

Table 1: Full questionnaire

1. How long have you been working in cystic fibrosis (CF) care? (years)	<ul style="list-style-type: none"> <li>• 1-4</li> <li>• 5-10</li> <li>• 11-20</li> <li>• &gt;20</li> </ul>
2. Which type of patients does your Center care for?	<ul style="list-style-type: none"> <li>• Adult patients only</li> <li>• Pediatric patients only</li> <li>• Both adult and pediatric patients</li> </ul>
3. How many CF patients does your Center care for?	<ul style="list-style-type: none"> <li>• &lt; 80 patients</li> <li>• 80-200 patients</li> <li>• &gt; 200 patients</li> </ul>
4. On the basis of available data on CFTR modulators (CFTRm) in <i>F508del</i> homozygous patients, to what extent do you expect such therapy to positively change the following conditions of the disease? (not at all, slightly, somewhat, a lot)	<ul style="list-style-type: none"> <li>• Pulmonary disease</li> <li>• Pancreatic exocrine disease</li> <li>• Pancreatic endocrine disease</li> <li>• Nutritional status</li> <li>• Hepatic disease</li> <li>• Ability to perform daily activities</li> <li>• Survival</li> </ul>
5. On the basis of available data on CFTRm in <i>F508del</i> homozygous patients, to what extent do you expect such therapy to change the following pulmonary conditions? (not at all, slightly, somewhat, a lot)	<ul style="list-style-type: none"> <li>• FEV<sub>1</sub> increase</li> <li>• Slowing down of FEV<sub>1</sub> yearly decline</li> <li>• Number of exacerbations</li> <li>• Imaging</li> </ul>
6. Considering the potential use of CFTRm in <i>F508del</i> homozygous patients < 12 years, how useful do you rate the following indicators? (useless, slightly useful, somewhat useful, very useful)	<ul style="list-style-type: none"> <li>• FEV<sub>1</sub></li> <li>• BMI Z-score</li> <li>• Number of exacerbations/year</li> <li>• Bacterial colonisation</li> <li>• LCI</li> <li>• Quality of life</li> </ul>
7. Considering the potential use of CFTRm in <i>F508del</i> homozygous patients > 12 years, how useful do you rate following indicators? (useless, slightly useful, somewhat useful, very useful)	<ul style="list-style-type: none"> <li>• FEV<sub>1</sub></li> <li>• BMI</li> <li>• Number of exacerbations/year</li> <li>• Exercise tolerance testing</li> <li>• Bacterial colonisation</li> <li>• LCI</li> <li>• Quality of life</li> </ul>

8. Considering the potential use of CFTRm in patients with residual function mutations, how useful do you rate the following indicators?  
(useless, slightly useful, somewhat useful, very useful)

- FEV<sub>1</sub>
- BMI
- Number of exacerbations/year
- Exercise tolerance testing
- Bacterial colonisation
- LCI
- Quality of life

9. Considering the potential use of CFTRm in *F508del* homozygous patients < 12 years, how useful do you rate the following indicators for periodic monitoring?  
(useless, slightly useful, somewhat useful, very useful)

- FEV<sub>1</sub>
- Growth percentiles
- Number of exacerbations/year
- Exercise tolerance testing
- Bacterial colonisation
- LCI
- Pulmonary Imaging
- Sweat chloride
- Quality of life
- Exocrine pancreatic function
- Endocrine pancreatic function

10. Considering the potential use of CFTRm in *F508del* homozygous patients >12 years, how useful do you rate the following indicators for periodic monitoring?  
(useless, slightly useful, somewhat useful, very useful)

- FEV<sub>1</sub>
- BMI
- Number of exacerbations/year
- Exercise tolerance testing
- Bacterial colonisation
- LCI
- Pulmonary Imaging
- Sweat chloride
- Quality of life
- Exocrine pancreatic function
- Endocrine pancreatic function

11. Considering the potential use of CFTRm in patients with residual function mutations, how useful do you rate the following indicators for periodic monitoring?  
(useless, slightly useful, somewhat useful, very useful)

- FEV<sub>1</sub>
- BMI
- Number of exacerbations/year
- Exercise tolerance testing
- Bacterial colonisation
- LCI
- Pulmonary Imaging
- Sweat chloride
- Quality of life
- Exocrine pancreatic function

12. In which *F508del* homozygous patients <12 years would you use therapy with CFTRm?  
(all, on a case by case basis, nobody)

- Endocrine pancreatic function
- Asymptomatic patients
- Patients with mild expression of disease
- Patients with complete expression of disease, stable
- Patients with complete expression of disease, worsening

13. In which *F508del* homozygous patients >12 years would you use therapy with CFTRm?  
(all, on a case by case basis, nobody)

- Asymptomatic patients
- Patients with mild expression of disease
- Patients with complete expression of disease, stable
- Patients with complete expression of disease, worsening
- Patients in end-stage disease
- Patients with low adherence to conventional therapy

14. In which patient with residual function mutations would you use therapy with CFTRm?  
(all, on a case by case basis, nobody)

- Asymptomatic patients
- Patients with mild expression of disease
- Patients with complete expression of disease, stable
- Patients with complete expression of disease, worsening
- Patients in end-stage disease
- Patients with low adherence to conventional therapy

15. On the basis of available data, in condition of clinical stability and absence of specific contraindications, which CFTRm would you select in *F508del* homozygous patients never previously treated with modulators?

- Lumacaftor/ivacaftor
- Tezacaftor/Ivacaftor
- I have no sufficient information to express preference

16. On the basis of which main aspect would you make the selection?  
(by order of importance)

- Clinical experience
  - Pharmacological interactions
  - Expected efficacy
  - Safety
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**Table 2: Criteria used to initiate CFTR modulator therapy**

	Somewhat/very useful			Very useful		
	<i>F508del</i> homozygous<1 2	<i>F508del</i> homozygous>1 2	Residual Function	<i>F508del</i> homozygous<1 2	<i>F508del</i> homozygous>1 2	Residual Function
<b>FEV<sub>1</sub></b>	69%	92%	88%	19%	29%	27%
<b>BMI z-score/BMI</b>	95%	95%	86%	27%	31%	24%
<b>Number of exacerbations/year</b>	95%	97%	90%	49%	51%	41%
<b>Bacterial colonization</b>	68%	56%	56%	7%	7%	5%
<b>LCI</b>	76%	61%	73%	25%	14%	15%
<b>Lung imaging</b>	71%	68%	71%	15%	14%	12%
<b>Ability to conduct daily activities</b>	80%	90%	80%	27%	36%	34%
<b>Exercise capacity test</b>	-	90%	80%	-	29%	17%

**Table 3: Criteria used to monitor CFTR modulator therapy**

	Somewhat/very useful			Very useful		
	<i>F508del</i> homozygous<12	<i>F508del</i> homozygous>12	Residual Function	<i>F508del</i> homozygous<12	<i>F508del</i> homozygous>12	Residual Function
<b>FEV1</b>	78%	88%	86%	22%	34%	32%
<b>Growth percentiles/BMI</b>	100%	95%	90%	44%	32%	27%
<b>Number</b>						
<b>exacerbations/year</b>	95%	98%	95%	51%	61%	51%
<b>Bacterial colonization</b>	69%	53%	56%	15%	7%	7%
<b>LCI</b>	85%	63%	75%	36%	10%	17%
<b>Lung imaging</b>	75%	75%	71%	15%	12%	15%
<b>Sweat chloride</b>	76%	73%	76%	15%	10%	19%
<b>Ability to conduct daily</b>						
<b>activities</b>	78%	88%	83%	29%	39%	39%
<b>Exocrine pancreatic</b>						
<b>function</b>	44%	41%	36%	5%	7%	5%
<b>Endocrine pancreatic</b>						
<b>function</b>	47%	41%	47%	3%	7%	5%
<b>Exercise capacity test</b>		90%	85%		31%	24%

**Table 4: Percentage of physicians who would consider use in all patients by disease stage and patient groups**

	<i>F508del</i> homozygous<1 2	<i>F508del</i> homozygous>12	Residual Function
Asymptomatic patients	11 (19%)	16 (27%)	10 (17%)
Patients with mild expression of disease	31 (53%)	33 (56%)	31 (53%)
Patients with complete expression of disease, stable	44 (75%)	46 (78%)	41 (69%)
Patients with complete expression of disease, worsening	53 (90%)	54 (92%)	53 (90%)
Patients in end-stage disease	-	29 (49%)	29 (49%)
Patients with low adherence to conventional therapy	-	10 (17%)	12 (20%)