Table S1: Overview of clinical trials on biologics in severe asthma which include pediatric/adolescent patients. The following studies were included: RCTs, post-trial follow-up regarding safety, PK studies in pediatrics, and post-hoc analyses of RCTs focusing on adolescent population included in the trial.

Reference	Treatment	Study name	Study population	Number of patients included <18 yrs	Study design	Duration of treatment	Primary outcome(s)
Milgrom et al. 2001	**Omalizumab**	Not specified	N=334; 6-12 yrs.; Allergic moderate-to-severe allergic asthma	334	RCT	24 wks	ICS dose reduction
Lanier et al. 2009	Omalizumab	NCT00079937	N=576; 6-12 yrs.; uncontrolled moderate-to-severe allergic asthma	576	RCT	52 wks	Exacerbation rate
Kulus et al. 2010	Omalizumab	NCT00079937	N=235; 6-12 yrs.; uncontrolled severe allergic asthma enrolled in NCT00079937	235	Post-hoc analysis	52 wks	Exacerbation rate
Busse et al. 2011	Omalizumab	NCT00377572	N=419; 6-20 yrs.; moderate-to-severe allergic asthma (uncontrolled)	Not specified	RCT	60 wks	Number of days with asthma symptoms
Busse et al. 2020	Omalizumab	008 009 011 SOLAR INNOVATE ALTO ETOPA EXTRA	N=340; 12-17 yrs, moderate-to-severe allergic asthma. Previously enrolled in other omalizumab RCTs.	340	Post-hoc analysis of 8 RCTs	16-53 wks	Lung function, eosinophil counts
Pavord et al. 2012	**Mepolizumab**	DREAM	N=621; 12-74 yrs.; severe eosinophilic asthma	1	RCT	52 wks	Exacerbation rate
Bel et al. 2014	Mepolizumab	SIRIUS	N=135; 16-74 yrs.; severe eosinophilic asthma	2	RCT	24 wks	Reduction of glucocorticoid dose
Ortega et al. 2014	Mepolizumab	MENSA	N=576; 12-82 yrs.; severe eosinophilic asthma	25	RCT	32 wks	Exacerbation rates
Lugogo et al. 2016	Mepolizumab	MENSA/SIRIUS	N=651; ≥12 yrs.; severe eosinophilic asthma (participants previously enrolled in MENSA or SIRIUS)	Not specified (max 27)	Post-trial follow-up	52 wks	Long-term safety and efficacy: number of AEs; exacerbation rates, durability of response and ACQ

Chupp et al. 2017	Mepolizumab	MUSCA	N=556; ≥ 12 yrs.; severe eosinophilic asthma	9	RCT	24 wks	SGRQ
Khatri et al. 2019	Mepolizumab	DREAM	N=347; 12-74 yrs.; severe eosinophilic asthma (participants previously enrolled in DREAM)	Not specified (max 1)	Post-trial follow-up	3.5 yrs average (4.5 yrs. max)	Long-term safety (AE; SAE; exacerbation rates; asthma control (ACQ); FEV1; blood eosinophil count)
Yancey et al. 2019	Mepolizumab	DREAM MENSA SIRIUS MUSCA	N=34; 12-17 yrs.; severe eosinophilic asthma (enrolled in DREAM, MENSA, SIRIUS/MUSCA)	34	Post hoc analysis of 4 RCTs	24 to 52 wks	Exacerbation rate
Gupta et al. 2019	Mepolizumab	NCT02377427	N=36; 6-11 yrs.; severe eosinophilic asthma	36	PK/PD study	12 wks	Pharmacokinetics: mepolizumab clearance Pharmacodynamics: blood eosinophil count
Gupta et al. 2019	Mepolizumab	NCT02377427	N=30; 6-11 yrs.; severe eosinophilic asthma	30 (	Post-trial follow up	52 wks	Long-term safety: Adverse effects; blood eosinophil count
Castro et al., 2018	**Dupilumab**	LIBERTY ASTHMA QUEST	N=1902 ≥12 yrs; uncontrolled asthma.	107	RCT	52 wks	Annual exacerbation rate and the absolute change from baseline to wk 12 in FEV1
Rabe et al., 2018	Dupilumab	LIBERTY ASTHMA VENTURE	N=210, ≥12 yrs; OCS treated asthma.	3	RCT	24 wks	% reduction in the glucocorticoid dose
FitzGerald et al., 2016	Benralizumab	CALIMA	N= 1306, 12-75 yrs, severe uncontrolled eosinophilic asthma	Not specified	RCT	52 wks	Annual exacerbation rate
Bleecker et al, 2016	Benralizumab	SIROCCO	N= 1205, 12-75 yrs, severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists	Not specified	RCT	48 wks	Annual exacerbation rate
Castro et al., 2015	**Reslizumab**	NCT01287039 NCT01285323	N=953, 12-75 yrs, uncontrolled eosinophilic asthma	Not specified	RCT	52 wks	Exacerbations
Bjermer et al., 2016	Reslizumab	NCT01270464	N=315, 12-75 yrs, uncontrolled eosinophilic asthma	15	RCT	16 wks	FEV1
Murphy et al., 2017	Reslizumab	NCT01290887	N=1052, 12-77 yrs, uncontrolled eosinophilic asthma, previously	28	Post-trial follow up	up to 24mth	AE, lung function, asthma control

	enrolled in NCT0128703, NCT01285323 or NCT01270464

ACQ = Asthma Quality of life Questionnaire, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, FEF25%-75% = forced exploratory flow between 25% and 75% of FVC, IgE = immunoglobulin, ICS = inhaled corticosteroids, OCS = oral corticosteroids, (P)AQLQ = (paediatric) asthma quality of life questionnaire, PEF(R) = peak expiratory flow (rate), QOL = quality of life, (S)AEs = (Severe) Adverse Events, SGQR = St George's Respiratory Questionnaire

wk(s) = week(s); mth(s). = month(s); yr(s). = year(s)

Table S2: ongoing European initiatives on biologics use in children and adolescents with asthma/allergies

Name	Description	Link
3TR	*Aims to provide fundamental new insights into the mechanisms of response and non-response to treatment.*	https://3tr-imi.eu/
ANCHORS	*Spanish cohort, long-term responses to omalizumab (over 6 years follow-up), with moderate to severe exacerbations as the primary outcomes*	Nieto et al. (1)
Danish National Study on Severe Asthma	*Identification of patients and cell phenotypes after 1-year course of biologics*	
German Asthma Net	*German Severe Asthma Register, aims to identify and differentiate distinct asthma subtypes (includes pediatric data)*	https://germanasthmanet.de/
PERMEABLE	*Identification of biomarkers to predict responses of pediatric patients to biologics*	https://www.permeable.eu/
SPACE	*ERS Clinical Research Collaboration to collect real-world data on severe pediatric asthma*	Rusconi et al. (3)
TREAT	*Pragmatic trial on comparison of the efficacy of mepolizumab vs omalizumab in reducing asthma attacks in children*	ISRCTN - ISRCTN12109108: Treating severe paediatric asthma: the TREAT trial

(1) Nieto García A, Garriga-Baraut T, Plaza AM, et al. Omalizumab outcomes for up to 6 years in pediatric patients with severe persistent allergic asthma. Authorea. October 29, 2020. DOI: 10.22541/au.160395134.43104166/v1 [*Preprint*]

(2) Lezmi G, Lejeune S, Pin I, et al. Factors associated with asthma severity in children: data from the French COBRAPed Cohort. J Allergy Clin Immunol Pract. 2020 Dec 24;S2213-2198(20)31359-3. doi: 10.1016/j.jaip.2020.12.027.

(3) Rusconi F, Fernandez RM, Pijnenburg MWH, et al. The Severe Paediatric Asthma Collaborative in Europe (SPACE) ERS Clinical Research Collaboration: enhancing participation of children with asthma in therapeutic trials of new biologics and receptor blockers. European Respiratory Journal 2018 52: 1801665; **DOI:** 10.1183/13993003.01665-2018