

DRUG INTERACTIONS WITH DIRECT ACTING ANTIVIRALS FOR HEPATITIS C: WHAT ABOUT IN PRACTICE? PHARMACEUTICAL IMPACT Hôpitaux de Toulouse

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BACKGROUND

Direct Acting Antivirals (DAA) introduction follows a MultiDisciplinary Team Meeting (MDTM), including a pharmacist who systematically analyzes potentials drug interactions between DAA recommended by the hepatitis C specialists and concomitant medications.

PURPOSE

To better define drug interactions consequences in practice, we analyzed and assessed their impact in terms of Pharmaceutical Interventions (PI) proposed after MDTM, differentiated according to an Impact Score (IS).

MATERIALS AND METHODS

This retrospective study analyzed for **5 months** the drug between DAA concomitant interactions and **medications** of patients presented at hepatitis C MDTM. Patient characteristics and concomitant medications are provided by the MDTM physician coordinator.

For each patient, drug interaction analysis were performed between all concomitant medications and all the DAA (and Ribavirine) recommended by MDTM

Drug interaction analysis sources:

- Summary of Product Characteristics (a)
- University of Liverpool hepatitis drug interactions website: hep-druginteractions.org (b)
- Scientific literature (c)
- French National Agency for Medicines Safety (ANSM) alerts (d)

Significant drug interactions generates Pharmaceutical

RESULTS

4: Laboratoire de virologie, CHU Toulouse, France

239 with DAA + concomitant medication(s) \rightarrow 145 with PI (30%) Patients: 486 at MDTM

2: Service de Médecine interne - pôle digestif, CHU Toulouse, France

1) <u>145 patients for whom a PI was formulated: characteristics</u>

	Characteristics	Average ; [Min-Max]		Total		
	Age	60 y.o ; [26 - 86]				
	Gender: Male / Female			83 (57%) / 62 ((43%)	
	HIV+ status			45 (31%)		
	Concomitant medications number	3;[1-15]		501		
	Genotype:		DAA recommended (+/- Ribavirine):			
	14%		6; 3% ³ ;	2%	Sofosbuvir/Le	edipasvir
07	12% Genoty Genoty	be 1 be 2 be 3		 Paritaprevir/Ombitase Ritonavir +/- Dasabuse Sofosbuvir + Daclata 		Ombitasvir/ Dasabuvir
	68% Genoty					Daclatasvir
	Genoty	pe 4			Sofosbuvir	
2)	ATC classes related to a l	<u>기</u> :	Sofosbuvir +		Simeprevir	
Pr of	roportion PI ^{30%}					

Intervention (PI) delivered by the Pharmacist to the MDTM physician coordinator, who relays them to patient's prescribing physician, in order to prevent adverse effects or lack of efficacy.

We ranked interventions according to an **Impact Score**.



3) Pharmaceutical interventions ranked by Impact Score (IS):190 DAA recommended at MDTM have revealed 257 interactions among 145 patients Impact Score 1 (IS1): clinical (74 PI) or biological monitoring (90 PI) recommended:

Example: Beta blocking agents (C07) AND Sofosbuvir: increase bradycardia or atrioventricular block risk, in patients with favoring factors or bradycardic drugs → Cardiac frequency and electrocardiogram monitoring are recommended during antiviral treatment. Source: d.

Impact Score 2 (IS2): dose (34 PI) or administration (32 PI) adjustment:

Example: Efavirenz (J05AG03) AND Daclatasvir: decrease in Daclatasvir concentrations is expected as a result of CYP3A4 induction, leading to lack of efficacy -> In case of co-administration with a potent CYP3A4 inducer, Daclatasvir dose should be augmented to 90mg daily, concentrations could be monitored. Sources: a;b;c.

Impact Score 3 (IS3): substitution or discontinuation of concomitant medicine or DAA (27 PI):

Example: Lopinavir/Ritonavir (J05AR10) AND Paritaprevir/Ombitasvir/Ritonavir +/- Dasabuvir: increase in Paritaprevir concentrations is expected -> Concomitant use is contraindicated: change of DAA (or otherwise antiretroviral class) is recommended during antiviral C treatment. Sources: a;b;c. Number of PI Number of PI / case

100



CONCLUSION

Our results underestimate the current number of interactions: PI orally formulated during MDTM are not counted, while they are generally of a high impact score (IS3). But even so, 30% of all patients presented at MDTM and 49% of patients with at least one DAA and one concomitant medication had a Pharmaceutical Intervention delivered. DAA's drug interaction analysis is effective (13% of analysis leading to a PI) for therapeutic management optimization and should be systematically performed.