Hyperechogenic foetal bowel: what now?

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UNIVERSITY HOSPITALS LEUVEN

Healthy 26-year-old pregnant woman

20 weeks

Routine Ultrasound
Hyperechogenic foetal bowel

22 weeks

Ultrasound UZ Leuven →
Confirmation of hyperechogenic and dilated bowel over an extended segment

Hyperechogenic fetal bowel

- +/- 1% ultrasounds at 20 w
- Bowel with similar or greater echogenicity than bone
- Attributable to hypoperistalsis and/or decreased fluid content of the meconium
- Nonspecific finding – associated with T21, bowel atresia, CMV infection, IUGR,…, in majority no abnormalities

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Ultrasound UZ Leuven
→ Confirmation of hyperechogenic and dilated bowel over an extended segment

22 weeks + 6 days

Parental screening: both carrier of the F508del CFTR mutation

Amniocentesis:
F508del homozygous CFTR mutation → CF diagnosis

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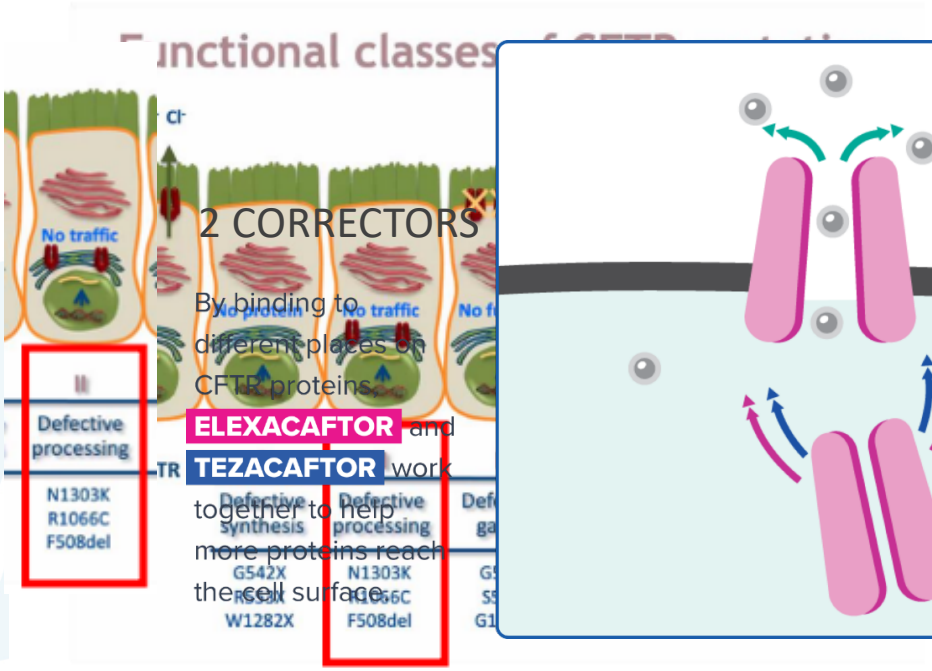
- CF: changes in the consistency of meconium because of abnormalities in pancreatic enzyme secretion
  - Hyperechogenic fetal bowel in 50-78% of all CF patients
  - CF in 0,8% tot 13,3% of fetuses with echogenic bowel
  - Meconium ileus in 10-20% of newborn babies with CF

Prenatal diagnosis CF with high risk of Meconium Ileus

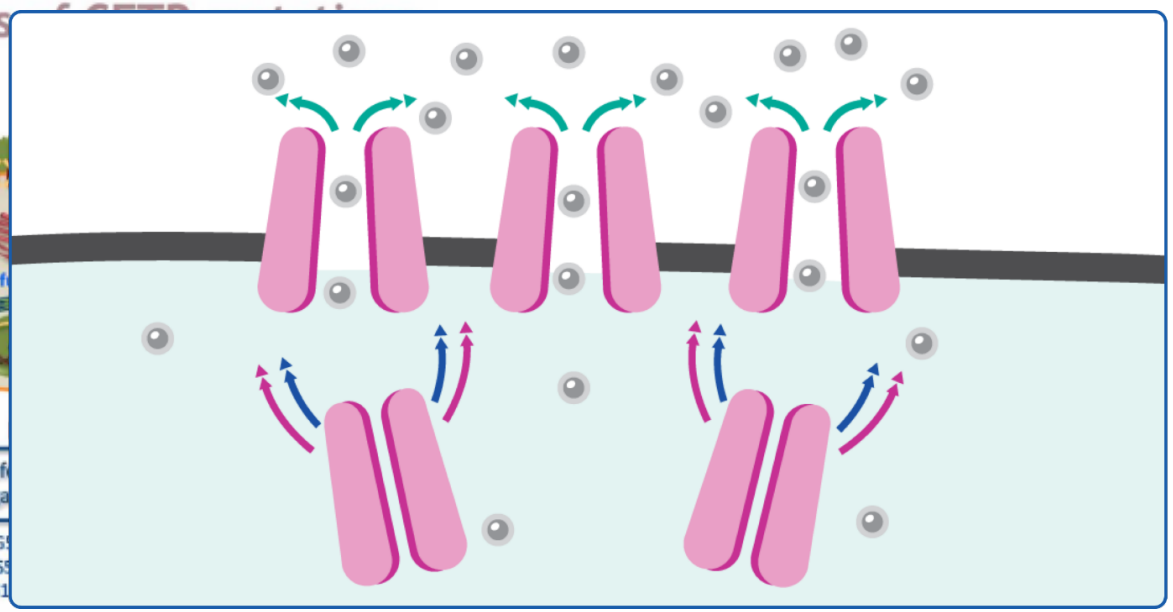
- Multidisciplinary counseling (CF team, gynaecologists and neonatologists)
  - Meconium ileus → bowel obstruction = high risk for surgery neonatally with/without temporary stoma
  - Possibility of maternal use of CFTR modulators? (Elexacaftor/Tezacaftor/Ivacaftor)
  - Goal = treating the foetus during the rest of pregnancy

Elexacaftor/Tezacaftor/Ivacaftor (Kaftrio®)



2 CORRECTORS

By binding to different places on CFTR proteins, **ELEXACAFTOR** and **TEZACAFTOR** work together to help more proteins reach the cell surface.

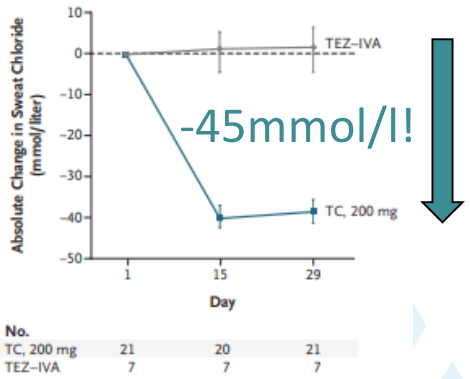


POTENTIATOR

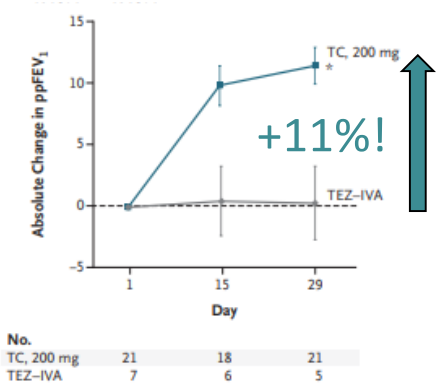
IVACAFTOR helps CFTR proteins stay open longer at the cell surface.

Elexacaftor/Tezacaftor/Ivacaftor (Kaftrio®)

- DF508



Sweat Chloride



Lung function

Keating NEMJ 2018

	6+ kaftrio kalydeco
Longfunctie	+10 tot 15% FEV_1
Zweetchloride	-40 tot -70 mmol/L
Gewicht	+0.6 tot +1.0 BMI Z-score
Exacerbaties	↓ met 2/3
'PRO' CFQ-R	+17 to +20

Min 1 DF508

- Pregnancy
  - ETI presumed safe during pregnancy and lactation *(Taylor J Cyst Fibros 2021, Elijah Pediatr. Pulmonol. 2023)*
  - Large prospective, multicenter study ongoing *(Jean BMJ 2022, MAYFLOWERS)*
  - Several cases of prenatal use in MI described

Prenatal diagnosis CF with high risk of Meconium Ileus

- Multidisciplinary counseling (CF team, gynaecologists and neonatologists)
  - Agreement on 'off-label' use, with close monitoring
    - Foetal MRI before start therapy + 2nd foetal MRI before birth
    - Foetal ultrasound two-weekly
    - Maternal follow-up of liver function and clinical signs
    - Animal studies: fetal cataract → ophthalmological check-up after birth
    - Admission NICU
    - No post-partum treatment of the neonate

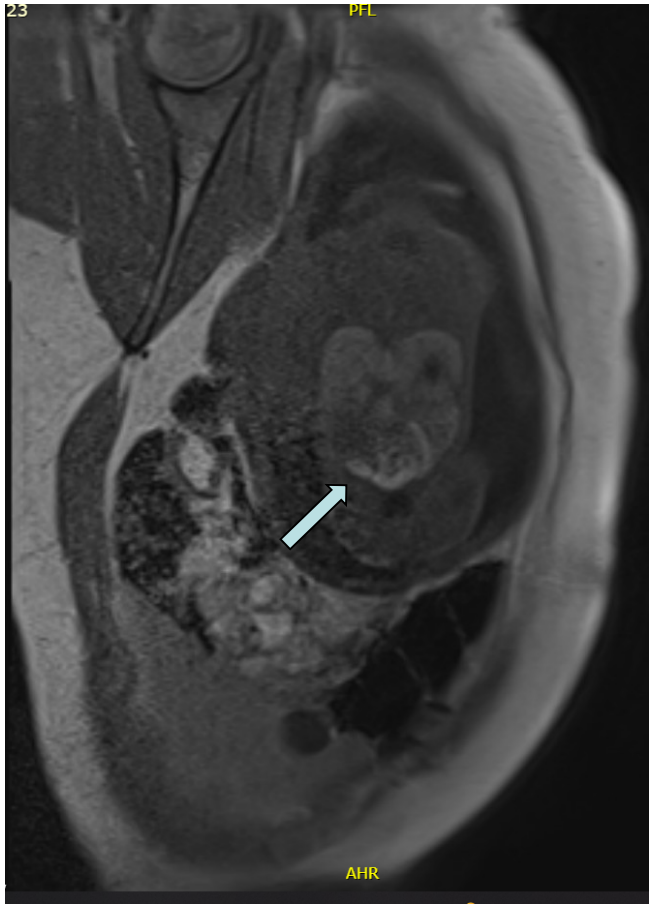
Fetal MRI

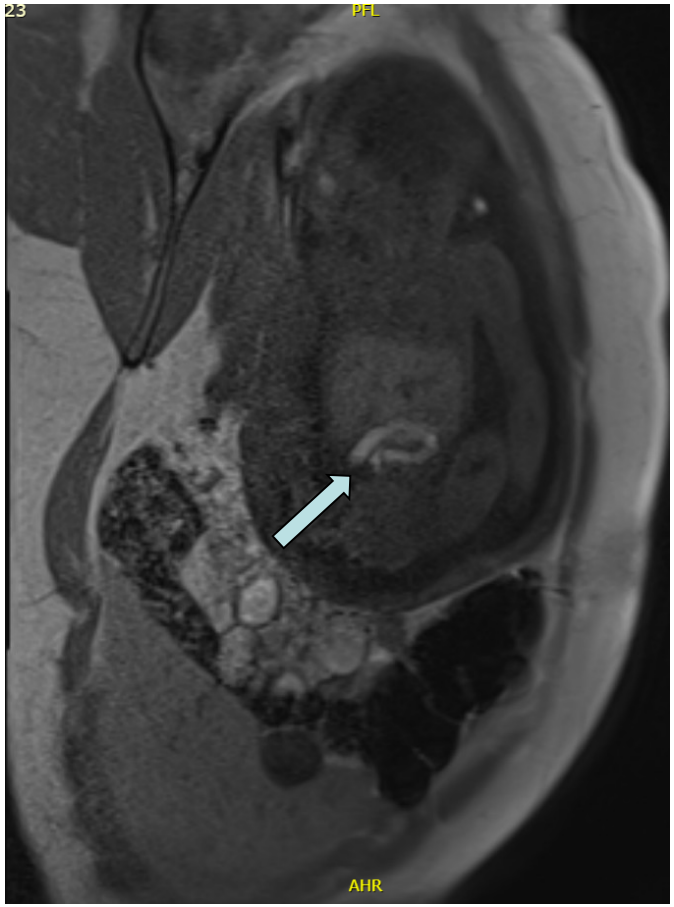
25 weeks

Dilated small bowel loops

Small calibre from the colon to the rectum

Meconium signal visible only in the small intestine





Maternal ETI Treatment

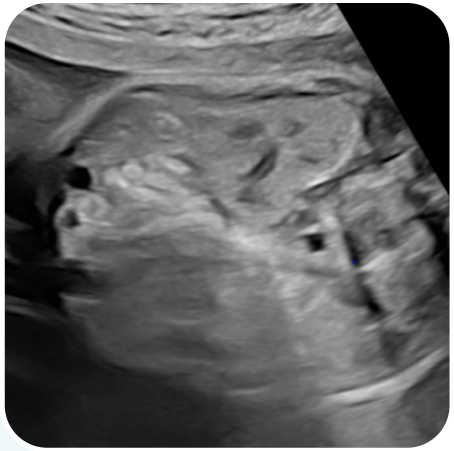
26 weeks + 6 days

Start maternal ETI treatment at normal adult dose

2 weekly liver and kidney function

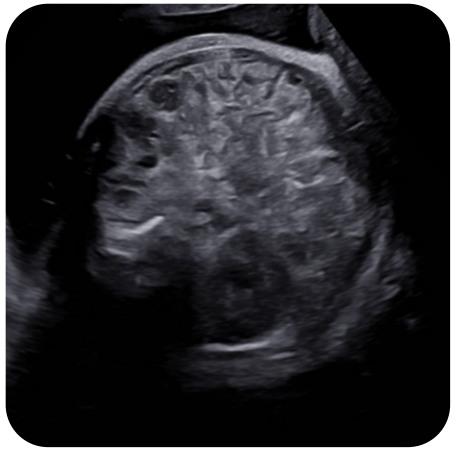
Good tolerance – mild diarrhoea

Ultrasound evolution



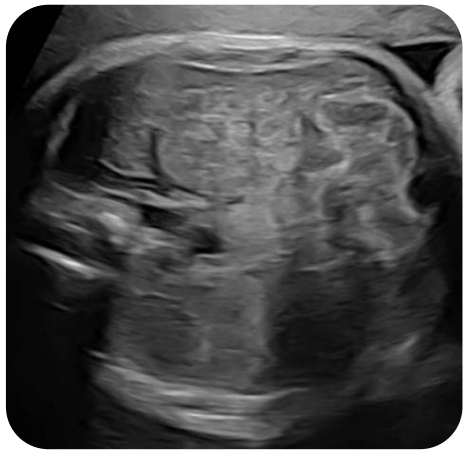
26w + 6d

- Before start therapy
- Hyperechogenic bowel & meconium plugs



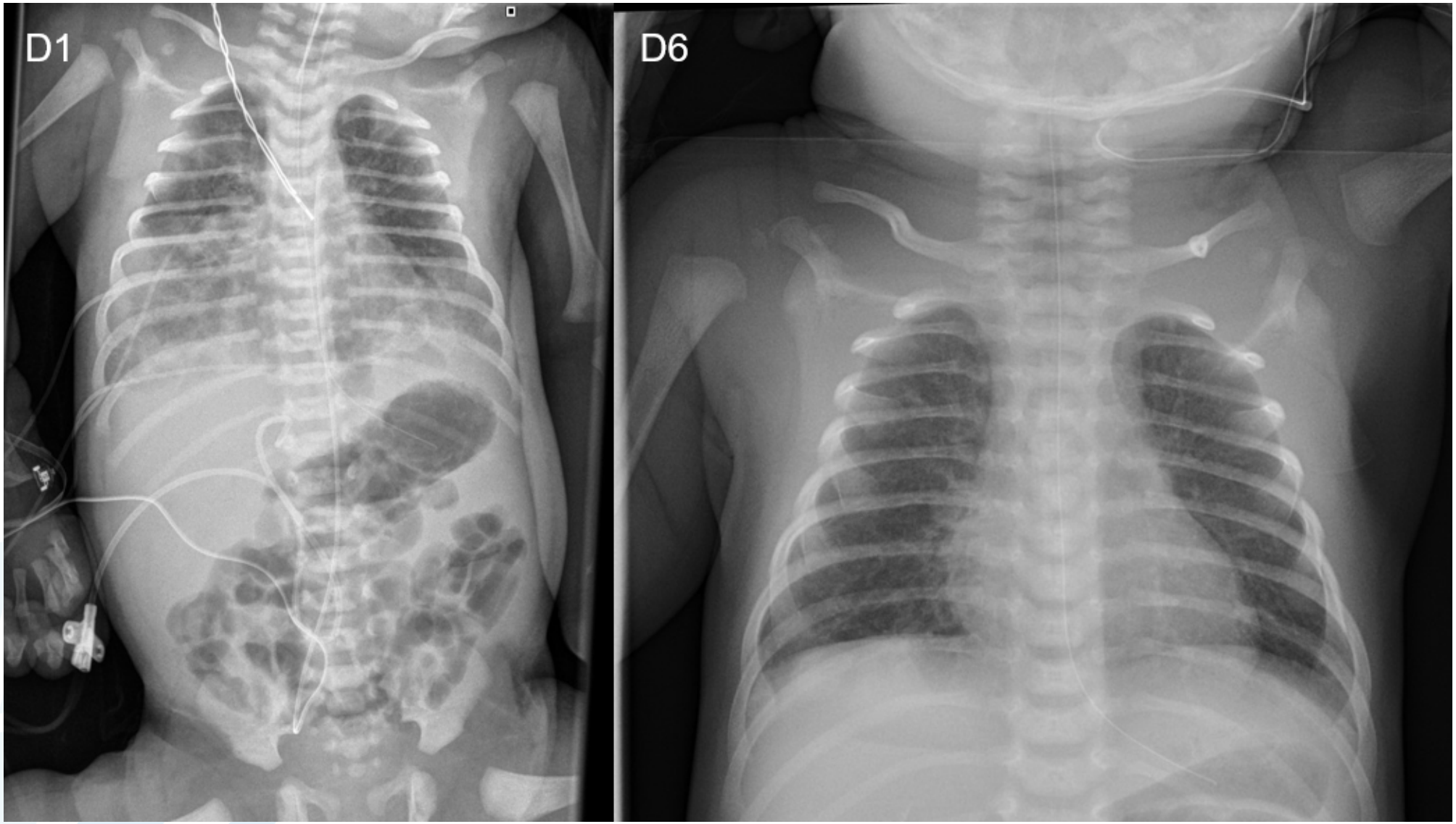
30w + 6d

- 4 weeks of ETI therapy
- Less obvious meconium plugs, good peristalsis & only mildly hyperechogenic bowel



34w + 6d

- 8 weeks of ETI therapy
- Normal ultrasound


D1
D6

NICU Admission

Laboratory

D3 sweat chloride **25.0 mmol/L** (<60mmol/l)

D2 Pancreatic elastase 115 µg/g

D3 Newborn screening
IRT **30ng/ml** (<55ng/ml)

Ophthalmology

D8: normal

Therapy

Pancreatic enzyme therapy (Creon®)

Vitamins + NaCl supplementation

Nebulizer with hypertonic saline

Pulmozyme

Respiratory physiotherapy

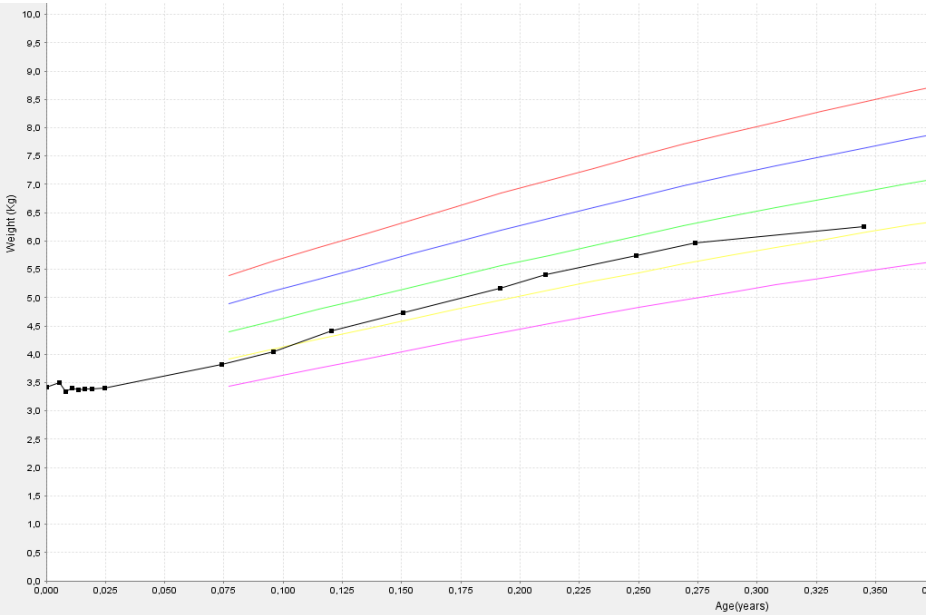
Neonatal Evolution

Discharge D10

Good weight evolution and stool pattern

KMEA

M3 Sweat chloride 89mmol/L
M3 Pancreatic elastase 70mmol/L



Conclusion

- ‘Off-label’ ETI was well tolerated in a healthy woman pregnant of a foetus with cystic fibrosis
- ETI cured neonatal meconium ileus with bowel obstruction.
- Neonatal respiratory distress with bilateral lobar atelectasis occurred, it is unclear whether this is linked to prenatal ETI treatment.

Questions?

Sources

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