Figure legends

Table 1
Table 1: Patient baseline characteristics for study stage 1 and stage 2.

Table 2
Pathogen isolates from 41 paired cough swab, sputum-induction, and BAL samples. Trial Event Number superscript “a-f” indicates 6 patients who contributed twice. Trial Event Number superscript “**” indicates patients who were asymptomatic.

Figure 1
Participant flow diagram.

Figure 2
Objective assessment of tolerance to the sputum-induction procedure in 200 attempted procedures. Pre and post procedure measurements of FEV1% (where applicable), respiratory rate, and heart rate.

Figure 3
3a) Total pathogen yield for concurrent cough swab and sputum-induction in the total cohort (n=167) and in subgroups aged <6 years of age (n=62), and >6 years of age (n=105).
3b) Specific pathogen yields for concurrent cough swab and sputum-induction in the total cohort (n=167).

Figure 4
4a) Total pathogen yield for concurrent cough swab, sputum induction, and 1-lobe, 2-lobe and 6-lobe BAL in 41 patients.
4b) Specific pathogen yield for concurrent cough swab, sputum induction, and 1-lobe, 2-lobe and 6-lobe BAL in 41 patients.
4c) Venn diagram indicating unique and overlapping pathogen yield for sputum induction, and 1-lobe, 2-lobe and 6-lobe BAL in 41 patients.

Figure 5
2 examples of Polymicrobial DNA signatures or RISA profiles from concurrent cough swab, sputum induction and BAL samples.
5a) The sputum RISA profile is directly related to BAL and discrete from the cough swab profile.
5b) The sputum RISA profile is a combination of contributions from multiple BAL samples sites, indicating that sputum-induction can be effective in sampling from a very wide lower airway compartment.

Figure e1
CF-SpIT Research protocol for sputum-induction sampling.

Table e1
Bacterial isolates from 167 paired cough swab and sputum-induction samples.
Patients enrolled (n=124)

Cough swab (n=200)
(Patients were allowed to contribute to the trial on more than one occasion, if >3 months apart)

**Intervention:**
Paired Sputum-induction procedure (n=200)

Unsuccessful Sputum-induction procedure (n=33)
Successful Sputum-induction procedure (n=167)

Analysis

**Stage 1 Analysis**
Comparison of pathogen yield from sputum-induction with paired cough swab (n=167). Intention to treat analysis (n=200).

Bronchoscopy & bronchoalveolar lavage (BAL) (n=41 in 35 patients).

**Stage 2 Analysis**
Comparison of pathogen yield from sputum-induction, with paired cough swab, 1-lobe BAL, 2-lobe BAL, and 6-lobe BAL (n=41).

**In all cases, samples were taken in strict order from all 6 lobes:**
Right middle lobe, left lingular, right lower lobe, right upper lobe, left lower lobe, left upper lobe

**Pathogen yield from bronchoscopy was defined as follows:**
1-lobe BAL: yield from right middle lobe
2-lobe BAL: summative yield from right middle lobe and left lingular
6-lobe BAL: summative yield from all 6 lobes
Figure 2

Box plots showing FEV1 %, RESP RATE, and HEART RATE pre and post treatment.
Figure 3a

Pathogens isolated

- COUGH SWAB
- SPUTUM INDUCTION

- whole cohort
- <6 yrs > 6yrs
Figure 3b

Pathogens isolated

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Cough Swab</th>
<th>Sputum Induction</th>
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<tr>
<td>H. influenzae</td>
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<td>S. aureus</td>
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<td>P. aeruginosa</td>
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<tr>
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<td>S. maltophilia</td>
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<td>A. xylosidans</td>
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<tr>
<td>K. pneum</td>
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</tbody>
</table>
Figure 4a
Figure 4b

Pathogen isolates

- H. influenzae
- S. aureus
- P. aeruginosa
- BCC
- S. Maltophilia
- MRSA
- A. Xylosoxidans
- AFB

Legend:
- COUGH SWAB
- SPUTUM INDUCTION
- BAL 1 LOBE
- BAL 2 LOBE
- BAL 6 LOBE
Figure 4c

Sputum induction

1-lobe BAL

2-lobe BAL

6-lobe BAL

17

5

3

2

3

3

5
COUGH SWAB

SPUTUM INDUCTION

BAL Sample 1 (RML)

BAL Sample 2 (LLi)

BAL Sample 3 (RLL, RUL, LLL, LUL)

Figure 5