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Use of contraindicated antiretroviral drugs in HIV/HCV coinfected persons receiving HCV treatment with direct-acting antivirals – results from the EuroSIDA study

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INTRODUCTION

- Modern direct-acting antiviral (DAA) therapy guarantees cure for almost all persons with hepatitis C. In HIV/HCV co-infected persons, the effectiveness of DAA is similar to what is seen in HIV mono-infected persons [1].
- HIV/HCV co-infected persons can be treated with the same DAA regimens, following the same rules as for people with HCV mono-infection [2].
- Potential drug interactions should be evaluated prior to initiating an antiviral regimen, especially in HIV/HCV co-infected persons who are receiving ART, as certain drugs may be incompatible, or dose adjustment may be required [2].

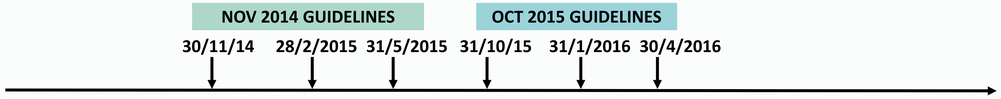
• AIMS:

- To determine whether antiretroviral (ARV) drugs are used according to EACS guidelines among HIV/HCV coinfected individuals treated with interferon-free direct acting antivirals (DAAs) in the pan-European EuroSIDA study.

METHODS

- At each EACS guidelines publication date, plus 3, 6 months, we calculated the numbers of persons on DAAs, with possible ARV interactions and with contraindications; defined as ARVs which should not be coadministered (‘red shading’ in EACS guidelines [2]). Table 1.
- Logistic regression with robust standard errors investigated factors associated with using contraindicated ARVs. Models were adjusted for gender, region of Europe, end stage liver disease, HCV genotype, age, guideline date and time since guidelines.
- Baseline is the first date the patient is on a DAA at a guideline check date (guideline date, plus 3 months, plus 6 months).

Table 1: Inclusion of patients and study baseline



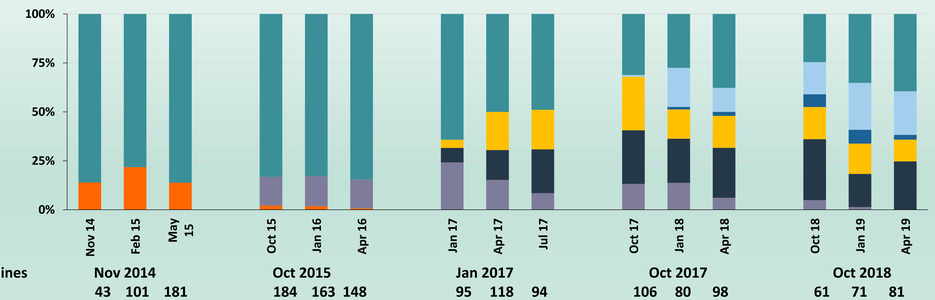
PATIENT								BASELINE	POSSIBLE CONTRA-INDICATION	CONTRA-INDICATION
1	DAA	SOFO/DACL						30/11/14	No	
	ART	LPV/r								
2	DAA		SIME		SOFO/LEDI			28/2/15	Yes	Yes
	ART		DRV/r		EFV					
3	DAA					OMBI		31/1/16	Yes	No
	ART					ATV/r				

Possible contraindication = ‘No’ if the patient is taking a DAA with no contraindications = ‘Yes’ if there is a potential contraindication
Contraindication= ‘Yes’ if possible contraindication= ‘Yes’ and they are on ART with contraindications

RESULTS

- Among 1,406 persons starting DAA, the baseline median age was 51 years (44-55), most were male (75%), had injecting drug use as HIV risk (57%), from Western Europe (76%) and had genotype 1 infection (52%). The median CD4 measured at baseline was 614 (423-828).
- Of 1,624 treatment episodes, 609 (37.5%) were receiving DAAs with possible ARV interactions, which increased over time (figure 1).
- Among those on DAA with possible ARV interactions, 38 (6.2%; 95% CI 4.3-8.2) received a contraindicated ARV of which 18 were NNRTIs, 16 PIs and two INSTIs.

Figure 1: Use of HCV direct-acting antivirals, possible ARV interactions & contraindications



EACS Guidelines	Nov 2014			Oct 2015			Jan 2017			Oct 2017			Oct 2018		
On DAA	43	101	181	184	163	148	95	118	94	106	80	98	61	71	81
Possible ARV interaction*	6	22	25	31	28	23	34	59	48	73	58	61	46	49	49
Contraindicated ARV*	0	5	3	1	1	1	3	5	0	6	4	6	0	1	2

***Based on EACS guidelines where drugs should not be co-administered (‘red shading’)**

Abbreviations: SMV: simeprevir; OMB: ombitasvir; SOF/VEL: sofosbuvir/velpatasvir; EBR/GRZ: elbasvir/grazoprevir; VOX: voxilaprevir; GLE/PIB: glecaprevir/pibrentasvir

RESULTS (continued)

- Adjusted odds (95% CI) of receiving a contraindicated ARV was higher (3.25, 1.40-7.57) among participants from East/Central East (vs. South) and lower (0.22, 0.08-0.65) for 2015-2018 guidelines (vs. 2014).
- SVR12 was 29/32 (90.6%) among those receiving a contraindicated ARV and 441/461 (95.7%) in those not receiving a contraindicated ARV (p=0.55).

LIMITATIONS

- SVR12 data was not available for all participants.
- We did not have sufficient power to compare across specific DAAs.

CONCLUSIONS

- In this large heterogenous European cohort, more than a third received DAAs with possible ARV interactions, but a low proportion received a contraindicated ARV (‘red shading’ in EACS guidelines [2]).
- Use of contraindicated ARVs declined over time which corresponds to the increased availability of ART regimens without interactions with DAA across Europe.
- Participants who received a contraindicated DAA and ARV combination still had a high rate of SVR12.

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https://chip.dk/Research/Studies/EuroSIDA/Study-group

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https://www.eacsociety.org/education/medical-exchange-programme/cdf/

REFERENCES

1. Amele et al. JAIDS. 2021 Feb 1;86(2):248-257
2. https://www.eacsociety.org/media/guidelines-10.1_30032021_1.pdf