Mesa 1

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Correlation Between Symptoms Pattern And Future Exacerbations: a Post-Hoc Analysis From The Spark Study

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Introduction:

Exacerbations of chronic obstructive pulmonary disease (COPD) are associated with accelerated deterioration of lung function and worsening prognosis but their underlying mechanisms remain poorly understood.

We conducted a post-hoc analysts of patient's e-diary twice daily reported symptoms in the SPARK study to better understand the nature and pattern of symptoms during exacerbations of varying severity.

Methods:

SPARK was conducted in 2224 COPD patients aged 240 years with severe/very severe COPD and ≥1 COPD exacerbation in the past year. Patients were randomized (1:1:1) to once-daily QVA149 110/50 µg (n=741), glycopyrronium 50 µg (n=741) or open-label tiotropium 18 µg (n=742) for 64 weeks.

Patterns of symptoms during the first and second exacerbations of varying severity (mild, moderate or severe) were compared by plotting total symptom scores over time for both unweighted (raw) and weighted scores (increment of 5 added to major symptoms).

Median area under the curve (AUC) values were calculated from each severity group profile and between-group differences were analyzed. Durations of exacerbations were also analyzed. P-values were determined using a Wilcoxon-Mann-Whitney test with adjustment for multiple comparisons.

Results:

Overall patterns of symptom increase from baseline were similar in exacerbations of varying severity, whether during the first (figure) or second exacerbation.

| Median (range) AUCs for total symptom scores	Mild	Moderate	Severe
First exacerbation	68 (1-6392)	129 (0-6441)	159 (31-7197)
Second exacerbation	58 (1-2730)	122 (0-4939)	146 (13-1399)

For both first and second exacerbations, significant differences were observed between the AUC or mild vs moderate or mild vs severe exacerbations (all p<0.0001) but not between severe vs moderate exacerbations (p=0.26, p=0.49).

Results:

Differences were primarily driven by the **longer duration or severe/moderate exacerbations** compared with mild exacerbations at both the first and second exacerbation (median durations 13 and 11 vs. 2 days. 17 and 11 vs.2 days; all p<0.0001).

Severe exacerbations were longer than moderate exacerbations at the second exacerbation (p=0.0002). No major differences In AUC were observed between first and second exacerbations of similar severity. Similar results were observed in the analysis of weighted symptom data.
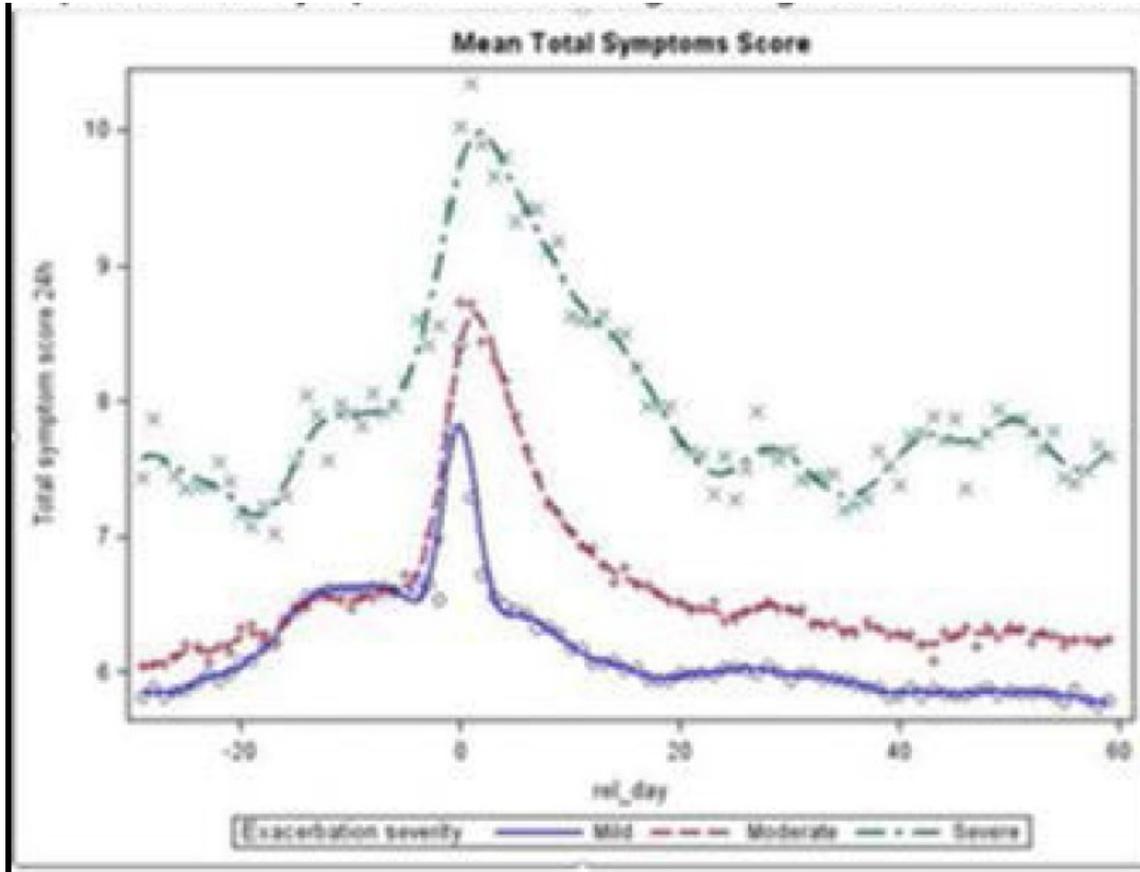
CONCLUSIONS

While overall symptom patterns were similar during exacerbations of varying severity, symptom burden is accentuated in the severe exacerbation and the time to return to baseline is higher in moderate to severe exacerbations. These results emphasize the importance of symptom monitoring during exacerbations to improve exacerbation management.