MEETING ABSTRACTS

Abstracts from the 25th Italian Congress of Cystic Fibrosis and the 15th National Congress of Cystic Fibrosis Italian Society

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S1
Tools to support quality of life in chronic diseases: perspectives in Cystic Fibrosis

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Regular physical activity has been recognized for many years as a key health factor by the scientific community. The focus is particularly high in the evaluation of quality of life perspectives of individuals with chronic disease (HRQoL), therefore also in FC. Recent studies have included a number of disciplines that combine physical and mental training.

Among these, Yoga is particularly interesting since it integrates physical exercise and stress management. To date, the main area of study are: mental health (anxiety, depression, PTSD), cardiovascular diseases, respiratory diseases (asthma and COPD), musculoskeletal disorders and oncological diseases. Among COPD patients, Yoga has proven to be effective in improving exercise capacity, respiratory function and QoL. Among children with chronic asthma, Yoga was found to be effective to reduce drug dependency, lower persistence of asthma symptoms and promote better asthma control. Two studies are currently available in FC, which have formulated the following conclusions: a personalized and individual Yoga program can be considered safe, well tolerated and effective in relation to the respiratory domain of CFQ-R, improvement of joint pain and reduction of anxiety in patients with mild to moderate CF (children and adolescent) [1,2]. The data collected to now, although quantitatively insufficient, encourage further experimentation. Yoga, as a complementary therapy for CF patients, can in fact contribute to: strengthening muscles (respiratory and pelvic floor), improving posture (trunk and rib cage), reducing joint pain, relaxing body-breathing-mind. Above all, the effectiveness of Yoga in CF should be evaluated in relation to its specific ability to control the mind, calming it and making it efficient in anxiety and stress management. Yoga practice develops self-esteem, as well as a positive aptitude to self-control. It also educates in self-discipline, thus training in adherence. A regular Yoga practice can help the CF patient to accept and make constructive a state of health discipline, thus training in adherence. A regular Yoga practice can help the CF patient to accept and make constructive a state of health.

perspectives in CF could be to make patients and caregivers share the same Yoga practice, and/or to create specific distance tools for caregivers, making them accessible online.

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Genetics / epidemiology

A1
Cystic fibrosis with residual function mutations: epidemiology and factors influencing lung disease

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Background

Patients with CF and Residual Function mutations (RFm) have often delayed diagnosis, milder lung disease and pancreatic sufficiency, compared with homozygous for F508del (FF). Here we wish to characterize Italian patients with RFm and describe the factors influencing the lung disease, comparing with patients FF.

Materials and methods

Data from the 2017 Italian Cystic Fibrosis Registry (ICFR) were retrieved for patients carrying RFm and with FF genotype. Furthermore, percent predicted (pp) FEV1 was analyzed over a 2-year period (2015 to 2017).

Results

904 subjects (452 males) with RFm were identified over a total of 5,563 (16.3%) with a median age of 25.5 years (IQR 11.4 – 42.4) and a median age at diagnosis of 5.9 (IQR 0.25 – 23.5). The mean BMI z-score was 0.3 (SD 1.1) in children and BMI 23.4 (SD 4.1) kg/m² in adults. Lung function was characterized by a mean ppFEV1 of 84.2
The longitudinal analysis showed no change over the period 2015–2017 in the ppFEV1% trend among FF patients.

1. Among subjects with RFm, strong evidence (p<0.001) of association between lung function and adult age. Evidence of worse lung function was also found among patients with chronic PA (Δ-16.9, 95% CI: -16.3 to -13.4). Weak evidence of difference in lung function was found between females and males (-3.0, 95% CI: -6.1 to 0.0, p=0.052).

2. Among FF subjects lung function was also negatively associated to increasing age from adolescence and to the colonization by PA. Lung function was not significantly different between females and males.

3. Patients with genotype 3849+10kbC>T/F508del reported significant worse lung function compared to all RF patients (-11.2, 95% CI: -16.9 to -5.4).

The longitudinal analysis showed no change over the period 2015–2017 in the ppFEV1% trend among RF and FF patients.

Conclusions

Patients with CF and RFm are numerous in Italy and have a milder clinical phenotype than FF. Lung disease of RF subjects is more evident since the early adult age and strongly associated to the colonization by PA. RF but not FF females might report more severe lung disease, but this issue needs further investigation. Patients with the genotype 3849+10kbC>T/F508del showed more severe lung disease. All patients provided informed written consent for data publication.

Table 1 (abstract A2). Genotypes, sweat chloride (SC) values and clinical features of this cohort of patients.

| Gender | 1st mutation | FEV1 | SC min | SC max | Last FEV1 | SC | Last SC | First SC | Clinical features |
|--------|--------------|------|--------|--------|-----------|----|---------|-----------|-------------------|
| M      | N1303K       | 110  | 62     | 61     | 110       | ND |         |           | pancreas sufficient; normal nutritional status; intermittent MSSA |
| F      | 2789+5G>A    | 46   | 49     | 42     | 49        | 89 |         |           | pancreas sufficient; at risk of obesity; intermittent MSSA |
| M      | [delta]F508  | 30   | 32     | 30     | 54        | 90 |         |           | pancreas sufficient; at risk of obesity; intermittent MSSA |
| F      | 2789+5G>A    | 85   | 49     | 40     | 85        | ND |         |           | pancreas sufficient; at risk of malnutrition |
| M      | 2789+5G>A    | 43   | 43     | 36     | 81        | 97 |         |           | pancreas sufficient; malnutrition; chronic MSSA |
| M      | [delta]F508  | 68   | 47     | 47     | 68        | 98 |         |           | pancreas sufficient; overweight; male infertility; intermittent MSSA |
| M      | R334L        | 72   | 71     | 68     | 72        | 53 |         |           | pancreas sufficient; normal nutritional status; 3 episodes of pseudo-Bartter’s syndrome; intermittent PA |
| M      | [delta]F508  | 24   | 49     | 24     | 49        | ND |         |           | pancreas sufficient; normal nutritional status |
| M      | [delta]F508  | 32   | 116    | 32     | 116       | ND |         |           | pancreas sufficient; normal nutritional status |
| M      | N1303K       | 29   | 84     | 29     | 87        | ND |         |           | pancreas sufficient; malnutrition; intermittent MSSA |
| M      | [delta]F508  | 34   | 93     | 31     | 93        | ND |         |           | pancreas sufficient; at risk of malnutrition; intermittent MSSA |
| F      | 621+1G>T     | 25   | 45     | 25     | 64        | ND |         |           | pancreas sufficient; at risk of malnutrition; intermittent MSSA |
| M      | 621+1G>T     | 39   | 50     | 39     | 50        | ND |         |           | pancreas sufficient; normal nutritional status |
| M      | 621+1G>T     | 24   | 57     | 24     | 57        | ND |         |           | pancreas sufficient; at risk of obesity; recurrent bronchiectasis |
| M      | L977F        | 16   | 36     | 16     | 36        | 93 |         |           | pancreas sufficient; normal nutritional status; bronchiectasis |
| F      | [delta]F508  | 60   | 34     | 32     | 63        | 98 |         |           | pancreas sufficient; normal nutritional status; recurrent respiratory infections |
| F      | [delta]F508  | 24   | 55     | 20     | 55        | 102|         |           | pancreas sufficient; at risk of obesity; intermittent MSSA |
| F      | G542X        | 47   | 57     | 47     | 57        | 62 |         |           | pancreas sufficient; normal nutritional status; bronchiectasis; kidney stones; hypertension |
| M      | N1303K       | 36   | 80     | 36     | 80        | ND |         |           | pancreas sufficient; normal nutritional status |
| F      | [delta]F508  | 37   | 35     | 26     | 52        | ND |         |           | pancreas sufficient; normal nutritional status |
| F      | [delta]F508  | 22   | 45     | 22     | 54        | 83 |         |           | atelectasis; normal nutritional status; bronchiectasis |
| M      | W1282X       | 21   | 48     | 21     | 136       | 95 |         |           | pancreas sufficient; normal nutritional status |
| M      | [delta]F508  | 99   | 94     | 94     | 102       | 82 |         |           | pancreas sufficient; obesity; type 2 diabetes mellitus; bladder cancer (surgery in 2011); male infertility |
| F      | [delta]F508  | 26   | 60     | 26     | 68        | ND |         |           | pancreas sufficient; normal nutritional status |
| M      | G542X        | 76   | 64     | 64     | 76        | 108|         |           | pancreas sufficient; overweight; CBAVD |
| F      | [delta]F508  | 26   | 157    | 26     | 157       | 101|         |           | pancreas sufficient; normal nutritional status; recurrent respiratory infections |
| F      | G81E         | 34   | 39     | 34     | 39        | ND |         |           | pancreas sufficient; normal nutritional status |

M=male; F=female; ND=not determined; MSSA=methicillin sensible Staphylococcus aureus; PA=Pseudomonas aeruginosa; CBAVD=congenital bilateral aplasia of the vas deferens
A3

Disease progression and burden in patients with cystic fibrosis homozygous for F508del across Europe in an observational registry (VOICE study)

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Background
The study objective was to assess the disease progression and burden of cystic fibrosis (CF) in patients aged ≥ 6 years homozygous for F508del in Europe.

Materials and methods
VOICE was an observational, encounter-based registry study of patients aged ≥ 6 years homozygous for F508del conducted at 37 CF centres in 7 countries in Europe. Data from 24 months before enrolment were collected retrospectively. Available data from the most recent 24-month period with no CFTR modulator therapy were analysed for all enrolled patients who had not participated in other Voice studies previously or concurrently. The rate of change in percent predicted forced expiratory volume in 1 second (ppFEV1) was estimated by mixed-effect model for repeated measures analysis. Pulmonary exacerbations (PEx; clinician defined), hospitalisations and intravenous (IV) antibiotic treatment were summarised descriptively.

Results
889 patients from Italy, the Netherlands, Spain, the UK, Ireland, Germany and Portugal were included (mean age [standard deviation], 22.6 years [11.8]). The observed annualised rate of change in ppFEV1 (95% confidence interval, CI) was −2.17 (−2.77 to −1.58) percentage points for all patients aged ≥6 years at the start of the analysis period (n=822), with the steepest rate of decline in patients aged 12–17 years (n=158; −3.92 [−5.03 to −2.81]). The observed rate of change in ppFEV1 (95% CI) was −2.06 (−3.23 to −0.90) percentage points in patients aged 6–11 years (n=196) and −1.46 (−2.27 to −0.64) percentage points in patients aged ≥18 years (n=468). The observed annualised PEx rate was 0.85 for PEx overall, 0.37 for PEx requiring hospitalisations and 0.42 for PEx requiring IV antibiotics (Table 1). PEx and hospitalisations were more common in patients with worse baseline lung function.

Conclusions
Findings reinforce the significant disease progression and burden in a European population homozygous for F508del.

Sponsor: Vertex Pharmaceuticals Incorporated.

New therapies and outcome measures

A4

Synthesis and biological characterization of new metalloprotease inhibitors for reducing lung inflammation in cystic fibrosis patients

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Italian Journal of Pediatrics 2020, 46(Suppl 1):A4

Background
Matrix metalloproteases (MMPs) are proteolytic enzymes restoring tissue architecture following injury. The importance of MMP activity in cystic fibrosis (CF) pathogenesis has been demonstrated. Particularly, the MMP-9 activity increases in CF patients undergoing acute exacerbation, and this correlates with the degradation of its natural tissue inhibitor. The reduction of MMP-9 activity in CF patients by MMP inhibitors (MMPIs) represents an attracting target, although this effort has been largely unsuccessful, mainly due to lack of appropriate drug delivery in the lungs, adverse effects, and poor enzymatic selectivity of compounds. The aim is to synthesize, purify, and fully characterize a new family of MMPIs, armed to be linked to carrier proteins and to determine their biological properties.

Materials and methods
The synthesis of new MMPIs relies on a gram-scale synthetic strategy previously optimized [1,2], starting from commercially available glycinine and inserting on the aminoacidic nitrogen the pre-formed spacers will be activated as N-hydroxysuccinimide for protein scaffold immobilization and inserting on the aminoacidic nitrogen the pre-formed spacers will be activated as N-hydroxysuccinimide for protein scaffold immobilization.

Table 1 (abstract A3). Summary of PEx and hospitalisations by baseline ppFEV1 subgroups

| Event | Overall (N=889) | Baseline ppFEV1 < 40% (n=114) | Baseline ppFEV1 ≥ 40%–< 70% (n=281) | Baseline ppFEV1 ≥ 70%–< 90% (n=406) | Baseline ppFEV1 ≥ 90% (n=277) |
|-------|-----------------|------------------------------|-----------------------------------|-----------------------------------|-------------------------------|
| All PEx | 491 (55.2) | 1.39 (0.85) | 1.08 (0.85) | 0.66 (0.85) | 0.58 (0.85) |
| PEx requiring hospitalisations | 296 (33.3) | 0.83 (0.37) | 0.52 (0.37) | 0.24 (0.37) | 0.15 (0.37) |
| PEx requiring IV antibiotics | 327 (36.8) | 0.97 (0.42) | 0.60 (0.42) | 0.28 (0.42) | 0.17 (0.42) |
| Hospitalisations | 386 (43.4) | 1.30 (0.57) | 0.78 (0.57) | 0.38 (0.57) | 0.28 (0.57) |
MTT assays and cell proliferation/IL-2 measurements [3]. The ability of each compound to inhibit MMP-9 activity will be measured on ex vivo human neutrophils by succinylated-gelatin assay.

**Results**

We developed and characterized a new family of MMPIs soluble in water. No compounds induced cytotoxicity at 12-24 h, demonstrating their fully biocompatibility. Cell exposure to each compound did not stimulate immune cell activation, ruling out possible immunogenicity. The ability of the compounds to inhibit of MMP-9 activity was at low nanomolar range, suggesting a good enzymatic specificity.

**Conclusions**

New biocompatible, no immunogenic, MMP-9 inhibitors, soluble in water and structurally useful to decorate endogenous proteins, were here described.

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**A5 Effectiveness of Ivacaftor in severe cystic fibrosis patients and CFTR residual function mutations**

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**A6 Phenotype effects by early treatment with Ivacaftor**

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**Background**

Ivacaftor is a CFTR potentiator approved in EU for class-III and for residual function (RF) CFTR mutations. Limited data are available on the effects of Ivacaftor on these patients with severe lung disease, usually excluded from RCT. Since 2016, subjects with CF and severe lung disease, with RF mutations, had access to Ivacaftor as compassionate use. We retrospectively describe the effectiveness and safety of this treatment.

**Materials and methods**

25 subjects (2 men). Median age: 46.7 yrs, range 21.3-58.4 yrs; Severe lung disease: Mean (SD) ppFEV1 31.5% (14.5).

- Genotypes:
  - 3849+10kbC-T7 / F508del (n=5), 3849+10kbC-T4382delA (n=1)
  - 2789+5G->A / F508del (n=3), 2789+5G->A / M11V (n=2), 2789+5G->A / W1282X (n=2), 2789+5G->A / M1602delCT (n=1)
  - D579G / F508del (n=3)
  - D1152H / F508del (n=2), D1152H / D110H (n=1), D1152H / N1303K (n=1)
  - R352Q / Delexon22-23 (n=1), R352Q / F508del (n=1)

**Lung function, BMI, use of antibiotics, sweat Cl, and microbiology were evaluated in the 12 months before starting Ivacaftor and every 3 months during the follow up. Mean treatment duration was 11.3 ± 6.9 months. 10/25 pts had therapy for greater than one year.**

**Results**

The mean absolute change (MAC) (95% confidence interval [CI]) in ppFEV1, from the baseline value was 7.1 (2.3 to 11.9) after 4 weeks (w), 7.8 (2.8 to 12.8) after 12 w, 9.74 (4.1 to 15.4) at 24 w, 8.5 (3.5 to 13.5) after 36 w and 8.6 (5.1 to 12.1) after 48 w. The MAC (95% IC) of BMI was 0.91 kg/m2 (-0.17 to 1.99) after 6 months and 1.03 (-0.59 to 2.65) after 12 months. Days of antibiotic therapy decreased by 80% in the first 12 months of follow up as compared to the 12 months before starting Ivacaftor. The MAC (95% IC) of sweat Cl was -19.7 mmol/L (-37.0 to -1.7). Sputum microbiology was unchanged. No safety concerns were registered. Results were independent of the presence of F508del in the genotype.

**Conclusions**

These cases expand our knowledge about potential benefits of Ivacaftor for patients with CF carrying RF mutations with severe lung disease. At this moment, subjects with CF and RF mutations without F508del on the 2nd allele do not have access to therapies with CFTR modulators. These results support the request of SIFC to AIFA of use of Ivacaftor in severely affected subjects with CF and RF mutations without F508del.

All patients provided informed consent for data publication.
Table 1 (abstract A6). Anthropometric measures, spirometric tests, CFQR, bacteriology over the follow-up

| Date | Age | Weight Kg | Height cm | BMI | FEV1 % | FVC % | MMEF | CFQR | Microbiology |
|------|-----|-----------|-----------|-----|--------|-------|------|------|-------------|
| 12/01/16 | 6.02 | 18.1 | 118 | 13 | 56.9 | 55.9 | 39.5 | 64 | SA + PA |
| 26/05/16 | 6.39 | 21.7 | 120 | 15.7 | 111.4 | 106.3 | 98.2 | 90 | SA + PA |
| 15/06/17 | 7.44 | 26.8 | 127.9 | 16.38 | 94.9 | 100.8 | 71 | 94 | SA |
| 10/07/18 | 8.51 | 32 | 136 | 17.3 | 95 | 89 | 86 | 95 | SA |
| 12/02/19 | 9.1 | 36 | 142 | 17.85 | 93 | 132 | 91 | Neg | |

SA= Staphylococcus aureus; PA= Pseudomonas aeruginosa

A7
Cystic fibrosis and new therapeutic strategies: Ivacaftor, a “bridge therapy” towards lung transplantation

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Background
Cystic fibrosis (CF) is the most common genetically determined, life limiting disease. The genetic origin of CF is the mutations in the CF transmembrane conductance regulator (CFTR). CFTR mutations may be classified into six categories. Class III mutations cause in patients with serious respiratory deficiency. Several parameters of the respiratory function and the general and metabolic state of the patient are evaluated by the Transplant Center in order to define specific clinical criteria to identify the “transplant window”.

Case report
We describe the clinical history of C., female, 45 years old. Genetics: DF508/ GT78R. Pancreatic failure since June 2013. Normal liver and kidney function. On the waiting list since June 2015 for bipulmonary transplant. She has been followed up by clinical examination, instrumental and laboratory tests. Auxological parameters and respiratory function were monitored. She was subjected to a quality of life assessment questionnaire: CFQ-R from the beginning of the therapy program, after about 3 years of treatment, an improvement of the auxometric parameters was observed, resulting in an increase in BMI from 19.9 to 25. Respiratory function has also improved (FEV1 from 19% to 25%).

After treatment with LUM/IVA we observed a significant increase of the mean values for ppFEV1 [before 72, SD 18 after 77, SD 17, p<0.002], ppFVC [before 89, SD 11 after 93, SD 12, p<0.01], BMI kg/m² [before 20.7 SD 2.7 after 21.2 SD 2.5, p<0.002]. After LUM/IVA the mean value of Sweat Cl mmol/L significantly decreased from 119 (SD 21) to 84 (SD 19, p<0.001). Concerning the CFQ-R scores, we found a significantly increase of the mean values for physical functioning [before 73, SD 21 after 78, SD 24, p<0.02], eating [before 87 SD 20 after 93 SD 15, p<0.05] and body image [before 69 SD 26 after 76 SD 22, p<0.03] domains. No significantly differences were detected in PHQ-9 and GAD-7 scores.

Conclusions
These real-life experiences in CF patients with F508del homozygous treated with LUM/IVA confirms the effectiveness of the treatment on lung function, BMI and sweat test Chloride. With regard to the psychological side effects our results prove that the positive influence of LUM/IVA seems to be limited to the domains related to body image and nutrition. Further evaluations are needed to explore the long term effect of LUM/IVA on the mental health and psychological wellbeing.

Patients gave informed consent to data publication.

A8
Real-life experience in a population of Cystic Fibrosis patients with homozygous F508del mutation treated with Lumacaftor/Ivacaftor (LUM/IVA)

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Italian Journal of Pediatrics 2020, 46(Suppl 1):A8

Background
Since 2016, CF patients with homozygous F508del had access to LUM/IVA treatment. We retrospectively describe the effectiveness of this treatment, focusing on psychological outcomes.

Materials and methods
33 patients homozygous for F508del (19 males), mean age: 30.5 yrs (SD 9.7), range 11-49 years were studied. The mean values of lung function, BMI, sweat Cl, CFQ-R, Patient Health Questionnaire 9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7) were compared in the 12 months before and after starting LUM/IVA. We used the Wilcoxon rank test and paired T Student for non parametrical and parametrical variables, respectively. We considered as statistically significant a p value< 0.05.

Results
After treatment with LUM/IVA we observed a significant increase of the mean values for ppFEV1 [before 72, SD 18 after 77, SD 17, p< 0.002], ppFVC [before 89, SD 11 after 93, SD 12, p<0.01], BMI kg/m² [before 20.7 SD 2.7 after 21.2 SD 2.5, p<0.02]. After LUM/IVA the mean value of Sweat Cl mmol/L significantly decreased from 119 (SD 21) to 84 (SD 19, p< 0.001). Concerning the CFQ-R scores, we found a significantly increase of the mean values for physical functioning [before 73, SD 21 after 78, SD 24, p<0.02], eating [before 87 SD 20 after 93 SD 15, p<0.05] and body image [before 69 SD 26 after 76 SD 22, p<0.03] domains. No significantly differences were detected in PHQ-9 and GAD-7 scores.

Conclusions
These real-life experiences in CF patients with F508del homozygous treated with LUM/IVA confirms the effectiveness of the treatment on lung function, BMI and sweat test Chloride. With regard to the psychological side effects our results prove that the positive influence of LUM/IVA seems to be limited to the domains related to body image and nutrition. Further evaluations are needed to explore the long term effect of LUM/IVA on the mental health and psychological wellbeing.

Patients gave informed consent to data publication.

A9
Improvement of lung clearance index in a homozygous F508del patient with mild cystic fibrosis in treatment with Lumacaftor/Ivacaftor

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Background
The lung clearance index (LCI) measured by multiple breath washout (MBW) has been shown to be a sensitive measure to capture lung function abnormalities in cystic fibrosis (CF) patients. LCI can also be used to detect treatment effects in interventional trials. Lumacaftor/Ivacaftor is available for CF patients aged 12 years and older who are homozygous for the F508del-CFTR but the timing when starting treatment in patients with mild CF lung disease is sometimes a matter of debate. Here we present the case of a patient with mild CF who started therapy with Lumacaftor/Ivacaftor using LCI to assess the response to treatment.

Case Report
13 year-old boy, genotype F508del/F508del, intermittent methicillin-sensitive Staphylococcus aureus colonization, last chest tomography (CT) showed some small central bronchiectasis, the forced expiratory volume in 1 s (FEV1) was 93% of predicted, body mass index (BMI) -1.18 SDS. We performed MBW test which showed a LCI of 9.51. In consideration of the aforementioned clinical features, we decided to enhance inhaled therapy, by starting the mucolytic Domnase Alfa, and to initiate therapy with Lumacaftor/Ivacaftor. At baseline, he had a total distance walked during the Six Minute Walk Test (6MWT) of 420 meters, a Cystic Fibrosis Questionnaire-Revised (CFQR) score for respiratory symptoms of 85, one pulmonary exacerbations during the previous year and a level of chloride of 111 mEq/l in the sweat test. After 12 months of treatment, we observed an improvement in all the clinical features as well as a reduction in LCI which was 7.25 (-23.7% than the baseline), as shown in Table 1.

Conclusion
Our case demonstrates how LCI can be useful in discriminating patients with mild CF lung disease to evaluate the start of therapy with LUM-IVA in this window of time using PRH.

Table 1 (abstract A9). Outcome measures

|                      | Baseline | After 12 months |
|----------------------|----------|-----------------|
| FEV1 (% of predicted)| 93       | 96              |
| LCI                  | 9.51     | 7.25            |
| BMI (SDS)            | -1.18    | -0.47           |
| 6MWT (m)             | 420      | 450             |
| CFQR                 | 85       | 100             |
| Sweat test (chloride mEq/l)| 111| 106             |
| Pulmonary exacerbations| 1 | 0               |

A10 Adherence to Lumacaftor-Ivacaftor in cystic fibrosis patients
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Background
Poor adherence rates to treatment is frequently reported in cystic fibrosis (CF). Specific data about CFTR modulators are currently lacking, with only one report showing suboptimal adherence to Ivacaftor [1]. Several methods of adherence assessment have been reported, such as daily phone diary, self-report, prescription refill history (PRH) and electronic monitoring. In Italy PRH data are hard to collect due to the absence of a network between territorial pharmacies and CF centers. In our region (Lazio, Italy), during 2016-2019 period, Lumacaftor-Ivacaftor (LUM-IVA) was delivered by in-hospital pharmacy, according to specific regional law. This offered us an unique opportunity to assess adherence to LUM-IVA in this window of time using PRH.

Materials and methods
We conducted a single-center, retrospective, observational study investigating adherence rates to LUM-IVA in 20 CF patients (11 males, 9 females) homozygous for F508del mutation (median age 20 years, range 10 – 44 years), referred to Bambino Gesù Children’s Hospital (Rome). Observation period spanned from October 2016 to July 2019. PRH data were recorded by in-hospital pharmacy service using Medical Possessions Ratio (MPR - total amount of medication obtained by the patient divided by the total amount of prescribed medication). At the end of the observation period, a phone interview was conducted assessing self-reported adherence (0-100%). Spearman coefficient was used to assess correlation between MPR and self-reported adherence.

Results
Average monitoring period was 26.7 months (range 5-32 months). Overall, median MPR derived adherence was 97%, ranging from 39% to 107%. Self-reported median adherence was 98.5%, ranging from 50% to 100%. In 4 out of 20 patients (15%) MPR derived adherence was < 65%. No significant correlation was found between MPR and self-reported adherence (r 0.31 p 0.17).

Conclusions
To our knowledge, this is the first attempt to assess adherence to LUM-IVA in CF patients. Our results show optimal adherence to LUM-IVA in the majority of our sample. Those results are in contrast with the current literature on adherence and may reflect the specificity of Italian CF population (not yet described elsewhere) and/or patients’ expectations on CFTR modulators. However, a consistent number of patients (4/20) shows a poor – to – suboptimal pattern of adherence. Routine adherence screening should be part of the standard care of CF patients, especially in the era of CFTR modulators. Cost-effectiveness analysis, clinical implications assessment and tailored countermeasures are needed.

Patients or their parents gave consent for the publication of clinical data.

Reference
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A11 Bridging CFTR-modulators to infection by defining the impact of therapies on airway microbiology and clinical response in CF patients
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Italian Journal of Pediatrics 2020, 46(Suppl 1):A11

Background
Cystic Fibrosis Transmembrane conductance regulator (CFTR)-modulators have been approved as a mutation-targeted personalized treatment for CF. Treatment efficacy is variable suggesting that individual factors may further influence drug effectiveness. New approaches that better support the identification of responders to CFTR-modulators are the clinical need. Here, we bridge CFTR-modulators to infection by defining the impact of these therapies on airway microbiology and clinical response in CF patients.

Materials and methods
Antimicrobial activity of CFTR-modulators and synergism with standard antibiotics were evaluated on a bio-bank of longitudinal Pseudomonas aeruginosa and Staphylococcus aureus isolates. Next, a cohort of CF patients homozygous for F508del-CFTR mutation is under investigation in a longitudinal study before and after Lumacaftor/Ivacaftor treatment.
Results
None or minimal antimicrobial effect was observed upon exposure of *P. aeruginosa* isolates to CFTR-modulators alone, including high concentrations up to 16 μg/ml for ivacaftor (IVA) and tezacaftor (TEZ) and 256 μg/ml for lumacaftor (LUM). Whereas, synergistic effect of CFTR-modulators with antibiotics was detected. IVA synergized with polymyxin and colistin in almost all *P. aeruginosa* isolates, while it did not show any synergy with other antibiotics. Differently, TEZ and LUM showed few synergies, even at high concentrations. Of note, IVA showed an antimicrobial activity per se against *S. aureus* isolates at clinically relevant concentrations, and synergized with antibiotics. LUM showed a similar activity although at higher concentrations. Conversely, TEZ was completely ineffective. We studied 14 patients, 12 years of age or older, homozygous for the F508del mutation, who had been taking LUMA/IVA for at least 2 years, with particular regard to their airways infections before and after treatment. Pulmonary exacerbations significantly decreased from baseline after both the first and the second year of treatment. Pulmonary function (FEV1, % predicted) and body mass index also improved from baseline but not significantly. After the first and second treatment year, no significant change in microbiological isolation was observed. The analysis of clinical data from additional 28 patients is in progress. In addition the antimicrobial activity of CFTR-modulators on patients’ isolates is under investigation.

Conclusions
So far, these results suggest that CFTR-modulators can have an anti-bacterial activity and influence antibiotic efficacy through a synergistic effect that varies depending on the isolate, modifying treatment efficacy. These initial clinical studies support the needs for further evaluation of their impact on infection.

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### GI / Nutrition

#### A12

**A screening system to test novel modulator drugs of CFTR gene transcriptional regulation**

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**Background**
The Cystic Fibrosis (CF) is an autosomal recessive disease caused by mutations in the *CFTR* gene, resulting in alteration of the chloride channel activity. Currently, the therapeutic strategies use drugs like potentiators and correctors or their combination. These drugs act in a mutation-specific manner, making these treatments limited to a few kinds of patients. For this reason, the research is focused on the development of novel classes of drugs: new potentiators and correctors, stabilizers, amplifiers, mRNA repairs and PTC readthrough molecules [1]. Among these, of great interest are the amplifiers that enhance the transcriptional level of *CFTR* gene. Our project is based on the hypothesis that a CF patient with CFTR mutations that retain a residual function may have a clinical benefit by increasing the amount of its mutated CFTR protein through a halide sensitive YFP assay [2] and to analyze this effect on the activity of the endogenous CFTR protein through a halide sensitive YFP assay [3].

**Materials and methods**
We constructed a bi-cistronic lentiviral vector (the pCFTR-LUC-YFP) containing two different expression cassettes: the LUC cassette to express the luciferase gene under the control of the CFTR promoter region3kb long; the YFP cassette expressing the yellow fluorescent protein and the puromycin gene for the endogenous CFTR activity analysis and cell selection. To test our CFTR promoter region in as many cell lines as possible, we used pCFTR-LUC-YFP vector for the production of lentiviral particles with VSV-G as envelope protein. Then, we transduced different cell lines with different CFTR gene expression levels (i.e., HEK293, A549, Calu3 and Caco 2 cell lines). After treatment with sodium butyrate (NaB), an inhibitor of histone deacetylases, we tested gene expression variation by luciferase assay and RT-PCR[4].

**Results**
Primary data show, as expected, that the basal CFTR expression levels are different in each cell line. Moreover, each cell line differentially responds to NaB treatment.

**Conclusions**

The preliminary data demonstrate that this model represents a good screening system for molecules with amplifier action, also by high throughput screening methods. Moreover, the use of lentiviral particles allows to test the activity of the CFTR promoter in almost all cell lines as well as in primary cells.
A nutritional support (oral nutritional supplements and/or enteral tube feeding) had been already prescribed one year before listing in 38% of cases, which increased to 56% and 59% at the time of listing and at the time of transplantation respectively. In addition a more aggressive nutritional intervention (partial parenteral nutrition) was required in 19% of cases.

Conclusions
In our patients, BMI was maintained during the waiting list by means of a progressive intensification of nutritional interventions. These findings confirm that therapeutic strategies aimed to maintain weight loss are associated to improve survival in CF patients in waiting list. An informed consent was obtained from all patients for data publication.

Table 1 (abstract A13). Nutrition interventions in patients with end stage lung disease 12 months before, at time of referral for LTx and at time of LTx

| Supplemented Patients (%) | 12 months before wait listing | Wait listing | Time of LTx |
|---------------------------|-------------------------------|--------------|-------------|
| Oral supplementation (%)  | 31                            | 41           | 44          |
| Enteral tube feeding (%)   | 9                             | 13           | 13          |
| Parenteral supplementation | 0                             | 19           | 25          |
| Kcal from supplementation % (mean ± SD) | 12.0 ±18.8 | 42.0 ±29.1 | 44.6 ±33.4 |

No deaths were registered in patients awaiting LTx

A14

The role of Bioelectrical Impedance in Cystic Fibrosis: the experience of a care Center

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Background
Malnutrition is a common complication in patients with Cystic Fibrosis (CF), and it directly affects the prognosis. Body composition (BC) should be evaluated to identify children at risk of malnutrition. Bioelectrical impedance (BIA) is extensively used to estimate BC. In particular BIA-derived phase angle (PhA) should be used to assess and monitor nutritional status.

Materials and methods
From enrolled patients we collected data including CFTR mutation, pancreatic insufficiency status (defined as fecal elastase value < 200 μg/g stool), anthropometric measurement (body weight, height and BMI) and glucose tolerance abnormalities. Body composition (BC) should be evaluated to identify children at risk of malnutrition. Bioelectrical impedance (BIA) is extensively used to estimate BC. In particular BIA-derived phase angle (PhA) should be used to assess and monitor nutritional status. Nutritional status strongly affects pulmonary function and survival in CF patients. In our preliminary study BIA PhA seems to have a good relationship with FEV1 values. BIA could be an early tool for nutritional evaluation in children with CF. More data are needed to establish normal values in this population. All parents gave informed consent to data publication.

A15

MyCyFAPP: a novel approach for the self management of pancreatic insufficiency in cystic fibrosis

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Background
The MyCyFAPP project was developed to promote self-management of pancreatic enzyme replacement therapy (PERT) in children with Cystic Fibrosis (CF) by means of a mobile application (app) that allows for a personalized and accurate control of pancreatic insufficiency and nutritional status.

Materials and methods
The initiative, coordinated by Hospital Universitario La Fe in Valencia, was financed by the European Commission under the Framework Program for Research and Innovation Horizon 2020 and involved CF centers, universities, patient representatives and ITC companies from Spain, Italy, Norway, Germany, Portugal, Belgium and the Netherlands.

Results
In the first stage 210 CF patients (30 from the Milan CF Center) completed a four days food record in order to characterize their nutritional habits and deliver common nutritional recommendations. At the same time in vitro digestion studies were carried out to estimate fat digestibility in real foods and meals under CF gastrointestinal conditions (intestinal pH, bile acid concentrations). Subsequently a pilot study was aimed at obtaining a personalized correction factor for each individual on the basis of the Theoretical Optimal Doses (TODs) obtained by in vitro studies. The study consisted of two consecutive stages, throughout which 42 patients (5 from our Center) received a standardized diet and a fixed dose of enzymes. Faecal samples were collected to assess the coefficient of fat absorption (CFA) while patients assumed the TODs. The use of this dose without any correction allowed to obtain a satisfactory CFA. The app was then developed and included an algorithm to calculate PERT-dose, a symptoms diary, a nutritional handbook and educational games. The app was linked to a professional web tool allowing healthcare professionals to evaluate patient’s data and give feedback. A clinical trial was planned to assess its usefulness; in the first stage a questionnaire specifically targeted to gastrointestinal symptoms (PEDS-QL-GI) was validated in different languages in 240 CF patients (62 from our Center) to be used as endpoint in the second part of the trial. Cystic Fibrosis Questionnaire-Revised (CFQ-R) and a Visual Analogue Scale (VAS) were also administered. A 6 months multicenter prospective trial involved 154 patients (20 from our Center) who used the app every day entering the meals and taking the PERT dosage calculated. In a subsidy of the clinical trial, faecal samples were collected to control CFA on a free diet.
Conclusions
The results show that MyCyFAPP improved GI QOL during a 6 months trial and may help patients to improve self-management of PERT.

A16
Night blindness in Cystic Fibrosis: the central role of vitamin A
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Italian Journal of Pediatrics 2020, 46(Suppl 1):A16

Background
In children with CF and pancreatic insufficiency, pancreatic enzymes and bicarbonate cannot be secreted into the duodenum, leading to impaired digestion of nutrients, bile acids precipitation, fat and liposoluble vitamins malabsorption. Deficiency of Vitamin A may cause ocular impairment.

Case Report
We present the case of a 9 years-old girl with CF diagnosed at birth following intestinal occlusion for meconium ileus (genotype: F508del/L1077P). In the first 6 months of life she underwent two surgeries for occlusion with bowel resection. After surgeries she ended up with 102 cm small bowel, without ileo-cecal valve, and ileocolic anastomosis. This anatomical situation is classified as short bowel syndrome type 2 and she needed parenteral nutrition (PN) support until the age of 14 months when PN was stopped. Despite the presence of a mild alteration of liver enzymes and a moderate degree of intestinal malabsorption, she had optimal weight and height gain. At the age of 4 years, during a hospital admission for respiratory tract infection, a severe vitamin A deficiency (VitA: 0 mg/l) was documented. This deficiency was associated with nocturnal blindness. Electroretinography (ERG) was performed and found normal. Despite nutritional adaptation of lipid and liposoluble oral intake, the deficit could not be corrected and was associated with important malnutrition which justified a new PN support. This was continued for 18 months with improvement of nutritional status and liposoluble vitamin profile (VitA:0.16mg/l, VitE:6.7mg/l, VitD:27.6 mcg/l). PN was stopped because of hepatic deterioration with cholestasis and evolution to cirrhosis. Two years after interruption of PN, despite normal growth and no clinical symptoms, retinal sufferance was found in a follow-up ERG. Vitamin A level was 0.11 mg/l with the rest of liposoluble vitamins in range. After an unsuccessful increase of oral supplementation, intramuscular administration was started leading to ERG normalization.

Conclusion
The peculiarity of this case is the coexistence of alteration in the three main protagonists of Vitamin A metabolism: pancreas, bowel and liver. Those three organs have a strong anatomic and functional linkage as testified by “the vitamin A vicious circle” [1]. The informed consent of the parents has been obtained.

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A17
Evaluation of the adherence of NaCl supplementation with Wadi (cps NaCl 1g + Mg) in CF
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Italian Journal of Pediatrics 2020, 46(Suppl 1):A17

Background
Sodium supplementation (as sodium chloride) is essential for patients with Cystic Fibrosis, however adherence to the nutritional therapy is often below the optimal value [1]. The are several causes: from the very low palatability of the products used to the huge daily therapeutic load of CF patients that leads nutritional supplementation therapy to take second place.

Materials and methods
Collection of data regarding drug withdrawals in terms of quantity and frequency at local patients’ pharmacies by telephone interview and / or email and comparison with the medical prescription.

Results
78% of patients shows adherence to sodium supplementation with Wadi (NaCl 1 g + Mg capsule).

Conclusions
Adherence to sodium supplementation with Wadi is very close to the optimal value of 80%. The limit of the study is that the withdrawal of the drug does not necessarily imply its intake. Although this drug has recently come on the market, the data of its use are encouraging, as it presents a neutral palatability and a format that meets the patient’s habits.

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Infection / inflammation

A18
Non Tuberculous Mycobacteria (NTM) in cystic fibrosis (CF) patients: real-life data from Verona CF center
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Background
NTM are one of the most challenging pathogens in patients with CF. Diagnostic- and specific treatments can be difficult in the clinical practice despite guidelines have been published. The aim of our study is to collect clinical and microbiological data of CF patients with NTM finding followed at our center.

Materials and methods
Data about CF patients with airway NTM isolation from June 2006 to June 2019 were extracted from our database (with prospectic insertion).

Results
Airway NTM was reported in 41 patients, representing 5.1% of the whole CF population followed at our center. Females represented 51.22% of our population; delF508 was in homozygosis in 19.51%, and heterozygosis in 56.1%; 73.17% was pancreatic insufficient, while 34.15% had CFRD. Chronic P. aeruginosa, MSSA, MRSA colonization had a prevalence of 82.93%, 36.58%, 12.19% respectively; Aspergillus was found in 61% of patients; S. apiospermum was isolated in 3 patients. First NTM finding resulted at 29.05 ±14.27 years old. M. abscessus, M. intracellulararum and M. avium spp were isolated in 46.34%, 24.39% and 9.76% respectively. In the transplanted patients included, NTM was isolated in 2 patients after transplantation, in 5 patients before transplantation. Mean FEV1 in the 12 months before NTM finding was 68.45 ±24.47 %pred, mean FEF25-75 in the 12 months preceding NTM was 46.80 ±49.37 %pred; no change was shown in the 12 months following NTM finding. Treatment for NTM was performed in 17 patients (41.46%). The therapy is still ongoing in 5 patients, in 4 of them spumum culture for NTM is still positive (all of them with M. abscessus). Twelve patients concluded the treatment after a minimum duration of 12 months, within this group NTM is still present in 4 patients (all of them with M. abscessus) and eradicated in 8 patients (50% with M. abscessus). Admission to hospital decreased in the 12 months following NTM finding in
comparison to 12 months preceding NTM, but this was significant only in the subset of patients treated for NTM.

Conclusions
NTM prevalence complies to literature. Even if therapy is still ongoing in some patients, NTM was eradicated only in 52.94%, proving the challenging nature of NTM treatment. This appears more evident for M. abscessus than the other species. Fewer hospital admissions in the treated population may suggest a control over infection and inflammation associated to treatment. Assessing treatment response and clinical data in the different NTM species requires wider populations and further studies.

A19
Early Pseudomonas Aeruginosa (PA) identification in 2003-2013 birth cohort cystic fibrosis (CF) patients: clinical, functional and radiological impact
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Background
Since early events in CF patients’ life can determine disease progression and burden in later years, there is increasing interest regarding these events. The aim of our study was to evaluate the effect of PA first identification in preschoolers.

Materials and methods
We retrospectively evaluated data regarding 150 2003-2013 birth cohort CF patients with regular follow-up. All patients had chest CT performed at 4-7 years of age, forced spirometry at 6 years and first N2-MBW measurement.

Results
We identified 3 groups: 61 patients with first PA identification before 2 years of age (group A); 47 patients with first PA at 2-6 years of age (group B); 42 patients without PA up until 7 years of age (group C). Class I or II mutations on both alleles were significantly more frequent in groups A and B (79% and 72.3% vs 36%), with an OR of 5.98 for PA identification before 7 years of age. Pancreatic insufficiency was significantly more frequent in groups A and B than in group C (91.8% e 85.1% vs 40.4%), with an OR of 11.76 for PA identification before 7 years of age. BMI percentile was higher in group C (p<0.01). FEV1%pred was worse in group A than in group C (98.66±15.38 vs 107.19±17.35, p=0.012), as was FVC (p=0.029). LCI 2.5% was worse in groups A and B than in group C (9.45 [8.93-12.6] and 10.82 [8.47-13.52] vs 7.91 [7.24-11.13], p=0.0023); analysis of LCI 2.5% pred was consistent with absolute values. Scond was also significantly worse in groups A and B; Scond was no different between groups. The prevalence of normal lung CT was lower in group A (19.67%, p=0.0006) and B (22.4%, p=0.005), than in C (52.38%); PA identification before 2 and 7 years of age associates with an OR of abnormal chest CT of 2.4 and 4.06, respectively. Peribronchial thickness and mucus plugs were significantly more frequent in groups A and B than in group C. No significant difference was shown between groups A and B for all examined parameters. Chronic colonization developed in 19.67% of group A and in 21.28% of group B. MRSA was found in 3.3% of A; 8.5% of B; 4.8% of C.

Conclusions
Of note, early PA isolation impacts on respiratory function and radiological status in CF preschool children. Nonetheless, chronic colonization only develops in a relatively small subgroup.

A20
Longitudinal genomic analysis of Pseudomonas aeruginosa as a tool for the definition of persistence/reinfection in the airways of Cystic Fibrosis patients
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Background
In cystic fibrosis (CF) patients chronic Pseudomonas aeruginosa (Pa) infection is associated with lung damage, a more rapid decline in lung function, and is an important prognostic factor of morbidity and mortality [1]. Pa earlier acquisition shortens life expectancy, therefore, eradication of initial Pa acquisition and delay chronic infection is crucial for patient care [2]. Aim of this study was to analyse the whole genome sequences (WGS) of Pa isolates obtained from a child over a 4 years period in order to define if she was subjected to uncommonly frequent reinfections or if she has acquired an early chronic Pa infection.

Materials and methods
Poisolates (n = 32) were subjected to WGS using the Nextera XT Flex DNA kit and the Miseq system (Illumina). Genetic characterization was performed by comparison of the obtained Pa genome sequences with specific databases such as virulence gene and antibiotic resistance databases. Moreover, phylogenetic relationship of the isolates was evaluated using a SNP-based approaches and SNPs matrix was used as input for phylogenetic analyses to determine the relationships between genomic sequences of Pa isolates obtained from this study and the ones that are present in databases.

Results
WGS analysis, using PAO1 as reference genome of Pa, highlighted the presence of two clusters whose isolates differ in about 1000 pairwise SNPs. Within the same cluster, Pa isolates had a maximum of 6 SNPs difference confirming the clonality of different isolates. The main cluster comprises all the Pa strains isolated in the period 2015-2017, when the child had two >6-months period of Pa-free cultures and some strains isolated in 2018/2019 (cluster I), whereas the cluster II contains only recent strains (years 2018-2019).

Conclusions
Results have shown that, starting the first Pa isolation, the child suffered from a chronic infection and that a superinfection occurred some years later. Evaluation of Pa clonality by WGS may support studies aimed to determine efficacy of eradication therapies and may help to manage patients for obtaining a better clinical outcomes.

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A21
Protective role of Palivizumab in the prevention of RSV respiratory infections in patients with Cystic fibrosis
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Background
Respiratory syncytial virus (RSV) is one of the most important pathogenic viruses with airway tropism. It is responsible for various clinical manifestations including bronchitis, pneumonia and bronchiolitis. Severe forms of bronchiolitis can affect pediatric patients, especially patients suffering from chronic respiratory diseases including cystic fibrosis. To date, active immunization is not yet available, but there is the possibility of carrying out passive immunization through the administration of monoclonal antibodies (Palivizumab). Few studies have evaluated protective efficacy of these antibodies especially in pediatric patients with cystic fibrosis (CF).

Materials and methods
We performed a retrospective analysis (2014-2019) involving all CF patients in follow-up in our Unit that presented respiratory symptoms with need of hospitalization, to evaluate the incidence of RSV related infections in pediatric patients younger than 24 months who had received prophylactic treatment with Palivizumab. All patients underwent RSV research in nasal mucus. All patients received five doses of Palivizumab in the first year of life.

Results
We identified 37 patients (22F e 15M) with CF born between 2014 and 2019 with diagnosis by screening or by symptoms, carried out within 2 years of age, who received prophylaxis with Palivizumab in the first year of life (five doses 15mg/kg/dose). 3 patients (8.1%) experienced RSV infection during hospitalization for respiratory problems, two of them with other comorbidities (extreme prematurity and bowel obstruction) and only one without other risk factors. 34 patients (91.9%) never had RSV infection.

Conclusions
Since there are no absolute indications about the administration of Palivizumab in CF patients, our analysis showed that this passive prophylaxis led to a low incidence of RSV infections. It therefore seems reasonable to implement a prophylaxis program with Palivizumab in patients suffering from chronic respiratory diseases such as CF.

A22
Potential role of serum and plasmatic biomarkers to predict clinical and functional response to antibiotic treatment for pulmonary exacerbation
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Background
Pulmonary exacerbations (PEx) frequently occur in cystic fibrosis patients, with an unfavorable impact on disease course [1]. The need of precocious markers of PEx as diagnostic tools and prognostic factors for treatment response, has increased the interest to biomarkers analysis in both sputum and blood samples. Several studies have investigated the role of acute phase reactants during PEx and little evidence exists for serum C-reactive protein (CRP) [2] and sputum interleukin-8 (IL8) [3]. In this study we measured several plasmatic and serum biomarkers to estimate their predictive and prognostic value in course of PEx.

Materials and methods
We prospectively enrolled 24 CF patients (17 F, 7 M) in course of PEx in need of intravenous antibiotic treatment. Patients were assessed at the diagnosis of PEx, at the fifth day of treatment and at the end of the antibiotic course. During each control patients performed clinical evaluation, pulmonary function test (forced expiratory volume in one second, FEV1) and blood test of plasmatic and serum biomarkers (fibrinogen, FBG; calprotectin, CP; interleukin-6, IL6; IL8; procalcitonin, PCT; white blood cells, WBC; reticulocyte, RCT; erythrocytes sedimentation rate, ESR; CRP). Informed consent was obtained from all patients for data publication.

Results
The main results of our study are:

1. High levels of at least two serum biomarkers at the diagnosis of PEx occurred in all but two patients;
2. All patient completed the antibiotic treatment (14 days) and we observed a significant reduction of IL6, CRP, CP, FBG and WBC at the end of the antibiotic course (Table 1), despite this reduction was independent with favorable and unfavorable response;
3. FBG seems to be the most earlier and predictive marker of treatment efficacy: the reduction of FBG after five days of therapy was associated to significant improvement in FEV1 values at the end of the antibiotic cycle.

Conclusions
Serum and plasmatic biomarkers seems to be simple and reproducible parameters to assess clinical and functional response during PEx and the trend of FBG may reflect the improvement of lung function. Further studies, with a large population, are needed to better investigate the role of such markers in clinical practice.

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Table 1 (abstract A22). Biomarkers trend during antibiotic course (T0 – T14)

| Biomarkers                  | Range    | Mean (SD)    | Median | p-value |
|-----------------------------|----------|--------------|--------|---------|
| Fibrinogen (mg/dl)          | 11690 – 5340 | 12841 (14978) | 860        | <0.0001 |
| Calprotectin (ug/ml)        | 4.9 – 55.8  | 6.80 (14.60)  | 1.7      | 0.0092  |
| White blood cells (10³/mm³) | 24900 – 62200 | 20799 (2786.60) | 1870.0    | 0.0022  |
| Procalcitonin (ng/ml)       | 0.9 – 0.1  | 0.03 (0.19)  | 0.0      | 0.334   |
| Interleukin 6 (pg/ml)       | 9.1 – 155.5 | 16.34 (39.45) | 2.2      | 0.0165  |
| Interleukin 8 (pg/ml)       | -506.8 – 37370 | 172.86 (926.87) | -2.1     | 0.6995  |
| Erythrocytes sedimentation rate (mm²/h) | -4.0 – 50.0  | 15.83 (18.21)  | 11.5    | 0.0073  |
| Reticulocyte (mm³)          | -900000 – 326000 | -16717.22 (30994.7) | -12550.0 | 0.0483  |
| C reactive protein (mg/dl)  | 0.2 – 7.3  | 1.26 (2.12)  | 0.3      | 0.0002  |
A23
Salivary cytokines and lung disease evaluation in patients with Cystic Fibrosis
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Background
In order to detect infections and quantify inflammatory biomarkers in patients with CF, bronchoalveolar lavage fluid (BALF) and/or sputum has been previously performed with conflicting results on their use. Saliva could represent an useful alternative tool being characterized by non-invasive collection and direct anatomical relationship with the lower airways [1]. The aim of this study was to investigate whether the salivary levels of interleukin-6 (IL-6), IL-8 and tumour necrosis factor-alpha (TNF-α) are associated with the clinical status of CF patients.

Materials and methods
Unstimulated saliva samples from 110 CF adults and 32 CF children have been collected at the Regional Cystic Fibrosis Center, Adult and Pediatric Section. and from 50 healthy subjects as controls. Lung disease severity was classified as severe, moderate and mild considering both the FEV1 and age of patients [2]. Salivary biochemical parameters were analyzed by automated clinical chemistry analyzer. Salivary IL-6, IL-8 and TNF-α were measured by specific ELISA methods.

Results
Biochemical analyses revealed that salivary chloride was significantly higher (p<0.05) in CF adults compared to controls, while calcium and phosphate resulted lower (p<0.005). Furthermore, salivary LDH, potassium and phosphate concentrations were significantly higher in CF children compared to those in CF adults (p<0.05). All three salivary cytokines, IL-6, IL-8 and TNF-α, resulted significantly higher in CF adults compared to controls (Table 1). No significant differences were observed between CF adults and children. Regarding the correlations between cytokines and the lung disease severity in CF patients significant correlations were observed only in CF children: i) Spearman’s rank-order analysis showed a positive significant correlations between IL-8 and FEV1 (rS: 0.388; p=0.031); ii) IL-6 positively correlated with FEV1/age ratio, an index of lung disease severity (rS: 0.412; p=0.019). No significant correlations of the salivary cytokines levels with the genotype and lung colonization were observed in neither CF adults and children.

Conclusions
This study showed that:

- salivary electrolyte and LDH concentrations were significantly different among healthy subjects, CF adults and children;
- IL-6, IL-8 TNF-α levels were significantly higher in saliva from CF patients compared to healthy subjects;
- in CF children, IL-6 and IL-8 correlated positively and negatively, respectively, with lung disease severity.

According with the literature [3], our results suggest that saliva could represent a valid matrix for the diagnosis and monitoring of CF patients. In particular, salivary IL-6 and IL-8 could represent useful biomarkers for monitoring lung disease in CF children. Further studies are needed to confirm the power of salivary markers and to define their potential predictive value.

Informed consent to data publication was obtained from all parents.

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Table 1 (abstract A23). Cytokines levels in controls subjects, adult and children CF patients as median (2.5-97.5 %ile)

| Cytokines | Controls (n = 50) | CF adults (n = 70) | CF children (n = 31) | Kruskal-Wallis (p value) |
|-----------|------------------|-------------------|---------------------|------------------------|
| IL-6      | 28.2 (4.1-66.8)  | 57.9 (18.3-202) * | 57.6 (17.7-357)     | 5.15*10^-10            |
| IL-8      | 55.0 (11.8-206)  | 307 (55.3-1031) * | 245 (33.4-889)      | 1.06*10^-13            |
| TNF-α     | 124 (0.5-56.1)   | 27.4 (2.4-94.1) * | 30.8 (12.6-87.2)    | 2.16*10^-6             |

* CF adults versus controls, p < 0.00001

Respiratory
A24
Therapeutic bronchoscopy with administration of recombinant human deoxyribonuclease in patients with cystic fibrosis
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Background
Cystic fibrosis is characterized by a progressive respiratory disease that is still the leading cause of morbidity and mortality. The accumulation of mucus with consequent neutrophil-mediated inflammation is responsible for the formation of bronchiectasis, which feeds the infectious-inflammatory vicious circle. Furthermore, during inflammation, there is a release of deoxyribonucleic acid (DNA) which contributes to increasing the density of secretions. To interrupt this vicious circle, in recent years, the method of bronchoscopy with therapeutic lavage has been taking hold with the instillation of recombinant human DNase to make the secretions more fluid and then aspirating them avoiding their accumulation and reducing inflammation [1].

Materials and methods
Herein we describe our experience using bronchoscopy with instillation of recombinant human deoxyribonuclease (rhDNase) in five adults with CF regardless the evidence of lobar atelectasis. rhDNase (2,500 IU/2.5ml diluted in 20 ml 0.9% saline) was administered into the most affected lobes (identified by chest radiograph prior to the procedure) by flexible bronchoscopy.

Patients data were the following:

- 36 year-old man, genotype F508del/R553X, chronic Pseudomonas aeruginosa colonization with dyspnea and increased
sputum production. Chest computed tomography (CT) revealed areas of mucus plugging above all in the right middle lobe; • 28 year-old woman, genotype F508del/F508del in treatment with Lumacaftor/Ivacaftor, chronic Klebsiella pneumoniae colonization with recent impairment in lung function. Chest X-ray showed consolidation of right middle and lower lobes; • 19 year-old male, genotype F508del/W1282X, chronic methicillin-resistant Staphylococcus aureus and areas of consolidation on chest X-ray in the right middle and lower lobes; • 18 year-old male, genotype F508del/G542X, allergic broncho-pulmonary aspergillosis in treatment with Oralzumab and atelectasis of the right upper lobe; • 38 year-old male, genotype F508del/E891Q in treatment with Lumacaftor/Ivacaftor, chronic Pseudomonas aeruginosa colonization and recent worsening of respiratory symptoms and lung function. Chest X-ray showed persistent consolidation of the left lower lobe.

Results
In four out of the five cases, the procedure resulted in an immediate improvement in symptoms, forced expiratory volume in 1 s (FEV1) and radiological features. Following the procedure, the patients resumed their regular medical regimen which included nebulised rhDNase.

Conclusions
In our hands, bronchoscopic instillation of rhDNase in patients with CF was safe and well-tolerated. These preliminary observations are encouraging. However, randomized controlled prospective trials of bronchoscopic instillation of rhDNase are needed to determine whether this form of treatment is justified.

All patients gave written informed consent for data publication.

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A25
Inhaled dry powder mannitol tolerability in cystic fibrosis (CF) patients is influenced by respiratory function and age
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Background
Inhaled mannitol dry powder is an osmotic agent which hydrates airway surface liquid and can be prescribed in adult CF patients with FEV1 >30%predicted (pp). A recent study showed its safety and tolerability also in patients aged 6-17 years [1]. The aim of our study was to evaluate tolerability in CF patients followed at our Center.

Materials and methods
We retrospectively evaluated data regarding patients who underwent mannitol tolerance test (MTT) between March 2017 and June 2019. Clinical and functional data regarding the year before and the period after MTT, were extracted.

Results
MTT was performed in 47 patients (F 68.08%), mean age 28.15 (range 11.38-50.51), mean ppFEV1 in the previous 12 months 71.6 ±17.7, MTT was tolerated (and mannitol treatment initiated) in 30 patients (63.83%) [group A], of which 7 were younger than 18; mean fall in ppFEV1 from baseline was 7.38 ±5.46%;17 patients (1 was younger than 18) did not tolerate MTT [group B]; mean fall of ppFEV1 from baseline was 14.1 ±7.44% (significantly higher than in group A); 6 patients presented delta ppFEV1 ≥20%, while 17 patients presented irritative cough. Patients in group B were older, though not significantly (mean age 30.20 ±9.86 vs 26.99 ±9.83); they had also lower mean ppFEV1 in the previous year (64.48 ±15.95 vs 75.7 ±17.57; p=0.03), and lower mean ppPEF25-75 in the previous year (29.11 ±16.73 vs 43.15 ±23.12; p=0.03); no difference was shown in sex and ppFVC.

Conclusions
MTT is feasible in pediatric and adult patients. MTT was proposed in patients with FEV1 >30% not tolerating hypertonic saline, or requiring an additional mucolytic agent, or a portable and faster mucolytic therapy. In our experience, mannitol therapy could be initiated in 64% of patients with these characteristics. The MTT positive outcome was shown to be influenced by a better respiratory function and a younger age.

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A26
Lung clearance index evaluation in detecting nocturnal hypoxemia in Cystic Fibrosis patients: toward a new diagnostic tool
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Italian Journal of Pediatrics 2020, 46(Suppl 1):A26

Background
Nocturnal hypoxemia adversely affects outcomes in patients with cystic fibrosis (CF). Although an early detection of this abnormality may be desirable, still its predictability remains uncertain. The Lung Clearance Index is a measure of lung ventilation distribution obtained from a multiple-breath washout technique (MBW), recently implemented in patients with CF. This study aimed to establish whether the LCI predicts nocturnal hypoxemia in patients with stable CF, with mild to moderate disease and normal diurnal gas exchange.

Materials and methods
31 stable patients (15 males, mean age 17.4±5.2 years) with mild to moderate CF, normoxic when awake, were enrolled. In all patients we performed nocturnal cardio-respiratory polygraphy, lung function measurement and MBW test to derive LCI values.

Results
Lung clearance index was abnormal in most of the patients and inversely correlated with mean nocturnal SpO2 (r=-0.880 p<0.01). A receiver operating characteristic (ROC) analysis, performed to assess whether LCI predicted nocturnal hypoxemia, revealed a high predictive accuracy of LCI for nocturnal desaturation (AUC=0.96; Youden index=0.79). Forced expiratory volume in 1 second (FEV1) was predictive only in patients with more severe airway obstruction, with a moderate degree of accuracy (AUC 0.71) (Table 1).

Conclusions
The LCI showed a high effectiveness in predicting nocturnal hypoxemia in stable patients with CF, particularly when compared with a traditional parameter of lung function such as FEV1.
A27 Chronic rhinosinusitis in cystic fibrosis: a review of surgical management and our surgical experience

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Background
Almost all the patients with Cystic Fibrosis (CF) present chronic rhinosinusitis (CRS). Clinical and basic scientific research, focusing on therapeutic strategies for CF-associated CRS, is limited; endoscopic sinus surgery (ESS) is an option for patients with CRS, it can help in management of infection, improve quality of life and stabilize lung function decline.

Material and methods
Pertinent studies published between January 2015 and January 2019 were selected by a Medline search accessed via PubMed and the Cochrane Library of titles and abstracts using the standard Boolean system; the words “endoscopic sinus surgery AND rhinosinusitis AND cystic fibrosis” were used as search string.

Results
Despite appropriate medical therapy, 20-60% of CF patients are going to require ESS; surgical intervention is generally reserved for those who have failed more conservative medical therapy [1]; to reduce pulmonary pathogen colonization, especially in transplant CF patients, is mandatory [2]. Proposed predictive criteria for ESS are: massive polyposis, prior history of ESS, high Lund-Mackay score, high SNORT-22 score and severe CFTR mutations [3]. Delay in surgery did not affect post-operative improvement [5]. A pre-operative image guidance can be useful due to anatomic differences in CF patients, especially in revision cases [6]. ESS procedure in pediatric patients is totally safe [7]. ESS also plays a critical role in reducing or eradicating pulmonary colonization of pathogens in CF patients [8]. Surgery leads to relieve nasal obstruction, decrease purulent nasal discharge, increase activity level and improve olfaction [9]. At our ENT-CF clinic, established 1989, CF patients are evaluated with CT and cone-beam CT (CBCT) for pediatric patients; radiological results are qualitatively and quantitatively evaluated using Lund-Mackay score and together with endoscopic Melzter’s Score and SNAQ-11 questionnaire are used for the assessment of a CF sinus score (CFSS). In the last 5 years, 88 patients (51.1% under 18 years old) underwent ESS with clinical and symptomatic improvement. Our experience is consistent with the results in the literature regarding similar strategies.

Conclusions
The treatment of CRS in CF is complex and challenging; currently available data are limited to mostly case series and further larger perspective studies are much needed. ESS has been shown to improve sinus and pulmonary bacterial colonization, as well as reducing patient symptoms. Increasing research suggested that a multi-disciplinary approach with ESS combined with topical and medical therapies offer the most optimal treatment for CF patients.

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Physiotherapy

A28 Effectiveness of energy conservation techniques in the performance of daily life activities in a group of patients with cystic fibrosis

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Background
The aim of pulmonary rehabilitation is to restore the cystic fibrosis (CF) patients to the highest possible level of independence. However, the natural history of CF is characterised by a progressive decline in lung function due to chronic pulmonary infections and recurrent exacerbations [1]. This leads to an increase in symptoms, such as dyspnoea and fatigue, and to intensification of treatments [2]; therefore, the advancement of the illness over-shadows the achieving of independence. Energy Conservation Techniques (ECTs), an educational intervention commonly used by occupational therapists, are recommended in the international pulmonary rehabilitation guidelines [3-4] and they help to avoid unnecessary or excessive use of energy during daily life activities (DLA) [5]. The primary objective of this study is to assess the effectiveness of ECTs in terms of reduction of energy expenditure, dyspnoea and fatigue perception.

Materials and methods
Seven patients were recruited from April to July 2019 in the Cystic Fibrosis Center ("Policlinico Umberto I" Hospital, Rome). All outcomes were measured during the execution of four tasks, using and not using ECTs: walking, tidying up, dressing, showering. Energy expenditure was measured using the accelerometer SenseWear Pro3 Armband, dyspnea was measured with the modified Borg scale, fatigue was assessed using a ten-point Likert type scale. Oxygen saturation (SpO2) and respiratory rate (RR) were also recorded at the end of each task.

Results
With ECTs, significant reductions in perceived breathlessness and fatigue scores were reported during walking (1.9±1.5 vs 0.8±1.1, p = 0.026; 1.5±1.0 vs 0.9±1.1, p = 0.034, respectively) and tidying up (1.4±1.0 vs 0.5±0.8, p = 0.039; 1.9±0.7 vs 0.8±0.7, p < 0.001, respectively). Significant decrease in energy expenditure was observed for activities as dressing (32.0±7.6 cal vs 22.6±12.5 cal; p = 0.041) and showering (40.0±15.0 cal vs 32.4±14.5 cal; p = 0.015). Walking SpO2 also improved with ECTs (93.3±2.7% vs 95.4±2.3%; p = 0.001) as well as RR during tidying up (20.7±1.7 vs 18.1±1.1 breaths/min; p = 0.026), dressing (21.0±1.3 vs 18.1±1.6 breaths/min; p = 0.027) and showering (20.4±0.8 vs 18.3±0.8 breaths/min; p = 0.017).

Conclusions
Occupational Therapy could supply an innovative contribution in the rehabilitation of patients with CF. It aims to enhance the patient’s independence, even in the context of frailty and advanced illness, by adopting Energy Conservation Techniques. Our data suggest that the use of ECTs in CF patients during DLA could reduce energy cost and dyspnoea and muscle fatigue perception, but further research is needed to support the use of energy conservation techniques among CF patients.

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A29
Intrapulmonary percussive ventilation (IPV): the effect on the frequency of pulmonary exacerbations in a group of pediatric patients with cystic fibrosis
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Background
In patients with cystic fibrosis (CF) the build-up of mucus in the lungs leads to infections and inflammation and eventually to deterioration in lung function [1]. To prevent them, chest physiotherapy is advocated for the clearance of mucus in the airways and the best airway clearance technique should be tailored to the individual [2]. Among these, Intrapulmonary Percussive Ventilation (IPV) is an intrathoracic device that provides continuous oscillation to the airways through the mouth and produces an alternating positive pressure. As a consequence, the vibration loosens the mucus allowing an easier expectoration and therefore improving the airway patency [3]. However, evidence on its efficacy, especially in children population, is still lacking. Therefore, the aim of this study is to assess the efficacy of IPV on the frequency of pulmonary exacerbations (PEx) and the changes in lung function in pediatric patients with CF.

Materials and methods
Pediatric CF patients followed at “Policlinico Umberto I” Hospital of Rome and prescribed with IPV treatment between November 2018 to July 2019 were retrospectively recruited. Data regarding number of PEx and lung function (FEV1, FVC, FEF25-75%) were collected and considered as primary and secondary outcomes, respectively. For each patient, comparison between data obtained after starting IPV and those collected from an equal time interval before starting IPV was performed.

Results
Nine patients (M/F: 3/6, mean age: 10.2 ± 3.2 years, mean body mass index: 16.5 ± 2.4 kg/m2) were recruited for analysis. Mean length of IPV treatment was 203 ± 94 days (range: 113 – 413 days). Spirometry at the moment of IPV prescription showed a mild-to-moderate impairment in lung function (FEV1: 77.4 ± 8.7% of predicted value). Use of IPV was associated with a significant decline in the rate of PEx (1.7 ± 1.3 with IPV vs 1.0 ± 1.2 before IPV, p = 0.014). A non-significant improvement in mean FEV1 (-1.7 ± 5.0% vs 2.5 ± 3.8% before and during IPV, respectively) and FVC (-1.6 ± 3.7% vs 2.5 ± 3.7% before and during IPV, respectively) changes was observed with IPV.

Conclusions
Use of IPV in children with CF is associated with a significant reduction in PEx and a positive trend in lung function. Further prospective studies are needed to confirm these results and to assess the efficacy of IPV on clinical and functional outcomes in CF pediatric populations.
Physiotherapy in a group of cystic fibrosis patients receiving extracorporeal lung support while awaiting lung transplantation: a retrospective observational study

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Italian Journal of Pediatrics 2020, 46(Suppl 1):A30

Background

Patients with cystic fibrosis (CF) waiting for lung transplantation (Tx) might need advanced therapies as extracorporeal lung support, that can be performed using extracorporeal membrane oxygenation (ECMO) and extracorporeal CO2 removal (Prolung®) [1]. These therapies can impede the implementation of a physiotherapy program, so determining a situation of deconditioning that can reduce the chances of survival before and after lung transplantation [2]. Primary aim of this study is to investigate the effect of a physiotherapy program on peri-transplant mortality and post-transplant ICU stay in CF patients that received extracorporeal lung support as a bridge to lung transplantation.

Materials and methods

A retrospective observational analysis was conducted on data collected from CF patients admitted to the Transplant Intensive Care Unit of “Policlinico Umberto I” Hospital of Rome from 2010 to 2017, receiving extracorporeal lung support while awaiting lung transplantation. Data were retrospectively collected from medical records: demographic data, tracheostomy status, days of extracorporeal lung support, days in ICU (total and post-Tx) and mortality rates. Patients were divided in two groups according to the level of physical activity (PA) performed during physiotherapy sessions, measured by the ICU Mobility Scale (i.e. low activity ≤ 4 points vs high activity > 4 points).

Results

Data from twenty patients were obtained for the analysis (13 F; mean age: 30.92 ± 10.32 yrs). Overall mortality was 55%. Among those who underwent lung Tx (15/20), peri-transplant mortality was 40% (6/15). Twelve out of twenty patients (60%) performed low levels of PA during their ICU admission. No differences were observed between groups with regards to anthropometric features. Peri-transplant mortality rates differed significantly between groups, being 85.7% vs 0% (p = 0.001) among patients with low and high levels of PA, respectively. Furthermore, length of post-transplant ICU stay was significantly higher for patients with low level of PA (27 [22 - 61] vs 14.5 [12.2 - 15.7] days, p < 0.001).

Conclusions

Higher levels of physical activity may provide better outcomes in terms of peri-transplant mortality and post-transplant ICU stay in CF patients receiving extracorporeal lung support while awaiting lung transplantation. Further studies on a larger sample are needed to fully evaluate benefits and risks of this treatment modality.

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Preventive use of nocturnal non invasive ventilation in Cystic Fibrosis: a pilot study

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Italian Journal of Pediatrics 2020, 46(Suppl 1):A31

Background

In patients with cystic fibrosis (CF) non-invasive ventilation (NIV) improves lung mechanics increasing airflow and gas exchange and decreasing the work of breathing; however, to date, there are no standardized criteria to indicate to whom and when NIV should be started. We investigated whether an early initiation of nocturnal NIV, as a prevention before respiratory failure occurs, affects Lung Clearance Index (LCI) and other clinical and functional outcomes.

Material and methods

7 normoxic patients (4 males, age 15-34 years, all BMI <18) without history of pneumothorax or presence of blebs were enrolled. All patients were stable at initiation of the treatment. In the first study day spirometry, multiple-breath washout of an inert gas to derive LCI, nocturnal cardiorespiratory polygraphy (PG) were performed. An acclimatization to NIV session, using a bi-level model, to establish the pressures tolerated by each patient was performed.

Results

Treatment with NIV significantly reduced nocturnal respiratory rate (28.4±4.2 vs23.5±4.9) and improved nocturnal SaO2 (91.9±1.0 vs 99.4±1.0), without affecting nocturnal mean values of TcCO2 (38.7±2.3 vs 39.7±2.3, ns). After one year of nocturnal treatment with NIV, FEV1% was stable but the LCI significantly improved (from 17.5 to 15.5). Moreover, the mean number of exacerbation was significantly decreasing during the treatment year (4.7±2.2, p<0.001). Gas exchange also remained stable as shown by unchanged values of SPO2 and TcCO2 (Table 1).

Conclusions

The early initiation of NIV significantly improved the LCI value, index of global ventilation distribution, and halved the number of exacerbations/year. The novelty of this finding relay in the fact that so far nocturnal NIV in CF has been used during exacerbations or in hypercapnic patients to slow the progression of respiratory failure. A preventive effect of early treatment with NIV has never been suggested. In addition, the effect of NIV on ventilation distribution has never explored before.
A32

High Flow Nasal Cannula (HFNC): an alternative to Non Invasive Ventilation in Cystic Fibrosis severe lung disease

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**Italian Journal of Pediatrics 2020, 46(Suppl 1):A32**

**Background**
Non Invasive Ventilation (NIV) in Cystic Fibrosis (CF) is a bridge to lung transplantation in patients (pts) with end-stage lung disease and a support during acute exacerbations, especially in those with hypercapnia, to avoid ventilator failure. A contraindication for NIV is the occurrence of pneumothorax (PNX), a fearsome complication in advanced CF lung disease. We report our experience using High Flow Nasal Cannula (HFNC) in adult CF pts with respiratory insufficiency secondary to severe lung disease which had to discontinue NIV for spontaneous PNX [1].

**Materials and methods**
3 adult CF patients (1 F, 42 years; 2 M, 28 and 43 years) with severe lung disease (FEV1 < 30%, at rest PaO2 50-60 mmHg, PaCO2>45 mmHg), on nocturnal oxygen therapy and NIV (PSV, IPAP 12-15, EPAP 6), chronic respiratory P. aeruginosa infection, > 3 respiratory exacerbations/year, pancreatic insufficiency and BMI < 19; 2 waiting for lung transplantation) presented with spontaneous PNX during an exacerbation (F with a small one < 2 cm, the others 2 with large PNX treated with chest tube).

**Results**
After the onset of PNX patients were switched to HFNC with flow of 25-35L/min, temperature 34-37°C and a FiO2 as required to maintain adequate blood oxygenation (> 93%). Arterial PaCO2 remained stable (<50 mmHg). At time of discharge HFNC was prescribed at home (Fisher and Paykel My Airvo and Optiflow Nasal cannulae). Observational period from acute exacerbation due to PNX ranges from 10 to 28 months: compliance to HFNC is optimal (8 hours/night), blood gases are stable and no concern about safety have raised. Reported comfort was high.

**Conclusions**
HFNC represents a safety alternative to NIV in CF patient with chronic respiratory failure and light compensated hypercapnia, when the use of NIV is not possible as on occurrence of PNX.

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A33

Occupational therapy: another ally against cystic fibrosis? A survey among patients and carers

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**Italian Journal of Pediatrics 2020, 46(Suppl 1):A33**

**Background**
Occupational therapy (OT) is a client-centered health profession concerned with promoting health and quality of life through occupation [1]. In the field of respiratory diseases, OT is highly recommended in the care of patients with chronic obstructive pulmonary disease [2], its practice is still not very common in cystic fibrosis (CF). The purpose of this study is to investigate patients’ experience and opinions about OT interventions.

**Materials and methods**
A survey was conducted among patients with CF and their carers using Survey Monkey®. Nine questions have been included, which investigated the level of usefulness of the OT interventions proposed in the survey cover letter. The survey was diffused through the website of the Italian patients’ association (LIFC Onlus), and by sending the link via social network.

**Results**
128 returned surveys were completed by patients (34%) and carers (66%). This survey shows that 83% of patients have never been offered any OT interventions, education in techniques of energy conservation, playful and manual-representative activities for anxiety management or environmental adaptations. The inclusion of OT in the treatment program is considered very helpful by 44% of respondents against the 3% that considered this useless. With regards to the questions on the relevance and usefulness of the other interventions proposed for patients with CF, five options have been included: not at all, not much, enough, greatly, very much. The possibility to benefit from learning and use of energy conservation techniques was considered “enough” by 38% of respondents. The help that the performance of gaming activities and manual-representative activities to alleviate a state of anxiety and the usefulness of devices and environmental adaptations have been considered “greatly” by 37% and 35% respectively of the respondents.

**Conclusions**
The last question of the survey was optional, but despite this there were 102 out of 130 responses. This result shows the great interest
that the OT has for CF patients and their carers, as many find it useful for improving the performance of daily life activities and for anxiety management. In particular, the answers show that the OT can be mostly useful to those who have a serious condition or are in an advanced stage of the disease. From these results, we can deduce that there is a great deal of interest by patients to try occupational therapy in CF, for which an implementation in clinical practice is suggested. It is also important to conduct clinical studies on this topic to increase scientific research.

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A34

“F (accio) C (entro)”: project for a smartphone application to increase adherence to aerosol treatment in adolescents with cystic fibrosis

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Italian Journal of Pediatrics 2020, 46(Suppl 1):A34

Background
Patients with Cystic Fibrosis are daily exposed to a high therapeutic burden represented by respiratory physiotherapy, therapy by aerosol, oral, intravenous and physical activity. Numerous studies underline how during adolescence the therapy adherence, that is undergoing treatments at the right time of the day, in the right sequence and dosage, considerably decreases with negative consequences in terms of: health status, quality of life and hospitalization [1,2]. From these considerations was born “Faccio Centro” the project of a smartphone application for adolescents with CF designed as a tool to increase the adherence to aerosol therapy and physiotherapy guiding them in the process of independence from a parental management of the therapy. Considering the age target, an application has been identified as the most appropriate tool to meet these needs, as the mobile phone is commonly used by adolescents and some studies underline how telemedicine could be a tool to improve the self-management in the FC [3,4].

Materials and methods
“Faccio Centro” is a project who integrating the results of the research conducted on the main biomedical databases, google scholar, apple store, android store and the interview with adolescents patient of the “cystic fibrosis centre” of the Bufalini Hospital in Cesena. In the app’s homepage the daily therapies appear in the temporal order of execution with notes about the correct assumption modalities, a graph indicates the percentage of therapy carried out and there is written the date of the next check with a customizable reminder attached. The patients can set a reminder alarm for each therapy and check if they have performed it or not and the checks will no longer be modifiable after midnight of the same day. In other sections user can interact autonomously with the professionals of the centre by sending an email directly to the most suitable figure to answer his question (doctor, nurse, physiotherapist) and also they can download a summary table of therapies conducted each month with indications on the trend of adherence.

Conclusions
The “Faccio Centro” APP designed to be tailored to the patients, simple, customizable, engaging and interactive could be a support tool for adolescents in the autonomous management of therapy and to contain the decline in adherence that has been recorded in the transition from childhood to adolescence. The next step will be to create a prototype of the APP for the patients of the centre to assess its impact on adherence.

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Quality improvement

A35

External Quality Assessment in Cystic Fibrosis Genetic Testing: the Italian Experience

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Italian Journal of Pediatrics 2020, 46(Suppl 1):A35

Background
Molecular analysis of CFTR gene is a key step in the diagnosis of Cystic Fibrosis (CF), carrier testing and prenatal diagnosis; it represent the most frequent genetic test carried out in Italy [1]. An error in the genotype analysis or an incorrect or inaccurate interpretation may have consequences on the life choices of patients and their family. In this context, it is essential that laboratories are competent to perform tests at an acceptable standard and to make sense of the information provided by the test. Monitoring genetic laboratories is an obligation for the National Health System as part of its mandate to protect the health and quality of life of citizens. The Italian External Quality Assessment (IEQA) for Cystic Fibrosis started in 2001; it was coordinated by the Istituto Superiore di Sanità (ISS) [2,3]. The aim of the activity is to monitor and to improve quality of genetic testing performed by Italian laboratories. In 2009 the activity was published in the Official Bulletin of the Italian Republic (G.U. n.199 del 28/08/2009) and a marking system was established.

Materials and methods
Participation is voluntary and open to both public and private Italian laboratories. Laboratories pay a fee to participate. The IEQA scheme organizer and national experts provide advice on the scientific context of the scheme and take decisions and educational actions for the development of the program. ISS provides four validated samples of genomic purified DNA, annually. All samples have been selected to represent typical mutations of the gene; they are distributed with mock data identifications, mock clinical patient detail and technical data. Poor performance was marked since 2013. All data are managed through a web utility designed to simplify communication and data sharing among ISS, laboratories and assessors. Laboratories are asked to process samples and to return results of genotyping and a full interpretative report. Scheme is strictly anonymous. Five National assessors evaluate laboratory results, according to established criteria.

Results
Until now 15 rounds have been completed and overall 90 Italian laboratories have been monitored. Participants laboratories returned acceptable analytical results, in recent years compared to previous ones, but we still registered a number of reports with not complete or not accurate interpretation.

Conclusions
Our observation highlight that laboratories that constantly participate to the EQA return more complete and accurate results. EQA should
be viewed as educational tool and used to help direct improvement efforts in the laboratory.

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A36
Single versus bilateral sweat chloride testing
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Italian Journal of Pediatrics 2020, 46(Suppl 1):A36

Background
The diagnosis of cystic fibrosis (CF) requires confirmatory diagnostic tests that should always include a sweat test, even when two CF-causing mutations are identified. Sweat testing requires experienced staff who should follow standard operating procedures. There are clear guidelines available for laboratories providing a sweat test service that recommend to collect sweat from both arms to decrease the probability of having an insufficient sweat quantity. Some evidences were published regarding the real impact of this practice. In our CF centre we changed our procedure in January 2018 from sweat test on one arm to sweat test on both arms. To evaluate the effectiveness of these two procedures we compared data.

Materials and methods
In our centre we regularly perform the sweat test using the Macroduct modified method (Iontophoresis stimulation with pilocarpin gel disc, collection on filter paper, chloride titration by coulometry). We compared sweat chloride records in 2 different periods: June 2016 – December 2017 (single sweat test) and January 2018 – July 2019 (bilateral testing). In these two periods the technical staff dedicated to sweat testing was the same. Our CF centre perform internal quality control as recommended (mean CV% for all 3 levels: 6.85%) and participate in the national External Quality Assessment scheme (overall performance in 2018: 100%). Statistical analyses included Chi-square test at 0.05 level of significance.

Results
Results are showed in Table 1
These results show that collecting sweat from both arms don’t improve the proportion of tests with sufficient sweat weight; anyway bilateral testing could be used as internal quality control.

Conclusions
Sweat testing is a crucial laboratory test for CF diagnosis. To maintain a high quality performance of this test it’s mandatory to retrain the technical staff and check the equipment regularly. A single test procedure can guarantee a good sweat test performance taking also into account the reimbursement of the test which is far from the real cost.

| Table 1 (abstract A36). Comparative analysis |
|-------------------------------------------|
|                                | Single sweat test | Bilateral sweat test |
| subjects with QS                | 310                | 229                  |
| subjects with at least 1 QNS     | 19                 | 14                   |
| subjects with 2 or more QNS      | 5                  | 6                    |
| subjects tested                  | 334                | 249                  |
| QS=sweat quantity sufficient; QNS=sweat quantity not sufficient |
| Chi square test = 0.642; p=0.725 |

Psychology
A37
A proposal for a new assessment tool of burnout in italian CF healthcare workers
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Italian Journal of Pediatrics 2020, 46(Suppl 1):A37

Background
The assessment of burnout is important to understand the wellness of healthcare workers and the quality of their performance. There are many tests for the analysis of burnout, such as the Maslach Burnout Inventory (MBI) [1], which are usually generic and not specific for workers that deal with chronic diseases, in particular with Cystic Fibrosis (CF). The aim of this project is to implement MBI tool with CF-related items to better understand burnout phenomenon in health care workers that take care of patients with Cystic Fibrosis and point out its characteristics.

Materials and methods
After a literature review [2,3] and analysis, specific fields were selected by psychologists focus group and proposed to multiprofessional group of Adult Committee of Italian Cystic Fibrosis Society.

Results
New nine statements were chosen, divided by three main psychological items (Powerlessness, Framework, Contention) and they will be presented to CF community of healthcare professionals, in addition to the MBI. A subgroup analysis will be performed to validate climetric properties of the new version of CF-related MBI. Descriptive and job related data were included.

Conclusions
The introduction of a questionnaire which is specific for the pathology could be a more accurate evaluation tool to assess burnout in CF healthcare workers, with the aim of finding and treating in advance the discomfort of the individual worker, but also of being able
to efficiently organize the team. Therefore, our purpose is to present this test to Italian CF healthcare workers to understand its effectiveness and its benefits in clinical practice.

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Comorbidities
A38 Early detection of glucose derangements in children with cystic fibrosis Giuseppe Napolitano, Emanuela Rossitti, Anna Coruzzo, Angela Sepe, Antonella Tosco, Enza Mazzoli, Valentina Fattorussi, Adriana Franzese, Valeria Raia Cystic Fibrosis Center, Department of Translational Medical Sciences University of Naples Federico II, Naples, Italy; 2Section of Pediatrics, Regional Center of Pediatric Diabetology, Clinical Department of Maternal and Child Health, University of Naples Federico II, Naples, Italy; 3Section of Pediatrics, Regional Center of Pediatric Diabetology, Department of Translational Medical Science, University of Naples Federico II, Naples, Italy

Materials and methods
We retrospectively collected data regarding children with CF in stable clinical condition annually evaluated by OGTT. Patients were classified according to ISPAD 2018 criteria: CFRD, fasting glucose > 126 mg/dl, CFRD, Non Fasting Hyperglycemia (CFRD-nonFH), 2 hours postload glucose > 200 mg/dl during OGTT; Impaired Glucose Tolerance (IGT), 2 hours postload glucose 140 to 199 mg/dl during OGTT; Indeterminate (INDET), fasting glucose < 126 mg/dl and 2 hours postload glucose < 200 mg/dl, but with glucose > a 200 mg/dl during intermediate times at OGTT (T30-T90 minutes). Moreover we classified as Abnormal Glucose Tolerance 140 (AGT140) those subjects with glucose 140 to 200 mg/dl at intermediate times of OGTT.

Results
Data from 72 patients (51.4%, F), 318 total OGTT, were collected. Mean age was 6.2±1.96 ys at first OGTT (range 3.7-9.5 ys). At the time of the first observation 50/72 (69.4%) showed glucose derangements: 3 CFRD (4.2%), 16 IGT (22.2%), 5 INDET (6.9%), 26 AGT140 (36.1%). 6/72 started insulin therapy (3 CFRD, 3 IGT). 59/66 (89.3%) subjects who did not start insulin therapy, annually performed an OGTT for a mean follow up of 5.8±3.4 ys. At the last OGTT, 42/59 (71.2%) showed a glucose derangement: 6/59 (10.2%) CFRD (mean age: mean 11±2.3 yrs), 11 IGT (18.6%), 5 INDET (8.5%), 20 AGT140 (33.9%). During follow-up no patient with normal glucose tolerance at first OGTT developed CFRD, while 9/24 AGT140 group (37.5%) developed IGT/CFRD. Preliminary data showed that there was no progression towards glyco-metabolic cathegories in patients who performed insulin therapy.

Conclusions
The high prevalence of glyco-metabolic derangements in CF children < 10 years of age suggests the relevance of OGTT as a metabolic screening tool before 10 years, differently from what reported in current recommendations. Moreover, the potential evolution to CFRD also for AGT140 group, not yet identified as at risk for glyco-metabolic derangements, suggests the need of longer-term studies to better define evolution of different glucose alterations in CF children.

A39 Prevalence of urinary incontinence in female with cystic fibrosis followed at the Cesena’s CF Regional Centre Elena Balestri, Virginia Magnani, Stefania Dall Ara, Cinzia Grazioli, Maura Ambromi, Fiorella Battisti U.O. Medicae Riabilitativa, Bufalini Hospital, Cesena, Italy; 2University of Bologna, Bologna, Italy; 3Cystic Fibrosis Regional Center, Bufalini Hospital, Cesena, Italy

Background
Urinary incontinence is today a recognized problem and it is reported in various studies in literature. The main cause of UI is chronic cough, which leads to a progressive weakness of the pelvic floor muscles. The aim of the study is to evaluate the prevalence of urinary incontinence in patients with cystic fibrosis followed at the Cesena’s CF Regional Centre and to determine the presence or absence of a correlation between incontinence and age, body mass index and lung function.

Materials and methods
The International Consultation on Incontinence Questionnaire Short Form (ICIQ-UI SF) was administered to female patients aged 10 years and older during routine visits, in a period from November 2018 to May 2019. Patients who received lung transplantation were excluded from the study. Clinical data of participants were collected including height, weight, forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and expiratory flow medium forced (MEF 75/25). FVC, FEV1 and MEF 75/25 were measured using spirometry, performed on the same day the questionnaire was administered. A statistical analysis was carried out by t-test, a significance level of 95% was considered.

Results
Forty-nine (98%) of 50 eligible patients (age: 10–53 years) participated. Twenty patients (41%) reported urinary incontinence. The presence of urinary incontinence was associated with increasing age. There is a correlation between incontinence and lung function (measured by FEV1 and MEF 75/25), although it’s not statistically significant (p = 0.06). No correlation was found between UI and body mass index or lung function measured by FVC (Table 1). All incontinent female reported stress UI; the situations that most commonly determine urine losses are coughing/sneezing, physical activity and laughing respectively in 80%, 20% and 10% of the patients. 94% of patients reported that the incontinence doesn’t impact on their daily life.

Conclusions
Urinary incontinence is a frequent and underestimated condition that commonly affects women with cystic fibrosis, although this problem is often not reported by patients to their physician or physiotherapist, probably due to embarrassment. It’s important to identify patients with incontinence because simple exercises to strengthen the pelvic floor muscles can improve the situation. Investigating the presence of UI should become part of routine visits.

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Table 1 (abstract A39). Clinical data of the Study Population

| Characteristics   | Incontinent (n=20) | Continent (n=29) | p-value |
|-------------------|-------------------|------------------|---------|
| Age (years)       | 27.4 (13.98)      | 18.14 (7.52)     | 0.01    |
| BMI (kg/m2)       | 20.41 (4.03)      | 20.01 (3.03)     | 0.70    |
| FEV1 (% predicted)| 74.29 (26.65)     | 86.91 (27.03)    | 0.06    |
| FVC (% predicted) | 87.39 (20.55)     | 95.10 (20.20)    | 0.20    |
| MEFF5/25 (% predicted) | 48.06 (33.56) | 63.83 (37.03)    | 0.06    |

Data are shown as mean with standard deviation

Case reports

A40

A rare association: Cystic fibrosis in patient with Down syndrome

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Background

Cystic fibrosis (CF) is a multisystemic hereditary, incurable and chronic disease which causes severe damages to respiratory and digestive tracts. It is the most common genetically inherited disease among caucasians. This disease is caused by defects in CF genes, the so-called mutations in cystic fibrosis transmembrane conductance regulator (CFTR) gene population.

Case Report

R.D.G. is a SGA newborn with signs of fetal malnutrition, clinical/dysmorphisms features compatible with Down Syndrome, born at 38.1 weeks of gestational age with caesarean section. Birth weight 2.035 kg. At birth he showed a mild respiratory distress and difficulty in feeding so was admitted to NICU for a month. Because of the presence of dysphormic features it has been performed a standard karyotype that showed 47 chromosomes and the presence of trisomy 21. The patient was asked to repeat a neonatal screening for abnormal value of IRT and a sweat test, which wasn’t performed because of recurrent bronchitis. After the discharge the patient showed many episodes of respiratory infections including some episodes of bronchitis with fever and cough. At the age of seven months, he was admitted to Hospital for cough, fever and dyspnea; it was therefore started empirical antibiotic therapy, first with amoxicillin/clavulanic acid then replaced with clarithromycin, but with very slow improvement. For an improved clinical evaluation, the patient had undergone further assessment: there were performed sweat tests that led to pathological results: 128 mEq/L, 137 mEq/L and 138 mEq/L. Chymotripsine and fecal elastases were abnormal in multiple evaluations. Chest X-ray showed multiple pneumonias. Colurtal sputum showed the presence of S. Maltophilia so we started intravenous cefalosporine with improved growth and respiratory symptoms.

Conclusion

The combination of two genetic pathologies with an unfavorable prognosis is very uncommon. In literature the association of cystic fibrosis and down syndrome is rare and accidental. Parents gave consent to patient data publication.

A41

A complicated association between two different genetic disorders: Spinal Muscular Atrophy and Cystic Fibrosis

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Background

Type 1 Spinal Muscolar Atrophy (SMA1) is a genetic disorder that affects the spinal motor neuron; the most common form is an autosomic recessive defect of the survival motor neuron gene 1 (SMN1); it generally onsets before 6 months of life presenting with severe hypotonic weakness in the lower limbs, respiratory distress, weak cry, and poor feeding [1]. In several cases Cystic Fibrosis (CF) poor nutritional status is associated to severe malabsorption. In this case the neuromuscular manifestations may involve legs with numbness, tingling, pain, weakness and unsteadiness of gait. We describe a rare case of a patient affected both by CF and SMA1 associated to concomitant clinical manifestations.

Case Report

A female 13 months-old was affected by CF with pancreatic insufficiency, diagnosed through a positive NBS and two CF-causing mutations [F508del/4016insT] at CFTR genetic analysis. In the first months of life, she was hospitalized for recurrent respiratory infections, poorly responsive to conventional treatment with oral/intravenous antibiotics and physiotherapy. Contemporary the patient showed a poor growth status despite PERT and progressively a severe hypotonia with delayed acquisition of developmental milestones, not elicitable osteotendinous reflexes, tongue fasciculations with lack of cough reflex. Based on these symptoms Motoreplex panel (analysis of genes causing muscle disorders) was performed resulting in a homozygous deletion for SMN1, compatible with diagnosis of type 1 SMA. A modified personalized physiotherapy program was promptly started, including airway clearance techniques with intrapulmonary percussive ventilation (IPV) and mechanical insufflation-exsufflation. Total enteral feeding by percutaneous endoscopic gastrostomy (PEG) was set up with improvement of clinical and nutritional conditions. The patient started experimental therapy with Nusinersen, a modified antisense oligonucleotide that increases the production of full-length SMN protein, approved for intrathecal use in paediatric and adult patients with SMA. It has been demonstrated that early treatment of this drug is crucial [2] to improve motor development in SMA.

Conclusion

Based on our knowledge, this is the first case in which these two genetic diseases occur in the same patient. The progressive neuromuscular weakness that characterizes SMA may impact on delayed mucociliary clearance affecting progressive lung disease and frequent pulmonary exacerbations. IPV is an adequate alternative to conventional chest physiotherapy in this case, also in order to impact upper airway muscle weakness and spinal deformity. We hope that therapy with Nusinersen, and a continuous personalized physiotherapy program may impact on natural history of both diseases and potentially on survival. Patient’s parents gave consent for the publication of clinical data.
Antiviral therapy\(^1\)\(^2\). Patient's parents gave consent for the publication of clinical data.

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Nursing

Evaluation of “home nursing service” for intravenous antibiotics administration in cystic fibrosis patients: 1-year experience in Livorno

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Background

Endobronchial infections in cystic fibrosis (CF) can require treatment with intravenous (i.v.) antibiotics for several days in the hospital, affecting health costs and quality of life for patients and their families. Home i.v. therapy can be an equally effective alternative\(^1\); in Italy usually the patient has to manage, prepare and administer the therapy himself or with the help of caregiver. Home care of qualified nurses (“home nursing service”, HNS) can lead to an improvement of assistance, quality of life and therapeutic compliance\(^2\).

Materials and methods

In Livorno, since August 2018, patients who needed i.v. antibiotic were offered the HNS, seven days a week, to reconstitute and administer i.v. drugs. Three qualified nurses trained in CF, performed the HNS. In every patient, we evaluated, with a written anonymous questionnaire the acceptance and satisfaction of HNS, the compliance with the prescribed therapeutic duration, the number and type of adverse drug reactions and the procedural anxiety.

Results

We enrolled 6 adult with CF (median age: 26.5 years), in follow-up in Livorno CF Support Centre, to receive HNS. In previous years, all these had already received i.v. therapy at home, with the help of a caregiver (usually a trained family member). In this year 10 antibiotic cycles were performed overall with HNS; during i.v. therapy 5/6 patients had peripheral venous catheter (PVC), 1/6 had central venous catheter. Five patients immediately accepted the HNS gladly, while one accepted afterward, for the initial fear of “privacy violation”. Contrary to the past, the therapeutic compliance was complete: always the prescribed duration of i.v. therapy has been maintained. None had any allergic drugs reactions; in two cases, with PVC, the presence of the nurse at home has allowed detection of early signs of phlebitis. HNS satisfaction was assessed positively by all patients (median score: 4.8/5). The level of procedural anxiety before the introduction of HNS and during HNS (self-declared with the questionnaire),
showed a reduction (median scores: 3.8/5 before HNS and 1.2/5 during HNS).

Conclusions
The results of this preliminary study showed that all patients are satisfied with their current HNS. The nurses played an important role in improving the home i.v. therapy by supervising the patient and identifying precisely the potential problems. Our experience, which we have intention to expand with other evaluations, suggests that HNS provides positive links between the hospital and patient’s home life, reducing anxiety and improving the therapeutic compliance.

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A44
Cystic fibrosis patient: proactive approach for venous heritage preservation
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Background
Cystic Fibrosis (CF) patients are admitted to hospital during their lifetime. In hospital, and at home, the drug administration frequently takes place intravenously. According to a proactive approach, a single vascular device should be placed, thus allowing to complete the whole diagnostic-treatment pathway. The benefits of such a choice have consequences both on the quality of life of the patient and on cost saving: nurses won’t waste time looking for a new vascular access, and there will be a reduction in phlebitis, infections and extravasation. Such an approach when numerous attempts to cannulate are necessary. Patients with chronic diseases are usually mistrustful towards changes, in particular about therapies or devices. In consideration of the fact the CF patient should benefit from a central access, due to the kind of drugs to administer, a compromise had to be reached. The nurses, sometimes have more difficulty in accepting new procedures or devices for their patients or for the work organization. A new vascular device needs a time of placement which cannot be very short. The aim of our work is to reduce the number of venipunctures and improve the quality of life of patients.

Materials and methods

• A long cannula has been chosen, power-injectable and in soft polyurethane so that it can be placed both in superficial and deep veins and could be used for blood collection too.
• Evaluation of the problem has been detected.
• National and international guidelines have been consulted.
• Getting in touch with devices producers has been made, as well as choice of the device (power glide).
• Theoretical and practical training have been carried out by the Clinical Specialist of the producer (BARD).
• Tutorship with Clinical Specialist until autonomy has been followed.
• Purchase of Ultrasound for venipuncture guidance has been used.

Results
Patients ‘point of view: Satisfaction for the dwell time of the device; they report less pain during placement; new patients asked for the device when admitted to hospital. Nurse ‘point of view: satisfaction for the dwell time of the device; decrease in the number of venipunctures; increase in technical skills (US guidance during venipuncture).

Preliminary data from 140 observations have the following results: average dwell time: 16 days; reasons for removal: end of therapy: 51%; thrombophlebitis: 4.4%; hematoma: 0.6%; pain: 2.5%; displacement: 2.5%; pre-dismissal change: 0.6%; malfunction: 3.1%.

Conclusions
Following suggestions:
• complications survey: phlebitis (which drug, which vein)
• promote and adopt other devices in order to reduce thrombophlebitis due to the drugs (PICC?)
• keep on with monitoring vascular access.

A45
Virtual reality as an alternative therapeutic option for the management of pain in children with Cystic Fibrosis
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Background
Virtual reality (VR) is defined by “the use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real world objects and events” [1]. VR quickly became a subject of study in the whole medical-therapeutic field, presenting itself as a valid alternative to Exposure Therapy [2], to improve the treatment of some pathologies and the recovery of cognitive, mental or motor functions.

Materials and methods
50 patients with Cystic Fibrosis aged between 8 and 18 years, were consecutively enrolled in a pilot study approved by the Ethical Committee of the University of Naples Federico II, in which VR was suggested as a tool for pain reduction during venipuncture and for anxiety reduction during intravenous antibiotics. To realize the VR, a head-mounted display and a cell phone inserted inside it were used. The display was positioned before the start of the procedure along with an oximeter, in order to investigate changes in heart rate and saturation; the display and the oximeter were removed only at the end of the procedure. The pain scale Numerical Rating Scale (NRS) was used to assess the perceived pain, while the State-Trait Anxiety Inventory questionnaire was used to assess the anxiety (S.T.A.I.). It was decided to set up the study as a case-control on the same patient. For each procedure questionnaires were administered before VR and at the end of the procedure.

Results
Preliminary results have shown a significant reduction in pain and anxiety when VR was used. The use of VR has also proved to be not harmful to patient safety, ensuring the completion of the procedure in safety. All but one patient who used VR reported lower pain than that reported without using it.

Conclusions
Although one of the most known use of VR in the scientific literature is for treating phobias and social disorders [3], VR has been demonstrated a safe method to control pain and anxiety in this cohort of patients. The reduction of the Heart Rate when the VR is used
indicates a general relaxation of the patient and alienation from the procedures, which helped to perceive less pain.

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