Poster

Acute exacerbations in patients with progressive fibrosing interstitial lung diseases: data from the INBUILD trial

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Acute exacerbations in patients with progressive fibrosing interstitial lung diseases: data from the INBUILD trial

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INTRODUCTION

- Acute deteriorations of respiratory function known as acute exacerbations are a feature of idiopathic pulmonary fibrosis (IPF) and other progressive fibrosing ILDs and are associated with high mortality.[1-3]

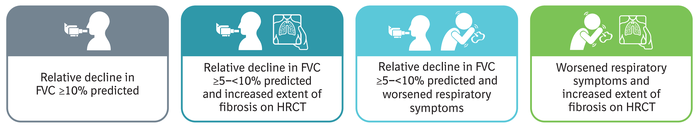
AIM

- To investigate the risk and impact of acute exacerbations in patients with progressive fibrosing ILDs other than IPF.

METHODS

Trial design[4]

- Patients in the INBUILD trial had diffuse fibrosing ILD (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted. Patients with IPF were excluded.
- Patients met ≥1 of these criteria for ILD progression at any time within the prior 24 months, despite management deemed appropriate in clinical practice:



- Patients were randomized to receive nintedanib or placebo.
- An acute exacerbation was defined as an acute, clinically significant respiratory deterioration characterized by evidence of new, widespread alveolar abnormality meeting all these criteria:
  - Acute worsening or development of dyspnea (typically <1 month duration)
  - Computed tomography with new bilateral ground-glass opacity or consolidation superimposed on a background pattern consistent with fibrosing ILD
  - Deterioration not fully explained by cardiac failure or fluid overload.
- Acute exacerbations were not adjudicated.

Analyses

- Risk factors for time to first acute exacerbation were identified by consecutively adding candidates into a Cox proportional hazard model, selecting the covariate with the smallest p-value at each step. Selection stopped when no further covariate achieved p<0.2.
- The time from first acute exacerbation to hospitalization and the time from first acute exacerbation to death were analysed using pooled data from both treatment groups (as there were only 58 events overall).

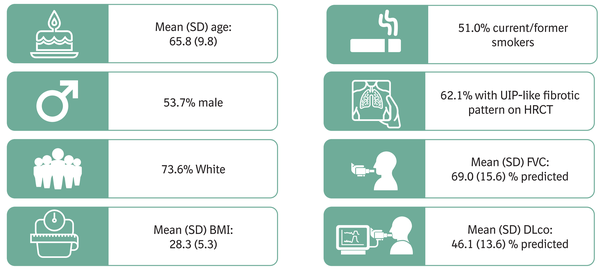
CONCLUSIONS

These analyses of acute exacerbations of progressive fibrosing ILDs other than IPF in the INBUILD trial suggested that:

- the risk of acute exacerbation was higher in patients who were older, had a lower DLco % predicted, or received placebo rather than nintedanib
- acute exacerbations were associated with a high risk of hospitalization and death in the next 180 days
- acute exacerbations of progressive fibrosing ILDs other than IPF may have a similar impact on outcomes as acute exacerbations of IPF

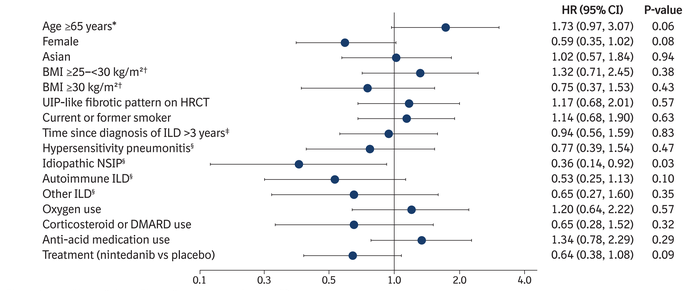
RESULTS

Baseline characteristics



BMI, body mass index. UIP, usual interstitial pneumonia.

Univariable associations between baseline characteristics and time to first acute exacerbation

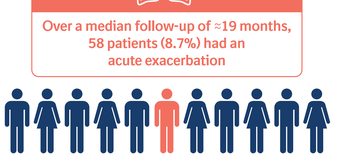


*Versus <65 years. †Versus <25 kg/m². ‡Versus ≤3 years. §Versus unclassifiable IIP.

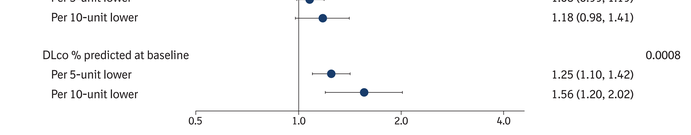
ILD diagnoses

Autoimmune disease-related ILDs: RA-ILD, SSc-ILD, MCTD-ILD, autoimmune ILDs in "Other fibrosing ILDs" category of case report form.
Other fibrosing ILDs: sarcoidosis, exposure-related ILDs and other terms in "Other fibrosing ILDs" category of case report form.
NSIP, non-specific interstitial pneumonia. IIP, idiopathic interstitial pneumonia.

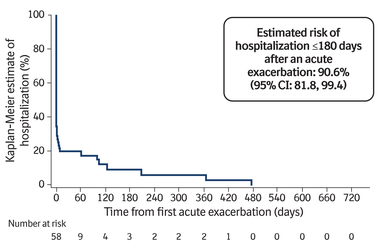
Risk of acute exacerbation



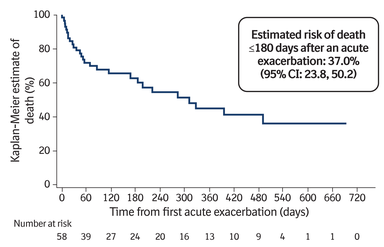
Univariable associations between FVC and DLco at baseline and time to first acute exacerbation



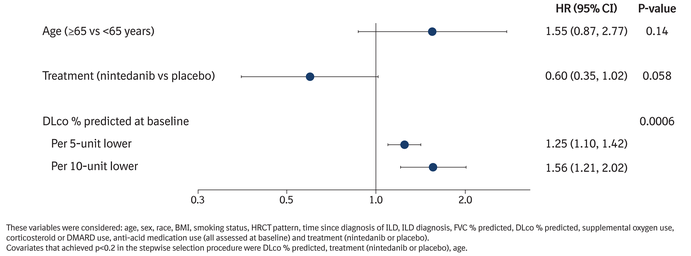
Time from first acute exacerbation to hospitalization



Time from first acute exacerbation to death



Final model for time to first acute exacerbation



These variables were considered: age, sex, race, BMI, smoking status, HRCT pattern, time since diagnosis of ILD, ILD diagnosis, FVC % predicted, DLco % predicted, supplemental oxygen use, corticosteroid or DMARD use, anti-acid medication use (all assessed at baseline) and treatment (nintedanib or placebo).
Covariates that achieved p<0.2 in the stepwise selection procedure were DLco % predicted, treatment (nintedanib or placebo), age.

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