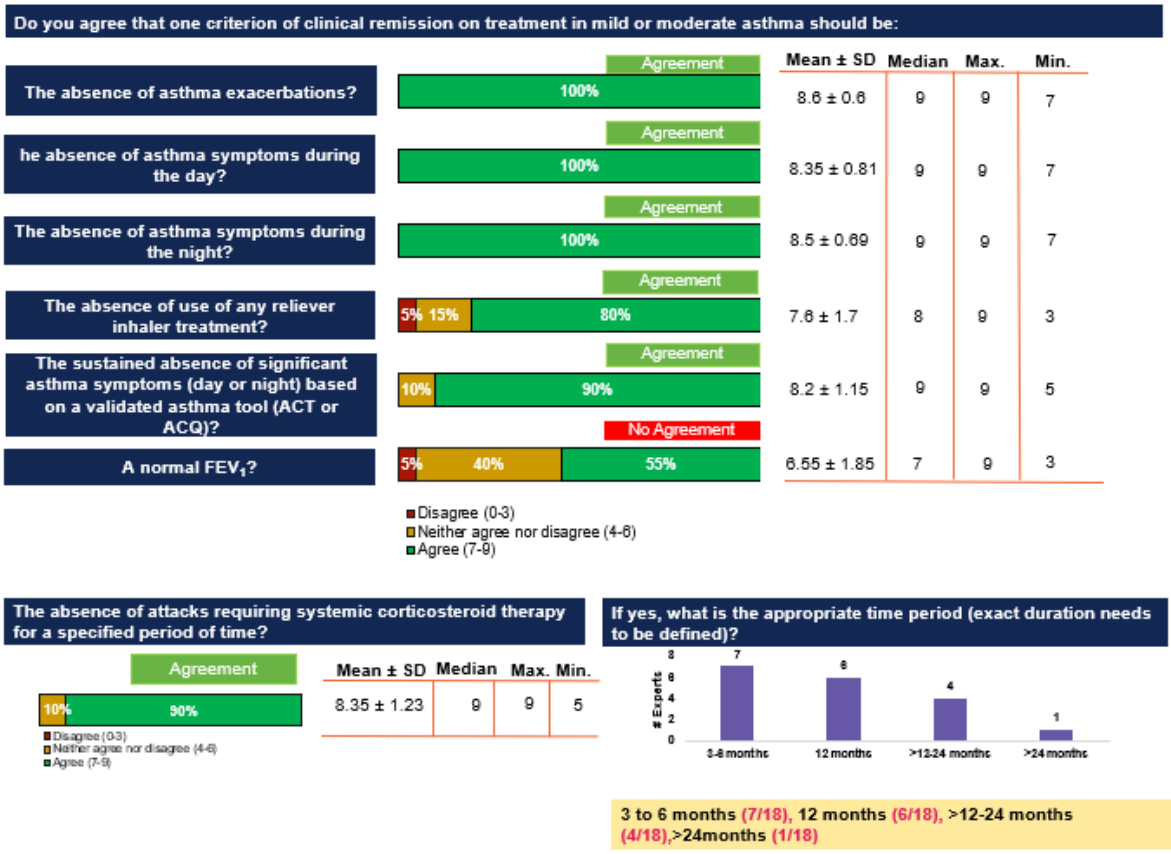


Figure S7: Criteria that could be included in a definition of clinical remission on treatment in mild or moderate asthma (survey 1)

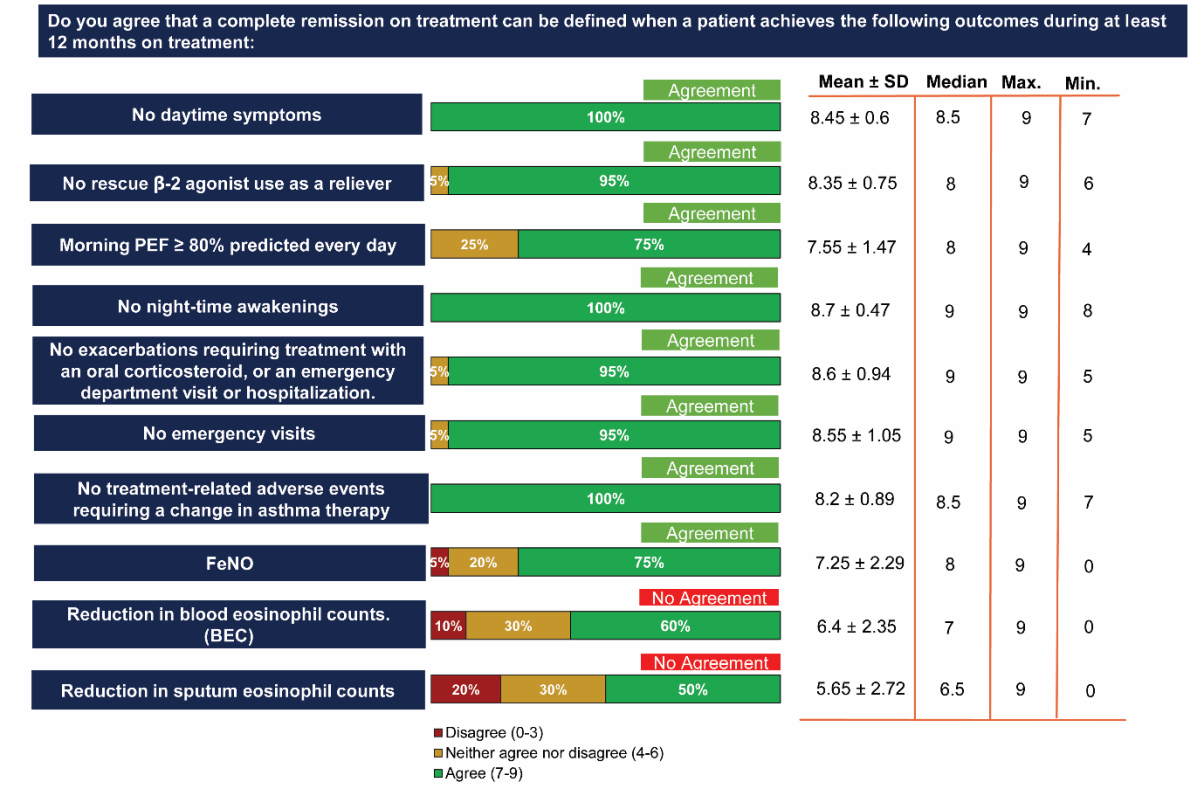


3 to 6 months (7/18), 12 months (6/18), >12-24 months (4/18),>24months (1/18)

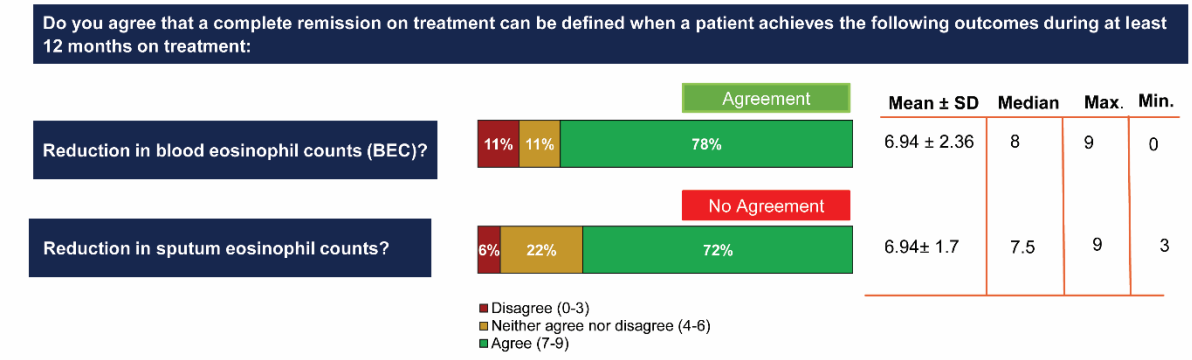
Figure S8: Concepts of asthma remission beyond clinical remission

Figure S9: Outcomes that could be included in a definition of remission beyond clinical remission on treatment

a. Survey 1



b. Survey 2



Appendix 1: Delphi survey 1 questions

Section I: Therapeutic Outcomes in Moderate Asthma

S.NO	Questions	Response
1	Do you agree that there is still no scientific consensus to support the expected/desirable therapeutic outcomes in moderate asthma (Step 3 & 4 of GINA recommendations)?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
2	Do you agree that a desirable therapeutic outcome in moderate asthma patient could be when a patient:	
	a) Has no moderate/severe exacerbations.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Did not use oral corticosteroids.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) Used rescue inhaler ≤2 days and ≤4 occasions per week.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	d) Achieved an ACT ≥ 20 in all last year/monthly checks. OR achieved an ACQ ≤ 0.75.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	e) Has a normal lung function. (FEV_1 ≥ 80% and FEV_1/FVC ≥ 70%)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	f) Has a stable lung function in one year. (Loss of the FEV_1 less than 10%).	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	g) Demonstrates no bronchodilator reversibility.	1. **On treatment** 0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		2. **Without treatment** 0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	h) Has a good QOL based on an objective QoL questionnaire assessment in your clinical practice.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	i) Does not have evidence of treatment related adverse effects that require or justify therapeutic change.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

	j) Has avoided any work or school due to asthma?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	k) Demonstrates no airway hyperresponsiveness. Or Has a negative methacholine challenge test.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	l) Has a FeNO: < 40 ppb for therapeutic purposes	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	m) Has a FeNO: < 40 ppb for adherence purposes.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	n) FeNO: < 25 ppb	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
3	How do you rank the above 14 therapeutic outcomes (based on their importance) to be considered in clinical practice to evaluate moderate asthma patient?	**Please rank the below therapeutic outcomes from 1-14 in the text box** No Moderate/Severe Exacerbations ☐ No use of oral corticosteroids ☐ Used rescue inhaler ≤2 days and ≤4 occasions per week ☐ ACT≥20 or ACQ≤0.75 ☐ Normal Lung Function (FEV_1 ≥ 80% and FEV_1/FVC ≥ 70%) ☐ Stable Lung Function (Loss of the FEV_1<10%) ☐ Bronchodilator Reversibility ☐ Good Quality of Life ☐ No evidence of treatment related adverse effects ☐ Avoided work or school ☐ Negative airway hyperresponsiveness (Methacholine challenge test) ☐ FeNO < 40ppb for therapeutic purpose ☐ FeNO < 40ppb for adherence purpose ☐

		FeNO < 25ppb ☐
4	Do you agree that therapeutic outcomes in moderate asthma require a composite outcomes measure for better asthma management?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
5	In your clinical practice, how many individual outcomes do you consider necessary to achieve a composite outcome definition?	**Open Text**
	a) Can you enumerate the number and type of outcomes you will be looking for a composite outcome definition?	☐ **No Moderate/Severe Exacerbations** ☐ **No use of Oral corticosteroids** ☐ **Used rescue inhaler =2 days and =4 occasions per week** ☐ **ACT = 20 OR ACQ = 0.75** ☐ **Normal Lung Function (FEV1 = 80% and FEV1/FVC = 70%)** ☐ **Stable Lung Function (Loss of the FEV1<10%)** ☐ **Bronchodilator Reversibility** ☐ **Good Quality of Life** ☐ **No evidence of Treatment Related Adverse Effects** ☐ **Avoided work or school** ☐ **Negative Airway Hyperresponsiveness (Methacholine challenge test)** ☐ **FeNO < 40ppb for therapeutic purpose** ☐ **FeNO < 40ppb for adherence purpose** ☐ **FeNO <25ppb**
6	Do you agree that treatment should or must be continued until composite control is achieved rather than individual outcomes?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
7	Do you agree that regular pharmacological treatment is recommended for the management of all patients with moderate asthma?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
8	Do you agree that the desirable therapeutic outcomes are achievable with symptom-driven treatment?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

9	Do you agree that continuing regular controller treatment is required even when clinical endpoints have been normalized?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
10	Do you agree that many months or even years of continued treatment is required to ensure improvement of the underlying airway hyperresponsiveness?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
11	The concept of desirable therapeutic outcomes in moderate asthma must include in the definition:	
	a) The duration of treatment and clinical outcomes (when a patient has reached an outcome in a sufficiently prolonged period).	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Time taken by a patient to reach desirable therapeutic outcomes	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) when a patient achieved therapeutic goals without changing their treatment	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	d) when a patient maintained all therapeutic outcomes for	○ 6 months ○ 12 months ○ >12 months
	e) Possibility of future relapses* in moderate asthma patient who achieved therapeutic goals *(*Relapse means an exacerbation in the last year or an ACT ≤ 20 points)*	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
12	The concept of desirable therapeutic outcomes in moderate asthma:	
	a) Applies to all patients, regardless of whether they are adherent or not to the treatment.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Only applies to adherent patients	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) Applies at all levels of disease severity	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
13	Do you agree that a moderate asthma patient who achieved therapeutic outcomes should be de-escalated from his/her treatment?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

14	Do you agree that normalizing airway hyperresponsiveness may be important for the prevention of exacerbations and improve long-term prognosis?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
15	In your clinical practice, do you agree that it's essential to measure airway hyperresponsiveness using bronchoprovocation test/methacholine challenge:	
	a) In mild asthma patients?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) In moderate asthma patients?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

Section II: Clinical Remission in Moderate Asthma

S.NO	Questions	Response
16	Do you agree that clinical remission is a desirable outcome for a patient with asthma?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
17	Do you agree that a definition of clinical remission in asthma should be stringent but achievable?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
18	Defining clinical remission, based primarily on patient symptoms, HCP assessment of disease activity, and routine clinical assessments (exact criteria to be defined), is an important first step in asthma management. Do you agree?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
19	Do you agree that any definition of asthma remission should be validated to determine its ability to predict long-term positive outcome?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
20	Do you agree that clinical remission in asthma should add value beyond the current definitions of asthma control based on ACT or ACQ?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
21	Do you agree that one criterion of clinical remission on treatment in mild or moderate asthma should be:	
	a) The absence of attacks requiring systemic corticosteroid therapy for a specified period of time?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	a1) If yes, what is the appropriate time period (exact duration needs to be defined)?	**Open text**
	b) The absence of asthma exacerbations?	

		0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) The absence of asthma symptoms during the day?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	d) The absence of asthma symptoms during the night?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	e) The absence of use of any reliever inhaler treatment?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	f) The sustained absence of significant asthma symptoms (day or night) based on a validated asthma tool (ACT or ACQ)?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	g) A normal FEV_1?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
22	Do you agree that clinical remission in mild and moderate asthma patients should be considered as a desirable a treatment goal for asthma treatment?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
23	Do you agree that it is required to have objective measures of disease activity for the Clinical Remission definition?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
24	Do you agree that clinical remission definition on-treatment requires to achieve outcomes measure for:	
	a) At least for 12 months?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) At least for 18 months?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) At least for 24 months?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
25	Do you agree that clinical remission of moderate asthma patients doesn't mean cure?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
26	Do you agree that a clinical remission on treatment can be defined when a patient achieves the following outcomes during at least 12 months on treatment:	
	a) No daytime symptoms.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) No rescue β-2 agonist use as a reliever.	

		0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) Morning PEF ≥ 80% predicted every day.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	d) No night-time awakenings.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	e) No exacerbations requiring treatment with an oral corticosteroid, or an emergency department visit or hospitalization.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	f) No emergency visits.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	g) No treatment-related adverse events requiring a change in asthma therapy.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	h) Reduction in blood eosinophil counts. (BEC)	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	i) Reduction in sputum eosinophil counts.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	j) FeNO	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	k) Any other criteria for clinical remission.	Open Text
27	Do you agree that a clinical remission off treatment can be defined when same criteria as mentioned above are maintained without asthma treatment for ≥12 months?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
28	For clinical remission in asthma, should any laboratory measures be included in the definition to provide an objective measurement of disease activity?	○ **Yes** ○ **No**
	a) If so, what criteria should be used:	☐ **FeNO** ☐ **Blood Eosinophils** ☐ **Pulmonary Function Test** ☐ **Impedance Oscillometry** ☐ **Histopathology** ☐ **Sputum Eosinophils**

		☐ **Airway Hyperresponsiveness**
29	What long-term outcomes should be used to test the predictive value of any asthma remission definition?	**Please explain your answer.**
30	What would be needed for GPs to understand and practice clinical remission in patients with moderate asthma?	**Open Text**
31	Are individual components of clinical remission easy to implement in the clinical practice of GPs?	**Open Text**
32	When should a GP consider a referral to a pulmonologist when considering clinical remission as an outcome?	**Open Text**
33	What would be needed for pulmonologists to communicate and implement the concept clinical remission in patients with moderate asthma with asthma management teams in their hospitals?	**Open Text**
34	Is there a need to evaluate the previous clinical studies or planned clinical trials to understand clinical remission as an endpoint?	**Open Text**

Section III: Complete Remission in Moderate Asthma

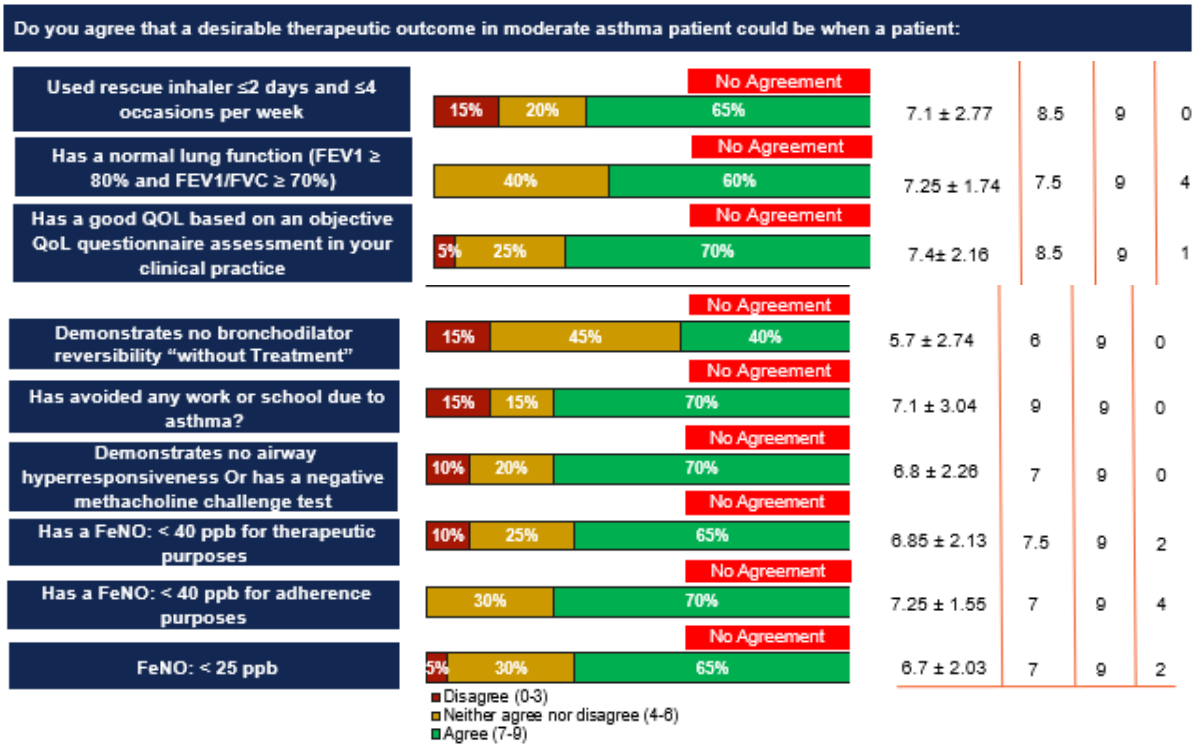
S.NO	**Questions**	**Response**
35	Do you agree that one objective measure for complete remission definition should include clinical remission definition and the absence of airway inflammation?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
36	Do you agree that one objective measure for complete remission on treatment in mild or moderate asthma patients could be:	
	a) To measure airway hyperresponsiveness?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

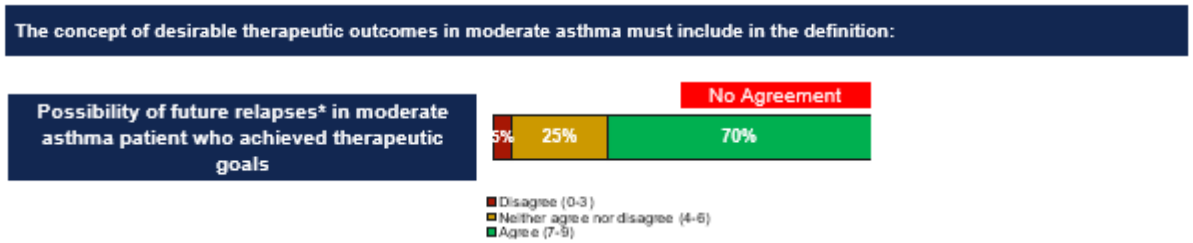
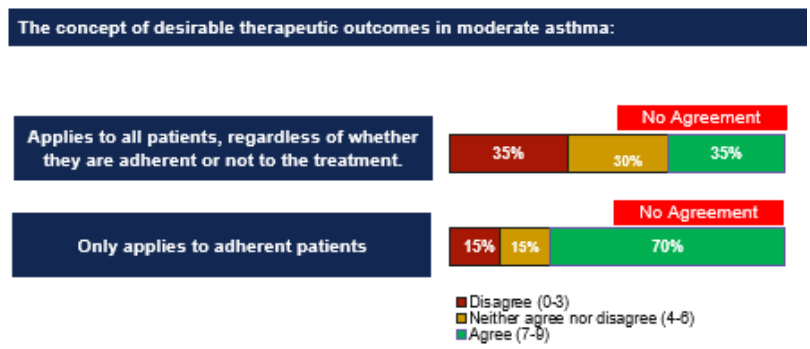
	a1) If your agreement answer score was 7 or higher, do you consider a normal airway hyperresponsiveness as the inflammation biomarker must for clinical remission?	○ Yes ○ No
	b) To measure blood eosinophil count (BEC)?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b1) If your agreement answer score was 7 or higher, what is the lower cutoff point of BEC expected for clinical remission?	**OPEN TEXT**
	c) To measure FeNO?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c1) If your agreement answer score was 7 or higher, what is the lower cutoff point of FeNO expected for clinical remission?	**OPEN TEXT**
37	The duration requirements for spontaneous remission in asthma have ranged from 6 months to 3 years. For remission in asthma that allows patients to be receiving treatment, should there be a duration requirement?	○ **Yes** ○ **No**
	a) If so, what duration should be required?	**OPEN TEXT**
38	Do you agree that a complete remission definition on-treatment requires achieving outcomes measure at least for 12 months?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
39	Do you agree that complete remission of moderate asthma patients doesn't mean cure?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
40	Do you agree that for a patient to be considered in remission, HCP and patient concurrence regarding asthma remission should be required, as there are no validated HCP-reported disease activity instruments for asthma?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
41	Do you agree that being in remission in asthma does not eliminate the risk of severe and even fatal asthma events?	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
42	Do you agree that a complete remission on treatment can be defined when a patient achieves the following outcomes during at least 12 months on treatment:	
	a) No daytime symptoms.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) No rescue β-2 agonist use as a reliever.	0☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

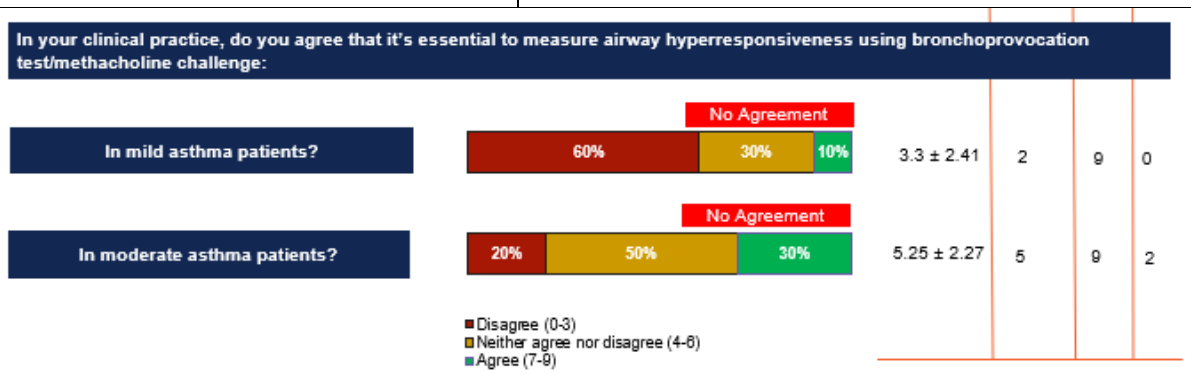
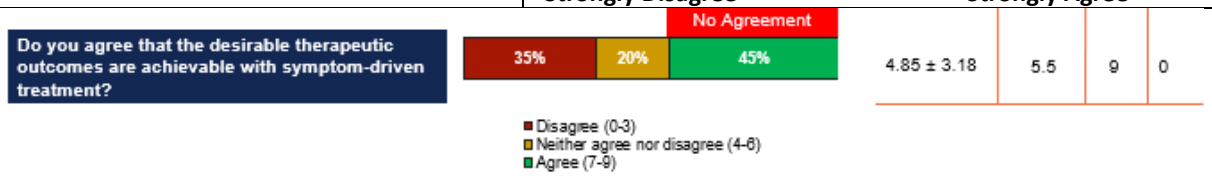
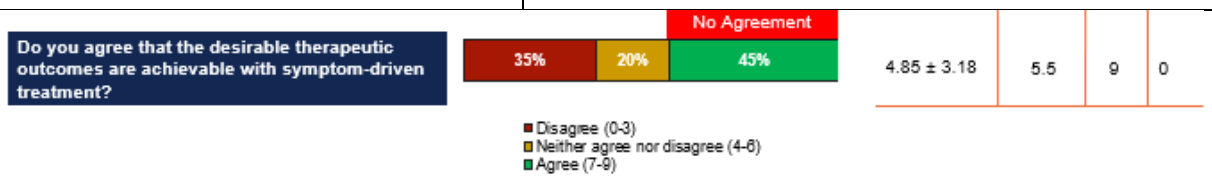
	c) Morning PEF ≥ 80% predicted every day.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	d) No night-time awakenings.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	e) No exacerbations requiring treatment with an oral corticosteroid, or an emergency department visit or hospitalization.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	f) No emergency visits.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	g) No treatment-related adverse events requiring a change in asthma therapy.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	h) Reduction in blood eosinophil counts. (BEC)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	i) Reduction in sputum eosinophil counts.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	j) FeNO	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	k) Any other criteria for complete remission.	**Open Text**
43	Do you agree that a complete remission off treatment can be defined when same criteria as mentioned above are maintained without asthma treatment for ≥12 months?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

Appendix 2: Delphi survey 2 questions and responses from survey 1 where no agreement reached

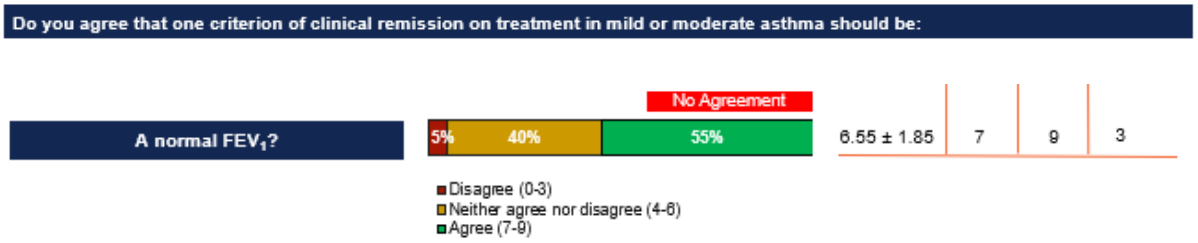
Section I: Therapeutic Outcomes in Moderate Asthma

S.NO	Questions	Response
	Do you agree that there is still no scientific consensus to support the expected/desirable therapeutic outcomes in moderate asthma (Step 3 & 4 of GINA recommendations)?	
Q1	Do you agree that there is still no scientific consensus to support the expected/desirable therapeutic outcomes in moderate asthma (Step 3 & 4 of GINA recommendations)?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q2	Do you agree that a desirable therapeutic outcome in moderate asthma patient could be when a patient:	
	a) Used rescue inhaler ≤2 days and ≤4 occasions per week.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Has a normal lung function. (FEV_1 ≥ 80% and FEV_1/FVC ≥ 70%)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) Has optimal and stable lung function (FEV1±10% of patient's baseline)?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	d) Has a good QOL based on an objective QoL questionnaire assessment in your clinical practice.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

	e) Demonstrates no bronchodilator reversibility "without treatment"	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	f) Has avoided any work or school due to asthma?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	g) Demonstrates no airway hyperresponsiveness. Or has a negative methacholine challenge test	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	h) Has a FeNO: < 40 ppb for therapeutic purposes (if FeNO is available)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	i) Has a FeNO: < 40 ppb for adherence purposes (if FeNO is available)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	j) FeNO: < 25 ppb (if FeNO is available)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q3	The concept of desirable therapeutic outcomes in moderate asthma must include in the definition:	
	a) Early response to treatment is less important than achieving overall control	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Possibility of future relapses* in moderate asthma patient who achieved therapeutic goals *(*Relapse means an exacerbation in the last year or an ACT ≤ 20 points)*	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q4	The concept of desirable therapeutic outcomes in moderate asthma:	

	a) Applies to all patients, regardless of whether they are adherent or not to the treatment.	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Only applies to adherent patients	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q5	In your clinical practice, do you agree that it is essential to measure airway hyperresponsiveness using bronchoprovocation test/methacholine challenge before and after reasonable interval (12 months) during maintenance anti-inflammatory regimen?	
	a) In mild asthma patients?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) In moderate asthma patients?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q6	Symptom driven treatment (**without** regular maintenance) will be insufficient to achieve desirable composite therapeutic outcomes in moderate to severe asthma [GINA 3-4].	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q7	Symptom driven treatment (**with** regular maintenance) will be insufficient to achieve desirable composite therapeutic outcomes in moderate to severe asthma [GINA 3-4].	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

Section II: Clinical Remission in Moderate Asthma

<table>
<tr><th>S.NO</th><th>Questions</th><th>Response</th></tr>
<tr><td></td><td colspan="2"> 
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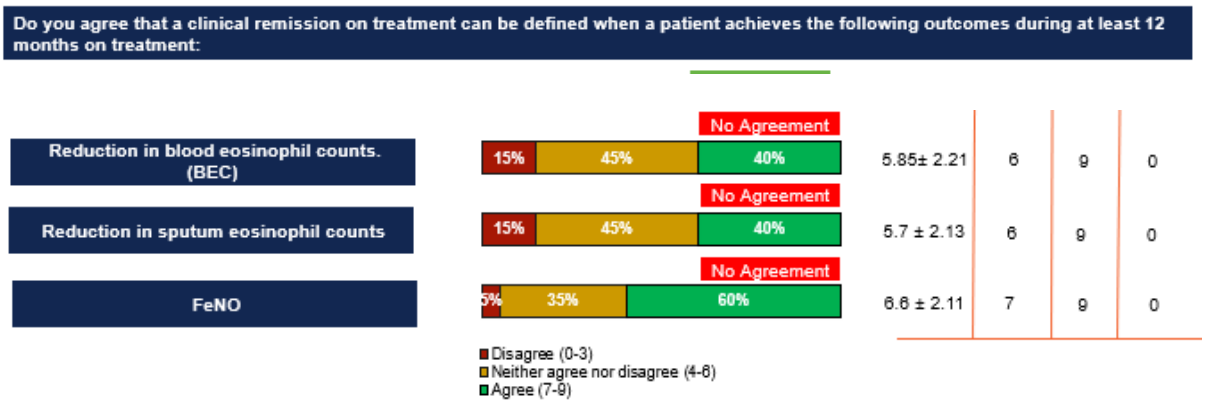
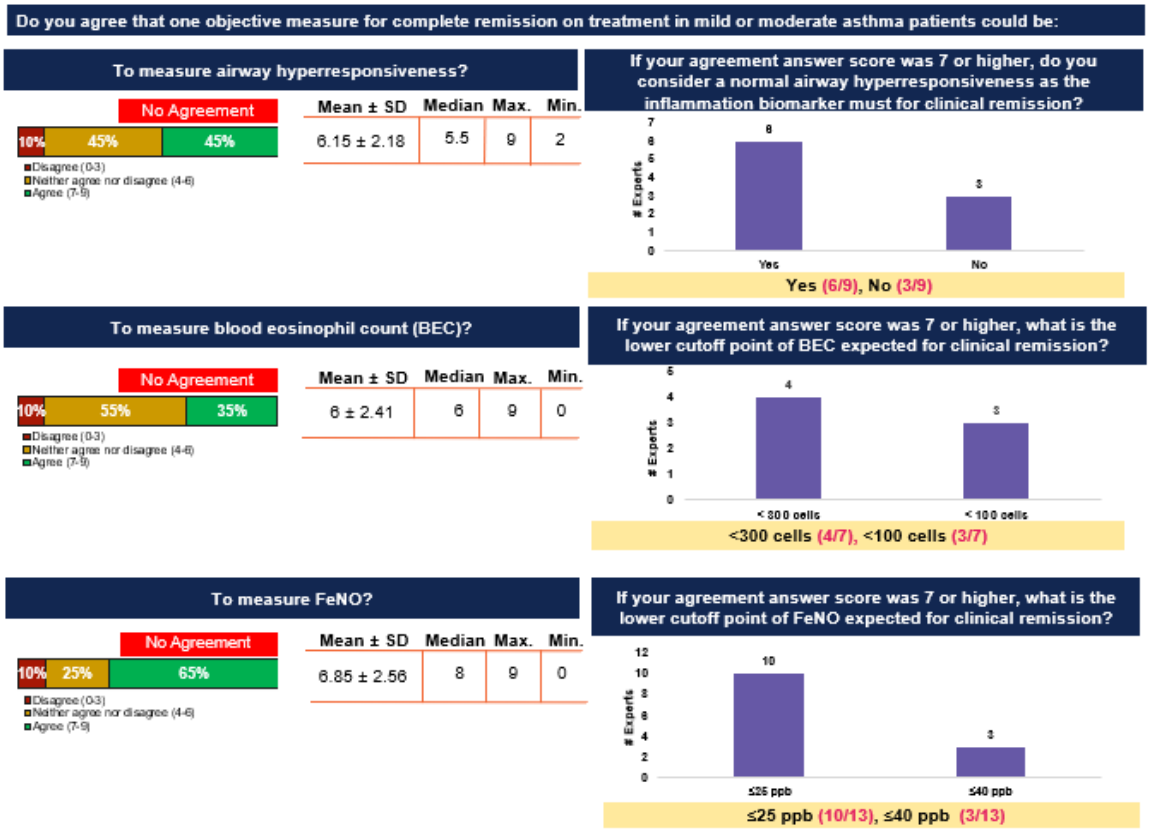
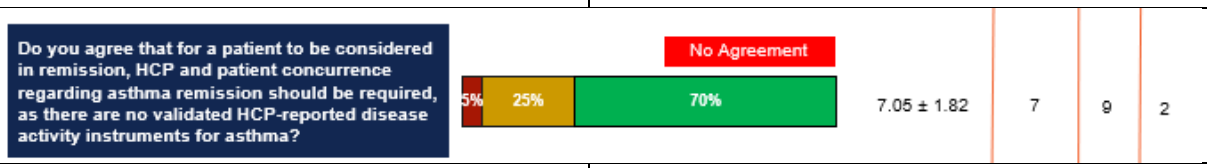
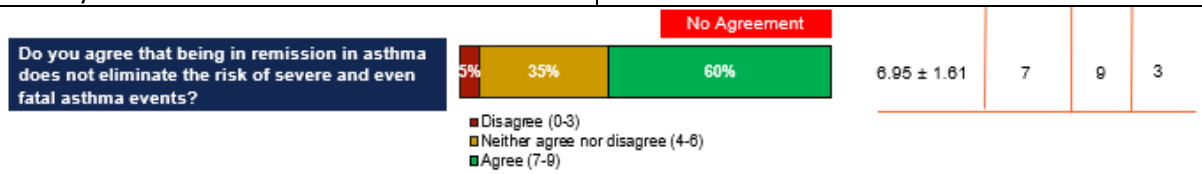
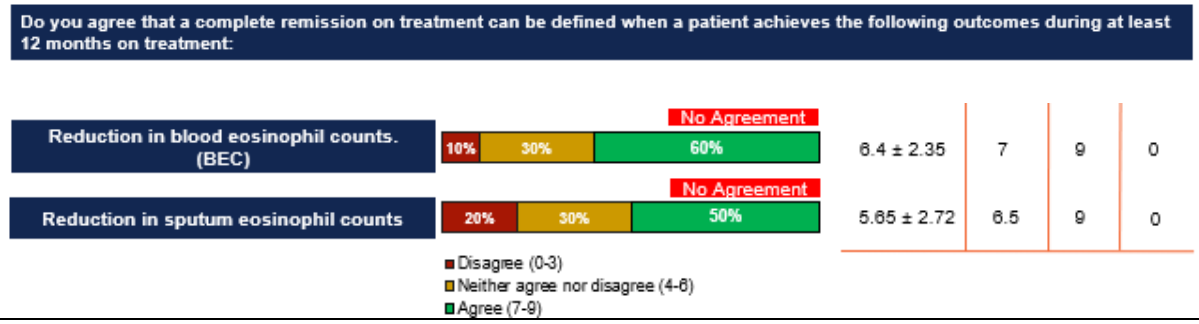
<tr><td>Q8</td><td>Do you agree that stable FEV1 (FEV1 ±10% of patient’s baseline) should be one criterion of clinical remission on treatment in moderate asthma?</td><td>0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐
Strongly Disagree Strongly Agree</td></tr>
<tr><td>Q9</td><td>Do you agree, that if a patient meets all other clinical remission criteria but still used some reliever (less than twice a month), it is still remission?</td><td>0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐
Strongly Disagree Strongly Agree</td></tr>
<tr><td>Q10</td><td>Would you agree that classifying a patient as clinical remission does not need any biomarkers assessment?</td><td>0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐
Strongly Disagree Strongly Agree</td></tr>
<tr><td></td><td colspan="2"> 
</td></tr>
<tr><td rowspan="4">Q11</td><td colspan="2">Do you agree that a clinical remission on treatment can be defined when a patient achieves the following outcomes during at least 12 months on treatment:</td></tr>
<tr><td>a) Reduction in blood eosinophil counts. (BEC)</td><td>0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐
Strongly Disagree Strongly Agree</td></tr>
<tr><td>b) Reduction in sputum eosinophil counts</td><td>0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐
Strongly Disagree Strongly Agree</td></tr>
<tr><td>c) FeNO (if available)</td><td>0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐
Strongly Disagree Strongly Agree</td></tr>
</table>

Q12	While on maintenance ICS containing regimen, clinical remission include lung function being?	
	a) Remains unchanged (stable FEV1 ±10% of patient's baseline)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Normalized (80% or more FEV1p)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	c) Improved by 20% or more from patient's personal baseline	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

Section III: Complete Remission in Moderate Asthma

S.NO	Questions	Response
Q13	Would you agree that complete remission is clinical remission with normal biomarker levels?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q14	Do you agree that in your clinical practice, one objective measure for complete remission on treatment in moderate asthma patients could be:	
	a) To measure airway hyperresponsiveness?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	a1) If your agreement answer score was 7 or higher, do you consider a normal airway hyperresponsiveness as the inflammation biomarker must for complete remission?	◯ Yes ◯ No
	b) To measure blood eosinophil count (BEC)?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b1) If your agreement answer score was 7 or higher, what is the lower cutoff point of BEC expected for complete remission?	**OPEN TEXT**
	c) To measure FeNO (if available)?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**

	c1) If your agreement answer score was 7 or higher, what is the lower cutoff point of FeNO expected for complete remission if available?	**OPEN TEXT**
		
Q15	Do you agree that for a patient to be considered in remission, HCP and patient concurrence regarding asthma remission should be required, as there are no validated HCP-reported disease activity instruments for asthma?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q16	Do you agree that being in complete remission in asthma does not eliminate the risk of severe and even fatal asthma events?	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
		
Q17	Do you agree that a complete remission on treatment can be defined when a patient achieves the following outcomes during at least 12 months on treatment:	
	a) Reduction in blood eosinophil counts. (BEC)	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**
	b) Reduction in sputum eosinophil counts	0 ☐ 1☐ 2☐ 3☐ 4☐ 5☐ 6☐ 7☐ 8☐ 9☐ **Strongly Disagree** **Strongly Agree**