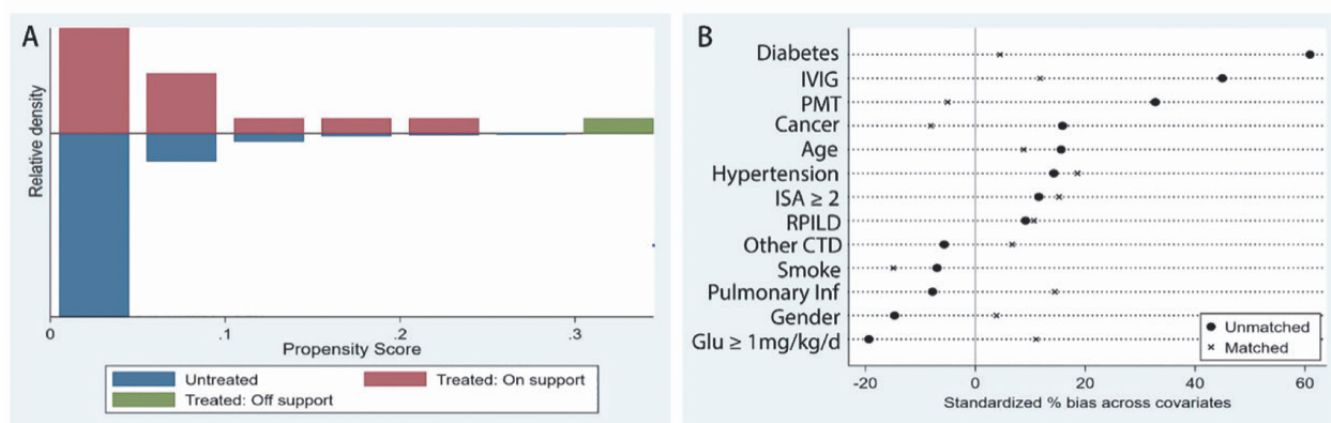


Supplementary Fig. S3. The Kaplan-Meier curves between patients receiving and not receiving nintedanib therapy.

Supplementary Fig. S1. Flow chart of the assembly of a matched cohort of patients with anti-MDA5+ DM, according to treated or not treated with nintedanib.



Supplementary Fig. S2. Results of propensity score-matched, by treated or not treated with nintedanib. (A) Histogram of the relative density of propensity scores for the cohort before matching. (B) Distribution of standardized bias across covariates before and after matching.

Supplementary Table S1. Comparison of baseline characteristics between anti-MDA5+ DM patients treated and not treated with nintedanib.

| Variable | Entire cohort | | | Propensity score-matched cohort | | |
|--|--------------------|---------------------|----------------|---------------------------------|--------------------|----------------|
| | Nintedanib+ (n=15) | Nintedanib- (n=379) | <i>p</i> value | Nintedanib+ (n=14) | Nintedanib- (n=56) | <i>p</i> value |
| Age, years | 48 (44, 60) | 50 (41, 58) | 0.689 | 49.5 (45.5, 60.5) | 51.5 (43.5, 57.8) | 0.774 |
| Female | 11 (73.3) | 252 (66.5) | 0.781 | 10 (71.4) | 41 (73.2) | 1.000 |
| History of smoking | 2 (13.3) | 60 (15.8) | 1.000 | 2 (14.3) | 11 (19.6) | 1.000 |
| ILD | 15 (100.0) | 359 (94.7) | 1.000 | 14 (100.0) | 54 (96.4) | 1.000 |
| RPILD | 10 (66.7) | 210 (55.4) | 0.389 | 9 (64.3) | 33 (58.9) | 0.714 |
| Pulmonary infection | 9 (60.0) | 242 (63.9) | 0.761 | 8 (57.1) | 28 (50.0) | 0.632 |
| Past medical history | | | | | | |
| Hypertension | 3 (20.0) | 55 (14.5) | 0.471 | 3 (21.4) | 8 (14.3) | 0.681 |
| Diabetes mellitus | 6 (40.0) | 34 (9.0) | 0.002 | 5 (35.7) | 15 (26.8) | 0.522 |
| Cancer | 1 (6.7) | 12 (3.2) | 0.401 | 0 (0.0) | 1 (1.8) | 1.000 |
| Other CTD | 1 (6.7) | 31 (8.2) | 1.000 | 1 (7.1) | 3 (5.4) | 1.000 |
| Treatment before admission | | | | | | |
| PMT | 3 (20.0) | 32 (8.4) | 0.139 | 2 (14.3) | 9 (16.1) | 1.000 |
| Prednisone use ≥ 1 mg/kg daily or equivalent GCs | 10 (66.7) | 263 (69.4) | 0.782 | 9 (64.3) | 31 (55.4) | 0.546 |
| CNI | 11 (73.3) | 205 (54.1) | 0.142 | 10 (71.4) | 26 (46.4) | 0.094 |
| CYC | 0 (0.0) | 82 (21.6) | 0.048 | 0 (0.0) | 12 (21.4) | 0.107 |
| MMF | 0 (0.0) | 25 (6.6) | 0.612 | 0 (0.0) | 5 (8.9) | 1.000 |
| JAKi | 3 (20.0) | 25 (6.6) | 0.082 | 3 (21.4) | 6 (10.7) | 0.370 |
| Biological agents | 0 (0.0) | 15 (4.0) | 1.000 | 0 (0.0) | 3 (5.4) | 1.000 |
| Immunosuppressant ≥ 2 # | 0 (0.0) | 14 (3.7) | 1.000 | 0 (0.0) | 5 (8.9) | 0.575 |
| IVIG | 10 (66.7) | 74 (19.5) | <0.001 | 9 (64.3) | 24 (42.9) | 0.151 |

Values are median (interquartile range) or number (%) unless indicated otherwise.

#Referring to the concurrent use of two or more immunosuppressants, including cyclophosphamide, calcineurin inhibitors, mycophenolate mofetil, Janus kinase inhibitors and biologic agents.

CNI: calcineurin inhibitors; CTD: connective tissue disease; CYC: cyclophosphamide; GCs: glucocorticoids; IVIG: intravenous immunoglobulin; JAKi: Janus kinase inhibitors; MMF: mycophenolate mofetil; PMT: pulse methylprednisolone therapy; RPILD: rapidly progressive interstitial lung disease.

Supplementary Table S2. Baseline clinical characteristics comparison in anti-MDA5+ DM patients using nintedanib: RPILD vs. non-RPILD.

| | RPILD (n=9) | Non-RPILD (n=5) | <i>p</i> value |
|--|-------------------|-------------------|----------------|
| Age, years | 48.0 (45.0, 59.5) | 51.0 (42.5, 67.5) | 0.364 |
| Female | 6 (66.6) | 4 (80.0) | 1.000 |
| Disease duration, month | 17.0 (7.0, 29.5) | 9.0 (5.5, 20.0) | 0.606 |
| Treatment | | | |
| PMT | 2 (22.2) | 0 (0.0) | 0.505 |
| Prednisone use ≥ 1 mg/kg daily or equivalent GCs | 6 (66.7) | 3 (60.0) | 1.000 |
| CNI | 7 (77.8) | 3 (60.0) | 0.580 |
| CYC | 0 (0.0) | 0 (0.0) | - |
| MMF | 0 (0.0) | 0 (0.0) | - |
| JAKi | 1 (11.1) | 2 (40.0) | 0.505 |
| Biological agents | 0 (0.0) | 0 (0.0) | - |
| Immunosuppressant ≥ 2 # | 0 (0.0) | 0 (0.0) | - |
| IVIG | 7 (77.8) | 2 (40.0) | 0.266 |

Values are median (interquartile range) or number (%) unless indicated otherwise.

RPILD: rapidly progressive interstitial lung disease; CNI: calcineurin inhibitors; CYC: cyclophosphamide; GCs: glucocorticoids; IVIG: intravenous immunoglobulin; JAKi: Janus kinase inhibitors; MMF: mycophenolate mofetil; PMT: pulse methylprednisolone therapy.

Supplementary Table S3. Baseline clinical characteristics comparison in anti-MDA5+ DM patients using nintedanib: refractory group vs. non-refractory group.

| | Refractory (n=5) | Non-refractory (n=9) | <i>p</i> value |
|--|-------------------|----------------------|----------------|
| Age, years | 48.0 (38.5, 57.0) | 51.0 (45.0, 64.5) | 0.606 |
| Female | 3 (60.0) | 7 (77.8) | 0.580 |
| Disease duration, month | 17.0 (7.5, 29.5) | 9.0 (6.0, 21.0) | 0.606 |
| Treatment | | | |
| PMT | 2 (22.2) | 0 (0.0) | 0.505 |
| Prednisone use ≥ 1 mg/kg daily or equivalent GCs | 4 (80.0) | 5 (55.6) | 0.580 |
| CNI | 5 (100.0) | 5 (55.6) | 0.221 |
| CYC | 0 (0.0) | 0 (0.0) | - |
| MMF | 0 (0.0) | 0 (0.0) | - |
| JAKi | 0 (0.0) | 3 (33.3) | 0.258 |
| Biological agents | 0 (0.0) | 0 (0.0) | - |
| Immunosuppressant ≥ 2 # | 0 (0.0) | 0 (0.0) | - |
| IVIG | 5 (100.0) | 4 (44.4) | 0.086 |

Values are median (interquartile range) or number (%) unless indicated otherwise.

RPILD: rapidly progressive interstitial lung disease; CNI: calcineurin inhibitors; CYC: cyclophosphamide; GCs: glucocorticoids; IVIG: intravenous immunoglobulin; JAKi: Janus kinase inhibitors; MMF: mycophenolate mofetil; PMT: pulse methylprednisolone therapy.