CLARIO.

Poster #11674

Adopting the 2019 ATS/ERS spirometry guidelines in clinical trials: impact on site and patient burden

Authors P. Lake[1], K. McCarthy[2], D. Patterson[3], M. A. Baumle[4], R. Farienfar[4], J. Ramos[5]
[1]Clario - Monmouth (United Kingdom), [2]Clario - Matthews (USA), [3]Clario - Philadelphia (USA), [4]Clario - Wurzburg (Germany), [5]Clario - Cleveland (USA)

Conflicts of Interest: All the authors are full time employees of Clario.

Rationale

ATS/ERS 2019 spirometry guidelines (GL) introduced a 4th phase that allows objective determination of full inflation. Lake et al has shown that the implementation of the 2019 GL within clinical trials has increased the average number of efforts required to meet acceptability criteria from 3.4 with the 2005 GL studies to 4.8 in a similar study using the 2019 GL (+41%). Initially, 30% of sessions required 8 efforts but this fell to around 6% after 3 months. We sought to explore the role of patient vs technician experience in driving this reduction over time.

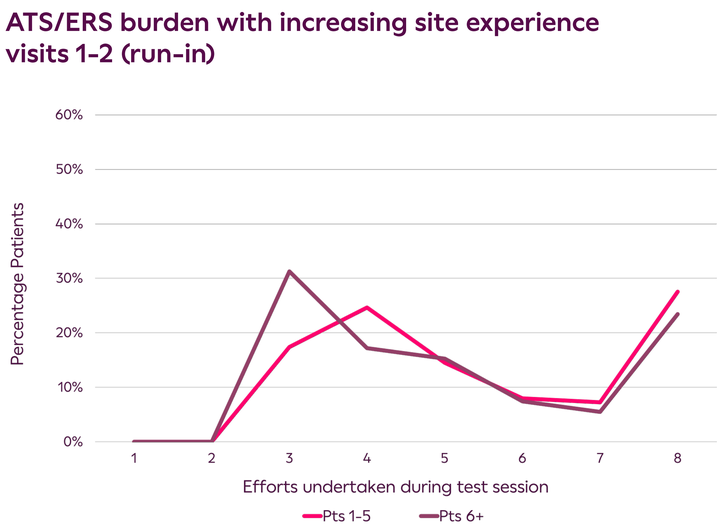
Methods

We analyzed the number of efforts required to meet the recommendations for acceptability and repeatability over time based on a patient's duration within the study (recent 2019 GL test experience) and on the prior number of patients enrolled by a research site in the same study (recent site 2019 GL experience). The average number of efforts required to meet the minimum 2019 GL standards of three technically acceptable and two repeatable efforts was compared for the different groups of interest.

Results

Around 25% of patients who progressed to randomization required the full 8 permitted efforts during the run-in phase of the trial. This dropped to 13.9% for the "Initial" (first 5 patients) and 5.8% for the subsequent (6 plus patients) by the baseline (3rd) study visit. The average number of tests for run-in visits was 5.45 and 5.1 for Initial and Subsequent patients, respectively, representing a 7% reduction in the number of efforts for Subsequent patients. By the study baseline (3rd) test visit, the average number of efforts required reduced to 4.5 and 4.1, respectively, for Initial and Subsequent patients representing a similar site learning effect of around 8%. The reduction in patient burden (average efforts required in run-in relative to baseline) was 18% for the Initial patients and 19.5% for the subsequent patients.

Figure 1. Number of Spirometry Efforts required to meet technical acceptability ATS/ERS 2019 GL



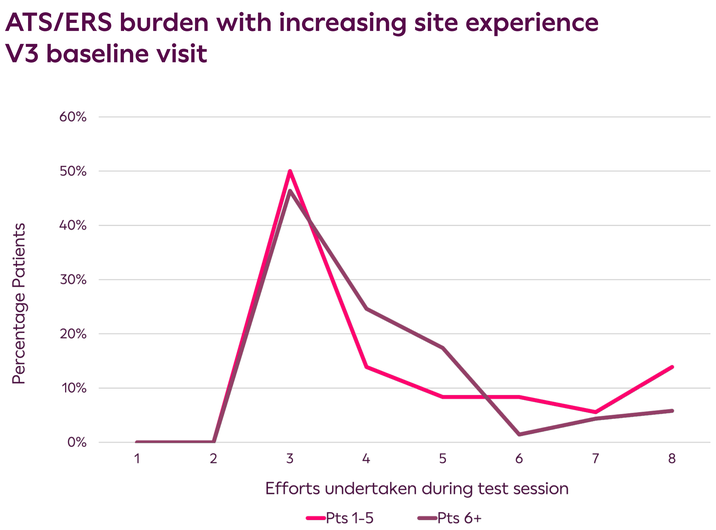


Table 1. Number of Spirometry Efforts required to meet technical acceptability ATS/ERS 2019 GL

	Number of efforts to reach technical acceptability run-in-phase							
Site experience	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Pts 1-5	0.0%	0.0%	17.4%	24.6%	14.5%	8.0%	7.2%	27.5%
Pts 6+	0.0%	0.0%	31.3%	17.2%	15.2%	7.4%	5.5%	23.4%

	Number of efforts to reach technical acceptability baseline visit							
Site experience	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Pts 1-5	0.0%	0.0%	50.0%	13.9%	8.3%	8.3%	5.6%	13.9%
Pts 6+	0.0%	0.0%	46.4%	24.6%	17.4%	1.4%	4.3%	5.8%

References

1. Lake P et al. Adopting the 2019 ATS/ERS spirometry guidelines in clinical trials: impact on site and patient burden. ERS 2022 poster 36816

CLARIO.

Poster #8040

Comparison of the old (2005) and new (2021) ATS/ERS methods for assessing bronchodilator response (BDR) by FEV1 in a clinical trial for asthma

Authors K. McCarthy[1], P. Lake[2], D. Patterson[3], M. A. Baumle[4], R. Farienfar[4], J. Ramos[5]
[1]Clario , Matthews (USA), [2]Clario - Monmouth (UK), [3]Clario – Philadelphia (USA), [4]Clario - Wurzburg (Germany), [5]Clario - Cleveland (USA)

Conflicts of Interest: All the authors are full time employees of Clario.

Rationale

The method for assessing BDR recommended in the 2005 ATS/ERS Interpretive Strategies document[1] set the threshold for significant response as a minimum absolute volume increase of 0.200L that also represented at least a 12% increase from the baseline measurement. The method recommended in the 2021 ATS/ERS Interpretive Strategies document[2] expresses the absolute volume increase as a percentage of the patient's predicted value. Greater than 10% increase by this method is considered a positive BDR. The GLI 2012 reference set was used to calculate predicted FEV1.

Methods

We compared both methods in 621 pairs of pre- and post-bronchodilator measurements meeting ATS/ERS 2019 acceptability and repeatability criteria, collected at baseline in a clinical trial for adult asthma. Patient characteristics are shown in Table 1.

Table 1	Patient characteristics
n	621
Gender, % female	51.5
Race, % white	65.1
Age, years	50.7 (12.9)
Height, cm	166.9 (10.1)
Baseline FVC, PP	66.9 (12.2)
Baseline FEV1, PP	81.9 (13.9)
BaselineFEV1/FVC	0.65 (0.11)

Results

Overall, the newly recommended method for assessing BDR agreed with the old method in 87.3% of assessments. 461 assessments (85.4%) showed agreement on positive BDR by both methods.

79 assessments (14.6%) that were called positive FEV1 BDR by the 2005 method were called negative by the 2021 method.

None of the assessments called negative BDR by the old method were called positive BDR by the new method.

Table 2 shows a comparison of how the two methods of assessing BDR to SABA compared in this study population.

Table 3 shows a comparison of demographic and spirometry results of patients when the methods for assessing FEV1 bronchodilator response agreed or disagreed.

	FEV1 BDR + ATS/ERS 2021	FEV1 BDR - ATS/ERS 2021	Total
FEV1 BDR + ATS/ERS 2005	461	79	540
FEV1 BDR - ATS/ERS 2005	0	81	81
Total	461	160	621

Table 2. Comparison of FEV1 response to SABA assess by the 2005 and 2021 ATS/ERS recommended methods

	+ BDR old + BDR new	+ BDR old - BDR new	p value
n	461	79	n/a
Gender, % female	50.7	52.8	0.69
Race, % white	65.1	87.3	<0.001
Age, years	49.5 (13.3)	52.3 (10.6)	0.07
Height, cm	166.6 (10.1)	169.1 (10.0)	0.04
Baseline FVC, PP	83.2 (13.7)	79.1 (12.5)	0.63
Baseline FEV1, PP	66.1 (11.3)	61.8 (10.1)	0.35
BaselineFEV1/FVC	0.65 (0.11)	0.63 (0.11)	0.15
Predicted FEV1	3.05 (0.74)	3.17 (0.70)	0.18
FEV1 change, L	0.53 (0.26)	0.28 (0.06)	<0.001
FEV1 change, % of baseline	27.0 (12.5)	14.5 (2.3)	<0.001
FEV1 change, % of predicted FEV1	17.2 (6.9)	8.8 (1.0)	<0.001

Table 3. Comparison of patient demographics and pulmonary function when methods for assessing bronchodilator response were concordant or discordant

Inclusion criteria for clinical trials for asthma often include demonstration of a significant FEV1 BDR. Further work is necessary to determine the impact of adopting the 2021 method for assessing BDR in clinical trials. Evaluation of the impact of removing data from patients demonstrating a negative BDR by the new criteria on the treatment response in a completed RCT may provide further insight into this question.

References

1. Pellegrino R, Viegi G, Brusasco V, et al. Interpretive strategies for lung function tests. Eur Respir J 2005; 26: 948–968
2. Stanojevic S, Kaminsky DA, Miller M, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. Eur Respir J 2021

CLARIO.

Poster #10060

Comparison of time to peak flow with rise time from 10 to 90% of peak flow

Authors J. Ramos[1], K. McCarthy[2], P. Lake[3], D. Patterson[4], M. A. Baumle[5], R. Farienfar[5]
[1]Clario - Cleveland (USA), [2]Clario – Matthews (USA), [3]Clario - Monmouth (UK) [4]Clario – Philadelphia (USA), [5]Clario - Wurzburg (Germany)

Conflicts of Interest: All the authors are full time employees of Clario.

Rationale

An explosive start of forced exhalation has always been a fundamental requirement for a good quality FEV1. In patients that have diminished elastic recoil this is necessary to avoid spuriously elevated FEV1s. Time to peak flow (TPEF) ≤ 0.120 s has been widely adopted as an objective criterion defining an explosive start in clinical trials but lacks empirical support. The 2019 ATS/ERS spirometry standards suggest using rise time from 10-90% of the peak expiratory flow rate (RT10-90%) ≤ 0.150 s as a possible means for evaluating an explosive start of test[1,2].

Methods

TPEF and RT10-90% collected from 15,123 acceptable efforts in 4,960 measurements made by 1,190 patients in a clinical trial for chronic obstructive lung disease were compared.

Results

The demographic and pulmonary function characteristics of the patients in this study are shown in Table 1.

14,492 of these efforts (95.8%) showed both RT10-90% ≤ 0.150 s and TPEF ≤ 0.120 s. 631 efforts (4.2%) showed RT10-90% ≤ 0.150 s but also showed TPEF > 0.120 s. The distribution of RT10-90% in the acceptable efforts as well as the number of efforts meeting RT10-90% ≤ 0.150s but show TPEF > 0.120 s is shown in Figure 1.

Inspection of the efforts that showed RT10-90% ≤ 0.150 s and TPEF > 0.120 s showed that most of these efforts showed no sharp peak on the expiratory flow-volume curve.

Patient characteristics	Mean (SD)
# patients	1,190
Gender, % male	61.7
Height (cm)	168.7 (10.2)
Ethnicity, % white	84.9%
FVC, % predicted	69.9 (22.7)
FEV1, % predicted	41.3 (20.8)
FEV1/FVC, %	0.46 (0.16)
PEF, LPS	1.40 (0.07)
RT 10-90% PEFR, s	0.115 (0.187)
Time to peak flow, s	0.074 (0.079)

Table 1. The demographic and pulmonary function characteristics of the patients

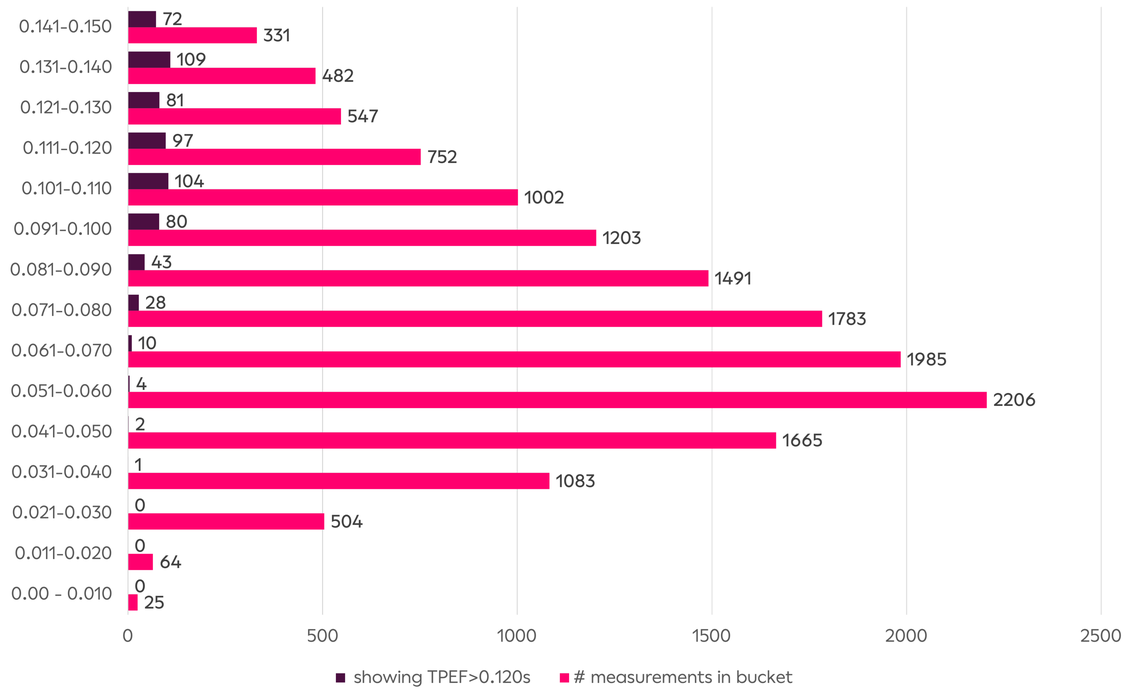


Figure 1. Distribution of rise time 10-90% of PEFR in 15,123 acceptable forced spirometry efforts

Conclusions

This comparison showed the new recommendation for an objective standard for an explosive start of test (RT10-90% ≤ 0.150 s) agreed with a previously used standard (TPEF ≤ 0.120 s) in 95.8% of the reviewed acceptable measurements. A small fraction (4.2%) of measurements meeting the RT10-90% ≤ 0.150 s standard showed TPEF > 0.120 s.

Visual inspection of the expiratory flow-volume curve, particularly during the collection of the measurement, still provides valuable guidance to the operator attempting to obtain maximum patient effort.

Failing to meet the TPEF ≤ 0.120 s standard while meeting the RT10-90% ≤ 0.150 s standard may serve as a useful objective means of identifying submaximal expiratory efforts.

References

1. Graham BL, Steenbruggen I, Miller MR, et al. ATS/ERS Task Force. Standardization of spirometry 2019 update. Am J Respir Crit Care Med. 2019 Oct 15; 200®: e70–e88. Published online 2019 Oct 15. doi: 10.1164/rccm.201908-1590ST.
2. Miller MR, Pedersen OF, Quanjer PH. The rise and dwell time for peak expiratory flow in patients with and without airflow limitation. Am J Respir Crit Care Med 1998;158:23–27