

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 interactions between **DAA and concomitant 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 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**.

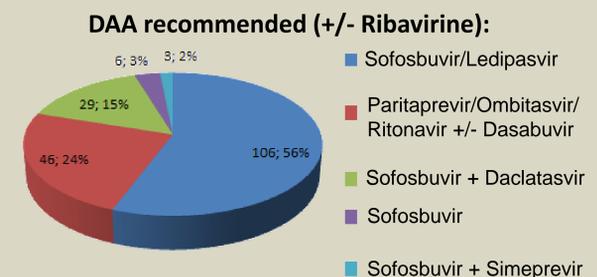
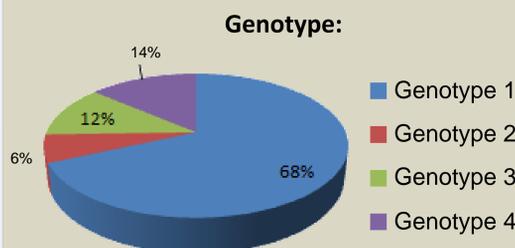
We ranked interventions according to an **Impact Score**.

RESULTS

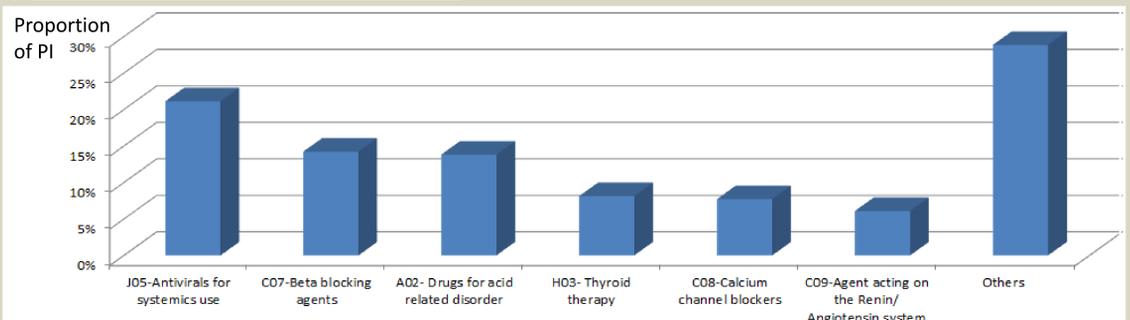
Patients : 486 at MDTM → 239 with DAA + concomitant medication(s) → 145 with PI (30%)
 → 2034 drug interaction analysis → total of 257 PI (13%)

1) 145 patients for whom a PI was formulated: characteristics

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



2) ATC classes related to a PI:



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:

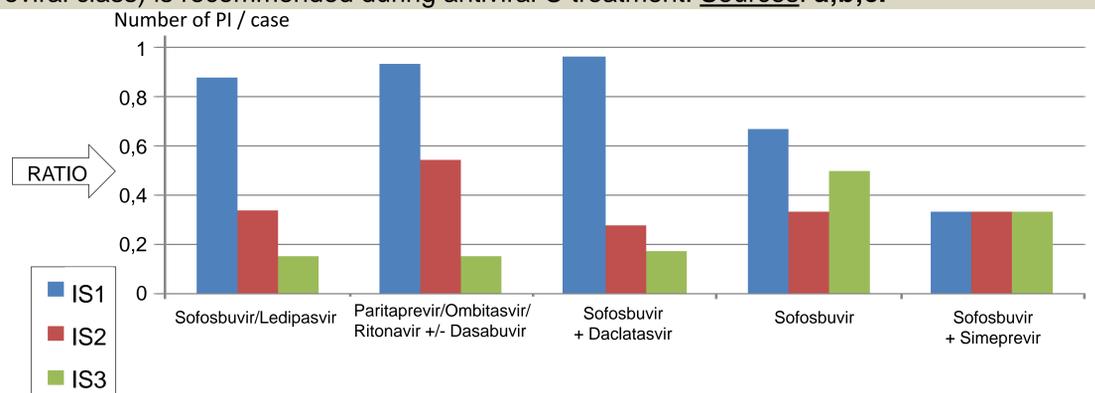
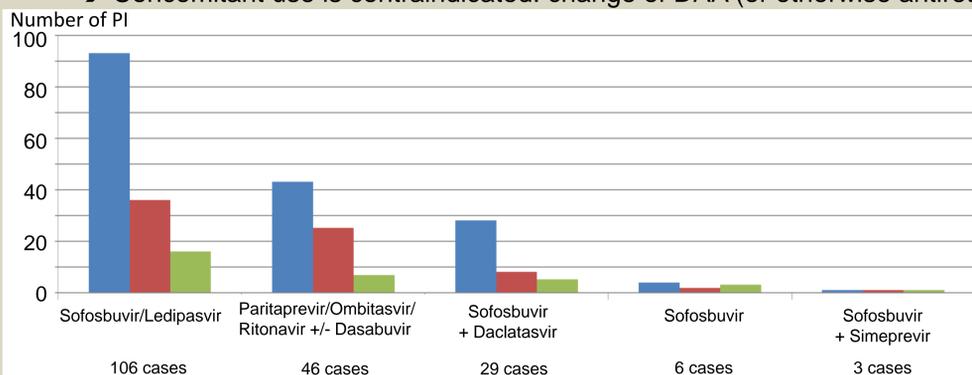
Example: **Beta blocking agents (C07)** AND **Sofosbuvir**: increase bradycardia or atrioventricular block risk, in patients with favoring factors or bradycardic drugs
 → Cardiac frequency and electrocardiogram monitoring are recommended during antiviral treatment. Source: d.

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.



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.