

DRUGS ABUSE AND CHEMSEX: A NEW CHALLENGE FOR ANTIRETROVIRAL DRUG-DRUG INTERACTION



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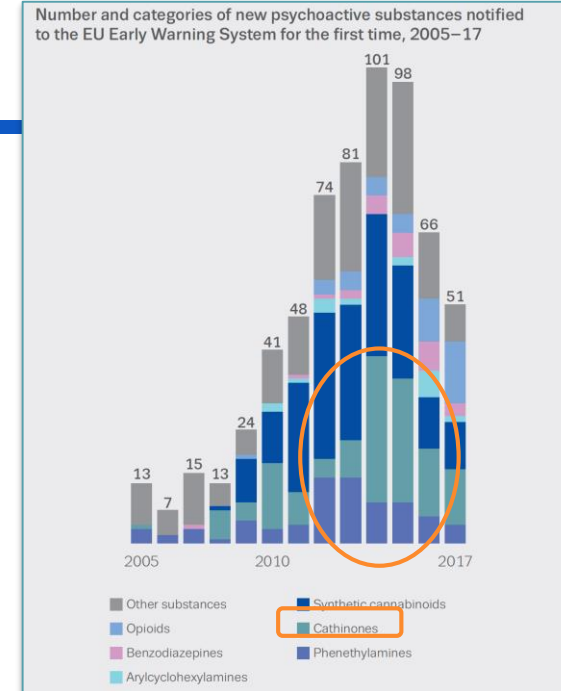
DISCLOSURE

No disclosure to declare

INTRODUCTION – Chemsex

- **Use of illicit /recreative drugs** : Cannabis, Cocaine, Ketamine, MDMA GHB/GBL, methamphetamine derivatives...
- **Emergence of new psychoactive substances (NPS) in the last decades**

➔ **In a sexualized context : CHEMSEX**



European Drug Report 2018

- **Chemsex has become a major and growing concern in the MSM population ...**
 - Pubmed references : 2015 (n = 6) to 2018 (n = 58)
 - Several national monitoring studies in United Kingdom 2014-2016
 - **Prevalence reported in Prep studies ranging from 30%² to 44%³**

²Trial Roux P1,2, 1Is on-Demand HIV Pre-exposure Prophylaxis a Suitable Tool for Men Who Have Sex With Men Who Practice Chemsex? Results From a Substudy of the ANRS-IPERGAY - J Acquir Immune Defic Syndr. 2018 Oct 1

³Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial Prof Sheena McCormack - Lancet. 2016 Jan 2;387(10013):53-60

INTRODUCTION – Chemsex & HIV

... **But not well known enough in the HIV-infected population !**

- **Prevalence among HIV-infected subjects ?**

- <5% to 28% according to the drugs in Astra study (MSM cohort)

Hockenhuil J Forensic science Int 2017; Schmidt et al. J of Drug Policy 2016

- **High potential of DDI between antiretrovirals and illicit drugs ?**

- **No DDI pharmacokinetic study or dose-effect relationships** between drugs and ARV

- Potentials severe interactions reported from **case reports**

Intensive Care Med (2012) 38:1239–1240
DOI 10.1007/s00134-012-2537-9

Surviving life-threatening MDMA
(3,4-methylenedioxymethamphetamine, ecstasy) toxicity caused
by ritonavir (RTV)

**Fatal interaction between ritonavir
and MDMA**

J A Henry, I R Hill

THE LANCET • Vol 352 • November 28, 1998

Possible fatal interaction between protease inhibitors
and methamphetamine

Gillian Hales¹, Norm Roth² and Don Smith³

Antivir Ther. 2000

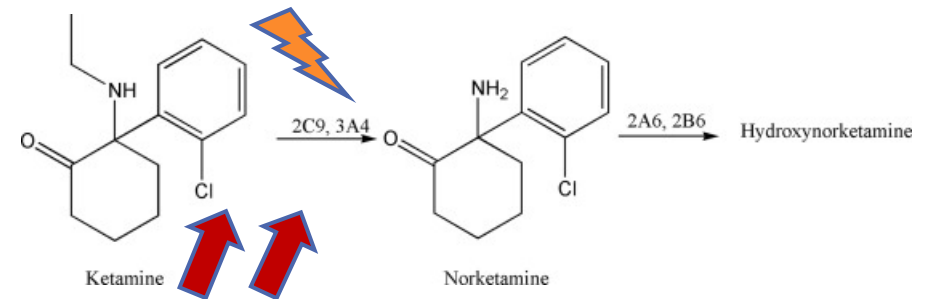
- Theoretical knowledge about the **metabolic pathways of drugs**

Increasing use of 'party drugs' in people living with HIV on antiretrovirals: a concern for patient safety - Bracchi M. AIDS. 2015

INTRODUCTION – Chemsex & Drug-Drug Interactions

- **Pharmacokinetic DDI : role of the CYP 450 family**

- **Ritonavir and cobicistat** : used as “booster” are strong **inhibitors** for **CYP 3A4 / CYP2D6**
- **Several drugs are metabolized by CYP450 family :**
 - *Ketamine, Benzodiazepines, Erectile dysfunction agents (EDA): CYP3A4++*
 - *MDMA, Cathinones, Methamphetamines: CYP2D6++*
 - *Cannabis, synthetic cannabinoids... : CYP2C9/1A2*
 - *GHB/GBL : non-cyp450 pathways but CYP450 unclear ??*



- **Pharmacodynamic DDI :**

- **Cocaine and rilpivirine** : both induce **QT prolongation**

STUDY OBJECTIVES

- **Describe illicit drugs consumption**
 - **Evaluate the risk of DDI with ARV treatment**
- In a cohort of HIV-infected patients
- **Monocentric study** : *APHM Sainte-Marguerite, Clinical Immuno-Hematological Unit, Marseille, France*

PATIENTS AND METHODS

- **Prospective survey initiated in March 2018** (*still ongoing*)
- **HIV-infected patients who attended the unit for a follow-up visit**
- **Self-administered questionnaires as part of the *Therapeutic Patient Education Program (TPEP)*:**
 - ✓ **Number of illicit drugs**
 - ✓ **Type of illicit drugs**
 - ✓ **Frequency of drugs consumption:** once in a while, \geq once a month, \geq once a week, \geq once a day, non reporting
- **Demographical characteristics and therapeutic data** from the electronical database **NADIS** : *age, sex, ARV regimen, HIV transmission mode, HCV co-infection*
- **DDI evaluation** :
 - ✓ **Online Expert Database of Liverpool**
 - ✓ **Knowledge on the drugs and ARV pharmacokinetics**



RESULTS – Population Characteristics

- Descriptive study including **286 HIV-infected patients on ART**
 - 315 questionnaires collected from March 2017 to January 2019
(1 patient responded to the questionnaire 3 times, 27 patients twice)
 - 75% male; median age: 52 years (range: 19-83)

ART Regimen in the cohort	
Triple therapy	62%
Single-Tablet Regimen (STR)	60%
Rilpivirine	34%
Booster (ritonavir or cobicistat)	33%

RESULTS – Prevalence of Drugs Consumption

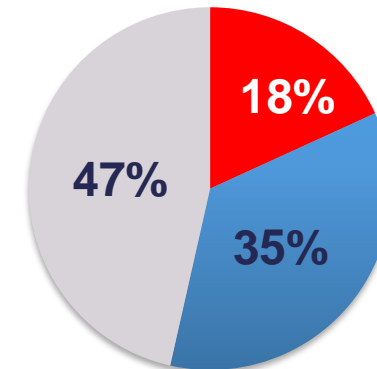
33% of drug users (93 / 286 patients)

Multiple drugs use : 41% of patients use **> 1 drug**

Mode of HIV transmission

- ☐ **MSM** : 52%
- ☐ **IVDU** : 28%
- ☐ **Heterosexual** : 13%

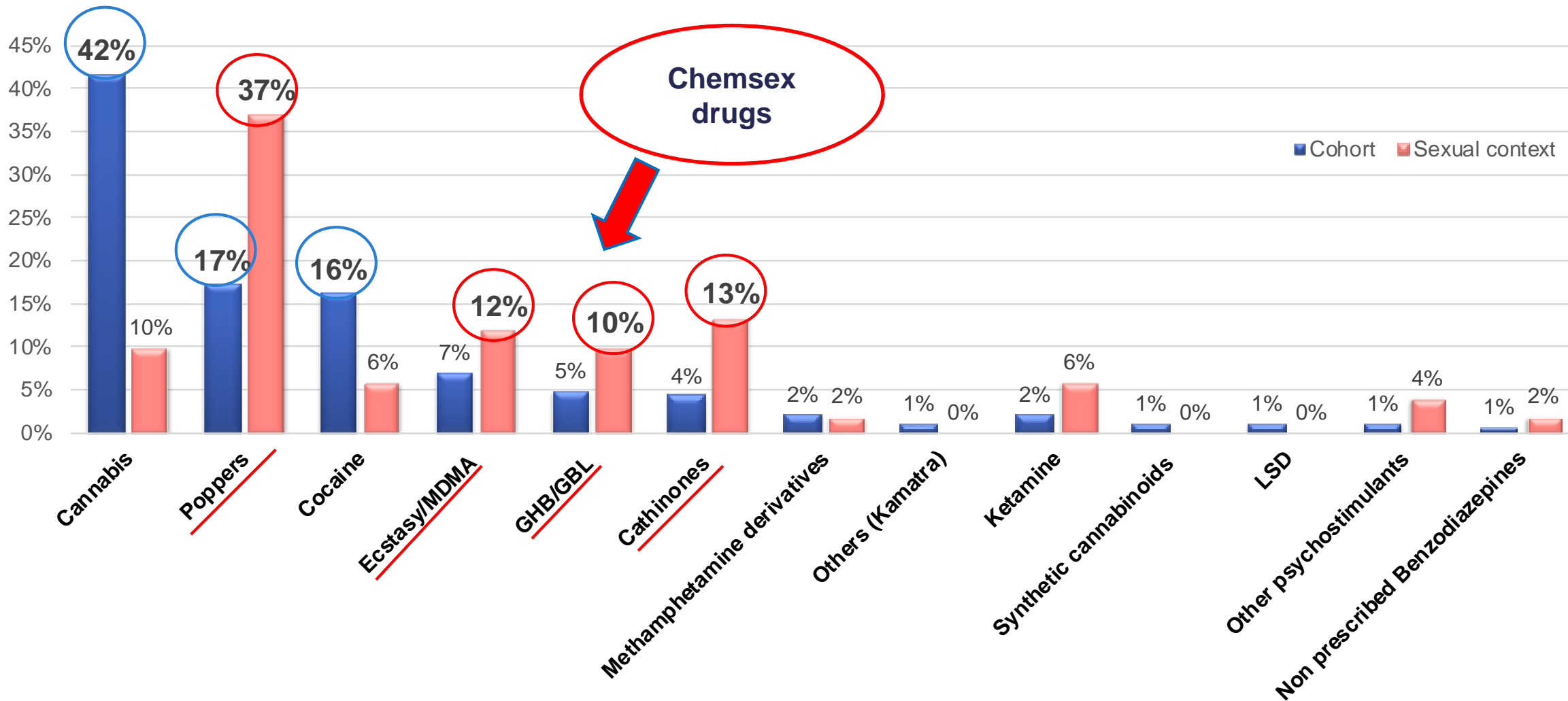
Chemsex Context



■ Sexual context ■ Non sexual context ■ Non reporting

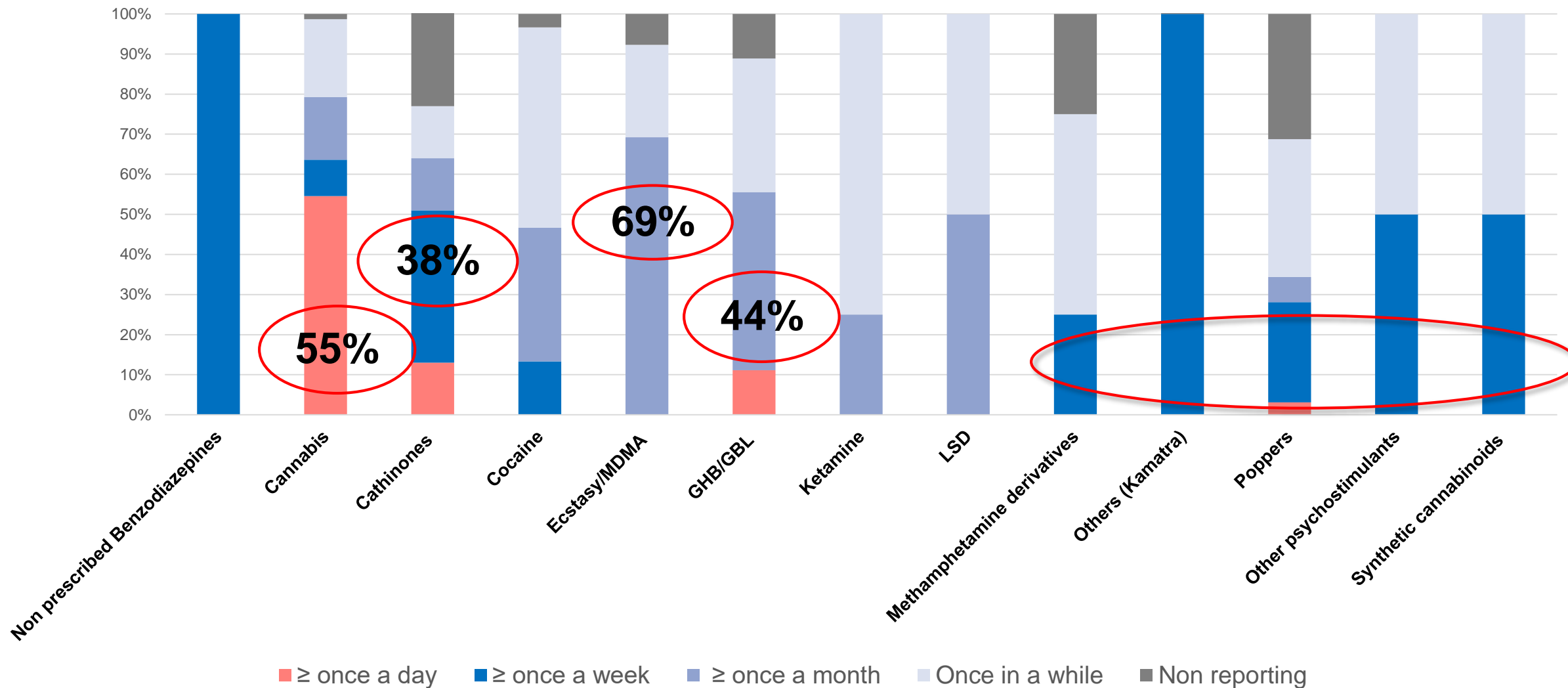


RESULTS – Type and Proportion of Drugs Use



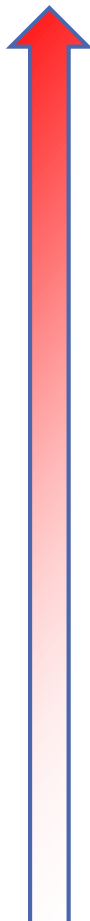


RESULTS – Frequency of Drugs Use



RESULTS – Drug-Drug Interaction Evaluation

DDI severity increase



DRUG	ARV REGIMEN	INTERACTION	EFFECT	n
Ketamine	Ritonavir Cobicistat	Inhibition CYP3A4	↗↗ drug exposure	2
MDMA, Cathinones, Methamphetamines		Inhibition CYP2D6		7
GHB/GBL		GHB DH CYP?	Unknown ? Narrow therapeutic index	1
Cannabis	Efavirenz Etravirine	Inhibition CYP2C9	↗ drug exposure	5
Cocaine	Rilpivirine	QT prolongation	Torsade de pointes	9
Cocaine	Ritonavir Cobicistat	Inhibition CYP3A4	↗ drug exposure	6
Poppers		Non CYP mediated		7
Cannabis	Nevirapine	Induction CYP3A4	↘ drug exposure	1

DDI in 38 cases (13,3%)

**→ Moderate to Severe in
24 cases (8,4%)**

CONCLUSION

- More than **1/3 of patients (33%) reported illicit drugs consumption**
- **18% in a “Chemsex” context**
 - Probably under-estimated as reported in the Ipergay study where 30% of pts who did not self-reported consuming drugs were positive to the hair screening
Chemsex drugs use by hair analysis among msm in the Anrs Ipergay trial. J Chas, J. Alvarez, Abstract Number: 1029 CROI 2018
 - **Poppers, cathinones, MDMA** and « **G** » were the most frequent drugs used in Chemsex
- The **risk** of consuming Illicit Drugs and ARV should **not be under-estimated** :

IDENTIFY illicit drugs consumption in HIV- infected patients

WARN the patient about risk of drug interaction and signs of toxicity

ADJUST the antiretroviral regimen

AVOID high risk of potential life-threatening toxicities

Aknowledgments

- Dr Caroline Solas
- Dr Isabelle Poizot-Martin

- **APHM Sainte-Marguerite, Clinical Immuno-Hematological Unit, Marseille, France**
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- **Patients**

