



# Tyrosine Kinase Inhibitors (TKI) and acid-inhibitory drugs (AID): strong concomitant dispensing and drug-drug interaction risk.

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## Introduction

Acid-Inhibitory Drugs (AID): 2001: First TKI (imatinib) 2015: 43 TKIs (1/4 treatment) antacids + anti-ulcerous drugs

1 mTOR inhibitor (imTOR) ORAL TREATMENT

intragastric pH >TKI solubility, > bioavailability and > treatment efficacy?

+ Proton Pomp Inhibitors (PPIs)

Are there concomitant prescription of TKI-AID in Pays de la Loire area (PL) inducing treatment efficacy decrease?

#### Material and Method

- Litterature synthesis to analyse TKI-AID interactions and effects
- Survey of oncologists about PPIs prescription in 2017 (15 days in December).
- Retrospective study of concomitant dispensing in 2016 conducted by the Medical Department of the French Regional Health Insurance (FRHI PL)
  - SNIIRAM database (>95% population)
  - No Hospital drugs dispensing
  - PL patients (pts) with at least 1 TKI or 1 imTOR dispensing in 2016 (n=2309 pts)

## Results of the clinicians' survey

43 answers: 98% have used to prescribed them.

#### Major reasons:

- 88% of clinicians presribe them for the treatment of gastroesophageal reflux
- 67% for the prevention/treatment of NSAID-associated ulcers and 55% for oeso-duodenal / stomach ulcers
- 31% for unknown reasons but required by patient
- 31% for Zollinger-Ellison syndrome.

Duration of treatment variable: more often between 7 days and 2 months

# Results

2309 pts with at least 1 TKI/imTOR dispensing in 2016

No AID dispensing: 967 pts

No AID-TKI concomitant dispensing: 274 pts (calendar month)

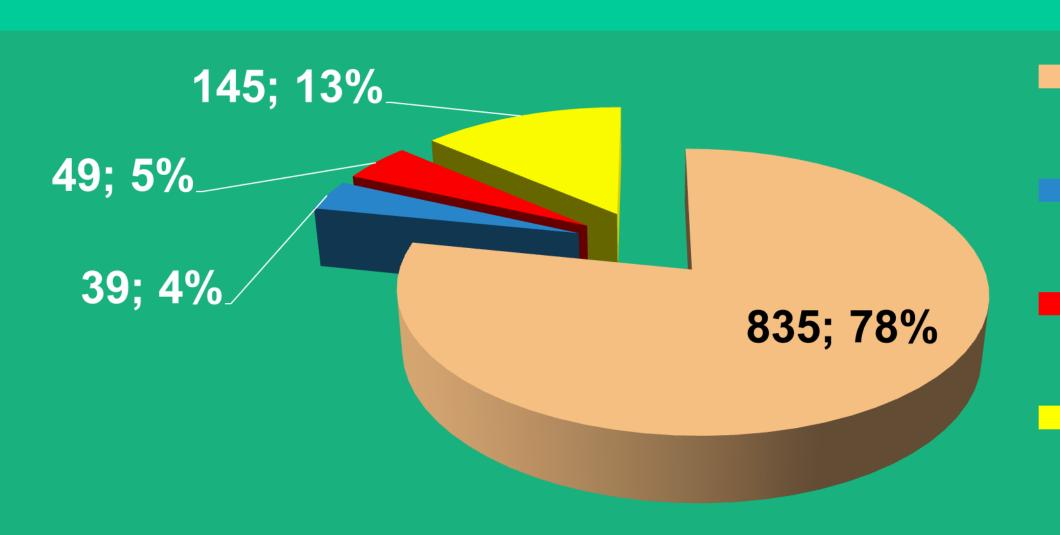
1068 pts with at least 1 concomitant AID-TKI dispensing in 2016: 46 %

> Antacids+anti-ulcerous drugs: 405 pts

Diosmectite concomitant dispensing: 172 pts

Pay attention to how this drug is taken

#### Pts' AID description



**■ PPI alone or** associated **Anti-ulcerous drugs** (aginate, ...) Antacids

Other AID association

835 with at least 1 concomitant PPI-TKI dispensing in 2016: 36 %

The solubility of some When used concomitantly tyrosine kinase inhibitors with diosmectite and/or locally acting antacids is pH- dependent Drug that reduced gastric (aluminum salts) acidity couldtherefore It is recommended to respect a reduce their absorption 2h delay Drug - Drug interactions Sometimes Very uneven data contradictory according to ITK data between the The fact that no data is Very general data different available does not mean referential and in major that the risk does not exist recommendations literature

concomitant dispensing: 37 % Analysis for each ITK the mentioned data concerning

absorption-modifying interactions in: - Micromedex

- Drug approval

**Total PPI-TKI** 

- ANSM drug interaction thesaurus

- Theriaque

TKIs/imTOR most concerned:

imatinib, everolimus, sorafenib,

ruxolitinib, erlotinib and sunitinib

- Stockley

- literature

The evaluation of the risk-benefit ratio of the coprescription of each ITK with the AIDs must be evaluated with regard to the AIDs indications. Concerning the diosmectite that acts on the absorption, the recommendation is not to take it at the same time as the TKI

## Discussion / Perspectives

>In 2017 in PL, half of the patients have a concomitant dispensing of TKI/imTOR and PPI with a potential interaction which should be considered for optimal TKI absorption. This study would be performed soon in another area (Brittany) to confirm our results. The current debate on the clinical impact of pharmacological interactions between TKI and PPI is ongoing. Variable information based on the consulted data sources have been found. There is a risk of less effective TKIs. Clinicians should know this risk and so assess again the TKI prescriptions and the duration of treatments or the use of others AID treatments.

>Moreover, TKI and PPIs could interact on cytochrome. The same analysis would be done soon.