

Figure S1 Swimmer plot of patients with acute exacerbation. Each time course of 4 patients were shown. Horizontal axis indicates days from start of trial treatment. y.o, year old; M, male; F, female; Ad, adenocarcinoma; Sq, squamous cell carcinoma; PR, partial response; SD, stable disease; PD, progressive disease.

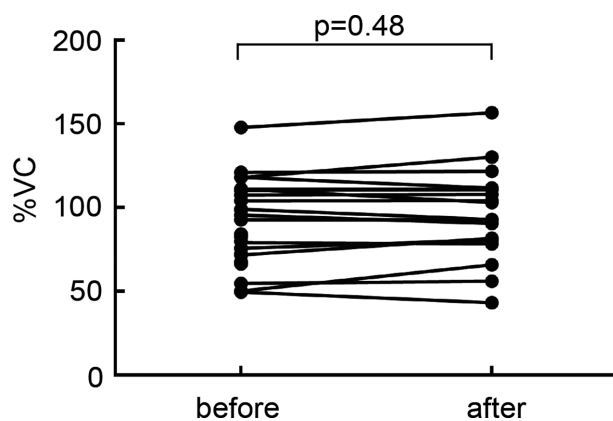


Figure S2 The comparison of predicted value of vital capacity between before and after the trial treatment.

Table S1 Exploratory cytokine analysis

	All patients	Exacerbation-experienced patients (n=4)	No exacerbation (n=23)	P value
IL-8 (pg/mL)	39.3±74.4	20.0±12.6	41.9±78.9	0.93
MMP-7 (pg/mL)	9392.1±11224.1	17200.0±26767.8	8034.3±6178.1	0.73
VEGF (pg/mL)	78.6±107.5	109.1±92.1	73.3±111.0	0.13
CCL18 (pg/mL)	51464.4±20769.8	44610.0±10870.5	52656.5±21992.7	0.68
TGFβ1 (pg/mL)	15547.5±12478.5	20745.4±12589.1	14602.5±12516.1	0.24
YKL40 (ng/mL)	224.6±254.8	161.0±116.3	234.2±270.3	1.0

IL-8: Interleukin 8, MMP-7: Matrix Metalloproteinase-7, VEGF: vascular endothelial growth factor, CCL18: Chemokine (C-C motif) ligand 18, TGF-β: transforming growth factor β, YKL-40: human Chitinase-3 like 1 protein. Data are expressed as mean ± SD.

Table S2 Subsequent anti-tumor therapy following trial treatment

	n
Second line	17
S-1	15
DTX+RAM	1
VNR	1
Third line	7
DTX	1
PEM	1
atezolizumab	3
nivolumab	2

DTX: docetaxel, RAM: ramucirumab, VNR: vinorelbine, PEM: pemetrexed.