**Supplementary Figure 1.** Comparison of patients' overall survival according to the extent of ILD.(a. ILD extent≥20% vs.＜20%: p=0.182; b. ILD extent≥25% vs.＜25%: p=0.090).

 

**Supplementary Table 1. Details of infections requiring hospitalization during follow-up.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | AAV-ILD | UIP | NSIP | OP | Unclassified ILD | p-value  |
| Infectious patients, no. (%) | 110(53.9) | 89(58.6) | 14(35.9) | 2(66.7) | 5(50.0) | 0.082 |
| Infectious episodes, no. (%) | 168 | 134 | 24 | 3 | 7 | - |
| First in-patient infection time, median (IQR)(weeks) | 3(2-17) | 3(2-18) | 4(2-16) | 5.5(4.3-6.8) | 3(2-3) | 0.326 |
| **Infection pathogens, no. (%)** |
| Bacteria | 162/168(96.4) | 129/134(96.3) | 23/24(95.8) | 3/3(100.0) | 7/7(100.0) | 0.939 |
| Fungus | 28/168(16.7) | 21/134(15.1) | 4/24(16.7) | 1/3(33.3) | 2/7(28.6) | 0.752 |
| Pneumocystis jirovecii | 7/168(4.2) | 5/134(3.7) | 1/24(4.2) | 1/3(33.3) | 0 | 0.338 |
|  Aspergillus | 7/168(4.2) | 5/134(3.7) | 1/24(4.2) | 0 | 1/7(14.3) | 0.695 |
|  Candida | 16/168(9.5) | 13/134(9.7) | 2/24(8.3) | 0 | 1/7(14.3) | 0.847 |
| Virus | 12/168(7.1) | 9/134(6.7) | 2/24(8.3) | 1/3(33.3) | 0 | 0.411 |
|  CMV | 6/168(3.6) | 4/134(3.0) | 1/24(4.2) | 1/3(33.3) | 0 | 0.300 |
|  EBV | 4/168(2.4) | 2/134(1.5) | 1/24(4.2) | 1/3(33.3) | 0 | 0.181 |
| Influenza virus | 2/168(1.2) | 2/134(1.5) | 0 | 0 | 0 | 0.823 |
| **Locations of infection, no. (%)** |
| Pulmonary | 157/168(93.5) | 124/134(92.5) | 23/24(95.8) | 3/3(100.0) | 7/7(100.0) | 0.619 |
| Genitourinary | 12/168(7.1) | 12/134(9.0) | 0 | 0 | 0 | 0.130 |
| Gastrointestinal | 2/168(1.2) | 2/134(1.5) | 0 | 0 | 0 | 0.823 |
| Catheter-associated | 4/168(2.4) | 4/134(3.0) | 0 | 0 | 0 | 0.608 |
| Sepsis | 6/168(3.6) | 5/134(3.7) | 1/24(4.2) | 0 | 0 | 0.859 |

AAV: ANCA-associated vasculitis; CMV: cytomegalovirus; EBV: Epstein-Barr virus; ILD: interstitial lung disease; IQR: interquartile range; NSIP: non-specific interstitial pneumonia; OP: organizing pneumonia; UIP: usual interstitial pneumonia.

**Supplementary Table 2. Characteristics of relapses during follow-up.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | AAV-ILD | UIP | NSIP | OP | Unclassified ILD | p-value |
| Relapse cases, no. (%) | 54 (26.5) | 42(27.6) | 8(20.5) | 1(33.3) | 3(30.0) | 0.813 |
| Relapse events, no. (%) | 85 | 69 | 11 | 1 | 4 | - |
| First relapsing time, median (IQR) (months) | 12(7-27)  | 12(5.5-32) | 12(9.5-27) | 7 | 18(17-51) | 0.421 |
| **Organ involvement at relapse, no. (%)** |
| Pulmonary  | 42/85(49.4) | 36/69(52.2) | 4/11(36.4) | 1/1(100.0) | 1/4(25.0) | 0.337 |
| Renal  | 47/85(55.3) | 36/69(52.2) | 6/11(54.5) | 1/1(100.0) | 4/4(100.0) | 0.102 |
| General 1 | 14/85(16.5) | 13/69(18.8) | 1/11(9.1) | 0 | 0 | 0.462 |
| Ear, nose, and throat | 2/85(2.4) | 1/69(1.4) b | 0 | 1/1(100.0) | 0 | 0.037 |
| Central nervous system  | 2/85(2.4) | 2/69(2.9) | 0 | 0 | 0 | 1.000 |
| Peripheral nervous system  | 4/85(4.7) | 3/69(4.3) | 1/11(9.1) | 0 | 0 | 0.831 |
| Gastrointestinal | 2/85(2.4) | 1/69(1.4) | 1/11(9.1) | 0 | 0 | 0.616 |
| Eye | 6/85(7.1) | 5/69(7.2) b | 0 | 1/1(100.0) | 0 | 0.058 |

AAV: ANCA-associated vasculitis; ILD: interstitial lung disease; IQR: interquartile range; NSIP: non-specific interstitial pneumonia; OP: organizing pneumonia; UIP: usual interstitial pneumonia.

1 General included fever or weight loss (≥2 kg).

b UIP vs OP.

**Supplementary Figure 2.** Relapse-free survival of patients with AAV-ILD (a) and compared with the types of ILD (b; log rank p=0.811). UIP (blue line), NSIP (green line), OP and unclassified ILD (yellow line). AAV: ANCA-associated vasculitis; ILD: interstitial lung disease; NSIP: non-specific interstitial pneumonia; OP: organizing pneumonia; UIP: usual interstitial pneumonia.

 

**Supplementary Table 3. Univariate analysis for predictors of mortality in AAV-related ILD.**

|  |
| --- |
| **FVC% pred. at baseline** |
| FVC% pred. <50% (vs. ≥50%-<90%) | 1.508(0.166-13.662) | 0.715 |
| FVC% pred. <50% (vs. ≥90%) | 1.065(0.321-3.540) | 0.918 |
| FVC% pred. ≥50%-<90% (vs. ≥90%) | 1.051(0.316-3.491) | 0.936 |
| FVC% pred. <80% (vs. ≥80%) | 1.172(0.393-3.494) | 0.776 |
| FVC% pred. <50% (vs. ≥50%-<80%) | 1.533(0.182-12.926) | 0.694 |
| FVC% pred. <50% (vs. ≥80%) | 1.128(0.363-3.503) | 0.836 |
| FVC% pred. ≥50%-<80% (vs. ≥80%) | 1.118(0.360-3.474) | 0.847 |

AAV: ANCA-associated vasculitis; FVC: forced vital capacity; ILD: interstitial lung disease; % pred.: % predicted.

**Supplementary Table 4. Multivariate analyses for predictors of mortality in AAV-related ILD.**

|  |  |  |
| --- | --- | --- |
|  | Model 5 | Model 6 |
| Age, years 1 | 1.036(0.994-1.080); p=0.092 | 1.035(0.993-1.079); p=0.106 |
| Male | 0.939(0.491-1.797); p=0.850 | 0.896(0.475-1.693); p=0.736 |
| Ear, nose and throat | 0.648(0.293-1.435); p=0.285 | 0.673(0.305-1.486); p=0.327 |
| Respiratory failure 2 | 4.770 (2.205-10.317); p<0.001 | 5.036(2.309-10.985); p<0.001 |
| Infection requiring hospitalization 2 | 1.439(0.639-3.240); p=0.379 | 1.368(0.607-3.082); p=0.450 |
| ILD extent≥30% (vs.＜30%) | 1.425(0.679-2.993); p=0.349 |  |
| Extent of ILD disease  |  | 1.596(0.187-13.660); p=0.669 |

Model 5 and model 6 incorporated age, sex, ENT involvement, respiratory failure, infection, and ILD extent. Data are presented as hazard ratio (95% CI) and p-value. AAV: ANCA-associated vasculitis; ILD: interstitial lung disease.

1 per 10 years increase.

2 both at baseline and during follow-up.

**Supplementary Table 5. Univariate and Multivariate analyses for predictors of mortality in AAV-UIP.**

|  |  |  |
| --- | --- | --- |
|  | Univariate analysis | Multivariate analysis |
|  | Hazard ratio (CI 95%) | p-value | Hazard ratio (CI 95%) | p-value |
| Age, years 1 | 1.412(0.897-2.221) | 0.136 |  |  |
| Male | 0.814(0.414-1.603) | 0.552 |  |  |
| Ever-smoker | 1.135(0.559-2.304) | 0.726 |  |  |
| MPA | 1.299(0.176-9.606) | 0.798 |  |  |
| GPA | 0.931(0.126-6.888) | 0.944 |  |  |
| MPO-ANCA  | 1.694(0.383-7.489) | 0.487 |  |  |
| PR3-ANCA  | 0.472(0.111-2.002) | 0.309 |  |  |
| Alveolar hemorrhage | 1.793(0.537-5.981) | 0.342 |  |  |
| Fever | 1.590(0.802-3.154) | 0.185 |  |  |
| Weight loss (≥2 kg) | 0.860(0.435-1.699) | 0.664 |  |  |
| Cutaneous | 1.149(0.272-4.860) | 0.850 |  |  |
| Ear, nose and throat | 0.594(0.268-1.319) | 0.201 |  |  |
| Eye | 1.013(0.137-7.482) | 0.990 |  |  |
| Peripheral nervous system | 1.411(0.625-3.183) | 0.407 |  |  |
| Renal  | 1.212(0.530-2.771) | 0.649 |  |  |
| Renal insufficiency  | 0.749(0.322-1.740) | 0.501 |  |  |
| BVAS  | 0.998(0.951-1.046) | 0.921 |  |  |
| FFS=1(ref.=0) | 0.920(0.433-1.952) | 0.827 |  |  |
| FFS≥2(ref.=0) | 0.704(0.255-1.948) | 0.500 |  |  |
| Serum creatinine, μmol/L1 | 0.999(0.986-1.012) | 0.827 |  |  |
| CRP, mg/L1 | 1.067(1.001-1.138) | 0.047 |  |  |
| **CT results**  |
| Extent of ILD  | 5.397(0.745-39.091) | 0.095 |  |  |
| ILD extent≥20% (vs.＜20%) | 1.352(0.655-2.787) | 0.414 |  |  |
| ILD extent≥25% (vs.＜25%) | 1.413(0.671-2.975) | 0.363 |  |  |
| ILD extent≥30% (vs.＜30%) | 1.933(0.900-4.155) | 0.091 |  |  |
| **BAL results**  |
| Lymphocyte percentage 1 | 0.612(0.246-1.520) | 0.290 |  |  |
| Neutrophil percentage 1 | 1.170(0.991-1.381) | 0.064 | 1.286(1.034-1.600) | 0.024 |
| Hemosiderin-laden macrophage percentage 1 | 0.989(0.754-1.298) | 0.938 |  |  |
| **PFT results** |
| Restrictive syndrome | 1.044(0.331-3.297) | 0.941 |  |  |
| FVC% pred. at baseline 2 | 0.985(0.726-1.337) | 0.924 |  |  |
| TLC% pred. at baseline 2 | 0.912(0.663-1.256) | 0.574 |  |  |
| DLCO % pred. at baseline 2 | 1.046(0.660-1.658) | 0.849 |  |  |
| Respiratory failure 3 | 4.750(2.343-9.632) | <0.001 | 6.342(1.370-29.368) | 0.018 |
| Relapse | 1.412(0.678-2.940) | 0.357 |  |  |
| ILD acute exacerbation | 1.730(0.774-3.868) | 0.182 |  |  |
| Infection requiring hospitalization 3 | 2.325(1.080-5.002) | 0.031 |  |  |

AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasm antibodies; BAL: bronchoalveolar lavage; BVAS: Birmingham Vasculitis Activity Scores; CRP: c-reactive protein; DLCO: diffusing capacity for carbon monoxide; FFS: five-factor score; FVC: forced vital capacity; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; MPO: myeloperoxidase; PR3: proteinase-3; TLC: total lung capacity; % pred.: % predicted; UIP: usual interstitial pneumonia.

1 Hazard ratio reported per 10 U increase.

2 Hazard ratio reported per 10 U decrease.

3 both at baseline and during follow-up.