

Indication TP: Mucoviscidose

DES pneumologie IDF

13/01/23

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Disclosure

No disclosure related to that presentation

116
Déclarations

€35 807
Euros au total

Nb déclarations et montant total par entreprise



^ Entreprise Émmetrice	^ Nb déclarations	^ Montant total (€)
BIOTEST	19	13 838
CSL BEHRING SA	11	8 217
Novartis	28	7 685
Astellas Pharma	17	2 432
Astrazeneca	8	1 801
Chiesi	3	1 184
OXYVIE S.A.S	2	262
MSD	17	130
Medtronic	4	120
LivaNova	1	36
LFB	2	35
SANOFI SA	1	32
GlaxoSmithKline	1	20

Indication TP: Spécificités de la Mucoviscidose

- **Patient Jeune**
 - Comorbidités stéréotypées/déjà prises en charge: diabète, SOD, hépatopathie
 - Maturité
 - Taille/poids (retard staturo pondéral)
- **Parcours de soins complexes**
 - Patients experts
 - Complications des soins:
 - Thrombose sur PAC/KT
 - Aminosides: surdité/ins rénale
- **Bactéries multirésistantes**
 - B. Cepacia Cenocepacia (genomovar 3)
 - M. Abcessus

Indication TP: Spécificités de la Mucoviscidose

Lung Transplant Referral for Individuals with Cystic Fibrosis: Cystic Fibrosis Foundation Consensus Guidelines

J Cyst Fibros. 2019 May ; 18(3): 321–333. doi:10.1016/j.jcf.2019.03.002.

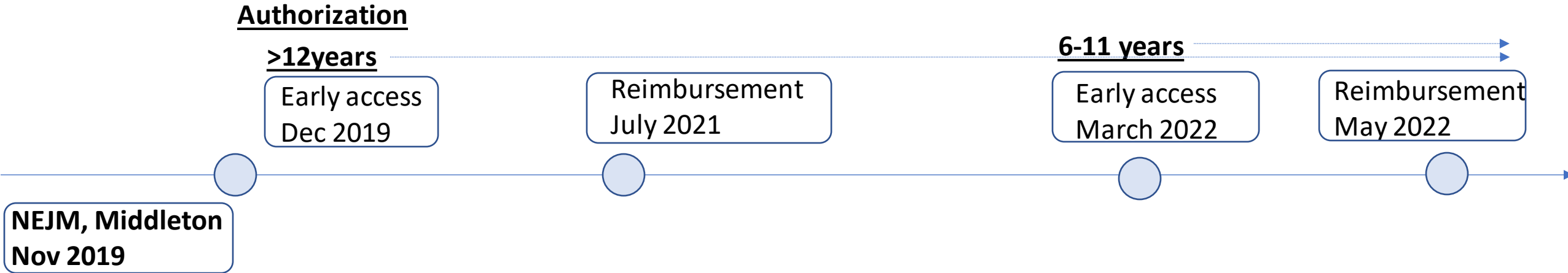
≠ scénarios

- IRC progressive
- ATB dpd+ fct ok
- PNO
- Hémoptysie



- IRC + PaO₂<60 mmHg ou PaCO₂>50mmHg
- VNI long terme
- HTAP
- Hospi fréquente pour EA
- Déclin rapide des EFR (baisse 30% VEMS)
- NYHA 4

Is CF still an indication for LTx?



Elexacaftor–Tezacaftor–Ivacaftor for Cystic Fibrosis with a Single Phe508del Allele

P.G. Middleton, M.A. Mall, P. Dřevínek, L.C. Lands, E.F. McKone, D. Polineni, B.W. Ramsey, J.L. Taylor-Cousar, E. Tullis, F. Vermeulen, G. Marigowda, C.M. McKee, S.M. Moskowitz, N. Nair, J. Savage, C. Simard, S. Tian, D. Waltz, F. Xuan, S.M. Rowe, and R. Jain, for the VX17-445-102 Study Group*

Is CF still an indication for LTx?

Authorization

>12years

Early access
Dec 2019

Reimbursement
July 2021

6-11 years

Early access
March 2022

Reimbursement
May 2022

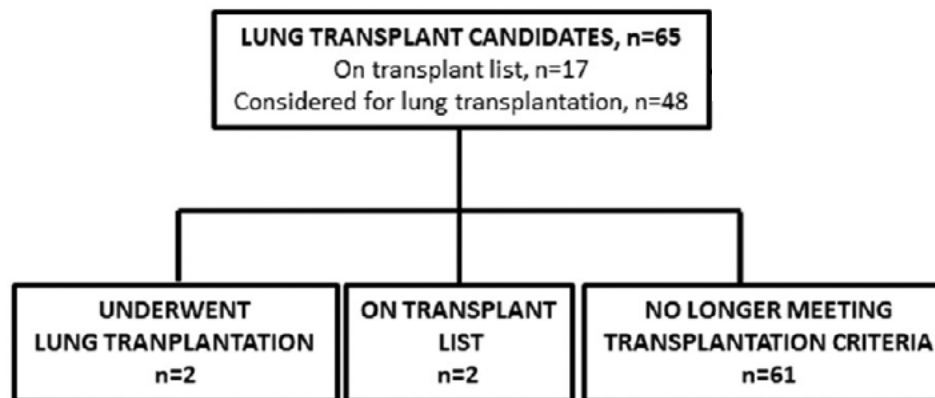
NEJM, Middleton
Nov 2019

<2020:

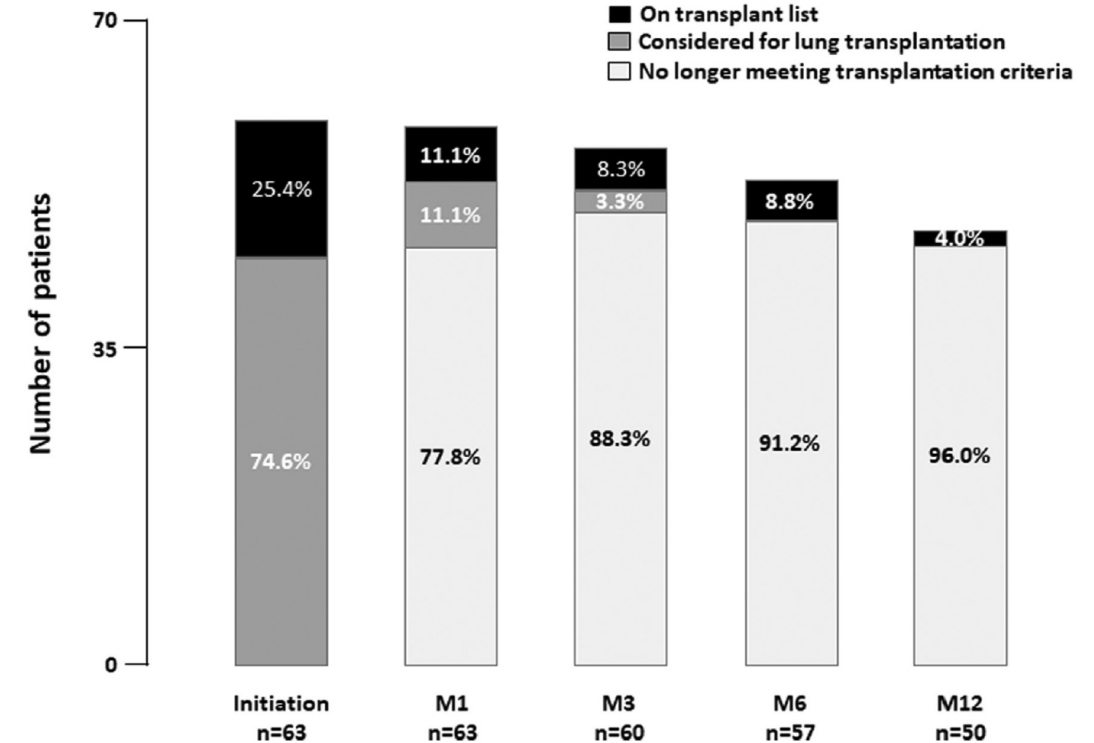
LTx = 7.5% of pwCF

LTx = 20% of adult pwCF

French CF registry



65 candidates >> 2 LTX



Is CF still an indication for LTx?

Authorization

>12years

Early access
Dec 2019

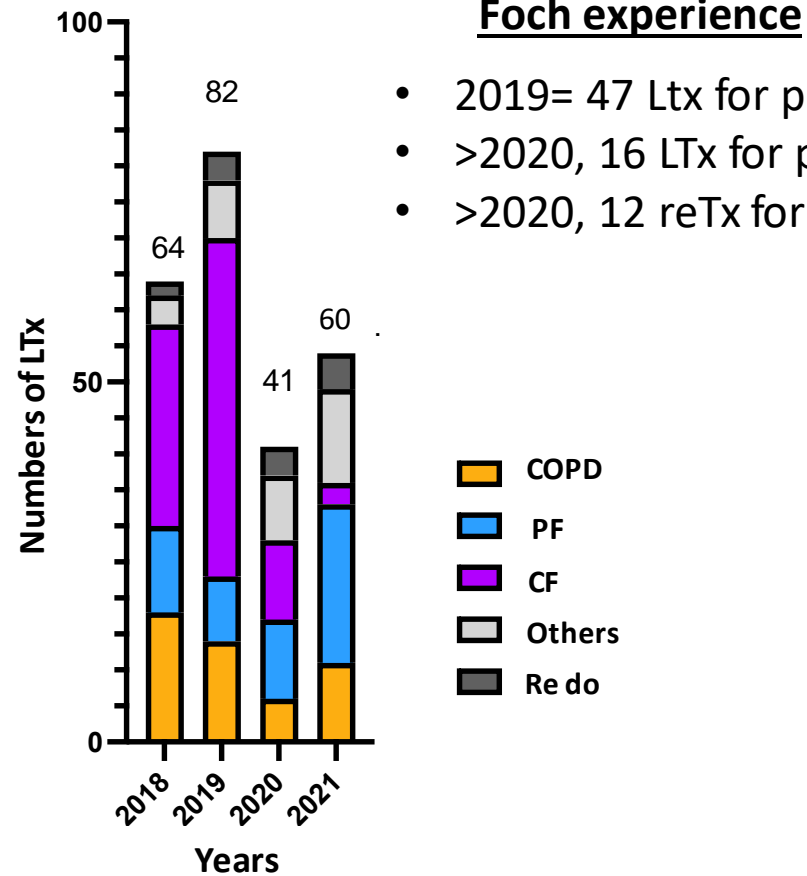
Reimbursement
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Early access
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May 2022

NEJM, Middleton
Nov 2019



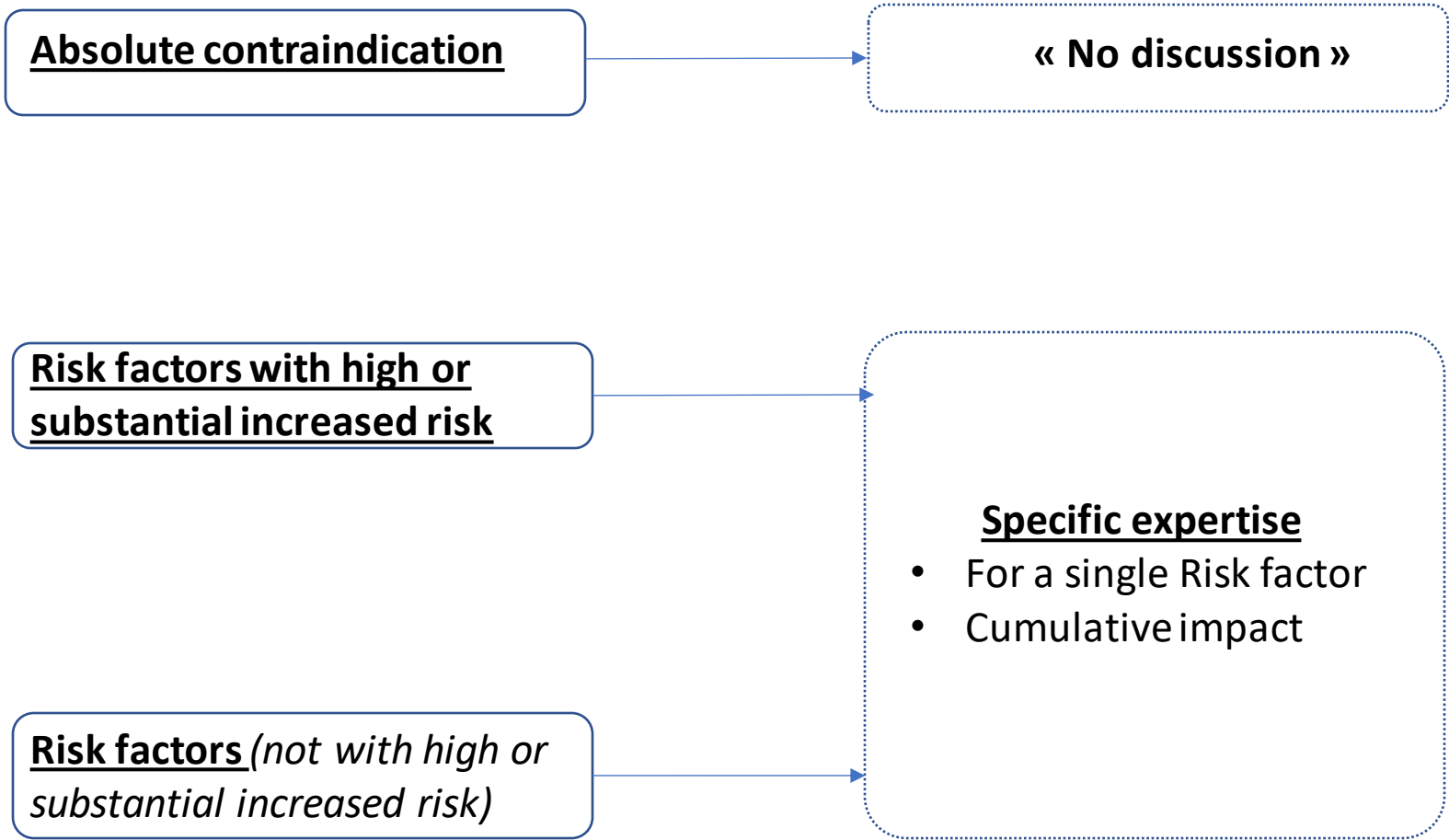
	No early access	Access (but late)	Not eligible mutation
2020, N=9	5	1	3
2021, N=5	-	-	5
2022, N=2	-	-	2

Remaining indication

- Not eligible Mutation (#10-15%)
- reTx for pwCF → Next leading indication?

Clinical situations not seen

- Loss of efficacy
- Stop for toxicity



Contraindication for LTx?

Absolute contraindication

ABSOLUTE CONTRAINDICATIONS:

- Candidates with these conditions are considered too high risk to achieve successful outcomes post lung transplantation.
- Factor or condition that significantly increases the risk of an adverse outcome post-transplant and /or would make transplant most likely harmful for a recipient.
- Most lung transplant programs should not transplant patients with these risk factors except under very exceptional or extenuating circumstances.

1. Lack of patient willingness or acceptance of transplant
2. Malignancy with high risk of recurrence or death related to cancer
3. Glomerular filtration rate < 40 mL/min/1.73m² unless being considered for multi-organ transplant
4. Acute coronary syndrome or myocardial infarction within 30 days (excluding demand ischemia)
5. Stroke within 30 days
6. Liver cirrhosis with portal hypertension or synthetic dysfunction unless being considered for multi-organ transplant
7. Acute liver failure
8. Acute renal failure with rising creatinine or on dialysis and low likelihood of recovery
9. Septic shock
10. Active extrapulmonary or disseminated infection
11. Active tuberculosis infection
12. HIV infection with detectable viral load
13. Limited functional status (e.g. non-ambulatory) with poor potential for post-transplant rehabilitation
14. Progressive cognitive impairment
15. Repeated episodes of non-adherence without evidence of improvement (Note: For pediatric patients this is not an absolute contraindication and ongoing assessment of non-adherence should occur as they progress through different developmental stages.)
16. Active substance use or dependence including current tobacco use, vaping, marijuana smoking, or IV drug use
17. Other severe uncontrolled medical condition expected to limit survival after transplant

➤ Unwilling patient

Well informed patient

➤ Non adherence

Without evidence of improvement

➤ Active uncontrolled disease

➤ Advanced chronic disease

Except if combined Tx

Contraindication for LTx?

Risk factors with high or substantial increased risk

RISK FACTORS WITH HIGH OR SUBSTANTIALLY INCREASED RISK:

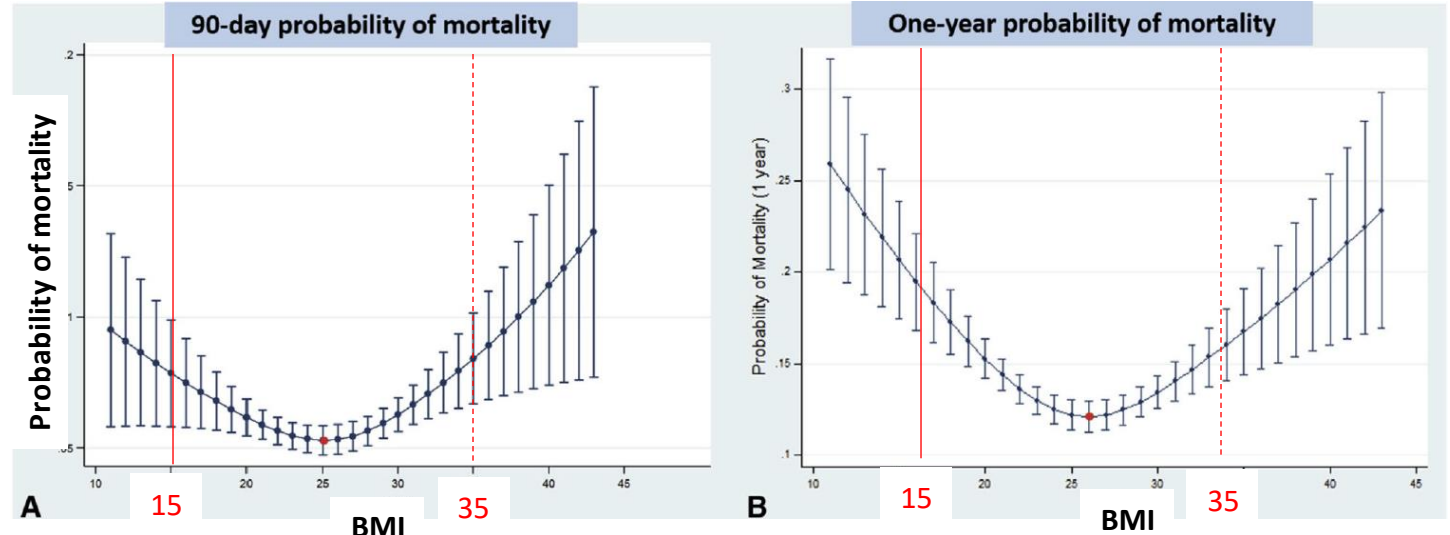
- Candidates with these conditions may be considered in centers with expertise specific to the condition.
- We may not have data to support transplanting patients with these risk factors or there is substantially increased risk based upon the currently available data, and further research is needed to better inform future recommendations.
- When more than one of these risk factors are present, they are thought to be possibly multiplicative in terms of increasing risk of adverse outcomes.
- Modifiable conditions should be optimized when possible.

Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation

Leard, 2021

- EXPERT centers
- Optimization
- Cumulative impact?

1. Age > 70 years
2. Severe coronary artery disease that requires coronary artery bypass grafting at transplant
3. Reduced left ventricular ejection fraction < 40%
4. Significant cerebrovascular disease
5. Severe esophageal dysmotility
6. Untreatable hematologic disorders including bleeding diathesis, thrombophilia, or severe bone marrow dysfunction
7. BMI > 35 kg/m²
8. BMI < 16 kg/m²
9. Limited functional status with potential for post-transplant rehabilitation
10. Psychiatric, psychological or cognitive conditions with potential to interfere with medical adherence without sufficient support systems
11. Unreliable support system or caregiving plan
12. Lack of understanding of disease and / or transplant despite teaching
13. *Mycobacterium abscessus* infection
14. *Lomentospora prolificans* infection
15. *Burkholderia cenocepacia* or *gladioli* infection
16. Hepatitis B or C infection with detectable viral load and liver fibrosis
17. Chest wall or spinal deformity expected to cause restriction after transplant
18. Extracorporeal life support
19. Retransplant <1 year following initial lung transplant
20. Retransplant for restrictive CLAD
21. Retransplant for AMR as etiology for CLAD



Extreme BMI associated with graft outcome

Fernandez, 2018

Contraindication for LTx?

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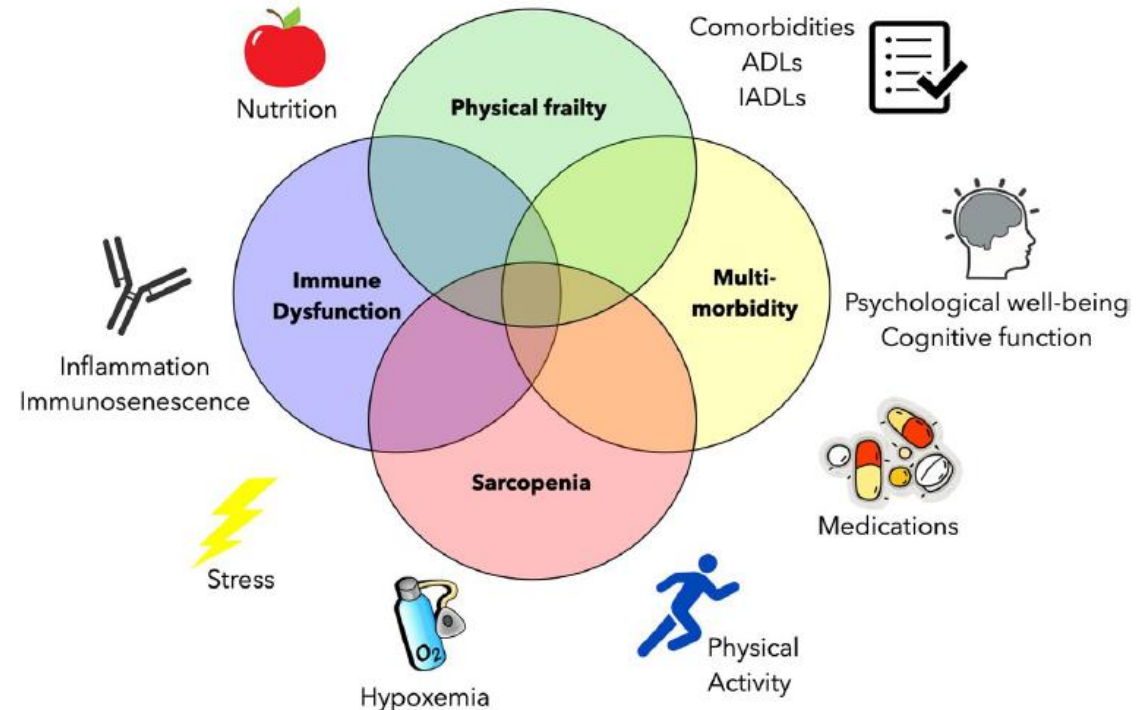
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FRAILITY



Schaenman, AJT, 2018

Contraindication for LTx?

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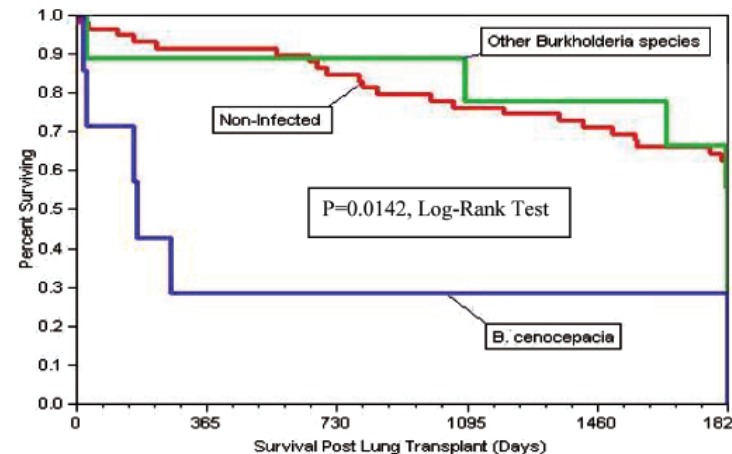
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Case of B.cepacia

Cohort of Duke University



Increased Mortality

Alexander, AJT, 2008

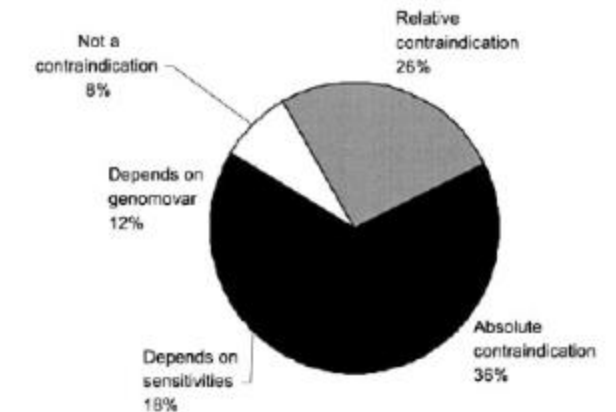


FIGURE 3. Program practices for transplanting patients colonized with *B. cepacia*.

Inter centers variability

Levine SM. Chest 2004

Contraindication for LTx?

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Active infection is contraindication

Besides Active infection:

- History of colonization
- Persistent colonization
- Role of the pathogen in the current clinical state

Pre Tx treatment:

- Do not expect negativation in airways
- Avoid active infection pre Tx
- Avoid peri operative infection (local or disseminated)

Post Tx treatment: very long time

Contraindication for LTx?

Risk factors (not with high or substantial increased risk)

RISK FACTORS:

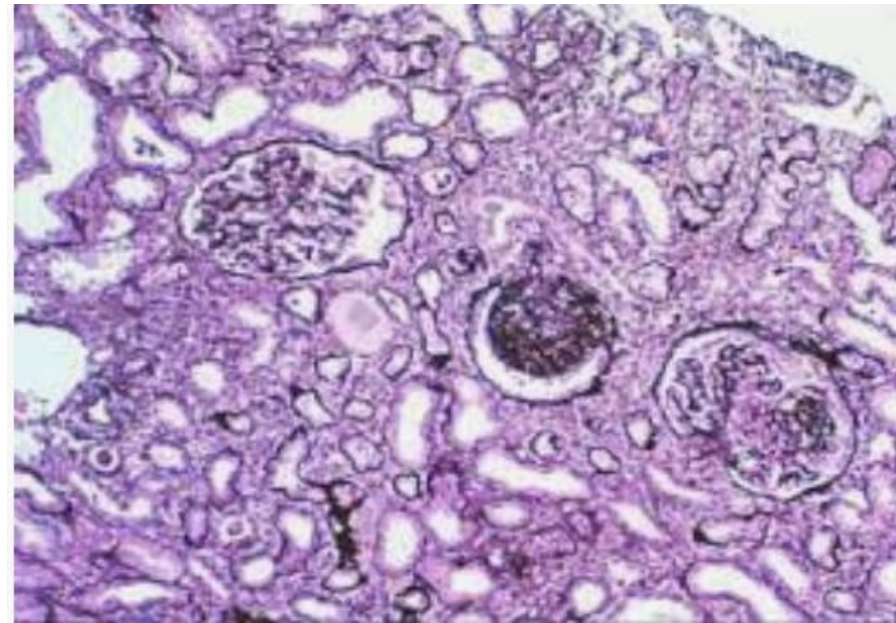
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- While acceptable for lung transplant programs to consider patients with these risk factors, multiple risk factors together may increase risk for adverse post lung transplant outcomes.

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1. Age 65-70 years
2. Glomerular filtration rate 40-60 mL/min/1.73 m²
3. Mild to moderate coronary artery disease
4. Severe coronary artery disease that can be revascularized via percutaneous coronary intervention prior to transplant
5. Patients with prior coronary artery bypass grafting
6. Reduced left ventricular ejection fraction 40-50%
7. Peripheral vascular disease
8. Connective tissue diseases (scleroderma, lupus, inflammatory myopathies)
9. Severe gastroesophageal reflux disease
10. Esophageal dysmotility
11. Thrombocytopenia, leukopenia, or anemia with high likelihood of persistence after transplant
12. Osteoporosis
13. BMI 30-34.9 kg/m²
14. BMI 16-17 kg/m²
15. Frailty
16. Hypoalbuminemia
17. Diabetes that is poorly controlled
18. Edible marijuana use
19. *Scedosporium apiospermum* infection
20. HIV infection with undetectable viral load
21. Previous thoracic surgery
22. Prior pleurodesis
23. Mechanical ventilation
24. Retransplant >1 year for obstructive CLAD

- GFR sufficient?
- Need Renal biopsy (glomerular fibrosis %)



Combined Tx?

Contraindication for LTx?

Risk factors (not with high or substantial increased risk)

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CV diseases: Frequent+++

- Coronary disease
- Atheromatosis
- Multiple venous thrombosis
- Treatment:

platelet aggregation inhibitors therapy

Anticoagulant therapy

Increase perioperative risk

Increase haemorrhagic risk

Conclusions

- Still a treatment for selected pwCF
- Re Tx : the next leading indication?
- Benefit from cumulative experience in CF transplanted patient
- Risk of Weakening of the knowledge/ practical experience
- Optimization of associated medical condition: earlier the better
- New specificities for older pwCF candidates? Benefit from LTx for COPD/Pulmonary fibrosis

Thank you for your attention

@drAntoineRoux

