

**Aim and objectives** The objective of this study was to perform a preliminary pharmacokinetic (PK) model of adalimumab to evaluate covariates potentially responsible for the PK variability in paediatric patients with IBD.

**Material and methods** A 3 year retrospective multicentre study was performed including children and adolescent ( $\leq 18$  years) diagnosed with IBD and treated with adalimumab. Demographic and clinical data were collected, including serum albumin, C reactive protein and faecal calprotectin. Pre-dose serum samples were carried out before administration. Adalimumab concentrations and anti-adalimumab antibodies (AAA) were determined by ELISA. The model was developed in NONMEM V.7.4 by approximating the non-linear mixed effects models. The first order conditional estimation method with interaction (FOCEI) was used for model building. Concentrations below the lower limit of quantification (LLOQ) were set to LLOQ/2. Body weight (WGT) was included in the PK parameters following an allometric relationship.

**Results** Twenty-three paediatric patients (10 women) were included, 3 were diagnosed with ulcerative colitis and 20 with Crohn disease. Median age (range) was 14.0 (5–18) years and weight 55.9 (20.4–80) kg. A total of 75 concentrations ( $2 < \text{LLOQ}$ ) were determined, with a medium concentration of 10.72 (0.1–24.7)  $\mu\text{g/mL}$ . Median (range) serum albumin level was 4.0 (2.8–5.0) g/dL. Only one patient developed AAA. Population PK model (PopPK): a one compartment with first order absorption and elimination described adequately the serum adalimumab concentration–time data. The absorption rate constant was fixed ( $K_a=0.008/\text{hour}$ ) according to Sharma *et al.* Among the clinical variables analysed, only albumin was significant on the apparent clearance (CL/F). The final PopPK model in the absence of AAA was as defined as:  $V/F=11.30 \times (\text{WGT}/56 \text{ kg})$  and  $\text{CL}/F (\text{L}/\text{day})=0.42 \times (\text{albumin}/4 \text{ g/dL})^{-2.32} \times (\text{WGT}/56 \text{ kg})^{0.75}$ . Covariate analysis reduced the interindividual variability associated with CL (IIVCL) from 34.1% to 21.3%. Proportional residual error estimated was 28.4%.

**Conclusion and relevance** Adalimumab PK in paediatric patients with IBD was best described by a one compartment model with first order absorption and elimination. WGT was included in the PK parameters following an allometric relationship. Albumin showed statistically significant differences on adalimumab CL/F, explaining 62.5% of its variability.

#### REFERENCES AND/OR ACKNOWLEDGEMENTS

- Sharma S, *et al.* *Inflamm Bowel Dis* 2015;21:783–792.

No conflict of interest.

#### 4CPS-127 ECONOMIC IMPACT OF INTENSIFICATION REGIMENS IN INFLAMMATORY BOWEL DISEASE

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10.1136/ejhp-pharm-2020-eahpconf.228

**Background and importance** Biological treatments have improved the therapeutic options for inflammatory bowel disease (IBD) and have shown high clinical efficacy. Nevertheless, some patients do not respond to initial treatment or present

loss of response over time. To prevent the loss of efficacy, treatment intensification has been employed, usually applied empirically based on the clinical condition of the patient and biochemical parameters. The introduction of tumour necrosis factor antagonist (anti-TNF) monitoring in clinical practice allows a more accurate selection of strategies.

**Aim and objectives** To analyse the number of patients receiving treatment with a biological agent for IBD and requiring an intensification regimen, including increasing dosage or shortening the administration interval, and to evaluate the economic impact of this intensification strategy.

**Material and methods** This was a retrospective observational study in patients diagnosed with IBD and under an intensified regimen of a biological agent. The cost per patient was estimated based on the extrapolation of the price of each medication for 1 year of treatment. In addition, the difference in costs per patient and year for each treatment and the total economic impact were calculated.

**Results** A total of 549 patients with IBD were receiving a biological treatment and 239 required an intensification regimen (table 1).

**Conclusion and relevance** Intensification regimens, including

Abstract 4CPS-127 Table 1

Drug	Intensification regimen	No patients (%) intensifications per drug	Patient annual cost (€)	Difference with respect to standard regimen (€)	Incremental annual total cost (€)
Adalimumab	40 mg q1 week	34 (18)	4860	2430	82620
Golimumab	100 mg q4 weeks	13 (52)	11082	725	9425
Ustekinumab	q8 weeks	52 (68)	16063	5362	278 824
	q6 weeks	9 (12)	21425	10725	96525
	q5 weeks	1 (1)	25700	15000	15000
	q4 weeks	13 (17)	32125	21425	278 525
Vedolizumab	q6 weeks	14 (19)	13791	3452	48328
	q4 weeks	16 (22)	20678	10339	165 424
Infliximab	10 mg/kg q8 weeks	77 (43)	6341	3170	244090
	5 mg/kg q6 weeks	9 (5)	4229	1058	9522
	5 mg/kg q4 weeks	1 (1)	6341	3170	3170
	5 mg/kg q4 weeks	1 (1)	6341	3170	3170
Total		239			1 231 453

increasing dosage or shortening the administration intervals, were frequent in our hospital, both for anti-TNF and for other biological agents used for the treatment of IBD. These strategies involve an important economic impact, as well as a high risk of infection for patients. Intensification should be guided by pharmacokinetic monitoring. More studies are needed to validate therapeutic algorithms that allow optimisation of resources for all biological agents used.

#### REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.