

A RARE CASE AND AN EFFECTIVE DRUG THERAPY: OFF-LABEL USE OF TACROLIMUS IN A PAEDIATRIC DYSIMMUNE DISEASE

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Background

A seven month child with an unremarkable previous medical history presented with a history of 18 days of severe secretory diarrhea.

Clinical and histological features were consistent with autoimmune enteropathy.

The patient could not tolerate foods, was started on total parental nutrition (TPN) and i.v. Methylprednisolone, without substantial clinical improvement.

Confirmed the resistance to traditional therapy and consulted hospital pharmacists, the use of Tacrolimus was identified as the best option.

Purpose

The aim of this work is to report several aspects of the hospital pharmacy involvement in the management of a difficult case, including: off-label approval, compounding, alternative therapies, nutritional support, costs.

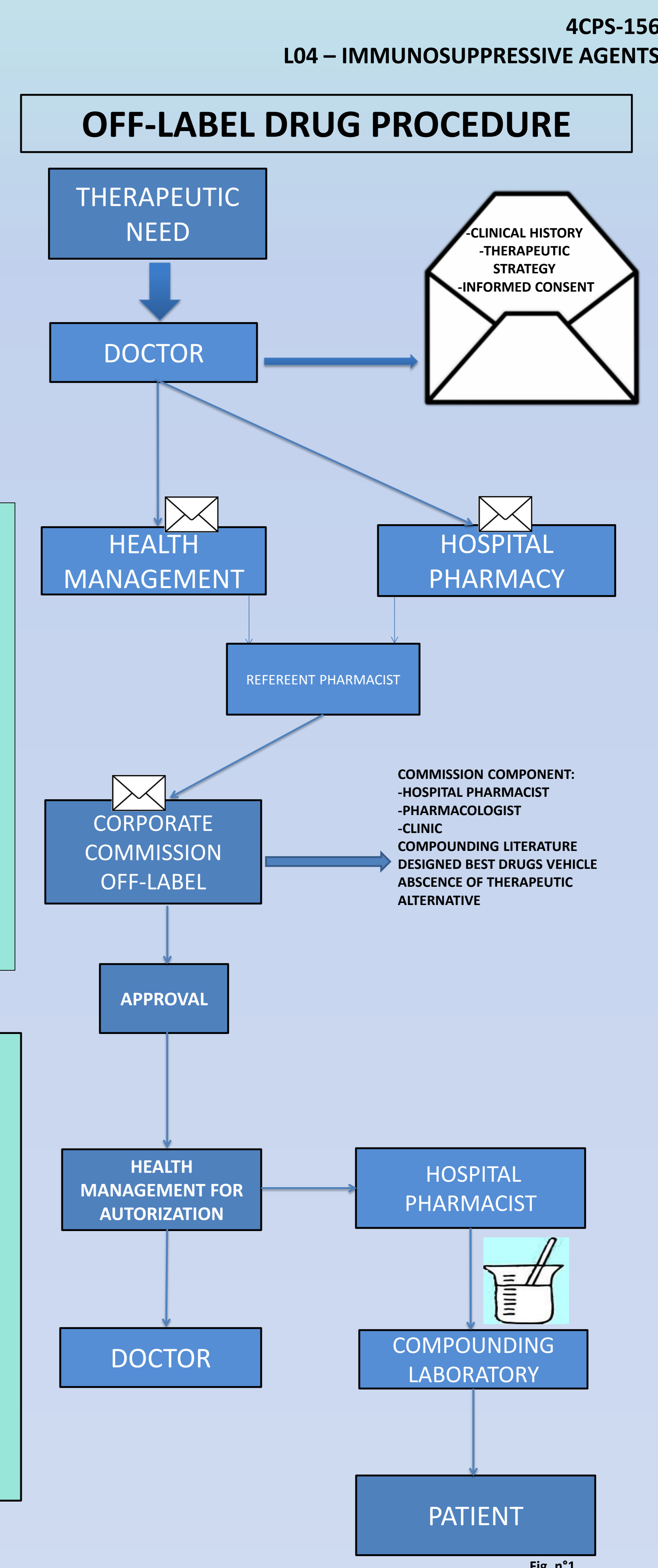
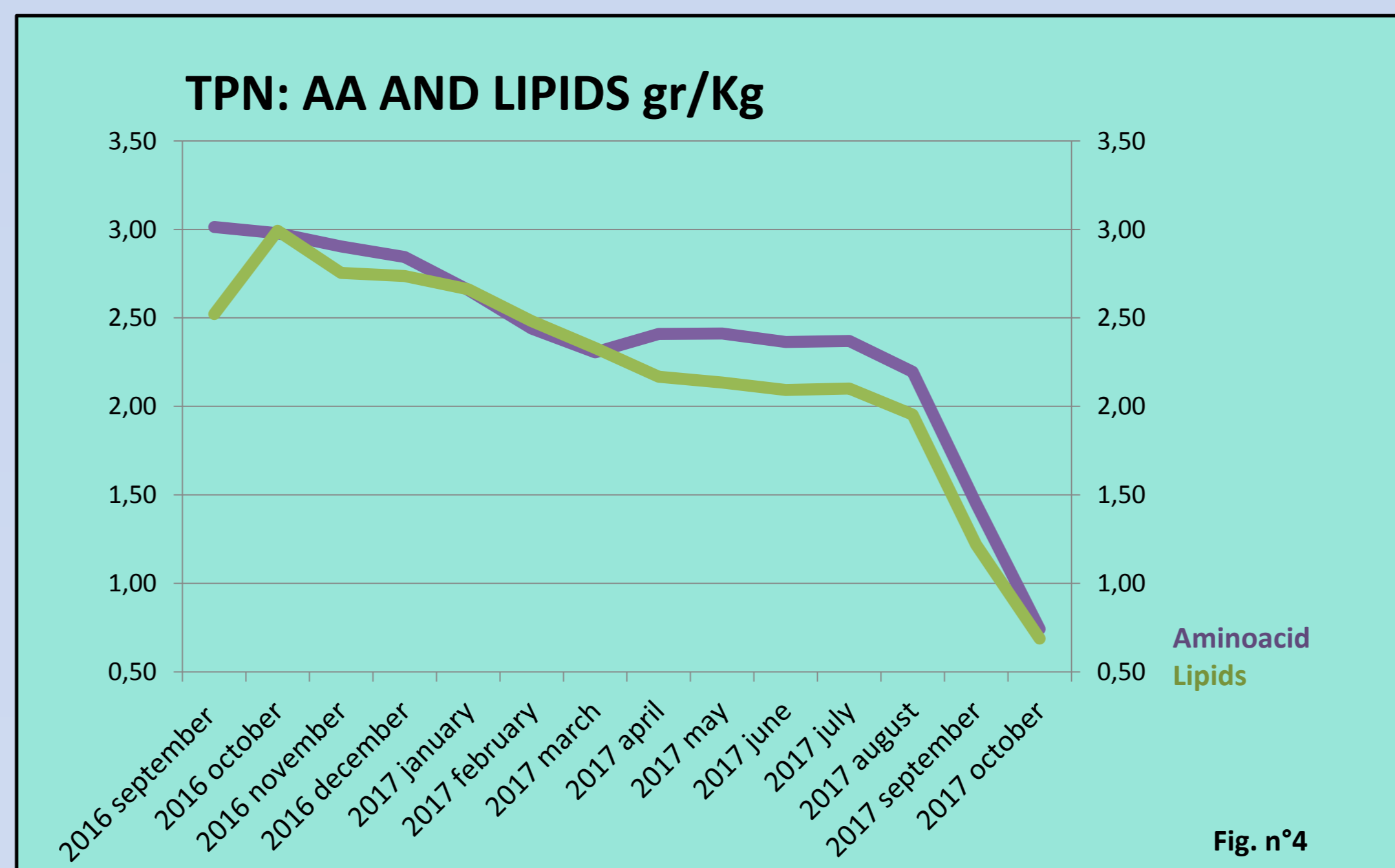
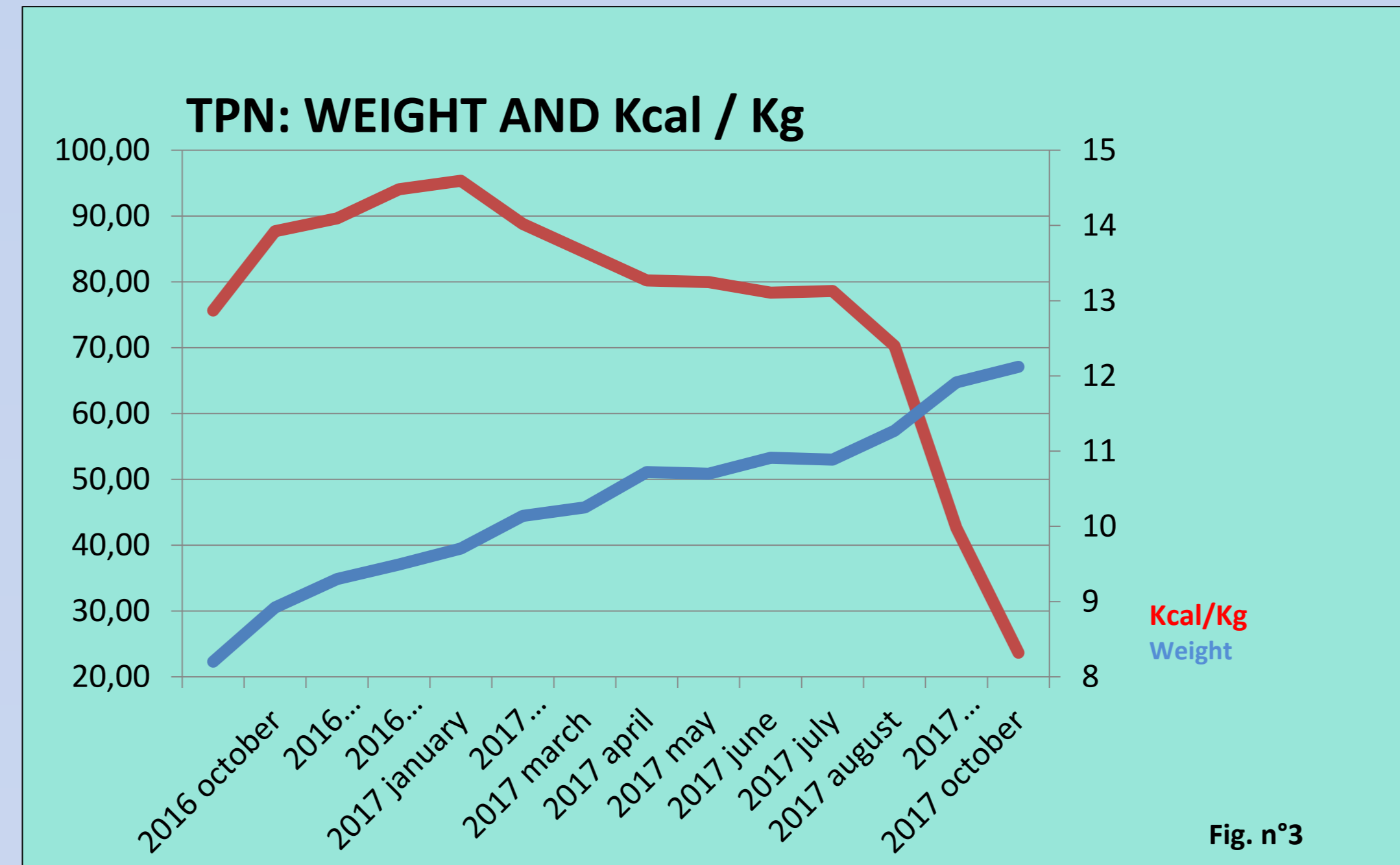
Material and methods

Being not registered for use, the corporate formal procedure for off-label drugs was submitted to "Corporate Commission off-label" involving designed pharmacist, pharmacologist and clinic. (Fig n°1)

Parents signed formal "informed consent" and medical records were verified.

Tacrolimus (Fig n°2) suspension 0,5mg/ml 40ml was prepared according to scientific literature and compounding formulas, using a basic vehicle for compounding of oral liquid dosage forms (stability 56 days, storage at 24-26°C).

An appropriate personalized TPN was formulated.



THERAPY	OCTOBER 2016	NOVEMBER 2016	DECEMBER 2016	JANUARY 2017	FEBRUARY 2017	MARCH 2017	APRIL 2017	MAY 2017	JUNE 2017	JULY 2017	AUGUST 2017	SEPTEMBER 2017	OCTOBER 2017
DRUGS													
METHYLPREDNISOLONE	1,5mg/kg/day	DOSE TAPERING											
TACROLIMUS		0,15mg/kg/day					0,055mg/kg/day		stop due fungal infections				
AZATHIOPRINE							2,5/mg/kg/day				2,5/mg/kg/day		

Results

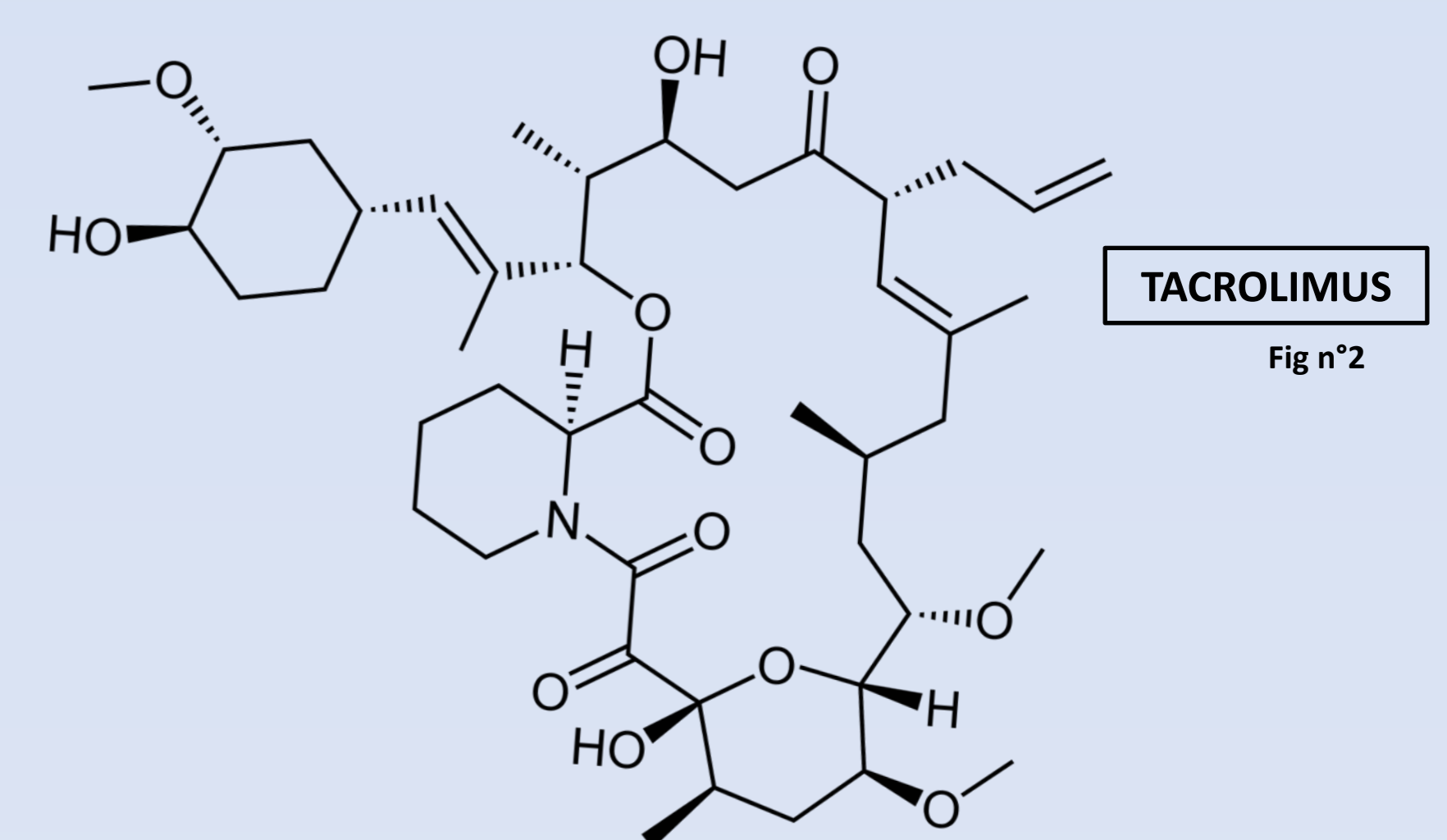
Drugs: i.v. Methylprednisolone was used at 1,5mg/kg/day for 1 month, with dose tapering in 3 months. Tacrolimus was used as unique therapy for 5 months, mean dose 0,15mg/kg/day and associated with Azathioprine at 2,5mg/kg/day for 2 months. (Tab 1)

Twenty-two bottles of Tacrolimus suspension 0,5mg/ml 40ml were prepared for 730 euros overall.

Tacrolimus and Azathioprine were stopped during a fungal infection, after which only Azathioprine was restarted. No adverse reactions were reported.

Artificial Nutrition: TPN for 3 months with soy-based lipid mixture (50% soybean-oil : 50% MCT 3g/kg/day) and for 11 months with fish-oil lipid mixture (30% soybean-oil : 30% MCT : 25% olive-oil : 15% fish-oil 2,5g/kg/day). (Fig.3) (Fig.4)

Optimal tolerance to parental nutrition (PN) and appropriate weight gain. PN was progressively reduced and elemental liquid oral formula was introduced. Overall after 16 months, clinical and histological condition were substantially improved, the patient currently tolerates enteral nutrition with elemental formula plus Azathioprine.



Conclusion

Rare paediatric diseases are always a challenge for the hospital medical staff. In this case the medical plan is to slowly reintroduce hypoantigenic foods and stop Azathioprine.

Given the disease rarity, we hope to increase available data and help the management of similar cases.