Pharmacokinetics of tezacaftor-ivacaftor (Symkevi) in children with cystic fibrosis

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON20087

Source
NTR

Brief title
SYM-CF

Health condition

Cystic Fibrosis

Sponsors and support

Primary sponsor: None
Source(s) of monetary or material Support: None

Intervention

Outcome measures

Primary outcome

To assess the exposure (AUC, Cmax) of tezacaftor-ivacaftor in a real life clinical setting in paediatric CF patients

Secondary outcome

1) To evaluate the relationship between covariates and PK parameters in order to explain inter-patient variability
2) To evaluate the relationship between AUC and through levels
3) To compare drug exposure in children of different age groups and compare with that in adults
4) To explore if there is a correlation between drug concentrations and clinical outcome measures (efficacy like exacerbation frequency, increase in weight, lung

Study description

Background summary

There are novel medicines in CF that target the CF transmembrane conductance regulator (CFTR) and increase its activity. Thesedrugs improve the lung function, quality of life and body mass index in patients with specific mutations and might decreasepulmonary exacerbations. The combination of tezacaftor-ivacaftor (Symkevi®) is registered for patients ≥ 12 years old and theexpectation is that at the end of 2020 it will also be registered for children from the age of 6 years. The clinical efficacy of thesedrugs is limited, some patients respond, while others do not or have side effects. The inter-individual variability (IIV) seems largeand therefore this study hypothesizes that we might be over- or undertreating specific groups of patients, which can affect efficacy,side effects and costs of these expensive drugs. Very little is known about the pharmacokinetics (PK) of tezacaftor-ivacaftor,especially in the paediatric population. Better knowledge of the PK may provide more insight into the exposure-responserelationships and IIV.

Study objective

The clinical efficacy of CFTR modulating drugs is limited, some patients respond, while others do not or have side effects. The inter-individual variability (IIV) in the PK seems large, and therefore we hypothesize that we might be over- or undertreating specific groups of patients, which can affect efficacy and side effects these drugs. There

Study design

0, 3, 6, 9, 12 months

Intervention

The intervention consists of additional DBS blood sampling for PK analysis.

Contacts

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Eligibility criteria

Inclusion criteria

- Use a combination therapy of tezacaftor-ivacaftor for a minimum period of 8 days in regular care or compassionate use
- CF patients aged 6 years and older who are homozygous for the F508del mutation or who are heterozygous for the F508del mutation and have one of the following mutations in the CFTR gene: P67L, R117C, L206W, R352Q, A455E, D579G,
- 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G, and 3849+10kbC→T.
- Signed informed consent from the patient when ≥16 years, from the patient and both parents for patients aged 12-15 years, from both parents aged 6-11 years.

Exclusion criteria

- History of poor compliance deemed by the physician
- Concomitant use of drugs that have an inhibitory or inducing effect on the CYP3A4 enzyme metabolism 14 days before the blood collection, if the patient uses one or more of these medicines the blood collection of the upcoming visit will be skipped:
o Inducers of CYP3A: rifampicin, rifabutin, phenobarbital, carbamazepine, phenytoin and St. John’s wort
o Inhibitors of CYP3A: ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, fluconazole, erythromycin and grapefruit juice
- Patient or parent refusal

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2021
Enrollment:	30
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	20-04-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9426
Other	METC AMC : METC 2021_021

Study results